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**SURGICAL TREATMENT
OF NEOPLASTIC LARYNGEAL LESIONS
VIA FLEXIBLE ENDOSCOPIC APPROACH**

321.20 – ONCOLOGY AND RADIOTHERAPY

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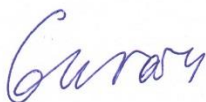
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LIST OF ABBREVIATIONS

AC - anterior commissure
BNELL – benign non-epithelial lesions of the larynx
CHL – chronic hyperplastic laryngitis
CHLK - chronic hyperplastic laryngitis with keratosis
CI – confidence interval
CIS – carcinoma in situ
CLP – cure with larynx preservation
CO₂ - carbon dioxide
CS - cold surgery
CT - computed tomography
DD – death due to the primary disease
DEX – diathermy loop/snare excision
DFS - disease-free survival
DSS – disease-specific survival
FELS– flexible endoscopic laryngeal surgery
GA – general anaesthesia
HLL - hyperplastic laryngeal lesions
HPV - Human Papilloma Virus
IMT - inflammatory myofibroblastic tumour
KTP – potassium titanyl phosphate
LA - laser ablation
LC – local control
LIN - Laryngeal Intraepithelial Neoplasia
LP – laryngeal papilloma/papillomatosis
LRc - local recurrence
Nd:YAG - neodymium-yttrium-aluminium-garnet
OBLS – office-based laryngeal surgery/outpatient laryngeal surgery
OPL - open partial laryngectomy
OS - overall survival rate
PDL - Pulsed Dye Laser
PSCC – papillary squamous cell carcinoma
RT – radiotherapy
SCC - squamous cell carcinoma
SD - standard deviation
SHFJV – superimposed high-frequency jet ventilation
SIL - squamous intraepithelial lesion
SIN - squamous intraepithelial neoplasia
SP - squamous papilloma
SpCC – spindle cell carcinoma
TLMS - transoral laser microsurgery
Tm:YAG - thulium:YAG
UDC – ultimate disease control
UDC FELS - ultimate disease control with FELS only
VC - verrucous carcinoma
VCL - verrucous carcinoma of the larynx
WHO - World Health Organisation

INTRODUCTION

Relevance and importance of the research topic

Laryngeal cancer is the second most common cancer of the respiratory tract and accounts for approximately 30–50% of all head and neck cancers [4]. Approximately 75% of laryngeal carcinomas are located in the glottic region [49, 141]. The prevention and treatment of laryngeal cancer represent one of the most pressing issues in oncology.

One approach to the prevention of laryngeal cancer is the effective screening and treatment of precancerous conditions of the larynx. Among the benign laryngeal lesions with the potential for malignancy, we mention: chronic hyperplastic laryngopathies/hyperplastic laryngeal lesions (HLL) and laryngeal papilloma (LP) in adults [23, 43, 101, 102, 123, 127, 140, 157, 188].

The preferred method for treating benign and precancerous laryngeal lesions is currently transoral microsurgery, including the use of CO₂ laser, angiolytic lasers, and diode lasers, performed under general anaesthesia (GA) with muscle relaxation [9, 14, 24, 31, 132, 188, 204].

In the treatment of early glottic cancer, three basic methods are traditionally used: (1) open partial laryngectomy (OPL), (2) radiotherapy (RT), and (3) transoral laser microsurgery (TLMS) using CO₂ laser. These methods have demonstrated comparable oncological outcomes in the treatment of early glottic cancer [13], but each has its limitations and disadvantages.

Flexible endoscopic laryngeal surgery (FELS) may overcome some of the limitations of traditional treatment methods, but this method is currently in the early stages of evaluation, with the experience reflected in scientific publications being limited to case reports or small case series [98, 118, 170, 181, 197, 205, 212]. Long-term outcomes of glottic cancer treatment using FELS, which are the most important for assessing the efficacy of any treatment in oncology, are not elucidated in the specialist literature.

The effective use of FELS in the treatment of benign and precancerous laryngeal lesions allows for increased patient comfort and considerable economic benefits, given the possibility of performing the procedure on an outpatient basis. This method offers a particular advantage in the treatment of lesions with a high potential for recurrence (LP, HLL, etc.) by avoiding repeated interventions under general anaesthesia in an inpatient setting, thereby reducing costs and postoperative morbidity. The study of the possibilities for using flexible endoscopy in early glottic cancer warrants attention, as the procedure can also be performed in an outpatient setting under local anaesthesia, making it a less invasive operation, which is particularly important for patients with poor general health and a high risk associated with traditional surgery, for patients with anatomical features that preclude transoral laser surgery, and for patients who have contraindications to traditional treatment methods.

There is little information available on the use of FELS in the treatment of tumours and precancerous conditions of the larynx. The indications for this approach have not been sufficiently evaluated, and there is a lack of consensus and guidelines. We therefore consider it reasonable to continue studying this surgical alternative, with the primary aim being to evaluate the method's efficacy based on long-term outcomes. These are the reasons for studying aspects of laryngeal neoplasm surgery using flexible endoscopy.

Research purpose:

To investigate the potential of flexible endoscopy in the treatment of benign neoplasms, precancerous lesions and early-stage malignant tumours of the larynx; to analyse factors associated with treatment efficacy; and to establish the value of the method in improving the management of patients with laryngeal neoplasms.

Research objectives:

- 1) To study the efficacy of various types of procedures using a flexible endoscope (cold ablation, diathermic excision, laser ablation) in the treatment of benign non-epithelial lesions of the larynx;
- 2) To develop an original endoscopic classification of hyperplastic laryngeal lesions;
- 3) To evaluate the efficacy of flexible surgical endoscopy (cold ablation, diathermic excision, laser ablation) and the importance of the method in the treatment of hyperplastic laryngeal lesions;
- 4) Assessment of the efficacy of various surgical techniques (cold ablation, diathermic excision, laser ablation) via a flexible endoscopic approach and determination of the value of FELS in the management of patients with laryngeal papilloma/papillomatosis in adults;
- 5) To estimate the long-term (5-year) oncological outcomes of the flexible endoscopic approach to early glottic cancer (T1-T2) and to determine the factors influencing treatment efficacy;
- 6) To assess the importance of the anaesthesia/ventilation method for the oncological outcomes of endoscopic treatment of glottic cancer;
- 7) Assessment of the efficacy of combined treatment (FELS and postoperative radiotherapy) for T1b-T2 glottic cancer;
- 8) To assess the potential of FELS in the management of patients with verrucous carcinoma of the larynx;
- 9) Assessing the efficacy of FELS in the treatment of recurrent and residual glottic cancer following radiotherapy failure;
- 10) To assess the applicability of FELS for the treatment of glottic cancer in an outpatient setting.

Study design

The study is retrospective. To address the set objectives, the results of surgical interventions using a flexible endoscope, performed by the author on patients with benign laryngeal lesions, precancerous lesions of the larynx, and early-stage (T1-T2) primary and recurrent/residual malignant tumours of the glottic portion of the larynx, between 1992 and 2025, in three institutions: the PMSI Oncology Institute, the PMSI „Timofei Moşneaga” Republican Clinical Hospital, and M.C. „Expert Endoscopy” SRL, were used. The treatment outcomes of patients in the following nosological categories were analysed (a total of 575 cases):

1. Benign non-epithelial lesions of the larynx (BNELL);
2. Precancerous lesions with 2 subcategories:
 - 2.a. Hyperplastic laryngeal lesions (HLL);
 - 2.b. Laryngeal papilloma/papillomatosis (LP);
3. Malignant lesions (T1-T2 glottic cancer).

Flexible endoscopic laryngeal surgery (FELS) was performed using the following equipment: flexible therapeutic endoscopes manufactured by „Olympus” (Japan) (models BF-1T10, BF-TE2, BF-1T60, BF-1TH1100); the suspended laryngoscopy set manufactured by „Carl Reiner” (Austria); the „Olympus” electrosurgical unit; endoscopic accessories (diathermy loops, biopsy forceps from „Olympus”, „Micro-Tech” and „Microvasive”); the Nd:YAG laser, model LTN-102 (Russia) (wavelength – 1064 nm); the diode laser, model Leonardo Dual 45 (wavelength – 980/1470 nm), manufactured by „Biolitec” (Germany); and the „TwinStream” superimposed high-frequency jet ventilation (SHFJV) device, manufactured by „Carl Reiner” (Austria).

Inclusion criteria:

The study included consecutive adult patients from the aforementioned nosological categories.

For the analysis of long-term oncological outcomes, patients with primary and recurrent/residual malignant lesions (T1-T2) with a 5-year follow-up period were included.

Exclusion criteria from the study:

For the analysis of long-term oncological outcomes, patients who were under observation for less than 5 years following endoscopic intervention, patients lost to follow-up up to 5 years after endoscopic intervention, and patients who died from causes unrelated to the primary disease up to 5 years after endoscopic intervention were excluded from the study.

The evaluation of the results of flexible endoscopic laryngeal surgery in patients with benign non-epithelial lesions and in patients with precancerous lesions (hyperplastic laryngeal lesions and papilloma/papillomatosis) was based on the following criteria: (1) feasibility of the

method; (2) immediate surgical outcome: eradication of the lesion; (3) short-term surgical outcome (1–3 months): complete epithelialisation of the postoperative wound and absence of residual lesion; and (4) lesion recurrence rate.

The oncological efficacy of flexible endoscopic laryngeal surgery in patients with malignant lesions was assessed according to the following criteria: ultimate disease control (UDC); overall survival; overall survival rate (OS); local control (LC); disease-free survival (DFS); disease-specific survival (DSS); ultimate disease control with FELS alone (UDC FELS); cure with larynx preservation (CLP); death due to the primary disease (DD); local recurrence (LRc).

The functional/vocal outcome after treatment was assessed using a grading system representing the patient's subjective assessment of their voice, as follows: (1) normal voice, (2) minor dysphonia, (3) moderate dysphonia, and (4) pronounced/severe dysphonia.

Investigative methods

Primary data collection was carried out by extracting data from medical records (archive). The data were recorded using Microsoft Office Excel 2007 (Redmond, WA, USA). Data analysis was performed using the open-source programming tools RStudio (<https://www.rstudio.com/>) and Python (<https://www.python.org/>), thereby ensuring the reproducibility of the statistical analysis. For numerical variables, the five basic indicators were estimated: the mean with standard deviation, the median with the interquartile range, the minimum and maximum values, supplemented by 95% confidence intervals for the mean; these indicators form part of the descriptive statistics, either for the cohort under examination or for the groups formed in the comparative evaluation of the groups examined. The comparative evaluation for numerical variables was carried out using non-parametric tests, depending on the number of groups and the relationships between the groups (Wilcoxon-Mann-Whitney test for dependent and independent groups or the Kruskal-Wallis test for independent groups, applying multiple comparisons and Holm corrections where necessary). For qualitative variables, relative frequencies were estimated, supplemented with 95% confidence intervals, as well as absolute frequencies. Hypothesis testing for categorical data was performed using Pearson's chi-square test, Monte Carlo variant (100 000 samples). For all the statistical tests described above, the significance level (α) was set at 0.05.

Novelty, scientific originality and theoretical significance of the research

For the first time, based on extensive clinical data, a comprehensive study was conducted on the potential of flexible endoscopy in the treatment of laryngeal neoplasms.

Endoscopic techniques applied for the first time in the management of patients with laryngeal neoplasms were analysed:

- a method for adequate exposure of the glottis in patients with limited cervical extension, which allows the limitations of conventional transoral surgery to be overcome;
- the method for the eradication of benign obstructive non-epithelial laryngeal tumours (schwannoma) affecting all parts of the larynx, which allows open surgery to be avoided;
- a method for the removal of laryngeal papilloma by combining diathermic excision and photoablation;
- a method for the endoscopic treatment of Reinke's oedema using a diathermic loop, which allows lesions to be removed on an outpatient basis, overcoming the limitations of previously proposed methods;
- a method of biopsy via diathermic excision in verrucous carcinoma of the larynx, which, when performed on an outpatient basis, allows for the collection of an adequate tissue specimen to obtain a conclusive histological result;
- a method for the eradication of glottic carcinoma by combining diathermic excision and photoablation.

An original clinical/endoscopic classification of hyperplastic laryngeal lesions has been developed and proposed, which will facilitate the identification of lesions with a high risk of malignancy and rationalise the diagnostic and therapeutic algorithm for this category of patients.

For the first time, the efficacy of FELS in early glottic cancer was studied based on long-term (5-year) outcomes.

The efficacy of combined treatment (FELS followed by postoperative/adjuvant radiotherapy) in the treatment of T1b-T2 glottic cancer was investigated.

The importance of the anaesthesia/ventilation method in FELS for laryngeal neoplasms was investigated.

For the first time, the applicability of FELS in the treatment of recurrent/residual glottic cancer following radiotherapy failure was investigated.

For the first time, the applicability of FELS for the treatment of glottic cancer on an outpatient basis was investigated.

An algorithm was developed for the follow-up management of patients with various laryngeal neoplastic lesions, operated on using a flexible endoscope.

Approval of research results

The research results were validated through the publication of 55 scientific papers, including: 1 monograph, 28 articles, including 15 international articles, of which 10 were published in journals with an impact factor (Clarivate summary IF = 14.7); 6 patents; 13 presentations at international conferences with abstracts [53–83].

The practical value of the work (educational, clinical, socio-economic, etc.)

The results of the investigations highlight the importance of flexible surgical endoscopy in the therapeutic arsenal for patients with laryngeal neoplasms.

The widespread use of the advantages of FELS in clinical practice will contribute to the optimisation of the treatment algorithm for laryngeal neoplasms.

Flexible surgical endoscopy allows for a more conservative treatment of patients with benign neoplasms and precancerous lesions of the larynx compared to other existing treatment methods, whilst also offering a considerable economic benefit.

Flexible endoscopic surgery broadens the range of curative procedures that preserve the organ in patients with malignant glottic tumours, in most cases avoiding the need for tracheostomy, and extends the indications for surgical treatment to those patients in whom, for various reasons, traditional treatment (surgical or radiological) cannot be applied.

The minimally invasive nature and safety of the method broaden the indications for outpatient endolaryngeal surgery for laryngeal neoplasms.

The curative efficacy, considerable economic benefits, good functional outcomes and low complication rate allow FELS to be recommended for use in institutions specialising in the treatment of laryngeal neoplasms.

Application of research results

The research results have led to the implementation of flexible endoscopic laryngeal surgery on an outpatient basis at the „Avangard-Med” clinic in Chişinău, Republic of Moldova.

Keywords: flexible endoscopy; endoscopic surgery; Nd:YAG laser; diode laser; benign laryngeal lesions; precancerous laryngeal lesions; hyperplastic laryngeal lesions; laryngeal papillomatosis; glottic cancer; office-based laryngeal surgery.

The research project received **the approval of the Research Ethics Committee of the “Nicolae Testemiţanu” SUMF** (08.10.2024, No. 6).

1. CURRENT DEVELOPMENTS IN THE MINIMALLY INVASIVE TREATMENT OF NEOPLASTIC LESIONS OF THE LARYNX

Neoplastic lesions of the larynx are divided into three major categories: (1) benign non-epithelial lesions, which include true tumours and tumour-like lesions; (2) precancerous lesions; and (3) malignant tumours.

1.1. Benign non-epithelial lesions of the larynx

Benign non-epithelial lesions comprise a wide spectrum of conditions, including both true tumours (fibroma, neurofibroma, schwannoma, lipoma, haemangioma, leiomyoma, inflammatory myofibroblastic tumour, etc.) and tumour-like conditions (vocal nodule and polyp, polypoid degeneration of the vocal cords (Reinke's oedema), non-specific granuloma, cyst, amyloidosis, etc.).

The traditional interventional approach to the management of patients with benign laryngeal lesions is transoral microlaryngoscopic surgery, which has been used successfully for several decades [16, 111, 188]. The application of this method involves suspending the larynx on a rigid laryngoscope and the mandatory use of general anaesthesia (GA) with muscle relaxation, in an inpatient setting.

The use of the laser has radically transformed endolaryngeal surgery. In 1972, Strong M.S. and Jako G.J. were the first to publish their experience of using the CO₂ laser in the treatment of various neoplastic lesions of the larynx [180]. The CO₂ laser remains, to date, the most widely used type of laser in endolaryngeal surgery, offering the following advantages over cold surgery: high precision, reduced bleeding, minimal reactive phenomena in the larynx, and favourable functional outcomes [154].

Transoral microsurgery, being the standard method for treating benign laryngeal lesions, has, alongside its indisputable advantages, certain disadvantages, including dental trauma caused by the rigid laryngoscope and risks associated with general anaesthesia.

With the development of flexible endoscopy and laser technologies, resulting in the possibility of transmitting the laser beam through a flexible guide, minimally invasive laryngeal surgery in an outpatient setting under local anaesthesia has become an attractive option. Office-based laryngeal surgery (OBLS) has become a growing trend in modern laryngology over the last two decades. Zeitels S.M. and Burns J.A. (2007) report, in a review article, that the concept of office-based laryngeal surgery was established in 2001 and first discussed within the American Laryngological Association in 2003 [207]. Currently, it is estimated that over 15% of laryngeal operations are performed on an outpatient basis, and this number is increasing due to

the many associated benefits [11]. Rosen C.A. et al. (2009), in a review article, note that the term „office-based surgery” also applies to procedures performed in the hospital’s endoscopy suite, provided that the key elements of the outpatient treatment concept are adhered to [161].

The advantages of OBLS include: avoiding hospitalisation; a faster diagnostic process; a minimally invasive treatment option for patients at risk or with contraindications for GA, and where the lesion is inaccessible via rigid laryngoscopy due to anatomical factors (limited cervical extension, dental limitations, etc.); a more timely intervention for patients with comorbidities; inclusion of patients ineligible for GA; the treatment of choice for conditions with a high recurrence rate; better visualisation of all laryngeal regions; preservation of oral tissues, which are subject to trauma during rigid laryngoscopy; reduced recovery time; minimal morbidity; safety, reduced health risks by avoiding general anaesthesia; lower costs; time savings, reduced operating time, the patient’s ability to leave the clinic without any lifestyle restrictions and even return to work almost immediately after the procedure, easier planning, shorter waiting lists; the ability to assess vocal outcome in real time; a marked patient preference for OBLS [11, 41, 88, 114, 170, 197, 198]. For some patients at high risk of GA, awake laryngeal surgery may be the only available treatment option [198]. According to data published by Lahav Y. et al. (2023), 90.2% of outpatient endolaryngeal laser operations were well tolerated by patients and completed [117]. Outpatient procedures under local anaesthesia are associated with significantly lower cardiovascular morbidity compared with procedures performed under general anaesthesia [166]. Lahav Y. et al. (2023) found no association between comorbidities such as hypertension, ischaemic cardiovascular disease, chronic obstructive pulmonary disease and the completion rate of outpatient laser treatment [117]. The authors consider this finding to be very important, as patients with the aforementioned comorbidities often have an increased risk of general anaesthesia and, therefore, may be considered eligible candidates for OBLS [117]. In a study conducted by Rees C.J. et al. (2006), the authors report on 54 patients who underwent both OBLS and traditional surgery in the operating theatre under general anaesthesia for the same condition. In this group, 87% of patients stated that they preferred PDL laser surgery on an outpatient basis without sedation to surgery in the operating theatre under GA, and 83% of patients reported that they found OBLS without sedation more comfortable than surgery in the operating theatre under GA [152]. A reduction in hospitalisation costs of up to 95% per procedure was noted when comparing outpatient procedures performed under topical anaesthesia with similar procedures performed under general anaesthesia [167]. The benefits of OBLS are particularly evident for conditions/lesions with a high recurrence rate (e.g., non-specific granulomas), which may require repeated/multiple interventions [117, 121]. For this category of

patients, avoiding repeated surgical interventions in the operating theatre is of particular importance.

Among the various techniques and instruments used in OBLs, the use of biopsy forceps, inserted through the working channel of the flexible endoscope, is mentioned for the removal of vocal nodules, polyps and non-specific granulomas [198]. The majority of publications on OBLs are dedicated to the use of two angiolytic lasers: the dye-based laser (PDL) with a wavelength of 585 nm and the potassium-titanyl-phosphate (KTP) laser with a wavelength of 532 nm. In 2018, a new angiolytic laser was launched – the blue diode laser (blue laser) with a wavelength of 445 nm, which appears set to gradually replace the two aforementioned angiolytic lasers in the future, demonstrating therapeutic results similar to those of the KTP laser [41, 117, 133]. Angiolytic lasers (PDL, KTP, blue laser) are strongly absorbed by the oxyhaemoglobin in the blood and cause photocoagulation of the subepithelial and intralaminar microvasculature, with subsequent regression/involution of the lesion. In the case of subepithelial lesions, the epithelium is not vaporised, which leads to the protection of the superficial lamina propria and the maintenance of vocal cord flexibility, associated with a better vocal outcome [207]. Zeitels S.M. et al. (2006) proposed a 4-level grading system for assessing the degree of lesion regression: (1) 0% to 50%, (2) 51% to 70%, (3) 71% to 99% and (4) 100% [205]. Hamdan A.L. and Ghanem A. (2023) present their experience of using a blue laser (445 nm) in the treatment of various vocal cord lesions, and report complete regression of the lesion in 50% of cases [86]. In another study, Hamdan A.L. et al. (2024) report complete regression of the lesion following blue laser treatment on an outpatient basis in 76% of cases (13/17) of vocal polyps and in 33% of cases (21/33) of Reinke's oedema [87]. Filastro M. et al. (2023) noted the comparable efficacy of outpatient procedures compared to the traditional microlaryngoscopic approach in the treatment of vocal polyps and Reinke's oedema and documented complete regression of Reinke's oedema in 85.7% of patients treated with blue laser on an outpatient basis [41]. Abi Zeid Daou C. et al. (2023), in a review article on OBLs for vocal polyps, note that the regression rate of vocal polyps in various studies ranges from 27.6% to 96.8% and conclude that OBLs is a safe alternative to conventional phonosurgery [2]. Chadwick K.A. et al. (2024) report comparable vocal outcomes for outpatient photoangiolytic treatment of vocal polyps using a KTP laser compared with traditional excision using transoral microlaryngoscopy in the operating theatre, regardless of lesion size [22]. It is worth noting that the use of angiolytic lasers in OBLs is based more on inducing lesion regression than on its complete removal during the procedure. Due to the delayed regression of the lesion, the final result is usually assessed after 4–5 weeks or more, and larger polyps require repeated procedures. In large lesions, these non-ablative techniques using angiolytic lasers are not recommended, due to the risk of airway obstruction in the postoperative

period [171]. Techniques for the removal of vocal cord polyps and granulomas, combining KTP laser and cold surgery using flexible forceps, have also been described [129, 193]. Polypectomy with flexible forceps, preceded by the application of the KTP laser, leads to faster therapeutic effects than the use of the laser alone [193].

Other types of lasers are less commonly used in clinical practice. There is very limited experience of using the diode laser during direct transoral microlaryngoscopy in the treatment of benign laryngeal lesions, with the authors noting the method's efficacy, the results being comparable to those obtained through traditional CO₂ laser microsurgery [9, 100, 106]. In a 2017 publication, Hu H.C. et al. present a series of 40 patients with benign laryngeal lesions (including 10 patients with benign non-epithelial lesions of the vocal cords), treated with a CO₂ laser via a flexible guide in an outpatient setting, with the lesions undergoing photovaporisation, yielding encouraging results [98]. The Nd:YAG laser (1064 nm), whilst very popular in interventional bronchology, is rarely used in laryngology. Poddubny B.K. et al. (2006) report on their experience of using the Nd:YAG laser under local anaesthesia in 205 patients with benign laryngeal neoplasms, noting the feasibility and efficacy of the method [212].

1.2. Precancerous lesions of the larynx

Reducing morbidity and mortality caused by laryngeal cancer largely depends on its detection at an early stage and the effective management of patients with precancerous lesions, which require accurate identification, early diagnosis and appropriate treatment. According to the 2022 WHO classification [200], premalignant/precancerous lesions are characterised by epithelial dysplasia (a histopathological term), which may occur in epithelial lesions of the larynx; these, in turn, can be divided into two categories: hyperplastic laryngeal lesions/chronic hyperplastic laryngopathies and squamous papilloma/papillomatosis.

1.2.1. Hyperplastic laryngeal lesions

There is considerable confusion in the specialist scientific literature regarding the definition of hyperplastic laryngeal lesions (HLL), their classification, and the relevant clinical and morphological terminology [17, 39, 47, 188]. There is no clear predictive relationship between clinical and histopathological terminology in the characterisation of HLL. The variety of classifications and categorisations of squamous intraepithelial lesions (SIL) reflects divergences within the multidisciplinary team regarding the identification, classification, clinical and histopathological diagnosis, management and prognosis of these lesions. Faced with a variety of histopathological terms used to describe squamous epithelial abnormalities in laryngeal biopsies, the surgeon often becomes confused. An appropriate classification and

unified terminology, which would allow for reproducible interpretations of HLL, reflect the biological progression of SIL, and distinguish lesions with high malignant potential from those with low malignant potential, is desirable, as it would result in the rational management of the disease. It is important to identify certain endoscopic criteria that would guide the clinician in the preoperative detection of lesions with high malignant potential. This would clearly contribute to the selection of a rational treatment approach and the subsequent monitoring of patients with HLL. Therefore, if the detected lesion does not have a high potential for malignancy, patients will not require intensive monitoring; however, if lesions with a high malignant potential are detected, patients will require surveillance and regular follow-up after primary treatment.

Clinical/endoscopic criteria

There is considerable uncertainty regarding the description, interpretation and classification of epithelial lesions of the larynx with malignant potential. Uloza V. (1986) considers chronic hyperplastic laryngitis, keratoses and papilloma in adults to be obligatory precancerous conditions [188]. Paches A.I. et al. (1988) include the following in the group of epithelial lesions with a high potential for malignancy: leukoplakia (whitish patch), leukokeratosis (whitish plaque with an irregular surface and villous projections), pachydermia (a pink, greyish or yellowish in colour, depending on the degree of keratinisation of the superficial epithelial layer, which may be located in the posterior portions of the vocal cords or in the interarytenoid region), and papilloma in adults, which may be non-keratinised (soft) or keratinised (hard) [210]. Pogosov V.S. et al. (1989) state that only adult papilloma is considered an obligatory precancer, whilst chronic hyperplastic laryngitis, as well as all benign tumours and dyskeratoses, are considered optional precancers [211]. Gallo A. et al. (2001) suggest classifying the clinical presentation of premalignant laryngeal lesions into three types: 1) leukoplakia (synonymous with keratosis) – white area; 2) erythroplakia – red area; 3) erythrokeratosis – mixed lesion, with foci of leukoplakia and erythroplakia. The term *leukoplakia* indicates thickening of the epithelium, whilst the term *erythroplakia* indicates thinning of the epithelium [47]. Poddubny B.K. et al. (2006) consider papilloma, chronic hyperplastic laryngitis, and various types of dyskeratosis to be precancerous: pachydermia (local hypertrophy of the keratinised epithelium), leukoplakia (flat, whitish patch with a smooth surface), leukokeratosis (distinguished from leukoplakia by its rough surface), and hyperkeratosis (appearing as a whitish plaque with an irregular surface and villous projections) [212]. Ferlito A. et al. (2012), in the clinical terminology of epithelial proliferative lesions, mention the following: leukoplakia (any whitish lesion on the mucosa that cannot be easily removed or attributed to a specific condition (e.g. candidiasis); erythroplakia (any red patch on the mucosal surface, characterised by epithelial atypia and the presence of invasive carcinoma in a substantial proportion of biopsies);

erythroleukoplakia (mixed forms of white and red mucosal changes); pachydermia (indicating extensive thickening of the mucosa) [39]. Chen M. et al. (2019) proposed classifying leukoplakia, based on macroscopic appearance, into three types: (1) flat and smooth, (2) elevated and smooth, (3) irregular type (elevated lesion with a wrinkled surface). Analysing the correlation between the endoscopic and histological appearance in a cohort of 375 patients with leukoplakia who underwent CO₂ laser excision, the authors found the absence of dysplasia in the surgical specimen in the three macroscopic types, at 68%, 13% and 1% respectively, and the presence of carcinoma at 0%, 5.2% and 30.6% [23]. Li C. et al. (2018) proposed a similar classification of the hist s of leukoplakia: (1) smooth and flat, (2) smooth and hypertrophic, and (3) irregular lesions (irregular, granular or verrucous appearance). The authors specify that no patients (0%) with smooth flat lesions were found to have high-grade dysplasia; in the group of patients with smooth hypertrophic lesions, severe dysplasia and carcinoma were detected in 28.1% of cases; and 87.8% of irregular lesions were morphologically characterised as severe dysplasia or carcinoma [126].

Histopathological aspects

The 2022 WHO classification of squamous intraepithelial neoplasia/lesions (SIN/SIL) [200] divides SIL into 3 categories: (1) low-grade dysplasia/SIL, which has a low potential for malignancy, with morphological changes occupying up to half the epithelial thickness, the upper part being unchanged; (2) high-grade dysplasia/SIN, which has a high potential for malignancy, with morphological changes occupying more than the lower half of the epithelial thickness; (3) carcinoma in situ (CIS), where the cytoarchitectural abnormalities occupy the entire thickness of the epithelium, which has the specific appearance of conventional carcinoma, but without invasion into the underlying stromal tissue.

Treatment of hyperplastic laryngeal lesions

At present, there is no consensus among specialists regarding the treatment of squamous intraepithelial lesions (SIL). There is a wide variety of proposed approaches: observation following biopsy and conservative therapy, radiotherapy (RT), vocal cord decortication, cold phonomicrosurgical excision, laser excision, and laser ablation. The choice of treatment method for hyperplastic laryngeal lesions depends largely on specialists' preferences, experience, and the availability of equipment. Some specialists consider that, due to its scarring effect, vocal cord decortication has no role in modern laryngology [107, 142]. Gale N. et al. (2016) report that RT is never used in Slovenia for the treatment of SIL with high-grade dysplasia, but is reserved solely for the management of carcinoma [45]. Taking into account both the possible complications and adverse effects, as well as the fact that typically only a single course of RT can be administered to a patient, it makes little sense to squander the potential of this method on

treating a premalignant lesion, rather than reserving it for the treatment of carcinoma [140]. On the one hand, otolaryngologists are concerned that insufficient measures may contribute to the progression of SIL to invasive carcinoma; on the other hand, excessive measures in cases of SIL that will not progress may cause vocal cord scarring and vocal defect. However, it seems reasonable to prioritise an oncological approach, with an awareness of the potential for SIL to become malignant, over voice quality [45]. According to the consensus statements reached by otolaryngologists and pathologists at a 2010 meeting dedicated to the diagnosis and treatment of laryngeal dysplasia, the following recommendations were suggested: maximal excision of the lesions will allow for a conclusive histological diagnosis and will constitute the primary management of the lesion; the general appearance of the lesion is considered the most important factor in determining management; solitary and multiple lesions require complete excision; in the presence of extensive leukoplakia with confluent lesions, multiple biopsies should initially be taken, followed by successive resections; complete excision of the visible margins is recommended; other factors, such as comorbidities and the patient's age, may be important in the surgeon's decision; all patients are encouraged to stop smoking; SIL are treated by transoral endoscopic surgery using cold instruments or CO₂ laser [132]. Li C. et al. (2018) select the treatment modality for leukoplakia based on the endoscopic appearance of the lesion. „Smooth flat” and „smooth hypertrophic” lesions are initially treated conservatively. Healing rates of 77.8% and 67.7% are reported, respectively. Surgical treatment is applied in cases of failure of conservative treatment and as initial treatment for „irregular” lesions [126].

Traditional transoral microsurgery is not always possible due to contraindications for general anaesthesia or anatomical difficulties (inadequate glottal exposure, short mandible, limited cervical mobility, ankylosis of the temporomandibular joint, etc.). OBLs under topical anaesthesia has become a developing trend in modern laryngology, particularly due to advances in flexible endoscopy and laser technologies based on flexible guidance. This approach is currently being successfully used for the treatment of premalignant laryngeal lesions thanks to its undeniable advantages: avoidance of general anaesthesia risks, cost-effectiveness, and time-saving [170, 181].

Given that hyperplastic laryngeal lesions are among conditions with a high tendency to recur and may therefore require repeated or multiple interventions, the benefits of OBLs are particularly evident due to the possibility of avoiding repeated surgical procedures in the operating theatre [117, 121]. OBLs also appears to be preferred by patients [152]. The transition of patients with recurrent disease to the doctor's office or outpatient clinic for photoangiolytic treatment following initial surgery in the operating theatre is noted as a trend by Karatayli-Ozgursoy S. et al. (2015) [107]. Zeitels S.M. et al. (2006), analysing the results of KTP laser

treatment via flexible endoscope in 29 patients with glottic dysplasia, report lesion regression of 75–100% in 62% of patients [205]. Koufman J.A. et al. (2007) report that 20 out of 25 patients (80%) with laryngeal leukoplakia, who underwent outpatient laryngeal surgery with a PDL laser, did not require further treatment [114]. Hu H.C. et al. (2017) report that in 9 out of 11 patients (82%) with leukoplakia, who were treated solely on an outpatient basis using a CO₂ laser equipped with a flexible guide, complete resolution of the lesion was achieved [98]. Wellenstein D.J. et al. (2020) report the results of SIL treatment with a CO₂ laser via a flexible guide on an outpatient basis, noting that in 10 out of 16 patients (63%) with leukoplakia and hyperkeratosis, no residual or recurrent lesions were detected after treatment [197]. Hamdan A.L et al. (2023) report the first series of patients with glottic leukoplakia (12 lesions/10 patients), treated with a blue laser on an outpatient basis, noting complete regression of the lesion in 75% of cases (9/12) [85].

When selecting a treatment method for HLL, both oncological efficacy and preservation of vocal function are important. There are always trade-offs, and priorities must be set after determining the lesion's malignant potential. In lesions with a low risk of malignancy, it seems reasonable to focus on preserving vocal function, whereas in lesions with a high risk of malignancy, the oncological approach appears to be the priority. The authors of several publications comparing CO₂ laser resection with laser ablation using angiolytic lasers (particularly the KTP laser) for glottic neoplasms report superior vocal outcomes following laser ablation [116, 182], however, it is not yet clear which factor is responsible for the better voice quality: the type of laser or the surgical technique [116]. There is no consensus regarding the types of lasers that should be used for the management of HLL and the advantages of one type of laser over another. Rosen C.A. et al. (2009), in a review article comparing different types of lasers used in OBLs (PDL laser, KTP laser, CO₂ laser, thulium laser, Nd:YAG laser), note that the choice of laser is largely theoretical. Claims of the superiority of one type of laser over others are not supported by thorough comparative studies on laryngeal tissues, particularly due to the large number of variables, apart from wavelength, involved in the interaction of the laser with biological tissue [161]. Wellenstein D.J. et al. (2018), in another review article dedicated to laryngoscopic procedures in an outpatient setting, note the absence of comparative studies on the efficacy of different types of lasers in the treatment of specific lesions [198]. Parker N.P. (2017), also in a review article on vocal cord leukoplakia, concludes that different lasers are merely different tools for achieving the same objective of lesion eradication [142]. Yan Y. et al. (2010) note that the efficacy of treatment with all lasers is highly dependent on the surgical technique and the surgeon's skills [203].

Given that leukoplakia, even without dysplasia, can progress to carcinoma, close monitoring of patients with HLL is recommended, regardless of the initial histological response [113, 140].

1.2.2. Laryngeal papillomatosis

Laryngeal papillomatosis (LP) is a chronic viral disease with an unpredictable course, characterised by exophytic tumour-like growths on the laryngeal mucosa, which can impair vocal function and obstruct breathing. Two types of human papillomavirus (HPV) – HPV6 and HPV11 – are responsible for the development of the disease in over 90% of cases [43]. The disease may go into spontaneous remission, may remain stable, requiring only periodic surgical treatment, or may take an aggressive course, requiring surgical treatment every few days or weeks and consideration of adjuvant therapy [31].

Laryngeal papilloma in adults is considered a precancerous condition, with a malignant transformation rate of 1–7% [43, 102, 157]. Recurrent respiratory papillomatosis poses a significant financial burden on both patients and society as a whole due to the multiple costly surgical interventions required throughout patients' lives [120].

There is currently no curative treatment for LP. The disease is typically recurrent. At present, surgical treatment is the priority in the management of patients with LP. The aim of surgical interventions is to ensure adequate phonation and respiration by removing tumour growths until the disease resolves spontaneously [32, 102, 120]. In approximately 20% of cases, when surgery cannot control the disease, patients require adjuvant therapy. The indications for adjuvant treatment are not clearly defined; however, the surgeon usually recommends adjuvant therapy for patients requiring more than four surgical procedures per year [31, 43, 102]. Multiple methods of adjuvant therapy have been proposed: systemic interferon, intralesional cidofovir, intralesional bevacizumab, HPV vaccine, etc. [31, 43, 102, 120]. The efficacy of adjuvant treatment is limited to merely increasing the interval between surgical procedures [102].

Currently, transoral microsurgery plays the primary role in the management of patients with LP. Several modalities of this type of treatment are practised, described and analysed: cold surgery [188], CO₂ laser [199], microdebridement [143], PDL laser [114], KTP laser [205], Nd:YAG laser [103]; diode laser [9]. Different lasers used in laryngology have different absorption characteristics due to different target chromophores, which determine the depth of penetration. The CO₂ laser targets water and therefore has minimal penetration depth and good cutting properties. Angiolytic lasers preferentially target oxyhaemoglobin and therefore affect small vessels and induce lesion regression. The Nd:YAG laser targets chromophores such as melanin and carbon, and is only partially absorbed by water and oxyhaemoglobin, resulting in a greater penetration depth of the laser irradiation (up to 10 mm) [82]. Currently, the most widely

used surgical treatment modality is transoral microsurgery, which utilizes a CO₂ laser. A disadvantage of using this type of laser is linked to the detection of active viral DNA in the laser smoke, which constitutes a potential source of infection [31]. Janda P. et al. (2004) report the use of the Nd:YAG laser during transoral microsurgery in a continuous, non-contact mode, using a rigid instrument with a flexible distal tip to guide the laser fibre for the treatment of LP. The authors note a reduction in the disease recurrence rate, which is believed to be attributable to the fact that the Nd:YAG laser, due to its deep coagulation properties, causes destruction of the basal layer of the mucosa, which is infected with HPV, the virus responsible for the regeneration of papillomatous tissue [103]. No surgical technique proposed to date can prevent the occurrence of tumour recurrence, due to the presence of viral particles in the visually intact laryngeal mucosa adjacent to visible papillomatous proliferations. Experts in the field of LP recommend avoiding excessive radicalism during the surgical procedure and protecting the anatomical structures important for phonation and respiration, in particular the anterior and posterior commissures, in order to reduce the risk of postoperative complications, such as synechiae and cicatricial glottic stenoses [31, 43, 102]. Tracheostomy should be avoided, if possible, as it has been demonstrated that tracheostomy promotes the growth of papillomas in the tracheostomy area and contributes to the spread of the tumour process into the distal airways [25, 31, 184]. Transoral microsurgery via suspended laryngoscopy, being the traditional method of treating LP, is sometimes difficult or impossible due to anatomical peculiarities (short mandible, limited cervical mobility, ankylosis of the temporomandibular joint, etc.).

With the advancement of flexible endoscopy and flexible-guide-based laser technologies, endoscopic surgical treatment of LP has become possible, avoiding general anaesthesia with muscle relaxants, which, when used repeatedly, increases the morbidity rate. Given the recurrent nature of the disease and the prospect of repeated/multiple surgical interventions, the benefits of OBLs are particularly evident [117, 121]. Avoiding repeated surgical interventions under general anaesthesia in the operating theatre is of particular value for these patients. Kuet M.L. and Pitman M.J. (2013) note that prior to the OBLs era, due to the risks associated with general anaesthesia, patients with LP typically waited until symptoms (dysphonia and dyspnoea) became sufficiently severe, enduring significant chronic morbidity, before deciding to undergo surgery in the operating theatre. Due to the advantages of OBLs (safety, time savings, etc.), the threshold for deciding in favour of surgery has lowered, and patients often prefer to be treated when symptoms are mild or minimal. Follow-up examination and surgery can often be carried out during a single outpatient visit, and patients can return to their normal routine on the same day. Consequently, OBLs, when performed for a limited lesion, has changed the treatment paradigm, resulting in reduced morbidity both associated with OBLs and with the disease itself [115]. Rees

C.J. et al. (2007) estimated that the savings per case amount to more than \$5,000 when performing PDL laser surgery for LP on an outpatient basis [153].

The flexible endoscope can be coupled with various types of lasers: pulsed dye laser (PDL) – 585 nm [170], KTP (potassium tetanyl phosphate) laser – 532 nm [181], thulium:YAG laser – 2013 nm, CO₂ – 10600 nm [114], diode laser – 810, 980, 445 nm [9, 133], Nd:YAG laser – 1064 nm [77]. Zeitels S.M. and Burns J.A. (2007) mention two types of angiolytic lasers used in OBLs: the PDL laser (585 nm) and the pulsed KTP laser (532 nm), giving priority to the KTP laser in the treatment of epithelial lesions [207]. The aim of surgical intervention in LP is to reduce the volume of tumour proliferations, improve vocal function, and maintain airway patency; the unpredictable natural course of the disease, manifested by relapses and remissions, poses a challenge for any study on the efficacy of LP treatment [115]. It has been demonstrated that treatment with photoangiolytic lasers (PDL, KTP) can lead to disease regression and improved voice quality [115]. Del Signore A.G. et al. (2016) note that 50% of patients with LP, treated with photodynamic lasers (PDL and KTP), required repeat treatment sessions [30]. Mao W. et al. (2023) report their experience of using the KTP laser in an outpatient setting for the treatment of LP, noting complete resolution of the condition in 66.7% of cases with a follow-up period ranging from 13 to 81 months [128]. More recent publications also mention the blue laser (445 nm) [50, 84].

One disadvantage of treatment with angiolytic lasers is the lack of a clear endpoint, resulting in suboptimal treatment that requires repeated unplanned surgical interventions in approximately 20% of cases [30]. Angiolytic lasers are used more to induce regression/involution of the lesion than to achieve immediate eradication/ablation of the lesion during the surgical procedure. Regression of the lesion may take several weeks (4–5 weeks or more) [22, 171]. Due to the delayed therapeutic effect, these non-ablative techniques are not suitable for the treatment of voluminous lesions, owing to the risk of airway obstruction in the postoperative period [171]. Lahav Y. et al. (2023) note that large papillomatous proliferations require particular caution when considering OBLs, due to the difficulty of delivering a sufficient amount of laser energy to the lesion [117]. Bar R. et al. (2024) mention the limited operating time following administration of topical laryngeal anaesthesia as a constraint for outpatient endolaryngeal procedures [11]. Consequently, if the lesion requires a longer operative time or if the patient is not sufficiently cooperative, the surgeon may not have sufficient time to complete the procedure.

There are few publications on the use of other types of lasers in the treatment of LP. Poddubny B.K. et al. (2006) report on the use of the Nd:YAG laser in 154 patients with precancerous lesions of the larynx, including LP (27.4%), with the majority of procedures

performed under local anaesthesia. In patients with limited LP, characterised by a few nodular lesions, treatment, carried out once or several times, was successful (patient recovery). In diffuse PL, the disease recurred after multiple laser ablations, with the authors assessing the results of surgical treatment as unsatisfactory [212]. Although the Nd:YAG laser (1064 nm) is widely used in interventional bronchology, we have not found any publications in the English-language literature regarding the use of the Nd:YAG laser via a flexible endoscope in the treatment of LP.

1.3. Laryngeal cancer

Laryngeal cancer accounts for approximately 30–50% of all head and neck cancers [4]. Approximately 75% of laryngeal carcinomas are located in the glottic region [49, 141]. The majority of patients (75–80%) present with early glottic carcinoma [141]. There is no clear clinical definition for early glottic cancer. Some authors include stages Tis, T1a and T1b in this definition [48]. Other authors also include T2 lesions [174]. Early glottic cancer is usually defined as disease at stages Tis, T1, and T2a (with unaffected vocal cord mobility) [146, 149, 174]. Although not endorsed by the latest AJCC (American Joint Committee on Cancer) TNM classification (2017) [7], stage T2 is often unofficially subdivided into the subcategories T2a (with unaffected vocal cord mobility) and T2b (with limited vocal cord mobility) [42, 90, 201]. The literature reports poorer oncological outcomes and, consequently, poorer prognoses in tumours that limit vocal cord mobility, compared with those that do not affect it [42, 90].

Currently, there is no consensus on the primary management of early glottic cancer. The choice of treatment strategy varies between countries and institutions and, to a large extent, depends on the clinician's preferences, the patient's preferences, and the availability of equipment.

The rate of occult cervical metastases for early glottic cancer is below 10%, and in T1 glottic cancer it is below 1%; therefore, there is a consensus among specialists, as per, that prophylactic neck dissection is not necessary if the tumour is radiologically classified as N0 [48, 89, 155, 174]. Open partial laryngectomy (OPL), radiotherapy (RT), and transoral laser microsurgery (TLMS), which utilizes a CO₂ laser, demonstrate high and comparable cure rates [13, 208], but all the aforementioned methods have drawbacks. When selecting the treatment modality, several factors are taken into account: duration of treatment, treatment costs, the patient's general medical condition, functional outcomes, preservation of future treatment options, and the patient's preference for RT or surgery [13, 208].

Open partial laryngectomy results in a local control rate of 91–98% for T1 glottic carcinoma and 84–86% for T2 lesions [149]. The disadvantages of OPL include (1) major surgical trauma, manifested by the cutting of normal anatomical structures (muscles, nerves,

vessels, cartilage), resulting in postoperative pain and oedema; (2) temporary tracheostomy (5–18 days); (3) temporary placement of a nasogastric tube, due to impaired swallowing and episodes of aspiration; (4) a long hospital stay (22–35 days); (5) poor voice quality after surgery; (6) high rate (up to 51%) of postoperative complications, many of which are severe (laryngeal stenosis, pneumonia, postoperative deaths) [13, 136, 149, 162]. For the reasons mentioned above, OPL is currently losing ground, being performed less and less frequently as a first-line treatment for early glottic cancer, and is reserved for more advanced disease [20, 89, 189].

External beam radiotherapy and CO₂ laser TLMS are the main treatment methods for T1–T2 glottic cancer, and the controversy between these two methods continues. Radiotherapy is still preferred for the treatment of early glottic cancer in many institutions, demonstrating a cure rate of 80–90% for Tis–T1 lesions and 50–75% for T2 lesions [105, 156]. The local recurrence rate following primary RT for early-stage glottic cancer ranges from 5% to 20% for stage T1 and from 25% to 50% for stage T2 [105, 148]. The disadvantages of RT include: (1) the long duration of treatment (6 weeks), associated with increased medical costs (RT is 2–15.5 times more expensive than TLMS), and burdensome travel commitments [18, 136, 155, 164, 209]; (2) radioresistance of some tumours (even small lesions) [156]; (3) risk (up to 17%) of serious long-term complications (xerostomia, hypothyroidism, damage to the skin and salivary glands, persistent glottic oedema and erythema, cervical myelitis, accelerated carotid artery stenosis, laryngeal chondronecrosis) [19, 89, 159, 176, 183]; (4) risk of developing radiation-induced secondary malignancies, particularly in young patients [4, 89, 97, 209]; (5) reduced efficacy in large/protruding tumours [156]; (6) reduced efficacy in cases of involvement of the anterior commissure [156]; (7) reduced efficacy in verrucous carcinoma [156] and risk of anaplastic transformation of this type of neoplasm [175]; (8) the inability to reuse RT in the event of a recurrent tumour or a new primary tumour in the head and neck region, which may occur in approximately 20% of treated patients, limiting subsequent treatment options [155]; (9) difficult and delayed diagnosis of persistent and recurrent tumours, due to persistent post-radiation oedema [4, 19]; (10) difficult salvage endoscopic laser resection in cases of irradiated larynx [190], resulting in an increased rate (75%) of total laryngectomy in the event of RT failure [18] and a lower larynx preservation rate compared with primary endoscopic surgery [1, 19, 52, 92, 168, 189]. Therefore, RT is far from being an ideal first-line treatment modality for early glottic cancer; consequently, for Tis and T1 tumours, it has been suggested (even by radiation oncologists) that RT should be reserved for situations where all surgical options have failed [89].

Transoral CO₂ laser microsurgery is considered the gold standard in the surgical management of early glottic carcinoma, having replaced OPL as the primary treatment modality [108, 174, 178]. The advantages of TLMS include: (1) minimal surgical trauma and preservation

of the integrity of the cartilaginous skeleton of the larynx [13, 135]; (2) avoidance of tracheostomy [13, 135]; (3) short treatment duration with minimal or no hospitalisation [13, 48, 202]; (4) easier and earlier detection of recurrent tumours than after RT or OPL [146, 202]; (5) complications, with the exception of persistent dysphonia, are rare [202]; (6) lower costs (by 50% or more) compared with RT and OPL [13, 18, 94, 136, 146, 164, 172, 209]; (7) the possibility of repeat treatment and the availability/preservation of all salvage treatment options in the event of tumour recurrence or a new primary tumour, resulting in a better larynx preservation rate compared with RT [1, 13, 19, 48, 52, 92, 145, 155, 168, 174, 189]. In a systematic review and meta-analysis of treatment outcomes for T1 glottic cancer, Vaculik M.F. et al. (2019) found that patients treated with TLMS are six times more likely to preserve their larynx than those initially treated with RT [189].

With the advent of fibre-optic laser technologies, other types of laser, in addition to the CO₂ laser, have been used over the last two decades in the treatment of early glottic cancer. In a review article, Karkos P.D. et al. (2021) present the advantages of TLMS using a 980 nm wavelength diode laser, compared to TLMS using a CO₂ laser, noting better access to distant, angled and hard-to-reach regions, such as the anterior commissure, thanks to the flexible fibre, and finding similar oncological outcomes for TLMS with the diode laser (980 nm) compared to the CO₂ laser [108]. In recent years, for the treatment of early glottic carcinoma, laser ablation using a KTP laser (532 nm) has been proposed as an alternative to laser resection [116, 121, 141, 178, 182, 206, 208]. This technique allows for better preservation of the structure and function of the vocal folds, with oncological outcomes reported to be similar to those achieved with CO₂ laser resection and better functional/vocal outcomes [178, 182, 206].

Transoral laser microsurgery also has limitations: (1) endoscopic exposure of the lesion is not possible in some cases due to difficult anatomy (short neck, insufficient cervical extension, hypertrophied tongue root, protruding incisors, retrognathism, ankylosis of the temporomandibular joint/limited mouth opening, etc.), resulting in the procedure being interrupted or inadequate resection; (2) the possibility of dental damage, in cases of tooth mobility or dental prosthetics in the anterior maxillary region, which is associated with additional health problems and extra costs for the patient; (3) patients with ischaemic cardiovascular disease cannot tolerate prolonged laryngoscopic suspension, which stimulates the vagus nerve and may cause cardiac arrhythmia or silent myocardial infarction; (4) risks of general anaesthesia with muscle relaxation, associated with the patient's comorbidities [52, 89, 149, 150, 155, 174, 187].

Following a study of treatment preference among patients with early-stage glottic cancer who were offered a choice between TLMS and RT, van Loon Y. et al. (2018) found that 168 out

of 175 patients (96%) opted for TLMS, largely due to the shorter treatment duration and the availability of more treatment options in the event of recurrence [190].

Flexible endoscopic laryngeal surgery (FELS), whilst retaining the advantages of TLMS, is able to address some of the disadvantages of traditional transoral laser surgery, being applicable in difficult anatomical situations (short neck, temporomandibular joint ankylosis, insufficient exposure of the anterior commissure, etc.), in patients at high risk of GA, and could be an alternative for patients who prefer OBL. FELS, whilst increasingly used in recent years for the treatment of benign and precancerous laryngeal lesions, has not yet become popular for the treatment of malignant lesions. The use of FELS in the treatment of glottic cancer is poorly documented in the specialist literature. Poddubny B.K. et al. (2006) report their experience of using the Nd:YAG laser in 24 patients with T1 glottic cancer, recording good results (tumour recurrence was detected in only one case of T1b tumour) [212]. Lai J.P. et al. (2001) were the first in the English-language literature to report the use of flexible endoscopy for the treatment of early glottic cancer with an Nd:YAG laser, performed on an outpatient basis under local anaesthesia. The authors present 27 patients with Tis-T1 glottic lesions, who were followed up for 3–7 years, with a cure rate of 85.2% [118]. In a review article, Wellenstein D.J. et al. (2018) note the absence of studies relating to OBL for early glottic cancer [198].

Minimally invasive procedures for neoplastic lesions of the larynx are therefore of clinical interest in terms of achieving a radical cure with minimal trauma. Both the traditional approach to managing these lesions via transoral microlaryngoscopy, using cold instruments or the CO₂ laser, and treatment with angiolytic lasers, whilst having advantages, demonstrate limitations in their applicability for certain categories of patients: transoral microsurgery is difficult or impossible in cases of anatomical peculiarities or limitations, such as insufficient cervical extension, a short mandible, ankylosis of the temporomandibular joint, etc., and in cases of contraindications for general anaesthesia, whilst treatment with angiolytic lasers is problematic in cases of voluminous laryngeal lesions. There is insufficient information in the specialist literature regarding the use of other types of lasers (non-angiolytic) and other surgical approaches in the treatment of neoplastic laryngeal lesions. Furthermore, there are very few studies addressing the treatment of malignant laryngeal lesions using FELS, particularly in an outpatient setting. For this reason, we set out to present and analyse our own experience in the treatment of neoplastic laryngeal lesions using FELS, employing different/non-traditional techniques, methods and approaches that could overcome the limitations of the aforementioned methods.

2. MATERIAL AND METHODS

2.1. Research materials and methods

Three studies were conducted as part of the project:

1. A study on the efficacy of different types of endoscopic interventions in the treatment of benign non-epithelial laryngeal lesions, as well as an analysis of the risk factors for their recurrence. This is a multicentre retrospective observational study.

For Study 1, the sample size was estimated in accordance with the need to test the hypothesis regarding the association between two dichotomous variables (the potential risk factor for recurrence and recurrence itself), the appropriate test being the χ^2 test. Therefore, the RStudio programme was used, specifically the 'pwr' library (<https://cran.r-project.org/web/packages/pwr/pwr.pdf>), with the calculation procedure and result shown in figure A2.1.

As shown in figure A2.1, for an effect size of 0.3, a significance level of 0.05 and a power (1- β) of 0.8, the minimum sample size is estimated at 88 patients with benign non-epithelial lesions who underwent endoscopic surgery.

2. Research on the efficacy of flexible surgical endoscopy in the treatment of precancerous lesions. A multicentre retrospective observational pilot study was conducted. The research was designed as a pilot study. The main purpose of such a study is not to draw definitive conclusions or to test hypotheses with high statistical power, but to assess the feasibility of the main study, to identify possible methodological issues and to obtain preliminary estimates for the variables of interest. Therefore, for this study, only patients available in the archives of the aforementioned institutions were considered; the arguments for not requiring an estimate of the minimum sample size are as follows [a, b, c, d, e]:

- a. Initial exploration: A pilot study is used to obtain exploratory data with the aim of better understanding the nature of the phenomenon under study. In this case, the sample does not need to be representative of the general population, but only large enough to provide a preliminary picture of the processes or factors under investigation.

- b. Feasibility and testing of methodology: The objective of a pilot study is to test procedures and determine whether the main study can be successfully carried out. For example, we can assess the time required for data collection, logistics, participant recruitment, and the functioning of measurement instruments and techniques. For this purpose, a small sample is usually sufficient.

- c. Lack of statistical validity requirements: In a pilot study, we do not focus on meeting rigorous criteria for statistical significance, such as 80% power. The sample size in a pilot study

should not be calculated using statistical power formulas, as the main aim is not to prove a hypothesis but to prepare for the main study.

d. Costs and resources: Pilot studies are often limited in terms of available resources. They are designed to minimise costs and completion time, so that we can test hypotheses and procedures with a smaller number of respondents, without requiring large samples.

e. Adjusting the sample size for the main study: Once the pilot study is complete, the preliminary data can be used to accurately estimate the minimum number of respondents required for the main study, meaning that the purpose of the pilot study is not to provide final results, but simply to guide the subsequent design of the research.

3. Research on the efficacy of flexible surgical endoscopy in the treatment of early glottic cancer (T1-T2), supplemented by an analysis of factors influencing treatment efficacy. A multicentre retrospective observational study was conducted. For this study, the sample size was estimated in accordance with the need to develop a predictive model within the survival analysis. Therefore, given that the variable of interest was a dichotomous characteristic, the RStudio software was used to estimate the minimum required number of respondents with glottic cancer in the two cohorts (the T1 cohort and the T2 cohort), specifically the ‘powerSurvEpi’ library (powerSurvEpi package - RDocumentation), with the calculation procedure and result shown in figure A2.2.

Thus, the minimum number of respondents for the group of patients with T2 glottic cancer is 53 respondents; meanwhile, for group T1, this number was 66 patients [93, 119, 125, 186, 191].

To address the set tasks, the results of surgical interventions using a flexible endoscope, performed by the author on patients with benign laryngeal neoplasms, precancerous lesions of the larynx, and early-stage (cT1-T2) primary and recurrent/residual malignant tumours of the glottic portion of the larynx, between 1992 and 2025, in three institutions: the PMSI Oncology Institute, the PMSI „Timofei Moşneaga” Republican Clinical Hospital, and M.C. „Expert Endoscopy” SRL. The treatment outcomes of patients in the following nosological categories were analysed: (1) benign non-epithelial lesions (n=338); (2) precancerous lesions (n=97); (3) malignant lesions (cT1-T2 glottic cancer) (n=140); a total of 575 cases.

Inclusion criteria:

The study included consecutive adult patients from the aforementioned nosological categories. For the analysis of long-term oncological outcomes, patients with primary and recurrent/residual malignant lesions (cT1-T2) with a 5-year follow-up period were included.

Exclusion criteria:

For the analysis of long-term oncological outcomes, patients who were under observation for less than 5 years following endoscopic intervention, patients lost to follow-up up to 5 years after endoscopic intervention, and patients who died from causes unrelated to the primary disease up to 5 years after endoscopic intervention were excluded from the study.

Evaluation of research results

The evaluation of the results of flexible endoscopic laryngeal surgery in patients with benign non-epithelial lesions and in patients with precancerous lesions (hyperplastic laryngeal lesions and papilloma/papillomatosis) was based on the following criteria: (1) feasibility of the method; (2) immediate surgical outcome: eradication of the lesion; (3) short-term surgical outcome (1–3 months): complete epithelialisation of the postoperative wound and absence of residual lesion; and (4) lesion recurrence rate.

The oncological efficacy of flexible endoscopic laryngeal surgery in patients with malignant lesions was assessed according to the following criteria:

- Ultimate disease control (UDC): absence of the primary tumour, regional metastases and distant metastases following treatment, including salvage therapy;
- Overall survival: the length of time from the start of treatment to death from any cause;
- Overall survival rate (OS): the percentage of patients who are alive after a certain period of time (e.g. after 5 years) from the start of treatment;
- Local control (LC): disappearance of the primary tumour and metastases in regional lymph nodes without locoregional recurrence, the endpoint for LC being the date of the first locoregional recurrence;
- Disease-free survival (DFS): the percentage of patients who are alive after a period of time (e.g. after 5 years) without locoregional recurrence, the endpoint for DFS being the date of the first locoregional recurrence;
- Disease-specific survival (DSS): the percentage of patients who have not died from laryngeal cancer within a defined period of time (e.g. 5 years from the start of treatment);
- Ultimate disease control with FELS alone (UDC FELS): definitive control of the disease following flexible endoscopic laryngeal surgery alone;
- Cure with larynx preservation (CLP): ultimate disease control with preservation of the larynx;
- Death due to the primary disease (DD): the percentage of patients who died due to the progression of laryngeal cancer;

- Local recurrence (LRc): LRc includes recurrences of the primary tumour (detected 12 months or more after surgery) and residual/persistent primary tumours (detected up to 12 months after surgery).

The functional/vocal outcome after treatment was assessed using a grading system representing the patient's subjective assessment of their voice, as follows: (1) normal voice, (2) minor dysphonia, (3) moderate dysphonia, and (4) pronounced/severe dysphonia.

Investigation methods

Primary data collection was carried out by extracting data from medical records (archives). The data were recorded using Microsoft Office Excel 2007 (Redmond, WA, USA). Data analysis was performed using the open-source programming tools RStudio (<https://www.rstudio.com/>) and Python (<https://www.python.org/>), thereby ensuring the reproducibility of the statistical analysis. For numerical variables, the five basic indicators were estimated: the mean with standard deviation, the median with the interquartile range, the minimum and maximum values, supplemented by 95% confidence intervals for the mean; these indicators form part of the descriptive statistics, either for the cohort under examination or for the groups formed in the comparative evaluation of the groups examined. The comparative evaluation for numerical variables was carried out using non-parametric tests, depending on the number of groups and the relationships between groups (the Wilcoxon-Mann-Whitney test for dependent and independent groups or the Kruskal-Wallis test for independent groups, applying multiple comparisons and Holm corrections where necessary). For qualitative variables, relative frequencies were estimated, supplemented with 95% confidence intervals, as well as absolute frequencies. Hypothesis testing for categorical data was performed using Pearson's chi-square test, Monte Carlo variant (100 000 samples). For all the statistical tests described above, the significance level (α) was set at 0.05.

2.2. Treatment methods

Treatment of neoplastic lesions of the larynx was performed using flexible endoscopic surgery, employing non-traditional techniques and instruments for endolaryngeal surgery (biopsy forceps, diathermy loop/snare, Nd:YAG laser (1064 nm), diode laser (980/1470 nm)), some of which were used for the first time. The surgeon who performed the procedures, having experience in interventional bronchology, applied certain techniques and skills from flexible bronchoscopy to surgical procedures on the larynx.

In the treatment of patients with neoplastic lesions of the larynx, we used the following instruments:

- flexible therapeutic bronchoscope with a 2.6–3.0 mm working channel (models: BF-1T10, BF-TE2, BF-1T60, BF-1TH1100 („Olympus”, Japan)) (figure A2.3, A2.4);
- flexible biopsy forceps with a jaw opening of 4.5 mm/6.7 mm („Micro-Tech”, China) (figure A2.5);
- oval-shaped diathermy loop, 10–15 mm in size („Micro-Tech”, China) (figure A2.6);
- electrosurgical unit (figure A2.7);
- Nd:YAG laser (wavelength: 1064 nm), model: LTN-102 (Russia) (figure A2.8);
- diode laser (wavelength: 980/1470 nm, model: LEONARDO Dual 45 („Biolitec”, Germany) (figure A2.9);
- superimposed high-frequency jet ventilator, model „TwinStream” („Carl Reiner”, Austria) (figure A2.10).

All endoscopic instruments/accessories (flexible forceps, diathermy loop, flexible laser guide, etc.) were delivered to the target lesion by being inserted through the working channel of the flexible bronchoscope (figure A2.11).

When procedures were performed under local anaesthesia, patients were secured in a sitting position (figure A2.12). The therapeutic flexible bronchoscope was inserted transnasally following local/topical anaesthesia of the nasal cavity and pharynx with 10% lidocaine spray. For laryngeal anaesthesia, 2% lidocaine (10–15 ml) was instilled into the larynx via a catheter (model: PR-2B („Olympus”, Japan)), inserted through the working channel of the flexible bronchoscope, during phonation, producing a „laryngeal gargle”. In some cases (at the patient’s request), minimal/moderate intravenous sedation/analgesia was administered. In such cases, pulse oximetry and appropriate cardiovascular monitoring were provided. When procedures were performed under general anaesthesia (GA) with superimposed high-frequency jet ventilation (SHFJV), the therapeutic flexible bronchoscope, together with the laser guide, flexible forceps or diathermy loop, was inserted via the suspended rigid laryngoscope (figure A2.13). Vocal rest was recommended for 7 days following the surgical procedure.

2.2.1. Benign non-epithelial lesions of the larynx

Flexible endoscopic surgical procedures were performed on 338 patients with various benign non-epithelial lesions of the larynx (BNELL). The procedures were performed in non-routine cases, for patients who were not considered suitable candidates for conventional microlaryngoscopy, and also in some routine cases, to assess the feasibility of the new technique. Patients’ preference to avoid general anaesthesia and to undergo surgery on an outpatient basis was also taken into account. Informed consent was obtained from all patients who underwent surgery.

The following methods were used to eradicate benign non-epithelial laryngeal lesions: cold surgery with flexible forceps, excision with a diathermic loop, Nd:YAG/diode (980/1470 nm) laser ablation, and combined techniques.

Small lesions (1–4 mm) were removed by cold surgery using flexible biopsy forceps, inserted through the working channel of the flexible endoscope (figure A2.14a–c).

In larger lesions with a prominent exophytic component, this was resected using a diathermic loop inserted through the working channel of the flexible bronchoscope. Diathermic excision was performed in cutting mode (figures A2.15a–e, A2.16a–e).

The Nd:YAG laser (1064 nm) or diode laser (980/1470 nm) was used, where necessary, following diathermic resection, for ablation of the residual lesion (figure A2.17a–e) or as the primary instrument in flattened lesions. The flexible guide of the Nd:YAG laser/980/1470 nm diode laser was inserted through the working channel of the flexible bronchoscope for ablation of the lesion, which was performed in continuous irradiation mode with the power set in the range of 20–40 W for the Nd:YAG laser and 20–30 W for the diode laser.

In patients with advanced stages (3 or 4) of Reinke's oedema, the polypoid lesions were grasped in the diathermic loop, which was fixed at their base, with subsequent resection using diathermic cutting (figure A2.18a–e). This technique was first applied for the treatment of patients with Reinke's oedema (Patent MD 1896 Z 2026) [71]. In our opinion, the use of the diathermic loop allows for a significant reduction in operative time, which is an important factor in OBLS. Another advantage of this method/technique is the possibility of applying OBLS even to large lesions, overcoming one of the main limitations of traditional non-ablative techniques using angiolytic lasers and enhancing the safety of the procedure [58, 62].

Good cooperation with the patient is required during the procedure. When the lesion is resected, the patient is encouraged to cough and expectorate the resected specimen, which is subsequently collected for histological examination. In the event of the specimen being aspirated into the tracheobronchial tree, it can be easily extracted as a foreign body. If histological examination is important and the specimen is swallowed, it can be located and retrieved via upper gastrointestinal endoscopy. Awake procedures are usually well tolerated by patients, provided that thorough anaesthesia of the vocal cords is performed during phonation, as well as anaesthesia of the tracheal carina. In cases where patients cannot control their reflexes, the solution is additional intravenous sedation, and if this does not help, general anaesthesia with SHFJV may be used, although this situation occurs quite rarely. If necessary, repeated treatment sessions are carried out at intervals of 2–7 days.

In cases of an obstructing tumour compromising the central airways, we have opted for a combined approach using flexible endoscopy in conjunction with rigid endoscopy. For the first

time, we have applied and described the method of resection of an obstructing laryngeal schwannoma via a non-traditional endoscopic approach, combining flexible and rigid endoscopy [74]. We now present the method (figure A2.19a–e; Patent MD 1895 Z 2026) [70]. Following preventive tracheostomy, a suspended direct rigid laryngoscopy was performed, combined with flexible laryngoscopy using a therapeutic flexible bronchoscope, under general anaesthesia with SHFJV. Initially, incisions were made at the upper and lower margins (through the tracheostomy opening) of the tumour base, using a 980/1470 nm diode laser (20W), with the flexible laser guide inserted through the working channel of the flexible bronchoscope (figure A2.19b). Subsequently, cold resection/„coring out” of the tumour was performed using the bevel of the rigid bronchoscope (figure A2.19c,d). Finally, laser vaporisation of the tumour remnants at the base and margins of the tumour bed was performed (figure A2.19e). The patient was extubated 3 days later and discharged home on the fifth postoperative day.

2.2.2. Precancerous lesions of the larynx

Flexible surgical endoscopy was performed on 97 patients with precancerous lesions of the larynx, who were divided into two subcategories: hyperplastic laryngeal lesions (HLL)/chronic hyperplastic laryngopathies and papilloma/laryngeal papillomatosis (LP).

2.2.2.1. Hyperplastic laryngeal lesions

Flexible endoscopic surgical procedures were performed on 46 patients with hyperplastic laryngeal lesions, who were grouped, according to the classification proposed by the author, into the following subcategories: chronic hyperplastic laryngitis with keratosis, leukoplakia, pachydermia, and verrucous neoplasia [77, 78].

The procedures were performed in non-routine cases, for patients who were not considered suitable candidates for conventional microlaryngoscopy, and also in some routine cases, to assess the feasibility of the new technique. Patients’ preference to avoid general anaesthesia and to undergo surgery on an outpatient basis was also taken into account. Informed consent was obtained from all patients who underwent surgery.

The following methods/techniques for the endoscopic treatment of HLL were used in isolation or in various combinations: cold surgery using flexible forceps, excision with a diathermic loop, Nd:YAG laser ablation/980/1470 nm diode laser ablation, and combined techniques.

Cold ablation using forceps was possible in the case of small flat lesions (1–3 mm). For lesions larger than 3 mm, we preferred Nd:YAG laser ablation or 980/1470 nm diode laser ablation. The laser guide, inserted through the working channel of the flexible endoscope, was brought close to the lesion, which was vaporised using continuous, non-contact irradiation

(figure A2.20a–c, A2.21a–c). In the case of lesions with a clearly evident exophytic component, this was resected using a diathermic snare in cutting mode, a procedure that allows a tissue specimen large enough to be obtained for a conclusive histological examination. The remaining lesion was treated with Nd:YAG laser/980/1470 nm diode laser ablation during the same session or the following session, after histological examination of the tissue specimen obtained by diathermic resection (figure A2.22a–e). We particularly prefer this approach in the case of verrucous neoplasia, so as not to miss carcinoma, which can easily be underdiagnosed if only traditional forceps biopsy is used.

Given that HLL, even without dysplasia, can progress to carcinoma, we recommend follow-up examinations after surgery at least once every 3 months for the first 2 years, and subsequently at least once a year.

2.2.2.2. Laryngeal papilloma/papillomatosis

Flexible endoscopic laryngeal surgery (FELS) was used to treat 51 patients with laryngeal papilloma/papillomatosis (LP). The procedures were performed in exceptional cases, for patients who were not considered suitable candidates for conventional transoral microsurgery due to the risks associated with general anaesthesia and anatomical difficulties, and also in cases where patients preferred to undergo surgery on an outpatient basis. Informed consent was obtained from all patients who underwent surgery.

The following methods/techniques for the endoscopic treatment of laryngeal papilloma/papillomatosis were used either alone or in various combinations: cold surgery using flexible forceps, excision with a diathermy loop, and ablation using Nd:YAG laser/980/1470 nm diode laser. The surgical technique was explained to each patient.

Surgery under local/topical anaesthesia was usually recommended for compliant patients with small lesions (up to 1.0 cm in size), following diagnostic flexible laryngoscopy with biopsy of the lesion. The option of undergoing surgery under general anaesthesia was also explained to patients.

For a period of time, we did not have access to a high-frequency jet ventilator, a CO₂ laser, and a surgical microscope, but we did have a flexible bronchoscope and an Nd:YAG laser, and we therefore gained experience using these instruments. Cases requiring multiple treatment sessions are associated with the aforementioned period of lack of necessary equipment. In cases of extensive obstructive lesions, during the first treatment session, we usually performed deobstruction by resection with a diathermy loop or vaporisation of the lesion with an Nd:YAG laser to avoid tracheostomy, and subsequently performed ablation of residual lesions during repeated sessions.

Currently, in cases of extensive lesions, we recommend GA (provided there are no contraindications for GA and transoral surgery) and, as a rule, we perform lesion ablation in a single session.

Small papillomas (1–4 mm) were removed using cold surgery with flexible forceps. Flat papillomas larger than 4 mm were initially treated with an Nd:YAG laser or a 980/147 nm diode laser. For laser ablation, the continuous non-contact mode was selected, with the power set in the range of 20–40 W (figure A2.23a–c). Prominent, pedunculated, racemose and obstructive lesions were preferably excised using a diathermy loop in cutting mode, with the Nd:YAG laser/980/1470 nm diode laser being used as a second-line instrument for the ablation of residual lesions (figure A2.24a–c, A2.25a–d). This method (excision of the prominent exophytic component of the papillomatous lesion using a diathermic loop, followed by photovaporisation of the remaining lesion using a non-angiolytic laser (Nd:YAG laser/980/1470 nm diode laser) was used for the first time in the endoscopic treatment of laryngeal papillomatosis (Patent MD 1492 Z 2021) [68]. Laser ablation/vaporisation, preceded by resection with a diathermic loop, compared to the use of the laser as a single instrument, reduces the duration of the procedure and thermal damage to adjacent tissues, and can be used in large and obstructive lesions, which present limitations for non-ablative techniques using angiolytic lasers, and enhances the safety of the procedure. If necessary, multiple treatment sessions are carried out at intervals of 2–7 days.

Good cooperation with the patient is essential during the procedure if the intervention is performed under local/topical anaesthesia. The patient's level of compliance is assessed during diagnostic flexible laryngoscopy, with a biopsy of the lesion, which is performed in a separate session prior to the surgical intervention. Communication with the patient during the procedure helps to increase patient compliance. Immediately after resection of the lesion with a diathermic loop, the patient is encouraged to cough and expectorate the resected specimen for subsequent histological examination. In the event of accidental aspiration of the resected specimen into the tracheobronchial tree, it could be easily retrieved using a flexible bronchoscope; however, this did not occur in any of our cases. If adequate vocal cord anaesthesia is performed, procedures carried out without sedation are usually well tolerated by patients. In rare cases, when patients are unable to control the gag reflex, even with additional intravenous sedation, we recommend general anaesthesia with SHFJV. When the surgical procedure is performed under GA with SHFJV, the flexible bronchoscope, together with the necessary accessories (laser guide, forceps, diathermy loop), is inserted through the jet-assisted laryngoscope. Vocal rest is recommended for 7 days following the surgical procedure.

The first follow-up endoscopic examination is usually scheduled 2 months after the procedure. Following this, subsequent examinations are scheduled 6 and 12 months after the

procedure, then once a year, provided there are no symptoms of disease recurrence (progression of dysphonia or dyspnoea), or immediately upon the onset of symptoms of disease recurrence. If the patient follows the recommendations and attends the follow-up endoscopic examination with a small recurrent lesion (up to 10 mm), we usually perform tumour removal under topical anaesthesia on an outpatient basis. In the case of massive, obstructive recurrent lesions, we recommend hospitalisation of the patient and endoscopic intervention under general anaesthesia with SHFJV.

2.2.3. Glottic cancer

Flexible endoscopic laryngeal surgery (FELS) was performed on 140 patients with cT1-T2 N0 M0 glottic cancer between 1993 and 2025. The first endoscopic procedure for glottic carcinoma in the Republic of Moldova was performed on 10 March 1993 [73]. At that time, the clinic had neither a CO₂ laser nor a surgical microscope, and the only treatment options available for patients with glottic carcinoma were radiotherapy or open surgery. Having experience in using the Nd:YAG laser via a flexible bronchoscope for the endoscopic ablation of tracheobronchial tumours, we proposed these instruments for the ablation of glottic tumours. Patients were informed about awake endoscopic surgery as an alternative to radiotherapy and open surgery, whilst retaining the availability of the aforementioned therapeutic methods in the event of failure of the endoscopic approach. Many patients were receptive to the proposed alternative.

The procedures were performed in exceptional cases, for patients who were not considered suitable candidates for RT and open laryngeal surgery (due to contraindications), and also in cases where patients preferred FELS. Informed consent was obtained from all patients who underwent surgery.

Procedures under local/topical anaesthesia, with spontaneous breathing, were chosen in cases of contraindications or major risk for general anaesthesia with muscle relaxation and/or transoral microsurgery, predominantly due to anatomical difficulties (short neck, insufficient head extension, temporomandibular joint ankylosis, insufficient exposure of the anterior commissure, etc.), the patient's wish to undergo endoscopic surgery whilst awake, good patient compliance, and the patient's ability to tolerate the procedure whilst awake. Patient cooperation is essential during endoscopic procedures whilst awake. The patient's level of compliance was assessed before FELS, during diagnostic flexible laryngoscopy with lesion biopsy, performed using flexible forceps. Cases requiring multiple treatment sessions relate to the aforementioned period when we did not have the necessary equipment for transoral laser surgery.

We applied Nd:YAG laser photoablation/photovaporisation for the majority of cases treated. From 2022 onwards, we began using the 980/1470 nm diode laser, which replaced the Nd:YAG laser in our practice. The 980 nm diode laser is equally absorbed by oxyhaemoglobin and water in the tissues, has excellent coagulation properties and allows for the vaporisation of a large volume of tissue. In our experience, with appropriate settings, the use of the 980 nm diode laser yields a surgical result/effect similar to that of the Nd:YAG laser (1064 nm).

Infiltrative and flattened tumours, without a clearly defined exophytic component (figure A2.26a), are treated by laser ablation alone. Immediately following laser ablation of the tumour, a wound forms, covered by a carbonised coagulation scab (figure A2.26b). One week after photoablation, the postoperative wound is covered with a dense, whitish-grey fibrin-necrotic scab (figure A2.26c). One month after the procedure, granulomatous proliferations are evident in the photoablation area, covered with focal whitish fibrin-membranous overlays. Two months after the operation, flattened, pink granulomatous proliferations without deposits are evident in the photodestruction area (figure A2.26d). Three months after laser ablation of the tumour, the postoperative wound usually heals and is completely epithelialised (figure A2.26e).

If there is a prominent exophytic component of the tumour (figure A2.27a), prior to photoablation, this is resected using a diathermic loop, inserted via the bronchoscope's working channel, in diathermic cutting mode (figure A2.27b). Next, the flexible guide of the Nd:YAG laser (1064 nm)/980 nm diode laser is inserted through the working channel of the bronchoscope for ablation of the remaining tumour, which is performed in continuous non-contact irradiation mode, with the power set within the range of 20–40 W, until the visible tumour lesion is completely vaporised (figure A2.27c). This method (excision of the prominent exophytic component of the tumour lesion using a diathermic loop, followed by photovaporisation of the residual lesion using a non-angiolytic laser (Nd:YAG laser/980/1470 nm diode laser) was used for the first time in the endoscopic treatment of glottic cancer (Patent MD 1464 Z 2021) [67]. Laser ablation/vaporisation, preceded by resection with a diathermic loop, compared to the use of the laser as a single instrument, allows for a reduction in the duration of the procedure (a very important factor, particularly for OBLs) and can be used in voluminous and obstructive lesions, which present limitations for non-ablative techniques using angiolytic lasers.

We consider the use of the diathermic snare to be very useful for the morphological confirmation of the tumour's nature in cases of verrucous neoplasia, which is very difficult/problematic to perform with conventional forceps biopsy due to the massive layer of keratin on the tumour's surface; this leads to an inconclusive histological result and, consequently, the tumour is often interpreted as benign, and appropriate treatment is delayed. In such cases, we have used flexible transnasal endoscopy, under local anaesthesia, with tumour

biopsy by excision using a diathermic loop (figure A2.28b, A2.29). This method allows for the collection of tumour fragments large enough (figure A2.30) to provide a conclusive morphological diagnosis and to perform the biopsy on an outpatient basis, avoiding general anaesthesia [54, 72, 77]. This biopsy method was first used in the diagnosis of verrucous carcinoma of the larynx (Patent MD 1473 Z 2021) [66].

In cases where the tumour does not affect the anterior commissure (AC), the postoperative defect is minimal, sometimes barely visible, with the postoperative scar mimicking the intact vocal cord (figure A2.31a-b). In such situations, the vocal defect is also minimal. In cases where the AC and, in particular, the contralateral vocal cord are affected by the tumour, some postoperative deformation and, possibly, scar-induced stenosis of the laryngeal lumen at the level of the glottis inevitably occur (figure A2.32a-b). Vocal function is impaired in such cases, with patients complaining of pronounced dysphonia.

If necessary, repeat treatment sessions are carried out at intervals of 2–7 days. A control biopsy of the tumour bed was performed only in cases of suspected residual or recurrent tumour.

When procedures were performed under general anaesthesia with SHFJV, the flexible bronchoscope, together with its accessories (flexible laser guide, diathermy loop, etc.), was inserted through the suspended rigid jet laryngoscope (figure A2.13). This method (access to the laryngeal tumour lesion by combining flexible and rigid endoscopy) was used for the first time in the endoscopic treatment of laryngeal tumours (Patent MD 1491 Z 2021) [69]. The proposed method is useful in cases where direct suspension laryngoscopy does not allow adequate exposure of the glottic portion of the larynx, in particular the anterior commissure, due to insufficient extension of the neck. In these situations, the rigid laryngoscope is inserted into the pharynx until the arytenoid cartilages are exposed (when the arytenoid cartilages become visible) (figure A2.33a). Next, the flexible bronchoscope is inserted through the suspended rigid laryngoscope until adequate exposure/visibility of the glottic portion of the larynx is achieved (figure A2.33b). Subsequent manoeuvres are performed using instruments (diathermy loop, flexible forceps, laser guide, etc.) inserted through the working channel of the flexible endoscope. The major advantage of the proposed method is that it overcomes the limitations of conventional transoral surgery, imposed by the patient's anatomical characteristics (short neck, voluminous base of the tongue, reduced cervical mobility, etc.), which lead to inadequate exposure/visibility of the glottis.

In some cases of cT1b-T2 glottic tumours, postoperative/adjuvant radiotherapy was also administered in addition to endoscopic treatment. The reasons for offering adjuvant RT for some cT1b-T2 tumours were as follows: (1) a large infiltrative tumour extending onto the AC (FELS was initially considered a method of achieving cytoreduction to enhance the efficacy of RT); (2)

the surgeon's uncertainty regarding the oncological radicality of the ablation performed; (3) an unfavourable histopathological appearance in tissue samples obtained via biopsy from the site of the eradicated tumour. The dose of postoperative external beam RT ranged from 22 Gy to 60 Gy.

2.2.4. Postoperative management of patients with laryngeal lesions

If the vibrating edge of the mucosa is removed during surgery, the lamina propria becomes exposed; therefore, it is advisable to minimise contact trauma to this region by maintaining vocal rest until the mucosal covering has been restored. We recommend absolute vocal rest for one week following the surgical procedure. After this, the patient transitions from absolute voice rest to limited voice use under the supervision of the ENT-phoniatrist. Voice rest under the supervision of the ENT-phoniatrist is maintained until the postoperative defect has completely healed/epithelialised. Given the adverse effect of gastric acid on the healing process of the postoperative laryngeal wound, we administer proton pump inhibitors to all patients in whom we suspect the presence of gastro-oesophago-pharyngeal reflux. Anti-reflux medication is administered to the majority of patients in the immediate postoperative period.

Following endolaryngeal laser procedures performed to eradicate massive obstructive lesions, precancerous lesions (leukoplakia, pachydermia, verrucous neoplasia, papilloma) and malignant lesions, a significant tissue defect often forms at the site of the ablated lesion, covered by layers of necrotic/charred tissue. Therefore, in addition to voice rest and the administration of proton pump inhibitors, we recommend the systemic administration of analgesic/anti-inflammatory drugs (2 days) for pain control, corticosteroids (2 days) for the control of postoperative local oedema, and antibiotics (5 days) for the prevention of infectious complications. We also recommend steroid inhalations (10 days). Postoperative wound healing and vocal rehabilitation in such cases take a longer period (usually up to 3 months).

3. FELLS OF BENIGN NON-EPITHELIAL LESIONS OF THE LARYNX

Flexible endoscopic surgery was performed on 338 patients with various benign non-epithelial lesions of the larynx (BNELL) (men – 220 (65.1%), women – 118 (34.9%)). The patients' ages ranged from 16 to 81 years, with a mean of 44.9±12.2 and a median of 44.0 years (IQR=18.0). All procedures were performed by a single surgeon.

Laryngeal pathology was represented by the following lesions: myxoid polyp (n=67 (19.8%)), polypoid degeneration of the vocal cords (Reinke's oedema) (n=17 (5.0%)), fibrous polyp (n=39 (11.5%)), angiofibrous polyp (n=76 (22.5%)), angiomatous polyp (n=43 (12.7%)), non-specific granuloma (n=28 (8.3%)), cyst (n=18 (5.3%)), lipoma (n=1 (0.3%)), neurofibroma (n=1 (0.3%)), schwannoma (n=1 (0.3%)), inflammatory myofibroblastic tumour (n=1 (0.3%)), and amyloidosis (n=1 (0.3%)). The dimensions of the lesions ranged from 0.2 cm to 4.5 cm (mean – 0.8±0.6 cm). In the majority of cases (96.4%), benign non-epithelial lesions affected the glottic portion of the larynx (table A3.1).

The following methods were used to remove laryngeal lesions (table A3.2): cold surgery using flexible forceps, excision with a diathermy loop, Nd:YAG laser ablation/980/1470 nm diode laser, and combined techniques. The number of treatment sessions ranged from 1 to 4 (table A3.3). In 97.0% of cases, treatment was completed in a single session.

In 327 cases (96.7%), the procedure was performed under local anaesthesia with spontaneous breathing, and in 11 cases (3.3%) we used general anaesthesia (GA) with superimposed high-frequency jet ventilation (SHFJV), the flexible endoscope being inserted via the rigid laryngoscope with a jet in suspension. In 286 cases (84.6%), the procedure was performed on an outpatient basis. Currently, we only opt for AG with SHFJV in cases where the airways are compromised due to obstructive lesions. Below, we present such a case, in which we employed a non-traditional endoscopic approach [70, 74].

Patient C., a 29-year-old man, presented to the clinic complaining of progressive hoarseness over a 12-year period and inspiratory dyspnoea at rest. Six years ago, the patient was examined at another hospital, where a laryngeal tumour was detected and open laryngeal surgery was proposed, but the patient refused the operation. A contrast-enhanced computed tomography scan revealed a broad-based, originating from the posterior and right lateral walls of the larynx, measuring 3.6×1.8×1.6 cm, occupying all three portions of the larynx and obstructing approximately 80% of the laryngeal lumen, with no signs of erosion of the adjacent cricoid cartilage (figure A2.34a–c).

On flexible laryngoscopy, an exophytic tumour was detected on the posterior wall of the larynx, with a broad base of attachment, irregular in shape, of a hard-elastic consistency, with a smooth, glossy surface and marked vascular pattern, measuring approximately 4.5×2.0×2.0 cm, which significantly obstructed the lumen of the supraglottic, glottic and subglottic portions of the larynx. The upper margin of the tumour was estimated to be 0.3 cm above the upper margin of the arytenoid cartilages, and the lower margin of the tumour was estimated to be 1.5 cm distal to the vocal cords. The endoscopic appearance was suggestive of a benign non-epithelial laryngeal tumour (figure A2.35a).

Endoscopic management was selected as the first-line approach for this case (figure A2.19a–e). Following prophylactic tracheostomy, suspended direct rigid laryngoscopy was performed, combined with flexible laryngoscopy using a therapeutic flexible bronchoscope, under general anaesthesia with SHFJV. Initially, incisions were made at the upper and lower margins (through the tracheostomy opening) of the tumour base, using a 980/1470 nm (20W) diode laser, with the flexible laser guide inserted through the working channel of the flexible bronchoscope (figure A2.19b). Subsequently, cold resection/„coring out” of the tumour was performed using the bevel of the rigid bronchoscope (figure A2.19c,d). Following cold resection, minor bleeding was observed from the site of the removed tumour. Finally, photocoagulation of the haemorrhage surface and laser vaporisation of the tumour remnants at the base and margins of the tumour site were performed (figure A2.19e). The patient was extubated 3 days later and discharged home on the fifth postoperative day. Histological examination revealed a schwannoma. Flexible laryngoscopy, performed 18 months after the operation, showed no tumour recurrence, a clear laryngeal lumen, and minor scarring of the mucosa of the posterior laryngeal wall (figure A2.35b). The patient’s voice and breathing had fully recovered.

The present case demonstrates that even large, obstructive laryngeal schwannomas, affecting all three portions of the larynx, can be successfully eradicated by endoscopic surgery in selected cases, by combining instruments such as the flexible bronchoscope, laser and rigid bronchoscope, provided there is no extraluminal tumour growth. The technique described makes a significant contribution to the diversity of approaches in the management of this rare nosological entity.

In all treated patients, the expected result was achieved – complete eradication of the visible lesion (figure A2.36a-c). There were no complications following the procedures performed.

Recurrent lesions were recorded in 9/338 cases (2.7%), of which: non-specific granuloma – 6/28 (21.4%), inflammatory myofibroblastic tumour – 1/1, myxoid polyp – 1/67 (1.5%),

angiofibrous polyp – 1/76 (1.3%). In 8 out of 9 patients (88.9%), treatment of the recurrences was performed via FELS, with the number of repeat procedures ranging from 1 to 2 (table A3.4).

The predominance of recurrences in patients with non-specific granuloma (6 out of 9 recurrent lesions observed (66.7%)) may be associated with the recurrent nature of this nosological entity. The reported rate of postoperative recurrence of non-specific granuloma of the vocal process varies in different studies between 30% and 90% [95, 158]. According to our data, the recurrence rate of non-specific granuloma is 21.4%, which is comparable to data published by other authors.

In one case, we encountered an inflammatory myofibroblastic tumour, which is an extremely rare lesion with a high potential for postoperative recurrence. The case is of particular interest due to its rarity.

Inflammatory myofibroblastic tumour (IMT) is a neoplasm composed of spindle cells, which, according to the 2020 WHO classification, is included in the category of „fibroblastic/myofibroblastic tumours” of the „intermediate/borderline” type (intermediate malignancies). This tumour has intermediate biological potential (it rarely metastasises) [3, 26]. The larynx is an extremely rare site for IMT. Laryngeal IMT was first described in 1992, and to date, only between 50 and 60 cases of IMT involving the laryngeal l have been reported. Laryngeal IMT is most commonly located in the glottic region, followed by the subglottic region and, more rarely, in the supraglottic region [109]. Despite their benign course, laryngeal IMT demonstrate local aggressiveness and have an increased tendency to recur. The recurrence rate of laryngeal IMT ranges between 8% and 18%. Recurrence usually occurs within 2–12 months after surgery. Distant metastasis is extremely rare [3]. Surgical excision with negative margins is the treatment of choice for laryngeal IMT, which can be performed via an endoscopic or open approach. The location of the tumour, which is challenging or „inconvenient” for minimally invasive (endoscopic) surgery, leads to difficult resection, resulting in an increased recurrence rate. Radiotherapy is used primarily for the treatment of local recurrences. Open surgery is reserved for tumour recurrences, cases with inadequate endoscopic exposure, or suspected malignancy. In some cases involving multiple recurrences, total laryngectomy may be considered [3, 185].

We shall now present our case. Patient C, aged 53, presented at the clinic on 28 March 2016, complaining of marked dysphonia that had been progressively worsening for 7 months. An emergency tracheostomy had been performed 5 days earlier at another institution. Diagnostic fibrolaryngoscopy: A tuberous exophytic tumour, pinkish-white in colour, with a broad base of attachment and a hard consistency, is affecting the anterior commissure, the anterior two-thirds of the right vocal cord, and the anterior one-third of the left vocal cord, extending into the

subcommissural space and the supracommissural region, with subtotal obstruction of the lumen of the glottic portion of the larynx. Endoscopic conclusion: Tumour formation of the glottic portion of the larynx (figure A2.37a). On 04.05.2016, surgery was performed: under general anaesthesia with SHFJV, a combined rigid suspended laryngoscopy and flexible laryngoscopy were carried out. The exophytic component of the tumour was removed by excision with a diathermy loop, followed by Nd:YAG laser photoablation (40W), with recanalisation of the laryngeal lumen (figure A2.37b). Histological findings: Inflammatory myofibroblastic tumour. The patient was extubated and discharged home in satisfactory condition, with a recommendation to attend a follow-up appointment in 1 month. The patient presented at the clinic 9 months after surgery, complaining of inspiratory dyspnoea on minimal exertion and marked dysphonia. Fibrolaryngoscopy: Exophytic tumour with a broad base of attachment, measuring 2.5×2.0×1.0 cm, with a smooth, red surface, is affecting the anterior commissure, extending to both vocal cords, the subglottic (subcommissural) space and the left laryngeal ventricle, with 70% stenosis of the laryngeal lumen. Endoscopic conclusion: Recurrent inflammatory myofibroblastic tumour of the larynx. The patient refused repeat surgery at our clinic. Subsequently, the patient remained under our observation for the next 8 years, during which he underwent repeated interventions for recurrent neoplasms via transoral CO₂ laser microsurgery on 13 occasions, at various clinics in the country and abroad, after which he disappeared from our records.

It should be noted that in 4 out of 338 patients with benign non-epithelial lesions (1.2%), who underwent FELS, malignancies (squamous cell carcinoma) subsequently developed during the observation period. In 3 cases, the malignant lesion was successfully eradicated by FELS (Nd:YAG laser ablation), and in one case (T2 squamous cell carcinoma), open partial laryngectomy was performed (table A3.5).

The functional effects of endoscopic treatment were assessed based on the patient's subjective evaluation of their voice. The majority of patients (92.0%) rated their voice as normal after surgery (table A3.6).

Minor dysphonia was observed postoperatively in 12 patients. In 8/12 patients in this group, lesion sizes ranged from 1.0 cm to 2.5 cm. Of the 4 out of 12 patients with smaller lesions (0.6–0.8 cm), in 3 patients the lesions were associated with chronic hyperplastic laryngitis, and in 1 patient the lesion was associated with vocal cord paresis.

Moderate dysphonia was recorded postoperatively in 10 patients. In all patients in this group, lesion sizes ranged from 1.0 cm to 2.0 cm, and in 6 out of 10 cases the lesions developed against a background of chronic hyperplastic laryngitis.

Severe dysphonia was observed postoperatively in 5 patients: (1) a patient with a recurrent inflammatory myofibroblastic tumour affecting the anterior commissure and both vocal cords, who had undergone multiple laryngeal operations; (2) a patient with a granulomatous polyp in the anterior commissure region, who had previously undergone open partial laryngectomy; (3) a patient with a myxoid polyp of the left vocal cord (measuring up to 2.0 cm) against a background of paralysis of both vocal cords; (4 and 5) patients with grade 4 polypoid degeneration of both vocal cords (Reinke's disease), associated with chronic hyperplastic laryngitis.

According to our data, the likelihood of vocal defect/dysphonia after surgery increases in patients with (1) large lesions (over 1.0 cm), (2) lesions associated with chronic hyperplastic laryngitis, (3) lesions against a background of vocal cord paresis/paralysis, and (4) lesions in patients with a history of laryngeal surgery (open partial laryngectomy).

The follow-up period after successful endoscopic treatment of benign non-epithelial lesions ranged from 1 month to 189 months (mean 10.8 ± 27.0 , with a median of 3.0 months (IQR=3.8) (table A3.7).

In the comparative analysis of the 338 patients included in the study, of whom 286 were treated on an outpatient basis and 52 on an inpatient basis, several statistically and clinically significant differences were observed between the two groups (table A3.7).

The mean age in the overall cohort was 44.9 years (standard deviation (SD) = 12.2). In the outpatient group, the mean was 44.0 years (SD = 11.4), with a 95% confidence interval (CI) between 43 and 45 years, whilst in the inpatient group the mean was significantly higher: 49.7 years (SD = 14.8), with a 95% confidence interval between 46 and 54 years. The Wilcoxon rank-sum test indicated a significant difference between the two groups (test value = 5.517, $p = 0.003$), suggesting that in-patient patients are, on average, older, possibly with more severe or complex comorbidities. It cannot be ruled out that the surgeon's choice of treatment strategy was influenced by this phenomenon.

The gender distribution was comparable between the groups. In the outpatient group, 65.7% of patients were men (confidence interval 60%–71%), and in the inpatient group – 61.5% (confidence interval 48%–75%). The proportion of women was 34.3% in the outpatient setting (CI 29%–40%) and 38.5% in the inpatient setting (CI 25%–52%). The chi-square test did not reveal any significant differences (test value = 0.34, $p = 0.6$), indicating that gender was not associated with the treatment regimen administered.

The nosological structure varied significantly between the two groups (χ^2 test value $_{\text{Monte Carlo}} = 43$, $p < 0.001$). Angiofibrous and myxoid polyps were more common in the outpatient group (24.5% and 21.3%, with confidence intervals of 19%–29% and 17%–26%), whilst non-specific granuloma (17.3%, CI 7%–28%) and Reinke's disease (15.4%, CI 5.6%–25%) had

higher prevalences in the inpatient group. These differences suggest a greater complexity of pathology in patients treated in hospital compared with those treated on an outpatient basis.

The location of the lesions was also significantly different. Glottic lesions were predominant in the outpatient group (98.6%, 97%–100% confidence interval), whilst in the inpatient group their proportion was 84.6% (95%–100% CI), and supraglottic, subglottic and combined localisations were present in higher proportions among inpatients. The differences were significant (χ^2 test value Monte Carlo= 32, $p < 0.001$), confirming the greater anatomical complexity of the cases treated as inpatients.

The mean size of the lesions was 0.8 cm (SD = 0.5) in the outpatient setting (confidence interval 0.71–0.83) and 1.2 cm (SD = 0.9) in the inpatient setting (confidence interval 0.92–1.4). The difference was statistically significant (Wilcoxon rank-sum test value = 5.379, $p = 0.001$), supporting the idea that inpatients present with larger lesions, which may be more difficult to treat using minimally invasive procedures.

The average number of therapy sessions was 1.0 (SD = 0.2) in the outpatient setting (confidence interval 1.0–1.0) and 1.2 (SD = 0.5) in the inpatient setting (confidence interval 1.0–1.3). The difference is significant (Wilcoxon rank-sum test value = 6.683, $p < 0.001$) and reflects the need for a multi-stage treatment in inpatients. The question remains as to whether this difference is relevant in practical terms.

Analysis of the endoscopic treatment applied revealed significant differences between groups (χ^2 test value Monte Carlo= 39, $p < 0.001$). DEX and CS were more frequently used in the outpatient setting (40.9% and 32.5%, confidence intervals 35%–47% and 27%–38%), whilst LA (19.2%) and combination treatments, such as DEX+LA (26.9%) and CS+LA (17.3%), were more common in the inpatient group, with wide confidence intervals (8.5%–30%, 15%–39%, and 7%–28%). These differences reflect the need for more complex therapeutic approaches in cases treated on an inpatient basis.

Local anaesthesia was used in almost all outpatient cases (99.7%, confidence interval 99%–100%) and in only 80.8% of inpatient cases (confidence interval 70%–91%). General anaesthesia with SHFJV was required in 19.2% of inpatient cases (CI 8.5%–30%). The differences are significant (χ^2 test value Monte Carlo= 50, $p < 0.001$), reflecting the likely more invasive or complex nature of procedures in hospitalised patients.

The recurrence rate was low in both groups (2.8% in the outpatient group and 1.9% in the inpatient group), and the difference was not significant (χ^2 test value Monte Carlo= 0.13, $p > 0.9$). This suggests that treatment efficacy is comparable between the two treatment regimens, provided that the intervention is appropriately tailored to each case.

Malignancy was a rare event, with four cases (1.2%) in the outpatient group and none in the inpatient group. The differences were not significant (test value = 0.74, $p = 0.6$), indicating a likely low risk that is independent of the treatment regimen.

Severe dysphonia was present in 7.7% of inpatients (confidence interval 0.45%–15%), compared with only 0.3% in the outpatient group. Mild and moderate dysphonia were also more common in the inpatient group. The differences are striking (χ^2 test value $_{\text{Monte Carlo}} = 35$, $p < 0.001$) and reflect the more severe functional impact of the condition in hospitalised patients, the reason being the need for more complex interventions with more problematic functional outcomes.

Consequently, the analysed data highlighted the existence of significant differences between patients treated on an outpatient basis and those treated as inpatients, both from a clinical perspective (age, size and location of lesions, severity of symptoms) and a therapeutic perspective (number of sessions, type of anaesthesia and type of treatment applied). These differences justify the proposal for a differentiated therapeutic approach, depending on the patient's profile, with an emphasis on individualised treatment. Taking into account the identified variables, such as age, the size of the lesions, the severity of postoperative dysphonia, the complexity of the pathology and the need for repeated interventions, we can rationally recommend outpatient or inpatient treatment for the patient. This approach supports the concept of personalised medicine, with efficient allocation of resources and superior clinical outcomes.

We support the view of Wellenstein D.J. et al. (2020) [197] and consider that the aim of endoscopic treatment should be the complete removal/eradication of the visible lesion. We used flexible biopsy forceps in 143/338 cases (42.3%), the diathermy loop – in 170 cases (50.3%), and the non-angiolytic laser (Nd:YAG (1064 nm)/diode (980/1470 nm)) – in 103 cases (30.5%) (table A3.2).

In our experience, the use of the diathermic loop leads to a significant reduction in operating time, which is very important for increasing the completion rate in outpatient surgery. Another advantage of this technique is the possibility of performing office-based laryngeal surgery (OBLS) for voluminous lesions (e.g. advanced Reinke's oedema, cysts, granulomas, etc.), which constitute the major limitation for non-ablative therapeutic techniques using angiolytic lasers, and increased procedural safety (figures A2.18a–e, A2.38a–c, A2.39a–e, A2.40a–c).

The Nd:YAG laser has been used successfully in interventional bronchoscopy for many years, but it is not widely accepted in laryngology, particularly due to specialists' concerns regarding the deeper penetration of this type of laser compared to other lasers, and the associated thermal damage to surrounding tissues [161]. We have applied laser vaporisation of benign non-

epithelial lesions in 30.5% of cases, and as the primary technique – in only 9.2% of cases. Our current approach involves using the laser as the primary instrument only for the treatment of extensive flattened lesions (figure A2.41a,b). Whenever possible, we prefer to use the laser in combination with other techniques (following cold surgery using forceps or diathermy loop excision), as a secondary/second-line tool, for the vaporisation of residual lesions only (figure A2.17a–e). This approach prevents the delivery of a significant amount of laser energy to the treated tissue and, consequently, reduces the risk of collateral thermal damage to adjacent tissues.

We consider the results obtained in this study to be encouraging and comparable to the possibilities of traditional transoral surgery, and we share the opinion of Wellenstein D.J. et al. (2018) [198] that outpatient laryngeal surgery is the future for rapid diagnosis and treatment, with minimal health risks for the patient.

Although the incidence of carcinoma following endoscopic intervention for benign non-epithelial lesions is low (according to our data, 1.2%), we consider endoscopic monitoring of patients to be advisable, at least once a year for at least the first 5 years following surgery.

The limitations of this study include (1) the retrospective nature of the study, (2) the absence of a control group, (3) significant variability in the observation period, (4) the lack of objective acoustic assessment and standardised subjective assessment (e.g. VHI score) of the voice, which would merit evaluation in future prospective studies.

Therefore, flexible endoscopic laryngeal surgery, using non-coagulating lasers (Nd:YAG (1064 nm), diode (980/1470 nm)), a diathermy loop and flexible biopsy forceps, can be considered an alternative to transoral microsurgery in the treatment of benign non-epithelial lesions of the larynx in selected patients, opening up a new direction in outpatient laryngeal surgery. The proposed techniques/methods allow the limitations of currently used surgical methods (transoral microsurgery and OBLs using angiolytic lasers) to be overcome and demonstrate applicability in OBLs even in the case of voluminous lesions, particularly in patients with risks and contraindications for general anaesthesia and suspended direct laryngoscopy. Although flexible endoscopic surgery, performed under local anaesthesia, is less precise than transoral microlaryngoscopy, the method is nevertheless attractive due to the reduced risks of the procedure for patients, particularly those with comorbidities, as well as lower costs and time savings, allowing patients to maintain a comfortable lifestyle. Flexible endoscopic surgery is worth considering, particularly in light of patients' preferences, as many opt to avoid general anaesthesia and prefer outpatient laryngeal surgery.

4. FELS OF PRECANCEROUS LESIONS OF THE LARYNX

Flexible surgical endoscopy was performed on 97 patients with precancerous laryngeal lesions, which were divided into two subcategories: hyperplastic laryngeal lesions (HLL) and laryngeal papilloma/papillomatosis (LP).

4.1. Classification of hyperplastic laryngeal lesions

Following analysis of the endoscopic appearance of HLL, we have developed our own endoscopic/clinical classification of HLL, which we consider relevant, use and propose [77, 78]:

1. Chronic hyperplastic laryngitis (CHL): the vocal cords are thickened, their mucosa is hypertrophied, the surface forming a slightly irregular or pleated relief, and the visibility of the laryngeal ventricles is reduced. Mucosal hypertrophy may also affect the laryngeal ventricles (manifesting as focal prolapse of the laryngeal ventricle mucosa into the lumen), the interarytenoid space and the vestibular bands. In cases of pronounced hypertrophy of the vocal cords and vestibular bands, the laryngeal lumen may be stenosed, causing dyspnoea. It is important to note the diffuse and symmetrical nature of the epithelial changes, which uniformly affect both laryngeal halves (figure A2.42);

2. Chronic hyperplastic laryngitis with keratosis (CHLK): on the hypertrophied mucosa, there are focal, semi-transparent, whitish overlays with a flaky appearance and indistinct borders (figure A2.43);

3. Leukoplakia: a flat lesion with a membranous overlay appearance, whitish in colour; its surface may be smooth or irregular, with well-defined or blurred borders. The lesion may be solitary or multifocal (presented as several separate or confluent foci) (figure A2.44);

4. Pachydermia: an elevated/raised, plaque-like lesion, whitish in colour, well-defined, with a surface that is smooth, rough, wrinkled or irregular, and of a hard consistency (figure A2.45);

5. Verrucous neoplasia: a lesion with the appearance of an exophytic tumour on a broad base. Its surface is tuberos, with villiform projections, hard in consistency and whitish in colour. The endoscopic appearance often evokes an association with sheep's wool (figure A2.46).

To briefly summarise the above classification of HLL, we shall highlight the following main features: CHL – only diffuse symmetrical hypertrophy (figure A2.42); CHLK – focal whitish, flaky overlays (figure A2.43); leukoplakia – a well-defined, flat, whitish lesion (figure

A2.44); pachydermia – an elevated/raised whitish lesion (figure A2.45); verrucous neoplasia – an exophytic whitish lesion with a verrucous appearance (figure A2.46).

Some authors consider the term „keratosis” to be purely histological [113]. We agree with the experts who use this term in clinical interpretations. Our findings reveal that, when a clinician observes a whitish lesion (flat or raised) on the laryngeal mucosa and takes a biopsy, it is unlikely that the histological examination will not reveal keratosis. The discrepancies that arise in clinical classifications can be explained by the fact that the same lesion may be perceived, interpreted, described and named differently by observers.

Analysing the data in the literature, leukoplakia, according to our classification, corresponds to type 1 (*flat and smooth leukoplakia*) according to Chen M. et al. (2019) [23]; pachydermia, according to our classification, corresponds to types 2 and 3 (*elevated and smooth leukoplakia* and *irregular-type leukoplakia*), according to Chen M. et al. (2019) [23]; and verrucous neoplasia, in our classification, corresponds to *keratinised papilloma*, described by Paches A.I. et al. (1988) [210] and Uloza V.(1986) [188] and, in part, to *irregular leukoplakia*, described by Li C. et al. (2018) [126].

We consider that behind the terms „*hyperkeratosis*”, „*irregular-type leukoplakia*”, „*keratinised papilloma*”, „*hard papilloma*” or „*white papilloma*”, often there is, in fact, verrucous carcinoma, which is difficult to diagnose due to the thick layer of keratin on the surface of the lesion and the high degree of differentiation of the tumour cells. Consequently, conventional forceps biopsy is usually unreliable, leading to an inconclusive histological result [130]. The rationale for this assumption is based on the fact that papilloma in adults is considered by some authors to be a mandatory precancerous condition [188, 211], with a rate of malignant transformation of up to 25% [188] and even up to 50% [210], whilst more recent data indicate that the rate of malignant transformation of papilloma is 1–7% [43, 102, 157]. Therefore, we consider the term „verrucous neoplasia” more appropriate for this type of lesion. The benign or malignant nature of this type of lesion can only be established histologically, following a thorough examination of the entire lesion or a sufficiently large fragment of the lesion, so that the pathologist examines not only the epithelial layer but also, without fail, the stromal component of the lesion.

Having performed over 10 000 endoscopic examinations of the larynx, we have never considered it acceptable to classify any laryngeal lesion as „*erythroplakia*” or „*erythroleukoplakia*” [77]. Upon analysing the interpretation of these lesions in the relevant literature, we found some confusion: some authors interpret *erythroplakia* as a sign of epithelial thinning [47], whilst others present it as a plaque-like hyperplastic lesion [39]. Taking into account the mention of a substantial rate of carcinoma in biopsy specimens obtained from these

lesions [39], we have most likely described these reddish mucosal areas as „hyperemia” and defined such lesions in our endoscopic reports as „carcinoma”.

Gale N. et al. (2000) note that precancerous lesions do not have a characteristic macroscopic appearance, and no laryngoscopic finding can be considered suggestive of a diagnosis of precancerous lesions [46]. Furthermore, based on data published by Chen M. et al. (2019) and Li C. et al. (2018) [23, 126], the presence of dysplasia and carcinoma in a white lesion increases as it becomes more elevated and its surface becomes more irregular. Li C. et al. (2018) found a strong correlation between the macroscopic appearance of the lesion and its degree of dysplasia [126]. A close correlation between the presence of vocal cord hyperaemia and high-risk leukoplakia was found by Fang T.J. et al. (2016) and Li L.J. et al. (2021) [37, 127]. The authors consider that hyperaemia/redness of the mucosa predicts the malignant potential of vocal cord leukoplakia.

Based on the aforementioned data, we consider that biopsy, taken during flexible laryngoscopy using wide/jumbo forceps, is an appropriate approach in cases of leukoplakia (flat lesion), but in cases of pachydermia (elevated lesion) or verrucous neoplasia (lesion with an exophytic tumour-like appearance), total or subtotal excisional biopsy of the lesion using a diathermy loop is preferable, as this allows for a conclusive histological result [77].

We performed endoscopic ablation in 30 cases of verrucous neoplasia, of which 28 cases (93.3%) were diagnosed as verrucous carcinoma, whilst in 2 cases the malignant nature of the lesion was not confirmed histologically. In 26 out of 28 cases (92.9%) of verrucous carcinoma, histological confirmation of the diagnosis was only possible following partial excision of the lesion using the diathermy loop. We acknowledge the possibility of verrucous carcinoma even in cases where the malignant nature of the lesion was not confirmed, as ablation of the lesion in those cases was performed following biopsy of the lesion with forceps. Currently, we perform the removal of verrucous neoplasia only after a conclusive histological result following the acquisition of a sufficiently large tissue fragment using a diathermic loop, so as not to miss any carcinoma. Therefore, based on our experience, the endoscopic appearance of verrucous neoplasia raises a high suspicion of malignancy [78].

4.2. FELS of hyperplastic laryngeal lesions

Flexible endoscopic surgical procedures were performed on 46 patients with LLH (men – 43 (93.5%), women – 3 (6.5%)). The patients’ ages ranged from 20 to 77 y , with a mean of 53.4±12.0 and a median of 55.5 years (IQR=16.5). All procedures were performed by a single surgeon.

Hyperplastic laryngeal lesions were represented by the following types of lesions: chronic hyperplastic laryngitis with keratosis (n=7 (15.2%)), leukoplakia (n=23 (50.0%)), pachydermia (n=14 (30.4%)) and verrucous neoplasia (n=2 (4.3%)).

The dimensions of the lesions ranged from 0.3 cm to 2.5 cm (mean – 1.1±0.6 cm).

In the majority of cases (44/46 (95.7%)), the glottic portion of the larynx was affected; in 2 cases (4.3%), pachydermia of the interarytenoid space was detected (table A3.8).

Based on the histopathological appearance of the lesions, according to the WHO classification (2022) [200], high-grade dysplasia was detected in one case (2.2%), low-grade dysplasia was detected in 7 cases (15.2%), and the absence of dysplasia was noted in the remaining cases (n=38 (82.6%)). Ultimately, in total, we performed FELS on 30 patients with verrucous neoplasia of the larynx, of whom 28 (93.3%) were found to have verrucous carcinoma. These cases of carcinoma are not included in the HLL group and are not discussed in this chapter, which is devoted to premalignant lesions, but are discussed in another chapter, devoted to malignant lesions.

The following methods/techniques for the eradication of hyperplastic laryngeal lesions were used in various combinations: cold surgery using flexible forceps, excision with a diathermic loop, and Nd:YAG laser/980/1470 nm diode laser ablation (table A3.9).

In 42 cases (91.3%), the procedure was performed under local anaesthesia with spontaneous breathing, and in 4 cases (8.7%), we used general anaesthesia with SHFJV, the flexible endoscope being inserted via the suspended rigid jet laryngoscope. In 31 cases (67.4%), the procedure was performed on an outpatient basis.

The number of treatment sessions ranged from 1 to 9. In 45 out of 46 patients (97.8%), treatment was completed in a single session. In one case (massive obstructive verrucous neoplasm), eradication of the lesion required 9 treatment sessions (figure A2.47a,b). This case was resolved by Nd:YAG laser ablation under local anaesthesia whilst the patient was awake, at a time when the clinic did not have the necessary equipment for transoral laser surgery or a high-frequency jet ventilator, and the patient preferred flexible endoscopic laryngeal surgery (FELS), under local anaesthesia whilst awake, performed in repeated sessions, to open laryngeal surgery. Following the first session of photoablation of the obstructing lesion, local oedema of the treated tissues occurred, with the patient complaining of increasing inspiratory dyspnoea, which led to the performance of an emergency tracheostomy. Subsequent endoscopic treatment sessions were performed with the tracheostomy in place, and following complete eradication of the lesion, the patient was extubated and discharged home in a satisfactory condition. Currently, with the available equipment, in cases where the airways are compromised due to massive obstructive

lesions, we prefer flexible endoscopy combined with suspended rigid laryngoscopy, under general anaesthesia with SHFJV.

Following endoscopic treatment performed on patients with hyperplastic laryngeal lesions, the expected result - complete eradication of the visible lesion - was achieved in all treated cases (figures A2.20a–c, A2.21a–c, A2.22a–e, A2.47a,b, A2.48a,b). No complications were recorded following the procedures performed, with the exception of the one mentioned above.

Recurrent lesions were recorded in 3/46 cases (6.5%) in patients with glottic pachydermia at 3, 11 and 93 months, respectively, following the endoscopic procedure. In 2 of the 3 cases, treatment of the recurrent lesions was performed by repeated FELS, and in the third case the patient refrained from repeated intervention, as he was in the postoperative period following prostatectomy for prostate cancer.

Invasive carcinoma was diagnosed in 2/46 patients (4.3%) who continued to smoke after surgery: one patient with CHLK, after 22 months, and one patient with pachydermia, after 103 months from endoscopic intervention.

The functional effects of endoscopic treatment were assessed based on the patients' subjective assessment of their own voices. More than half of the patients who underwent surgery (54.3%) rated their post-operative voice as normal. The remaining patients presented with varying degrees of dysphonia following surgery (table A3.10).

Voice quality depended largely on the size and location of the lesion. Involvement of the anterior commissure (AC) and a diffuse bilateral process worsen the prognosis regarding voice quality. Severe dysphonia was observed postoperatively in 6 patients, of whom: in 2 cases, the patients had previously undergone cordectomy for carcinoma of the contralateral vocal cord; in 3 cases, diffuse involvement of both vocal cords was observed; and in one case, vocal cord pachydermia developed against a background of chronic hyperplastic laryngitis.

In the treatment of HLL, both oncological efficacy and the preservation of vocal function are important. There are always trade-offs, and priorities are set following the assessment of the lesion's malignant potential and the patient's preferences. In this regard, we agree with Gale N. et al. (2016), who argue that the oncological approach, recognising the potential for malignancy in HLL, must take precedence over voice quality [45].

The period of clinical observation without local recurrence following endoscopic intervention ranged from one month to 266 months (mean: 62.4±72.0, with a median of 24.0 months (IQR=99.5) (table A3.11).

As with BNELL, we support the position of Wellenstein D.J. et al. (2020) [197] and consider that the aim of endoscopic treatment should be the complete removal/eradication of the visible lesion.

The non-angiolytic laser (Nd:YAG (1064 nm) or diode (980/1470 nm)) was the primary instrument for treating hyperplastic laryngeal lesions, being used in 45 out of 46 cases (97.8%), biopsy forceps were used in 3 cases (6.5%) and the diathermy loop in 3 cases (6.5%) (table A3.9). In our experience, the use of the diathermy loop leads to a significant reduction in operating time, which is very important for increasing the completion rate in outpatient surgery. Currently, we use the diathermic loop as the first-line instrument in all verrucous neoplasms, so as not to miss verrucous carcinoma, which can easily be underdiagnosed when using traditional biopsy via forceps [72].

We consider the results obtained in this study to be encouraging and comparable to the capabilities of traditional transoral CO₂ laser microsurgery, and superior to the results obtained in OBLs of HLL using angiolytic lasers; we believe that OBLs is the optimal modality for the diagnosis and effective treatment of HLL.

Given that leukoplakia, even without dysplasia, can progress to carcinoma, close monitoring of patients with HLL is recommended, regardless of the initial histological response [113, 140]. We recommend follow-up examinations after surgery at least once every 3 months during the first 2 years, and subsequently at least once a year.

The limitations of this study include: (1) the retrospective nature of the study, (2) the insufficient number of observations to make categorical statements, (3) the lack of a control group, (3) significant variability in the observation period, (4) the lack of objective acoustic assessment and standardised subjective assessment (e.g., the VHI score) of the voice, which would merit evaluation in future prospective studies.

4.3. FELs of laryngeal papilloma/papillomatosis

Flexible laryngoscopic laryngeal surgery was performed to treat 51 patients with laryngeal papilloma/papillomatosis (LP) (men – 29 (56.9%), women – 22 (43.1%). The patients' ages ranged from 19 to 77 years, with a mean of 44.1±15.7 years and a median of 44.0 years (IQR=22.0). All procedures were performed by a single surgeon.

The size of the lesions ranged from 0.2 cm to 3.0 cm (mean – 1.6±0.8 cm).

In the majority of cases (46/51 (90.2%)), the glottic portion of the larynx was affected; in 4 cases (7.8%), isolated involvement of the vestibular/supraglottic portion was recorded, and in 2 cases (4.0%) of the – extension of the laryngeal lesion into the trachea (Table A3.12). The diagnosis of LP was confirmed histologically by biopsy performed under local/topical anaesthesia.

We applied the following methods/techniques for the eradication of papillomatous lesions, in various combinations (table A3.13): cold surgery using flexible forceps, excision with a diathermy loop, and Nd:YAG laser/980/1470 nm diode laser ablation.

In 40 cases (78.4%), the procedure was performed under local anaesthesia with 2% lidocaine and spontaneous breathing, and in 9 cases (17.6%), the procedure was performed under general anaesthesia, combining flexible laryngoscopy with suspended rigid laryngoscopy using SHFJV. In 2 patients (3.9%), both types of anaesthesia were used in different sessions.

In 24 cases (47.1%), the procedures were performed on an outpatient basis.

The number of sessions per course of treatment required for the ablation of papillomatous proliferations ranged from 1 to 7 (mean: 1.4 ± 1.4). In 43/51 patients (84.3%), ablation of the lesions was performed in a single session, and in 8 cases (15.7%), repeated treatment sessions were required (table A3.14). In 3 patients with extensive papillomatous lesions, 6–7 sessions of endoscopic treatment were performed to eradicate the lesion (figure A2.49a–e). These cases were resolved by Nd:YAG laser ablation under local anaesthesia whilst the patient was awake, at a time when the clinic did not have the necessary equipment for transoral laser surgery and a high-frequency jet ventilator, and the patients preferred FELS under local anaesthesia whilst awake, performed in repeated sessions, to open laryngeal surgery. Currently, with the available equipment, in cases where the airways are compromised due to massive obstructive lesions, we prefer flexible endoscopy, combined with suspended rigid laryngoscopy, under general anaesthesia with superimposed high-frequency jet ventilation.

Following endoscopic treatment in patients with LP, the expected outcome (complete eradication of the visible lesion) was achieved in all treated patients (figures A2.23a–c, A2.24a–c, A2.25a–d, A2.50a,b). In one case, a toxic reaction to lidocaine was observed, arising from an overdose of the local anaesthetic during the surgical procedure, which was successfully resolved. No other complications associated with the procedure were recorded.

Tumour recurrence was established in 18/51 cases (35.3%), necessitating repeat procedures at intervals ranging from 1 month to 188 months. The number of repeated courses of surgical treatment per patient ranged from 1 to 6 (average – 2.7) (table A3.15).

Malignancy (the development of invasive carcinoma) was observed in only one case (2%) during the follow-up period for patients with LP. We present this case below.

Patient S, a 35-year-old woman, presented to the clinic complaining of severe dysphonia that had persisted for 3 months. Fibrolaryngoscopy: In the anterior third of the left vocal cord, a flattened polypoid formation with a broad base, measuring 0.3×0.6 cm, was noted; the surface was slightly irregular and pink in colour. Conclusion: Polyp of the left vocal cord. Complete removal of the visible polypoid lesion was performed via cold surgery, using biopsy forceps.

Histological examination: Squamous cell papilloma with koilocytosis. The patient attended a follow-up appointment 188 months (15 years and 8 months) after the operation, complaining of moderate dysphonia for 3 months. Fibrolaryngoscopy: Both laryngeal halves are mobile during phonation. The vocal cords are slightly thickened, with their mucosa being slightly hypertrophied. In the anterior third of the left vocal cord, an exophytic mass is evident, with a broad base of attachment, measuring 0.3×0.5 cm; the surface is slightly irregular, whitish in colour, and soft in consistency. Conclusion: Polypoid lesion (possibly a papilloma) of the left vocal cord against a background of chronic hyperplastic laryngitis. Complete cold endoscopic excision of the laryngeal lesion was performed using biopsy forceps. Histological examination: Squamous cell papilloma with moderate dysplasia. The patient attended a follow-up appointment 24 months (2 years) after the last operation, complaining of pronounced dysphonia for 3 months. Fibrolaryngoscopy: The vocal cords are thickened, and their mucosa is slightly hypertrophied. A scar membrane (synechia) is evident in the region of the anterior commissure. In the anterior two-thirds of the left vocal cord, a flattened polypoid formation is evident, with an elongated appearance, elastic consistency, and a smooth surface. In the anterior third of the left vocal cord, on the superior surface, a raised lesion is evident, measuring up to 0.8 cm, with a tuberous surface and a whitish colour. Biopsy. Conclusion: Chronic hyperplastic laryngitis. Synechia in the region of the anterior commissure. Oedematous polyp of the left vocal cord. Carcinoma of the left vocal cord or, possibly, pachydermia (figure A2.51a). Histological examination: Keratinised squamous cell carcinoma (G2). Complete ablation of the visible tumour was performed using a 980/1470 nm diode laser, under local anaesthesia, with spontaneous breathing, on an outpatient basis (figure A2.51b).

The functional/vocal outcome of endoscopic treatment of LP was assessed based on the patient's subjective assessment of their voice. More than half of the operated patients (58.8%) rated their voice as normal after surgery. The remaining patients presented with varying degrees of postoperative dysphonia (table A3.16). The functional outcome was largely influenced by the location and extent of the lesion, as well as previous surgical interventions on the larynx. Involvement of the anterior commissure, extensive bilateral lesions, and scarring of laryngeal tissues following repeated surgical procedures worsen the vocal outcome. Both patients with severe dysphonia had a history of recurrent juvenile LP, with multiple laryngeal surgeries.

The period of clinical observation without local recurrence following endoscopic intervention ranged from 2 months to 268 months (mean – 72.0±67.1, with a median of 56 months (IQR=88.5)) (table A3.17). In the group of patients without established recurrence (n=33), the observation period ranged from 2 months to 203 months (mean – 74.6±64.8, with a median of 56 months (IQR=91.0)), and in the group of patients with recurrent disease (n=18),

following the last surgical procedure, this period ranged from 3 months to 268 months (mean – 67.2 ± 72.9 , with a median of 41 months (IQR=74.5)).

Although many experts in the field of LP treatment consider it prudent to avoid excessive radicalism during surgery, emphasising the protection of anatomical structures important for phonation and ensuring an airway calibre sufficient for breathing, the recurrent nature of the disease presenting a challenge for any study on the efficacy of LP treatment [31, 43, 102, 115], our aim was the complete eradication of all visible papillomatous lesions, taking into account the potential for LP to become malignant. In the surgical treatment of LP, complete eradication of the lesion is often associated with a more guarded prognosis regarding voice quality, particularly when the lesion affects the anterior commissure. Priorities were set based on the lesion's potential for malignancy and the patient's preferences. In our experience, patients opted for complete eradication of the visible lesion following surgery, preferring the removal of the papillomatous lesion - even with the prospect of a poorer vocal outcome - over preserving the residual lesion, with the prospect of its progression, in order to achieve a better vocal outcome.

The non-angiolytic laser (Nd:YAG (1064 nm) or diode (980/1470 nm)) was the primary instrument in the endoscopic treatment of LP, being used in 46/51 cases (90.2%), biopsy forceps were used in 7 cases (13.7%), and the diathermic loop in 17 cases (33.3%) (table A3.13).

In the English-language literature available to us, we found no publications regarding the use of the Nd:YAG laser or the 980/1470 nm diode laser via a flexible endoscope in the treatment of LP. Based on the available information, the material presented (51 patients with LP, for whom the non-angiolytic laser (Nd:YAG/980/1470 nm diode) was used separately or in combination with other endoscopic techniques) is the largest series reported in the literature to date [81]. The caution shown by laryngologists regarding the use of the Nd:YAG laser in the treatment of laryngeal lesions can be explained by the fact that the penetration capacity of this type of laser into biological tissues is greater than that of other types of lasers used, resulting in concerns regarding excessive thermal damage to adjacent tissues, scarring of the superficial lamina propria and the formation of synechiae in the anterior commissure region. We consider that collateral thermal damage caused by the Nd:YAG laser can be minimised by using the laser following cold surgery or diathermy loop excision, as a second-line tool, for the ablation of residual lesions only.

We prefer to use the diathermic loop as a first-line instrument in cases where there is a clearly evident exophytic component of the lesion, and the non-angiolytic laser is applied for the eradication/vaporisation of the residual lesion only. This technique was used for the first time in the endoscopic treatment of LP (Patent MD 1492 Z 2021) [68]. In our experience, the use of the diathermic loop leads to a significant reduction in operating time, which is very important for

increasing the rate of completed treatment in OBLs. Furthermore, laser ablation/vaporisation, preceded by resection with a diathermic loop, compared to the use of the laser as a single instrument, allows for a reduction in thermal damage to adjacent tissues, and can also be used in large and obstructing lesions, which present a major limitation for non-ablative techniques using angiolytic lasers, and enhances the safety of the procedure (figure A2.25a–d). We consider Nd:YAG (1064 nm)/diode (980/1470 nm) laser ablation, preceded by diathermic excision, to be safe and effective, particularly for large and obstructing papillomatous lesions.

We consider the results of applying FELS techniques/methods, as obtained in this study, to be encouraging and comparable to the capabilities of TLMS using a CO₂ laser and superior to the results obtained in OBLs of LP using angiolytic lasers; the proposed methods are applicable, including for the eradication of voluminous lesions, which present a significant limitation for non-ablative laser techniques in the treatment of LP.

Our data on complete resolution of the disease (absence of recurrence was recorded in 64.7% of our cases) are comparable to the data presented by Mao W. et al. (2023), who reported their experience of using the KTP laser in an outpatient setting for the treatment of LP, noting complete resolution of the disease in 66.7% of cases [128].

According to data published by Del Signore A.G. et al. (2016), 50% of patients with LP treated with angiolytic lasers (PDL and KTP) required repeat treatment sessions [30]. Our data show that only 15.7% of treated patients required repeat treatment sessions to eradicate the lesion. We therefore consider that the use of non-angiolytic lasers (Nd:YAG (1064 nm) and diode (980/1470 nm)) allows for a considerable reduction in the number of sessions required to eradicate the lesion. Another disadvantage of treatment with angiolytic lasers is the lack of a clear endpoint, resulting in suboptimal treatment that requires repeated unplanned surgical interventions in approximately 20% of cases [30]. The techniques we propose are free from this disadvantage, as lesion eradication is visually/endoscopically monitored during the procedure, and the endpoint (vaporisation/disappearance of the visible lesion) can be documented at the end of the endoscopic operation (figure A2.24b, A2.52b).

According to the results obtained, the techniques proposed for the treatment of LP fit perfectly within the OBLs concept, which is a solution for rapid diagnosis and treatment, with minimal risks to the patient. Taking into account the recurrent nature of the disease and the prospect of repeated/multiple surgical interventions, OBLs via FELS offers patients the opportunity to avoid multiple general anaesthetics with muscle relaxation in the operating theatre, which are associated with increased morbidity.

Among the limitations of this study, we note: (1) the retrospective nature of the study, (2) the insufficient number of observations for categorical statements, (3) the lack of a control

group, (4) significant variability in the observation period, (5) the lack of objective acoustic assessment and standardised subjective assessment (e.g., VHI score) of the voice, which would merit evaluation in future prospective studies.

Therefore, FELS using non-angiolytic lasers (Nd:YAG (1064 nm), diode (980/1470 nm)), a diathermic loop and flexible biopsy forceps, can be considered an alternative to transoral microsurgery in the treatment of precancerous laryngeal lesions in selected patients, opening up a new direction in OBLs for this patient group. The proposed techniques/methods allow for the overcoming of certain limitations of currently used surgical methods (transoral microsurgery and OBLs using angiolytic lasers) and demonstrate applicability in OBLs, particularly in patients with risks and contraindications for general anaesthesia and direct suspended laryngoscopy. The proposed method is attractive due to the reduced risks of the procedure for patients, particularly those with comorbidities, as well as cost savings and time efficiency, allowing patients to maintain a comfortable lifestyle. Given that both HLL and LP are lesions with a high potential for recurrence, FELS, being performed on an outpatient basis, offers this category of patients the possibility of avoiding repeated interventions under general anaesthesia in an inpatient setting, which are associated with increased morbidity. Flexible endoscopic surgery is worth considering, taking into account patients' preferences, as many of them opt to avoid general anaesthesia and prefer outpatient laryngeal surgery. Prospective studies, involving a larger number of patients and a longer follow-up period, are required to validate the proposed approach to the treatment of precancerous laryngeal lesions and to draw definitive conclusions.

5. FELS OF GLOTTIC CANCER

Flexible endoscopic surgery was performed on 140 patients with glottic cancer (men – 131 (93.6%), women – 9 (6.4%)). The patients' ages ranged from 18 to 83 years, with a mean of 58.7 ± 10.5 and a median of 59.0 years (IQR=13.3). The histological structure of the tumours was as follows: squamous cell carcinoma – 108 (77.1%), verrucous carcinoma – 24 (17.1%), verrucous carcinoma of the hybrid type – 4 (2.9%) and spindle cell carcinoma – 4 (2.9%). Depending on tumour extent, 41 patients (29.3%) were diagnosed with a cT1a-stage tumour, 36 patients (25.7%) with cT1b (vocal cord carcinoma involving the anterior commissure was staged as cT1b), 56 patients (40.0%) – cT2a (due to supraglottic and/or subglottic extension of the tumour, without impairment of vocal cord mobility), and in 7 patients (5.0%) – cT2b (due to supraglottic and/or subglottic extension of the tumour, with impairment of vocal cord mobility) [7, 201]. Given that the eradication of neoplastic lesions via photoablation precludes histological examination of the margins of the resected specimen, the assessment of tumour stage according to the „T” criterion was performed clinically, based on endoscopic and imaging findings. Therefore, when the „T” criterion is mentioned in this paper, the „cT” criterion is implied.

All procedures were performed by a single surgeon. No complications associated with FELS were recorded during or after the procedure. No patient reported swallowing difficulties in the postoperative period.

5.1. Survival analysis of patients with glottic cancer

We performed an analysis of overall survival (figure A2.53), cumulative mortality rate (figure A2.54), univariate analysis of survival according to the treatment method applied (figure A2.55) and tumour stage (figure A2.56) , as well as a multivariate survival analysis, with the included predictors being sex, age, treatment methods, endoscopic techniques, tumour stage and histological type of tumour (figure A2.57).

5.1.1 Kaplan–Meier curve for overall survival

The vertical axis (figure A2.53) shows the probability of survival, and the horizontal axis shows time (in months). The blue curve represents the Kaplan–Meier estimate, and the light blue band shows the 95% confidence interval. A steady decline in survival is observed over the follow-up period, with a rapid reduction in the first 200 months. After approximately 200–220 months, the curve stabilises around a survival rate of ~20%, suggesting that some patients have survived for a longer period. The shape of the curve indicates significant early and intermediate mortality, with a plateau after ~200 months, which may reflect the selection of a group of patients with a better prognosis.

5.1.2. Kaplan–Meier curve for the cumulative rate of events/deaths (cumulative incidence)

In this case (figure A2.54), the vertical axis represents the cumulative probability of experiencing the event (death) over time. The curve rises progressively throughout the follow-up period, reaching ~80% at 300 months. The confidence interval widens after 200 months, reflecting the decreasing number of patients still at risk. The interpretation of this curve complements that of the survival curve: if survival at 300 months is ~20%, then the probability of death by that point is ~80%.

The median survival time was 156 months. The 95% confidence interval for median survival ranges from 100 to 192 months. This means that half of the patients survived for 156 months or less, whilst the other half survived longer than this. The relatively wide CI suggests significant variability in prognosis, which is consistent with the diversity of clinical factors (age, tumour stage, histological type) identified also with the Cox model as determinants of survival.

5.1.3. Univariate survival analysis

Comparative analysis of patient survival in different treatment groups (Kaplan–Meier and log-rank test)

The Kaplan–Meier plot shows patient survival according to the treatment method used (figure A2.55): FELS (flexible endoscopic laryngeal surgery) and FELS+RT (endoscopic surgery + adjuvant radiotherapy). The curve for patients treated with FELS alone (orange) remains visibly above the curve for patients treated with FELS+RT (blue), indicating better survival in the FELS group. The difference becomes evident from the very first months and persists throughout the follow-up period. At 200 months, survival in the FELS group is higher (~40%) compared with the FELS+RT group (~25%). The log-rank test confirmed the difference between the two groups: $\chi^2 = 13.76$, $p = 0.0002$, $-\log_2(p) \approx 12.23$. In this dataset, patients treated exclusively with FELS had significantly better overall survival than those who received combined treatment (FELS+RT). This result may reflect the fact that patients in the FELS+RT group initially had more advanced tumours or more unfavourable clinical characteristics, which necessitated adjuvant RT. Therefore, the difference in survival could be explained by both the effect of the therapy and the initial selection of cases.

Kaplan–Meier analysis of survival by tumour stage

The graph shows the survival curves for patients with glottic tumours classified as stages T1a, T1b, T2a and T2b (figure A2.56).

Statistical results (log-rank test, pairwise comparisons)

- **Overall comparison (all stages):** $\chi^2 = 10.71$, $p = 0.013$ (the difference between stages is significant).
- **Pairwise comparisons:**

T1a vs T1b: $p = 0.45$ → no significant difference.

T1a vs T2a: $p = 0.20$ → no significant difference.

T1a vs T2b: $\chi^2 = 13.61$, $p < 0.001$ → significant difference, with reduced survival at T2b.

T1b vs T2a: $p = 0.37$ → no significant difference.

T1b vs T2b: $\chi^2 = 9.54$, $p = 0.002$ → significant difference, with a poor prognosis for T2b.

T2a vs T2b: $p = 0.054$ → no significant difference.

Interpretation of the Kaplan–Meier curves

T1a and T1b: the curves are similar, suggesting a similar prognosis; both show relatively good survival, with a gradual decline. T2a: survival is noticeably lower than in T1, but the difference did not reach statistical significance (probably due to the number of patients). T2b: the curve drops rapidly, indicating a dramatically worse prognosis compared to all other stages. Therefore, stage T2b is associated with the lowest survival and represents a major negative prognostic factor. T1a and T1b do not differ significantly from one another, suggesting a comparable prognosis in the early stages. The progressive difference in survival between T1/T2a and T2b validates the results obtained in the Cox model, where T2b emerged as an unfavourable prognostic factor (see section below).

5.1.4. Multivariate survival analysis

Multivariate survival analysis was performed using a Cox proportional hazards model (CoxPH), with time to event/death (months) and patient status (death) as dependent variables (figure A2.57). The analysed cohort included 140 patients, of whom 62 events (deaths) were observed during the follow-up period. The baseline function was estimated using the Breslow method.

The overall model proved to be statistically significant according to the chi-square test ($\chi^2 = 31.43$, $df = 10$, $p < 0.001$), confirming that the included variables contribute significantly to explaining the variation in survival. The goodness of fit (C-index) was 0.68, suggesting moderate predictive power of the model. The partial AIC value (494.49) indicates a reasonable fit of the model to the data.

Analysis of included predictors

The coefficient for sex was positive (coef = 0.57, HR = 1.76), indicating a trend towards increased risk of death in men compared with women. However, the confidence interval (95% CI: 0.50–6.21) is wide, and the p-value (0.38) shows that the difference is not statistically significant.

Age was a significant predictor (coef = 0.05, HR = 1.05, 95% CI: 1.02–1.08, $p < 0.005$). Thus, each additional year of age is associated with an approximately 5% increase in the risk of death. This result highlights the importance of age as a major prognostic factor in glottic cancer.

The use of different endoscopic techniques did not significantly influence survival (coef = -0.23, HR = 0.80, 95% CI: 0.36–1.76, $p = 0.58$). This suggests that the type of endoscopic technique used is not a determining factor for prognosis.

The treatment methods analysed (FELS vs FELS+RT) showed a non-significant reduction in risk (coef = -0.21, HR = 0.81, 95% CI: 0.36–1.85, $p = 0.62$). This result suggests that, within the study cohort, the choice of treatment method did not significantly influence overall survival.

Tumour stage:

T1b: coef = 0.32, HR = 1.38, 95% CI: 0.64–2.96, $p = 0.42$ – non-significant, but indicates a trend towards a poorer prognosis compared with T1a.

T2a: coefficient = 0.33, HR = 1.39, 95% CI: 0.67–2.87, $p = 0.38$ – also non-significant, but confirms the trend towards increased risk.

T2b: coefficient = 1.88, HR = 6.53, 95% CI: 1.50–28.55, $p = 0.01$ – statistically significant, indicating a six-fold increase in the risk of death compared with T1a. These results confirm the importance of T2b tumour stage as a negative prognostic factor.

Histological type:

Squamous cell carcinoma: coef = -1.55, HR = 0.21, 95% CI: 0.06–0.81, $p = 0.02$ – significant, with a clear protective effect. Patients with conventional squamous cell carcinoma have an approximately 5-fold lower risk of death compared with the reference group (hybrid variant verrucous carcinoma).

Spindle cell carcinoma: coef = -0.85, HR = 0.43, 95% CI: 0.08–2.22, $p = 0.31$ – not significant, but suggests a possible reduction in risk.

Verrucous carcinoma: coef = -1.26, HR = 0.28, 95% CI: 0.07–1.10, $p = 0.07$ – borderline significant, indicating a protective trend.

Overall interpretation:

The results highlight three main factors associated with survival in patients with glottic cancer: (1) advanced age consistently and significantly increases the risk of death; (2) T2b stage correlates with a significantly poorer prognosis, being a major negative factor; (3) the

histological variant of conventional squamous cell carcinoma represents a favourable factor, being associated with a significant reduction in the risk of death. Factors related to sex, treatment methods and endoscopic techniques did not demonstrate statistically significant effects on survival. Our results support the observations reported in other studies, which mention more modest oncological outcomes of treatment for T2b-stage glottic carcinoma, compared to those achieved in stage T2a, both with RT and TLMS [42, 90], a fact which has likely led to the subdivision of stage T2 into the subcategories T2a and T2b in some scientific publications [42, 90, 201].

5.2. Five-year oncological outcomes in the endoscopic treatment of glottic cancer

For the analysis of long-term oncological outcomes, the following patients were excluded from the study: those who were under observation for less than 5 years following the endoscopic procedure (n=20), patients who were lost to follow-up within 5 years of the endoscopic procedure (n=6) and patients who died from causes unrelated to the primary disease within 5 years of the endoscopic procedure (n=18).

A total of 96 patients met the selection criteria for this study: 88 men (91.7%) and 8 women (8.3%). The patients' ages ranged from 18 to 83 years (mean 57.1±10.5 years, with a median of 57.0 years (IQR=14.0)). The histological structure of the tumours was as follows: squamous cell carcinoma – 75 (78.1%), verrucous carcinoma – 15 (15.6%), hybrid verrucous carcinoma – 4 (4.2%) and spindle cell carcinoma – 2 (2.1%). The primary tumour was recorded in 87 (90.6%) of cases, and 9 patients (9.4%) presented with a recurrent (n=4) or persistent (n=5) tumour following RT. Depending on tumour extent, 27 patients (28.1%) were diagnosed with T1a-stage tumour, 26 patients (27.1%) with T1b, 40 patients (41.7%) with T2a, and 3 patients (3.1%) - T2b. Involvement of the anterior commissure (AC) was recorded in 66 cases (68.8%). The macroscopic appearance of the tumour lesions in the is shown in table A3.18. Tumours with exophytic and mixed growth patterns without ulceration predominated (76.0%).

In 71 cases (74.0%), only endoscopic treatment was administered, whilst in the remaining 25 cases (T1b (n=2), T2 (n=23)) (26.0%), postoperative RT was also administered. The reasons for offering adjuvant RT to some of the patients with T1b-T2 tumours were as follows: (1) a large infiltrative tumour extending to the anterior commissure (FELS was considered from the outset as the method for achieving cytoreduction, to enhance the efficacy of RT); (2) the surgeon's uncertainty regarding the oncological radicality of the ablation performed; (3) an unfavourable histopathological appearance in the tissue samples obtained by biopsy from the site of the eradicated tumour.

The following endoscopic techniques were used for tumour eradication: Nd:YAG laser (1064 nm)/diode laser (980/140 nm) ablation – in 64 (66.7%) cases and laser ablation preceded by tumour excision with a diathermic loop – in 32 (33.3%) cases. The number of treatment sessions ranged from 1 to 9 (mean – 1.6 ± 1.2 , with a median of 1.0 (IQR=1.0)). In 68 (70.8%) cases, treatment was completed in a single session.

Procedures under local/topical anaesthesia, with spontaneous breathing, were performed in 57 (59.4%) patients, whilst general anaesthesia with muscle relaxation and SHFJV was used in 39 (40.6%) cases.

Five-year overall survival and ultimate disease control, including salvage treatment, was achieved in 82/96 cases (85.4%).

Disease-free survival (DFS) was achieved in 75 cases (78.1%).

Local control was recorded in 76 cases (79.2%).

Recurrence/persistence of the primary tumour was recorded in 17 cases (17.7%). In 15 out of 17 cases (88.2%), disease recurrence was diagnosed within the first 2 years following surgery, and in 2 cases – more than 4 years later. Successful salvage treatment for tumour recurrence was performed in 7/17 patients (41.2%): 3 patients underwent repeat flexible endoscopic laser surgery (FELS), salvage RT was administered to 1 patient, open partial laryngectomy was performed in 1 patient, and 2 patients underwent total laryngectomy.

Death due to the primary disease was recorded in 14 out of 96 cases (14.6%). Progression of the primary tumour was observed in 10 of these cases, regional lymph node metastasis without recurrence of the primary tumour in 3 cases, and cerebral metastasis was found in one case. Within one year of the endoscopic surgery, 3 patients (21.4%) died; after the first year – 3 (21.4%); after the second year – 3 (21.4%); after the third year – 1 (7.2%); and after the fourth year – 4 (28.6%).

Cure with preservation of the larynx was achieved in 80/96 (83.3%) cases.

Ultimate disease control by FELS alone (without radiotherapy and/or salvage OPL) was achieved in 78/96 (81.3%) of patients.

We analysed the 5-year outcomes of glottic cancer treatment according to tumour stage (table A3.19). The data obtained show a decline in the oncological outcomes of treatment in relation to increasing tumour stage across all analysed criteria, with statistical significance observed for 8 out of 9 criteria (UDC, OS, DSS, DFS, LC, UDC FELS, CLP, DD). The best outcomes were achieved in the group of patients treated at stage T1a, with all patients alive, cured of the disease and with their larynx preserved, whilst the most unfavourable outcomes were recorded in the group of patients at stage T2b (all 3 patients died as a result of progression of the primary disease).

Analysis of the long-term (5-year) outcomes of glottic cancer treatment according to anterior commissure (AC) involvement shows that patients with tumour extension to the AC had less favourable oncological outcomes compared with those in whom the AC was not affected. AC involvement worsens treatment outcomes according to all oncological criteria analysed, with statistical significance observed according to the CLP criterion ($p=0.039$) (table A3.20).

General anaesthesia with muscle relaxation and SHFJV showed no advantage over local/topical anaesthesia with spontaneous breathing in terms of long-term (5-year) oncological outcomes, with statistical significance observed for 5 out of 9 criteria analysed (UDC, OS, DSS, CLP, DD) (table A3.21).

Our expectations regarding the combination of FELS with postoperative RT in T1b-T2 glottic tumours were associated with improved oncological outcomes, but the results obtained do not support this hypothesis. The results in the group of patients who received the combined treatment proved to be even inferior to those in the group of patients treated with FELS alone according to all the oncological criteria analysed, reaching statistical significance for 8 out of 9 criteria (UDC, OS, DSS, DFS, LC, UDC FELS, CLP, DD) (table A3.22, A3.23).

The functional outcome (voice quality) was largely dependent on the extent/stage of the tumour and, in particular, on tumour involvement of the AC. The results obtained demonstrate, with statistical significance ($p<0.001$), that the functional/vocal outcome is impaired in relation to increasing tumour stage and AC involvement (table A3.24). In the majority of patients with T1a lesions (70.4%), satisfactory voice quality or minor dysphonia was recorded. Over half of patients with T2-stage disease (51.6%) presented with severe dysphonia after treatment, and moderate or severe dysphonia was recorded in 77.3% of patients with T1-stage disease with AC involvement. It is worth noting that none of the patients observed with a preserved larynx expressed any regrets regarding their choice of treatment method, regardless of voice quality.

Based on currently published data, this study presents the largest series of patients treated by FELS and followed up for 5 years [63].

We note that the 5-year oncological outcomes of FELS for glottic cancer, presented in this study, are comparable to the published long-term results obtained with TLMS and RT.

According to our data, the UDC, including salvage therapy, for T1 and T2 glottic cancer was 94.3% (T1a – 100%, T1b – 88.5%) and 74.4% (T2a – 80%, T2b – 0%), respectively. The UDC rate, including salvage therapy, reported in the literature following TLMS was: for T1 disease: 97% [35], 96% [208]; for T2 disease: 80% [208]. The UDC rate, including salvage therapy, reported in the literature following RT for T1 disease was: 98% [144], 90.3% [40]; for T1a disease: 90.3% [134].

According to our data, the LC/DFS for T1 and T2 disease was, respectively: 86.8% (T1a – 92.6%, T1b – 80.8%) and 69.8%/67.4% (T2a – 72.5%, T2b – 33.3%/0%). According to the literature, LC/DFS following TLMS was: for T1 disease: 85% [145], 86.3% [35], 85–87% [174], 75% [36]; for T1a disease: 76.1% [21], 92.3% [124], 93.1% [33], 69% [36]; for T1b disease: 74.1% [124], 75% [4], 77% [49], 55.6% [33]; for T2 disease: 72.7% [124], 66–82% [174], 59% [147], 77.3% [195], 75.4% [20]. Following primary RT, LC/DFS was, according to the literature: for T1 disease: 85–88% [136], 93% [144], 88% [104], 82.1% [40], 73.6%–94% [138], 79% [134], 87% [36]; for T1a disease: 94% [110], 86.5% [138], 77% [134], 78% [36]; for T1b disease: 87% [49], 83% [110], 83.6% [138], 81% [134]; for T2 disease: 70–73% [136], 73% [144], 67% [104]; 18% [35], 77% [29], 75.8% [195], 75.6% [20], 71% [36].

Ultimate disease control achieved solely through endoscopic surgery, according to our data, was as follows for T1 and T2 disease, respectively: 90.6% (T1a – 96.3%, T1b – 84.6%) and 69.8% (T2a – 75.0%, T2b – 0%). According to the literature, ultimate disease control (UDC) achieved solely by TLMS was: for T1 disease: 87% [146], 90% [145], 93–95% [174]; for T1a disease: 94% [48], 98% [124], 98% [24]; for T1b disease: 91% [48], 83.3% [124], 90% [24]; for T2 disease: 81.8% [124], 79–86% [174], 76% [147].

According to our data, cure with larynx preservation was: for T1 and T2 disease, respectively, 92.5% (T1a – 100%, T1b – 84.6%) and 72.1% (T2a – 77.5%, T2b – 0%). According to the literature, the larynx preservation rate following TLMS was: for T1 disease: 91.7% [35], 99% [208], 94–98% [174]; for T1a disease: 97.3% [21], 95% [168], 69–100% [36]; for T2 disease: 80% [208], 82–95% [174], 88.8% [92], 84% [147]. The larynx preservation rate following primary RT was, according to the literature: for T1 disease: 82% [134]; for T1a disease: 77% [168], 77–93% [36]; for T2 disease: 60.4% [44].

Death from the primary disease, according to our data, was: for T1 and T2 disease, respectively, 5.7% (T1a – 0%, T1b – 11.5%) and 25.6% (T2a – 20%, T2b – 100%). The mortality rate from the primary disease following TLMS, as reported in the literature, was: for T1 disease: 1.5% [202]. Mortality from the primary disease following primary RT, according to the literature, for T1-T2 disease was 11.2% [134].

The local recurrence rate, according to our data, for T1 and T2 disease was: 13.2% (T1a – 7.4%, T1b – 19.2%) and 23.3% (T2a – 20.0%, T2b – 66.7%). According to the literature, the local recurrence rate following TLMS was: for T1 disease: 11.2% [35], 12.3% [187], 12.9% [18], 14% [202], 18% [146]; for T2 disease: 26% [146]. Following primary RT, the local recurrence rate was, according to the literature: for T1 disease: 16% [18]; for T1a disease: 14% [169]; for T1b disease: 16% [169], for T2 disease: 36% [169].

According to our data, AC involvement worsens the outcomes of laryngeal cancer treatment, although we were unable to establish the statistical significance of the results obtained, except for one criterion (CLP), due to the insufficient number of observations (table A3.20). The treatment of glottic carcinoma involving the AC is controversial [24, 174]. At the point where the vocal cords attach to the thyroid cartilage via the Broyles ligament, the perichondrium is absent; consequently, some authors consider this site to be a vulnerable point that facilitates tumour invasion of the thyroid cartilage, transforming a T1 tumour into a T4 tumour [4, 174]. Lesions affecting the AC are often understaged, with invasion of the thyroid cartilage being overlooked, leading to T3-T4 tumours being treated as T1-T2 tumours, with consequently poor outcomes [149]. In some publications, tumour extension to the AC is considered a contraindication for endoscopic management [149, 187]. On the other hand, other specialists consider the Broyles ligament to be a protective factor for the thyroid cartilage and emphasise the negative impact of AC involvement only for T2 tumours, which cross the AC vertically [145, 174, 209]. The higher recurrence rate of infiltrative and exulcerated tumours is associated with deep superior and/or inferior extension of the tumour along the inner perichondrium of the thyroid cartilage [89]. Shvero J. et al. (2003) argue that, in cases of AC involvement in the tumour, laser resection must include the AC up to the thyroid cartilage, at least 0.5 cm of the subglottic area, and the anterior third of the contralateral vocal cord [172]. Stephenson K.A. and Fagan J.J. (2017) recommend TLMS with adjuvant RT as the primary treatment for glottic cancer involving the AC in patients with unfavourable morphopathological findings (positive or uncertain margins) [177]. Regardless of the therapeutic method applied (RT, partial laryngectomy, TLMS), tumour involvement of the AC (particularly for infiltrative and ulcerated tumours) is considered an unfavourable prognostic factor [4, 10, 19, 89, 156]. Alkan U. et al. (2017) reported a 75% local control rate at 5 years following TLMS for glottic cancer with AC involvement [4]. Wang Q. et al. (2025) reported a 61% local control rate at 5 years following TLMS for T1 glottic cancer with severe AC involvement [194]. Bron L.P. et al. (2001) reported a 66% local control rate at 5 years following RT for glottic cancer with AC involvement [19]. Vasudevan S.S. et al. (2025) reported a 77.2% local control rate following primary RT for T1-T2 glottic cancer with AC involvement [192]. Pradhan S.A. et al. (2003) reported a recurrence rate of 35.7% after TLMS for glottic cancer with AC involvement [149], Bassani S. et al. (2025) reported a recurrence rate of 55.5% after TLMS for early-stage glottic cancer with AC involvement [12], and Balica N.C. et al. (2016) noted that, regardless of the therapeutic method applied (RT, open partial laryngectomy, TLMS), in glottic cancer with AC involvement the recurrence rate is up to 70% [10]. Thus, our data (table A3.20) are consistent with and comparable to the long-term results observed following the use of TLMS and RT in the

treatment of glottic cancer with AC involvement. We consider that the oncological outcome is more important than the vocal outcome in patients with glottic cancer; therefore, sparing the AC during surgery to achieve better voice quality is not relevant for this category of patients due to the high risk of persistent tumour.

Anterior commissure involvement was also one of the main reasons for offering adjuvant radiotherapy to some patients with T1b-T2 disease; however, our data do not support the assumption that postoperative RT would improve the oncological outcomes of FELS. Surprisingly, the results obtained in the group of patients undergoing combined treatment (FELS and postoperative RT) were inferior to those in the group of patients undergoing endoscopic laser surgery alone, according to all the oncological criteria analysed (tables A3.22, A3.23). Our data support the findings published by Djuckic V. et al. (2019), who reported lower overall survival and disease-specific survival rates in patients who underwent postoperative RT compared with those who underwent endoscopic surgery alone [33].

Regarding functional/vocal outcomes after treatment, both RT and TLMS can result in an abnormal voice. Impaired voice quality following RT is caused by oedema, stiffness, scarring and atrophy. Voice quality following TLMS may be reduced due to scarring of the operated vocal cord or glottic incompetence, related to the depth of excision [145]. The advantage of one method over the other remains debatable. In a systematic review and meta-analysis, Greulich M.T. et al. (2015) found no significant clinical difference in vocal outcomes between RT and TLMS [51]. Brandenburg J.H. (2001) notes that the size and location of the tumour may have a greater impact on voice quality than the selected treatment modality (for example, AC involvement will result in poor voice quality, regardless of the treatment modality applied) [18]. Functional impairment following treatment for early glottic cancer is often considered acceptable [178]. Our data confirm that tumour extent has a statistically significant impact on voice quality (table A3.24). A satisfactory voice/minor dysphonia was recorded in 70.4% of patients with T1a disease, whilst more than half of patients with T2 disease presented with severe postoperative dysphonia.

The disadvantage of tumour ablation compared to tumour resection lies in the inability to perform a histological examination of the margins of the resected specimen. The clinical significance of positive resection margins remains debatable. It is generally accepted that some patients with positive margins following TLMS for glottic carcinoma will not develop tumour recurrence, and the relationship between the status of resection margins and tumour recurrence is unclear [24, 174]. The evaluation of histological specimens following laser excision is problematic due to charring and shrinkage of the specimens [13, 24]. There is no consensus among specialists regarding positive resection margins. Some authors consider that, in the case

of positive margins, additional treatment is mandatory [8]. Others propose a „wait and see” strategy [91, 173, 174]. Sigston E. et al. (2006) found that 84% of their patients with positive resection margins would have undergone unnecessary additional treatment had the „wait and see” strategy not been followed [173]. Aluffi Valetti P. et al. (2018) report that in 83% of patients with positive resection margins who underwent re-excision, no residual carcinoma was detected [5]. Bertino G. et al. (2015) consider that, if the surgical margins are tumour-free during the surgical procedure, secondary treatment can be avoided, even if the histological specimens are positive [13]. Lee H.S. et al. (2013) report that oncological outcomes in cases with positive margins do not differ significantly from those recorded in cases with negative margins and suggest that the identification of the surgical margin by an experienced surgeon may be reliable and considered more clinically predictive than histological assessment [124]. We advocate and practise the „wait and see” strategy [173, 174], taking into account the accessibility of the glottic region for visual examination, and do not routinely take a biopsy from the site of the eradicated tumour unless a persistent/recurrent lesion is suspected during the follow-up flexible laryngoscopy. The importance of patient cooperation and follow-up examinations via flexible laryngoscopy, scheduled at close intervals, cannot be overestimated for the early detection of a possible tumour recurrence. Given the increased risk of local tumour recurrence in the first 2 years after surgery (according to our data – in 88.2% of cases), our recommendations for postoperative follow-up examinations by flexible laryngoscopy are as follows: once a month during the first year after surgery, once every 2 months during the second year, once every 3 months during the third year, once every 6 months during the fourth and fifth years, and once a year after 5 years. In addition, for patients with T2 disease, we recommend performing an ultrasound scan of the cervical region every 3 months during the first 2 years after surgery.

The limitations of the present study are as follows: the retrospective nature of the study, the lack of a control group to compare the results obtained (TLMS and/or RT), and the lack of an objective assessment of the voice post-operatively, which could have been useful for the study, although this was not the objective of the present study.

Therefore, FELS for early glottic cancer demonstrates oncological outcomes comparable to RT and TLMS; from an oncological perspective, it can be considered an effective method for treating T1-T2a glottic cancer and an alternative to traditional approaches, primarily for patients with risks/contraindications for RT, GA with muscle relaxation, and transoral microsurgery, as well as for patients who prefer outpatient laryngeal surgery.

5.3. Characteristics of FELS for verrucous carcinoma of the larynx (VCL)

The aim of the study was to evaluate the efficacy of FELS in the diagnosis and treatment of verrucous carcinoma of the larynx (VCL) [54, 72].

The study group consisted of 28 patients with glottic verrucous carcinoma, treated by a single surgeon using flexible endoscopic laser surgery (FELS) between 1993 and 2024. Informed consent was obtained from the treated patients. All patients in the study cohort were men aged between 38 and 80 years (mean age – 58 ± 9.4 years). In all cases, the tumour affected the glottic portion of the larynx. According to the extent of tumour spread, patients were classified as follows: T1a – 8 (28.6%), T1b – 7 (25.0%), T2 – 13 (46.4%). Traditional biopsy using forceps, inserted through the working channel of the flexible laryngoscope, was inconclusive in 26 out of 28 cases (92.9%). The histological findings received, in most cases, were as follows: „leukoplakia”, „pachydermia”, „hyperkeratosis”, „papilloma”. To obtain adequate specimens for histological confirmation of the tumour, tumour excision with a diathermic loop was performed via a flexible endoscope under local anaesthesia with 2% lidocaine, with spontaneous breathing [72, 77]. Following histological confirmation of the tumour, laser ablation of the tumour was performed via a flexible endoscopic approach, using an Nd:YAG laser (1064 nm) or a diode laser (980/1470 nm) and a flexible therapeutic bronchoscope. The number of sessions ranged from 1 to 9 (mean – 2.0 ± 1.8) (table A3.25). In 17 cases (60.7%), tumour eradication was achieved in a single session. In 18 cases, the procedure was performed using flexible endoscopy, under local anaesthesia with mild/moderate intravenous sedation and spontaneous breathing. In 10 cases, suspended laryngoscopy under general anaesthesia with SHFJV was performed, combined with flexible endoscopy, the reasons being the patient’s preference or the surgeon’s preference, taking into account, in particular, the size of the tumour and airway compromise. In 1 patient (T2, hybrid form of VCL), postoperative RT was administered.

Ultimate disease control was achieved in 24 cases (85.7%). In 22 cases (78.6%), no recurrence was detected (table A3.26). The recurrence-free observation period in this group ranged from 12 to 247 months (mean – 85.4 months) (table A3.27). Residual or recurrent tumours were detected in 6 cases (21.4%), of which in 2 cases, ultimate disease control with organ preservation was achieved through repeated FELS (one patient) and open surgery (one patient). In 4 cases (14.3%), treatment failed, and the patients died as a result of tumour progression (in all cases, the hybrid form of VCL was observed).

Verrucous carcinoma of the larynx (VCL) is a rare form of laryngeal cancer, accounting for 1–4% of malignant laryngeal tumours, and is often difficult to diagnose [6]. Establishing a diagnosis of VCL poses a major challenge for both the clinician and the pathologist, which is why we pay particular attention to this tumour. VCL is characterised by a discrepancy between

the macroscopic and microscopic appearance of the tumour, whereby the tumour has a macroscopically „malignant” appearance but a microscopically „benign” appearance. Consequently, the laryngologist is usually impressed by the macroscopic appearance, whilst the pathologist is less impressed by the microscopic appearance [139]. If the clinician does not suspect the presence of VCL and takes a conventional biopsy of the tumour, he will almost always receive a „benign” morphological result, such as: „epithelial hyperplasia with keratosis, parakeratosis and acanthosis” or „papilloma”. The pathologist, not having been guided or made aware by the clinician, will not issue a conclusive VCL diagnosis based on a routine biopsy. Consequently, VCL is frequently underdiagnosed, resulting in late diagnosis at an advanced stage, inappropriate treatment and an unfavourable prognosis for the patient [122]. Orvidas L.J. et al. (1998) report a high rate (52%) of initial misdiagnosis, with the lesion being classified as benign, and a higher incidence of total laryngectomies in the group of patients with an initial misdiagnosis [139]. In some publications from previous years, devoted to laryngeal precancer, the authors mention „white papilloma”, classifying it as a precancer with a malignancy rate of up to 50% [210]. In more recent publications, the possibility of laryngeal papilloma becoming malignant is acknowledged, but with a much lower rate: 1–7% [43, 102, 157]. This huge discrepancy in the rate of malignant transformation of laryngeal papilloma across different bibliographic sources, in our opinion, is explained by the fact that behind the diagnosis of „papilloma” or „hyperkeratosis” there is, in reality, often undiagnosed laryngeal verrucous carcinoma.

The macroscopic appearance of verrucous carcinoma is, in practice, unmistakable or pathognomonic [38]. The lesion presents as an exophytic growth, with a broad base of attachment, well-defined margins, a hard consistency, a tuberous surface, and a greyish-white colour (cauliflower-like appearance), often with bizarre frond-like or villous projections, giving a „hairy” appearance (figure A2.58).

The microscopic appearance of the tumour is characterised by the following features (figure A2.59): a massive layer of keratin on the surface of the lesion (hyperkeratosis); a papillary surface with deep fissures containing masses of decomposing keratin; the presence of cells with nuclei in the keratin layer (parakeratosis); villiform projections without fibro-vascular axes, consisting of well-differentiated squamous epithelium; absent or rare mitoses in the basal and parabasal layers; minimal or absent cellular atypia; wide epithelial invaginations with blunt tips („elephant’s feet”), which extend into the underlying stromal connective tissue, with a compressive, locally destructive edge appearance at the interface with the underlying connective tissue; the basement membrane usually remains intact; tumour growth through compression of adjacent structures; marked lympho-plasmacytic inflammatory reaction in the connective tissue

stroma; the presence of epithelial pearls, small cysts, microabscesses and foreign body granulomas adjacent to the epithelial pearls and keratin masses; metastases to regional lymph nodes are absent or extremely rare [38].

A definitive histological diagnosis requires obtaining sufficiently large tissue fragments, including the epithelial-stromal interface, which would allow examination of the entire epithelial thickness and the underlying stromal tissue; this is difficult due to the massive layer of keratin on the tumour surface and its hard consistency, and requires a greater effort on the part of the clinician, which is not usually necessary in the case of biopsy of squamous papilloma or typical squamous cell carcinoma (SCC). Damm M. et al. (1997) report that biopsy specimens taken during transoral microlaryngoscopy were insufficient for a conclusive histopathological diagnosis of VCL in 40% of cases, arguing for the need for multiple biopsies [28]. We used flexible transnasal endoscopy under local anaesthesia, with tumour biopsy by excision using a diathermic snare (figure A2.28b, A2.29). This method allows for the collection of tumour fragments large enough for a conclusive morphological diagnosis (figure A2.30) and enables the biopsy to be performed on an outpatient basis, avoiding general anaesthesia [66, 72].

It should be noted that in approximately 20% of cases, the hybrid form of VCL is observed, where elements of VCL and classic SCC are detected in a single lesion [137]. The biological behaviour of the hybrid form of VCL is similar to that of classic SCC. Multiple tissue specimens may be required to rule out the presence of a conventional SCC component in the lesion. Half of patients with an initial diagnosis of a hybrid tumour are subsequently diagnosed with a recurrent tumour [139]. The differential diagnosis of VCL most often needs to be made with squamous papilloma (SP) and papillary squamous cell carcinoma (PSCC). Even an experienced pathologist may misdiagnose VCL as a papilloma, particularly if the biopsy specimen is small. Papilloma and papillomatosis are purely exophytic lesions, with acanthosis and, only occasionally, with keratosis and parakeratosis. For VCL, massive superficial keratosis is a key criterion, being associated with villiform projections and a „hairy” appearance. Cellular morphometry may be helpful. Cooper J.R. et al. (1992) found, through morphometric analysis of the dimensions of the intermediate layer cells, that there is a significant difference between VCL and SP. The authors’ conclusion is that a mean cell area greater than 300 μm^2 supports the diagnosis of VCL, whilst a mean area less than 250 μm^2 supports the diagnosis of papilloma [27]. Papillary squamous cell carcinoma is the term used for invasive squamous cell carcinoma with a papillary exophytic component. Microscopically, the tumour has all the characteristics of classic SCC (cellular atypia, invasion of the basement membrane, etc.). A tumour showing atypia on biopsy is likely not VCL, but well-differentiated papillary squamous cell carcinoma [38]. The correct diagnosis is imperative for determining the most appropriate treatment. Both

underdiagnosis (e.g., papilloma) and overdiagnosis (e.g., papillary squamous cell carcinoma) can have serious consequences for the patient. In laryngeal papillomatosis, during surgery, the emphasis is on ensuring adequate phonation and respiration. It is recommended to avoid excessive radicalism and to preserve anatomical structures important for phonation and respiration, in particular the anterior and posterior commissures, in order to reduce the risk of postoperative complications, such as synechiae and cicatricial glottic stenoses [31, 43, 102]. In the case of VCL, the approach is entirely different: complete tumour ablation is essential for the patient's cure, with oncological radicalism being the priority.

Verrucous carcinoma, having the same dimensions and extent as PSCC, may be treated with a more conservative approach. For example, in the case of VCL involving the vocal cord, the anterior commissure, with extension into the subglottic and supraglottic regions and reduced laryngeal mobility (figure A2.60a), we proposed and successfully performed endoscopic laser ablation of the tumour (figure A2.60b). However, had we obtained a PSCC result following biopsy in this case, the patient would likely have required a total laryngectomy. Cervical lymph node dissection is not indicated in cases of VCL, even in advanced cases, whereas in cases of PSCC with T3 extension, prophylactic cervical dissection is performed, given the possibility of cervical metastasis [38].

The diagnosis of VCL is always clinical-morphological; the macroscopic appearance must be correlated with the microscopic findings, which requires a high level of expertise from both the laryngologist and the pathologist, as well as good collaboration between them, in order to arrive at the correct diagnosis [38, 139].

Due to the rarity of VCL, the existing literature consists mainly of case reports and small case series; consequently, there is currently no definitive treatment strategy. From the time of the tumour's first description to the present day, strategies for managing VCL remain the subject of ongoing debate. Surgical resection is currently the main method of treating VCL, ensuring local control in 80–83.6% of cases [6, 34, 96, 122]. The use of RT in treating VCL is controversial. Many clinicians do not recommend RT as a primary treatment, as several studies have demonstrated that RT can cause anaplastic transformation of VCL, increasing the rate of recurrence and regional metastases following irradiation [96, 112, 130, 131, 175]. This hypothesis is debatable, as there are publications that challenge it [99, 179], but the main treatment method for resectable tumours at present is surgery, with RT being reserved for lesions that cannot be resected whilst preserving laryngeal function, recurrent tumours, persistent tumours, and hybrid tumours [96, 131, 137].

There are publications on the use of CO₂ laser in endoscopic surgery of the laryngeal vestibule with encouraging results. Damm M. et al. (1997), presenting results of treating 21

patients, recommend transoral endoscopic surgery with CO₂ laser as the method of choice for T1-T2 VCL [28]. Hod R. et al. (2010) report the results of CO₂ laser cordectomies performed on 18 patients with T1 VCL. The authors mention the advantages of CO₂ laser resection: precise application; minimal surgical trauma; resection with almost no bleeding; rapid wound healing; and reduced morbidity. Among the disadvantages of the method, the authors mention the problematic manoeuvrability of the endoscope in patients with a short neck and/or cervical pathology, associated with the risk that the surgeon will be unable to visualise the AC and, consequently, the surgical intervention will not be as radical as it should be. The authors argue that CO₂ laser cordectomy is a feasible procedure for patients with VCL, provided they have a normal neck, no subglottic extension of the tumour, no stridor, and no extensive lesions. In the event of tumour recurrence, repeated laser cordectomies are considered appropriate. For patients with a short neck or AC involvement, the authors propose laryngofissure, followed by laser cordectomy [96].

In the available English-language literature, we found no references to the use of FELS for VCL. Based on our experience, FELS for VCL demonstrates similar results compared to traditional TLMS using a CO₂ laser, and allows the difficulties encountered in patients with cervical problems or AC involvement to be overcome, avoiding laryngofissure and tracheostomy. The less aggressive biological behaviour of VCL, compared to typical SCC, often allows for a conservative ablation of the tumour via FELS, even in large tumours that obstruct the laryngeal lumen (figure A2.60a,b).

Therefore, close collaboration between the clinician and the pathologist is vital for the correct diagnosis of VCL. Obtaining a large tissue specimen during a biopsy is critical for a conclusive histological diagnosis. Excision with a diathermic loop via a flexible endoscope allows for an adequate biopsy to be performed under local anaesthesia on an outpatient basis. Flexible laser endoscopic surgery can be considered a valid therapeutic alternative for patients with VCL, provided they are closely monitored endoscopically. Among the advantages of the method are: the possibility of performing the procedure under local anaesthesia, which avoids general anaesthesia and the risks associated with it; applicability to patients with contraindications for general anaesthesia and to patients with anatomical features that make transoral surgery impossible (short mandible, insufficient neck extension, ankylosis of the temporomandibular joint, inadequate exposure of the larynx, etc.), making it possible to avoid laryngotomy and tracheostomy. In the hybrid form of VCL T2, achieving local control is more problematic than in typical VCL. Further studies are needed to confirm whether postoperative RT can promote treatment success in such cases.

5.4. Flexible endoscopic surgery for recurrent/residual glottic cancer following radiotherapy

The aim of the study was to evaluate the long-term (5-year) efficacy of FELS in the treatment of recurrent and residual glottic cancer following RT [60, 83]. The present study is retrospective. Informed consent was obtained from all treated patients. The following selection criteria were used for the study: (1) consecutive patients with recurrent and residual glottic carcinoma, cT1-T2N0M0, (2) a 5-year follow-up period after treatment.

Nine patients with recurrent (n=4) and residual (n=5) glottic cancer following RT, at cT1-T2 stage, were selected for the study: 8 men and 1 woman, aged 47–66 years (mean 55.4±7.8 years). The histological structure of the tumours consisted of keratinised squamous cell carcinoma (n=7) and non-keratinised squamous cell carcinoma (n=2). Depending on tumour extent, 2 patients were diagnosed with a T1a tumour, 1 patient with a T1b tumour, and 6 patients with a T2 tumour (due to supraglottic and/or subglottic extension of the tumour, without affecting vocal cord mobility). Anterior commissure involvement was recorded in 6 cases (66.7%).

In 7 cases, only endoscopic treatment was administered, and in 2 cases of residual T2 carcinoma, postoperative RT was also administered at a dose of 20–22 Gy. The rationale for providing adjuvant RT for the 2 cases of residual tumours was to complete the preoperative RT dose (40 and 46 Gy, respectively) and to consolidate the therapeutic effect of FELS. In 8 cases, treatment was performed in a single session, and in one case – in 2 sessions. Procedures under local/topical anaesthesia, with spontaneous breathing, were performed in 5 patients (55.6%), and general anaesthesia with muscle relaxation and SHFJV was used in the other 4 cases.

No complications were recorded during or after the procedure. Five-year overall survival and ultimate disease control, including salvage treatment, were achieved in 6/9 cases (66.7%). Recurrence-free survival (LC/DFS) was achieved in 5 cases (55.6%). Local recurrence of the primary tumour was recorded in 3 cases (33.3%). Successful salvage treatment (total laryngectomy) for tumour recurrence was performed in 1 patient. Death, caused by progression of the primary disease, was recorded in 2 cases (22.2%), 48 and 53 months, respectively, after the endoscopic procedure. In one case, at 7 months after FELS, the patient died from a brain tumour, which was considered to be metastatic, although there is no firm certainty of an association between the brain tumour and the laryngeal tumour. Cure with preservation of the larynx was achieved in 5 (55.6%) cases. Ultimate disease control, achieved solely through FELS, was registered in 5 (55.6%) patients. All three patients with stage T1 remained alive, cured of the disease, and with their larynx preserved, thanks to FELS (table A3.28).

Radiotherapy is still the preferred treatment for early-stage glottic cancer in many institutions, with a cure rate of 80–90% for Tis–T1 lesions [156]. The tumour recurrence rate following RT is 5–20% for stage T1 and 25–50% for stage T2 [105, 148]. A major disadvantage of this type of treatment is the inability to reuse RT in the event of tumour recurrence [155]. Consequently, the management of RT failures is always surgical. Open partial laryngectomy (OPL) may be used to treat RT failures, but the procedure is associated with significant surgical trauma and a high rate (up to 51%) of postoperative complications [13, 136, 149, 162]. Incision of the thyroid cartilage on the larynx, which has previously been irradiated, promotes the development of severe postoperative complications, including chondritis, chondronecrosis and fistula [160]. Consequently, in the event of RT failure, total laryngectomy is performed in the majority (75%) of cases [18], resulting in a substantial reduction in patients' quality of life. Transoral CO₂ laser microsurgery is considered the gold standard in the surgical management of early primary glottic carcinoma, having replaced OPL as the primary treatment modality [108, 174, 178]. In contrast to primary glottic cancer, experience with the use of TLMS for the treatment of recurrent/residual cancer following RT failure is still limited. More modest results are reported for TLMS when applied to recurrent/residual cancer following RT, compared with primary cancer [155], a higher complication rate than in the treatment of primary tumours, and the frequent need for repeat procedures to achieve disease control [165]. Blakeslee D. et al. (1984), analysing a series of 15 patients, report a 40% local control rate in the treatment of recurrent carcinoma following RT for T1 glottic cancer [15]. Ramakrishnan Y. et al. (2014), in a review and meta-analysis based on 11 studies, report local control following the first intervention of 56.9% [151]. Weiss B.G. et al. (2017), in a retrospective study, found the 5-year local control rate following TLMS for 93 patients with early recurrent glottic cancer to be 57.5% [196]. Roedel R.M. et al. (2010), analysing the oncological outcomes of TLMS for early recurrent glottic cancer following primary RT, report a cure rate of 42% after the first operation [160]. Russo E. et al. (2023), in a recent review and meta-analysis, analysing the results of salvage TLMS following primary RT for 235 patients, estimate the 5-year summary local control rate to be 39.1% [163].

Flexible endoscopic laryngeal surgery may overcome some of the limitations of TLMS mentioned earlier (Chapter 1), but in the available literature, we have found no studies on the use of FELS for treating recurrent and residual glottic cancer. Based on currently published data, this study presents the first and largest series of patients treated by FELS and followed for 5 years. The first endoscopic laser ablation under local anaesthesia for recurrent glottic carcinoma following RT was performed in 1994, with the patient remaining tumour-free for over 9 years [83]. Although there is no substantial evidence to support adjuvant re-irradiation following

salvage surgery, the rationale for such a decision in two of our cases was as follows: the two patients mentioned did not receive the full dose of radiation prior to salvage endoscopic treatment, with the persistent tumour being detected after the first half of the RT course. Therefore, completing the RT regimen (up to 60–70 Gy) following substantial surgical cytoreduction was considered rational to enhance the chances of local control.

The small number of cases included in this study, which constitutes a limitation of the study, does not allow for categorical statements, but the achievement of local control, disease-free survival, cure with larynx preservation, and ultimate disease control through FELS alone at 55.6% allows us to conclude that the oncological efficacy of FELS is comparable to that of TLMS, and the method is worthy of use as a salvage treatment following RT failure, offering patients the chance of organ preservation, particularly in limited lesions (T1).

5.5. Endoscopic surgery for glottic cancer on an outpatient basis

Flexible endoscopic laryngeal surgery on an outpatient basis was performed on twenty-four patients (23 men, 1 woman) with primary glottic carcinoma cT1-T2, aged between 38 and 81 years, with a mean of 58.2 ± 10.4 years, with a median of 56.2 years (IQR=11.4). Histological examination revealed squamous cell carcinoma in 16 cases (66.7%), verrucous carcinoma in 6 cases (25.0%), and spindle cell carcinoma in 3 cases (8.3%). In 7 patients, the tumour was diagnosed at stage T1a, in 8 patients at stage T1b, in 6 patients at stage T2a, and in 3 patients at stage T2b (with vocal cord mobility impairment). Anterior commissure involvement was observed in 15 patients (62.5%). In 20 cases, only endoscopic surgery was performed. In 4 cases (all T2), postoperative/adjuvant RT (36–70 Gy) was also administered. In one case (T2a), the patient decided to undergo postoperative RT, with no evidence of persistent tumour; in another case (T2a), the reason for offering postoperative RT was the detection of adverse changes in biopsies taken from the site of the eradicated tumour; and in two other cases (T2b), endoscopic surgery was initially planned as a means of achieving significant tumour reduction for large/protruding tumours in patients who refused open surgery, in order to increase the chances of successful radiotherapy.

Laser ablation of the tumour was performed in all cases, preceded by diathermic loop excision in 12 cases (50%). The number of treatment sessions ranged from 1 (n=13 (54.2%)) to 3 (n=1) (mean – 1.5).

Tumour persistence was detected in one case (4.2%) at 10 months after FELS for T2b glottic carcinoma, and the residual tumour underwent repeated laser ablation on an outpatient basis, followed by postoperative RT. Laryngeal preservation was achieved in all treated patients. Ultimate disease control by FELS alone on an outpatient basis was achieved in 19 (79.2%)

patients, and the recurrence-free survival period since the last organ-preserving procedure ranged from 4 to 270 months, with a mean of 72.5 ± 91.7 months and a median of 16 months (IQR=133.5). One-third of patients (33.3%) were followed up for over 5 years (table A3.29).

Fourteen patients presented with minor postoperative dysphonia, 5 patients presented with moderate dysphonia, and 5 patients presented with severe dysphonia.

No intra- or postoperative complications were recorded. All therapeutic procedures were completed on an outpatient basis, without subsequent referral for surgery in the operating theatre under inpatient conditions. All treated patients were discharged home within 1–2 hours of the operation.

In the available literature, we found no references regarding the use of the Nd:YAG laser, the 980 nm diode laser, and the diathermy loop in outpatient laryngeal surgery. We also found no studies regarding the treatment of primary glottic carcinoma on an outpatient basis. This study claims to be the first to present a series of patients with primary glottic carcinoma (n=24) treated on an outpatient basis, including 79.2% of patients followed for over 1 year and 33.3% of patients followed for over 5 years [62].

We consider the results obtained to be encouraging and comparable to the outcomes of traditional surgery performed in an inpatient operating theatre.

Among the limitations of the study, we note its retrospective nature, the absence of a control group, a relatively small number of patients, a relatively short follow-up period for some patients, and the lack of both objective measurements and detailed subjective assessments of voice quality (e.g., the VHI score), which would merit further evaluation in the future.

Consequently, OBLs using the Nd:YAG laser, the 980 nm diode laser, and the diathermic loop can be considered an alternative to traditional endoscopic surgery, performed in the operating theatre, for selected patients with glottic cancer. The proposed techniques overcome the limitations of previously suggested methods and demonstrate the applicability of OBLs, including for primary malignant lesions, particularly in patients with contraindications for GA and direct rigid laryngoscopy. Large-scale prospective studies, involving a large number of patients and a longer follow-up period, are welcome to validate the described approach and draw definitive conclusions.

GENERAL CONCLUSIONS

1. Flexible endoscopic laryngeal surgery using non-angiolytic lasers (Nd:YAG (1064 nm), diode (980/1470 nm)), a diathermy loop and flexible biopsy forceps is an effective method for the treatment of benign non-epithelial lesions of the larynx, offering a relevant therapeutic alternative to currently used surgical methods (transoral microsurgery and outpatient laryngeal surgery using angiolytic lasers), particularly for patients with contraindications for general anaesthesia or transoral microsurgery, and opening up a new direction in outpatient laryngeal surgery. The proposed techniques/methods allow the limitations of the aforementioned surgical methods to be overcome, demonstrating applicability in outpatient laryngeal surgery even in the case of voluminous lesions. Among the advantages of the method, the positive economic impact and time savings are worth noting, as the procedure can be performed on an outpatient basis for the majority of patients.

2. Endoscopic classification of hyperplastic laryngeal lesions ((1) chronic hyperplastic laryngitis, (2) chronic hyperplastic laryngitis with keratosis, (3) leukoplakia, (4) pachydermia, and (5) verrucous neoplasia), developed and proposed by the author, contributes to a clearer distinction between hyperplastic laryngeal lesions with increased malignant potential and those with reduced malignant potential. The last two types of lesions (pachydermia and verrucous neoplasia) raise a heightened suspicion of malignancy and warrant a more aggressive approach than the first three types. To obtain a conclusive histological result, traditional forceps biopsy may be appropriate in cases of CHL, CHLK, and leukoplakia, whilst in cases of pachydermia or verrucous neoplasia, total or subtotal excision of the lesion using a diathermy loop is relevant.

3. Surgical treatment via flexible endoscopy using non-angiolytic lasers (Nd:YAG (1064 nm), diode (980/1470 nm)), a diathermic loop, and flexible biopsy forceps may be a relevant alternative to the traditional approach to hyperplastic laryngeal lesions (via transoral CO₂ laser microsurgery), offering significant advantages such as: the ability to avoid the risks of general anaesthesia, applicability to patients with risks and contraindications for general anaesthesia and transoral surgery, a favourable cost-effectiveness ratio, and time savings. FELS using non-angiolytic lasers (Nd:YAG (1064 nm), diode (980/1470 nm)) overcomes the limitations of outpatient surgery using non-ablative techniques with angiolytic lasers by eradicating the lesion during the procedure. Surgical treatment via flexible endoscopy can be performed both on an outpatient basis under topical anaesthesia and in combination with direct suspended laryngoscopy under general anaesthesia with SHFJV. FELS in an outpatient setting is particularly attractive for patients with recurrent lesions, as it offers the possibility of avoiding repeated general anaesthesia with muscle relaxation, which is associated with increased morbidity. Inpatient FELS is preferred in cases of obstructive lesions with compromised airways,

and in patients with unfavourable/unstable cardiopulmonary status. Prospective studies, involving a larger number of patients and a longer follow-up period, are required to validate the proposed approach to the treatment of hyperplastic laryngeal lesions and to draw definitive conclusions.

4. Flexible endoscopic laryngeal surgery using non-angiolytic lasers (Nd:YAG (1064 nm), diode (980/1470 nm)) as the primary instrument is a safe and effective approach, which may be a relevant and feasible alternative to the conventional approach in the treatment of laryngeal papillomatosis, given the recurrent nature of the disease, with advantages including: (1) the possibility of avoiding repeated general anaesthesia with muscle relaxation, along with the associated risks; (2) applicability for patients with contraindications for general anaesthesia and transoral microsurgery; (3) the possibility of performing the procedure on an outpatient basis, which leads to a significant reduction in medical costs; (4) time savings. Nd:YAG laser /980/1470 nm diode laser ablation, preceded by resection with a diathermic loop, compared to the use of the laser as a single instrument, reduces the duration of the procedure and thermal damage to adjacent tissues, and can be used in large, obstructing lesions, which present a major limitation for non-ablative laser techniques.

5. Flexible endoscopic laryngeal surgery for early glottic cancer demonstrates oncological outcomes comparable to radiotherapy and transoral laser microsurgery; from an oncological perspective, it can be considered an effective method for treating T1-T2 glottic cancer and an alternative to traditional approaches, primarily for patients with risks/contraindications for radiotherapy, general anaesthesia with muscle relaxation and transoral microsurgery, as well as for patients who prefer outpatient laryngeal surgery.

6. Flexible endoscopic laryngeal surgery under local anaesthesia is not inferior to FELS under general anaesthesia with SHFJV in terms of oncological efficacy and is a safe procedure that can be recommended for the management of early glottic carcinoma on an outpatient basis, particularly for T1a lesions.

7. Tumour involvement of the anterior commissure reduces the oncological outcomes of FELS for early glottic cancer. Further studies on a larger clinical sample are required for definitive conclusions.

8. Combining FELS with adjuvant RT does not lead to improved oncological outcomes in the group of patients with T1b-T2 glottic cancer compared with FELS alone. Further studies on a larger clinical sample are required for definitive conclusions.

9. Impairment of vocal cord mobility (T2b stage) has a major negative impact on the outcomes of glottic cancer treatment; it correlates with a significantly poorer prognosis and is a major negative factor.

10. Flexible endoscopic laser surgery may be considered as an alternative treatment method for patients with T1–T2 verrucous carcinoma of the larynx, including large obstructive lesions, provided that patients are closely monitored endoscopically. In the hybrid form of T2 VCL, achieving local control is more problematic than in typical VCL. Further studies are needed to confirm whether postoperative RT can promote treatment success in such cases.

11. Flexible endoscopic laryngeal surgery for recurrent and residual glottic cancer following RT in stages T1–T2 demonstrates oncological outcomes comparable to transoral laser microsurgery; from an oncological perspective, it can be considered an effective method for treating recurrent/residual T1 cancer and is worthy of use as a minimally invasive surgical alternative for curing the disease whilst preserving the larynx, primarily for patients with risks/contraindications for general anaesthesia with muscle relaxation and transoral microsurgery. Prospective studies involving a larger number of patients are required to validate the proposed approach and draw definitive conclusions.

PRACTICAL RECOMMENDATIONS

1. Flexible endoscopy with biopsy is, in most cases, possible on an outpatient basis and is recommended as the most appropriate method for establishing a correct clinical and histopathological diagnosis of neoplastic lesions of the larynx.
2. Although the incidence of carcinoma following endoscopic treatment for benign and precancerous laryngeal lesions is low (according to our data, 1.2% for benign non-epithelial lesions, 2% for papilloma and 4.3% for hyperplastic laryngeal lesions), we consider it advisable to stop smoking, manage gastro-oesophageal reflux disease and monitor patients endoscopically at least once a year for at least the first 5 years following surgery. Patients with precancerous laryngeal lesions (hyperplastic laryngeal lesions and papilloma) should attend for endoscopic review as soon as possible after the onset of symptoms suggestive of recurrence or disease progression (change in voice quality, sensation of a foreign body in the throat, etc.), in order to benefit from early-stage diagnosis and minimally invasive treatment.
3. Given the potential for HLL to become malignant, we recommend follow-up examinations following endoscopic surgery at least once every 3 months for the first 2 years, and thereafter at least once a year.
4. Following FELS for LP, the first follow-up endoscopic examination is recommended 2 months after the procedure. Subsequent examinations should be scheduled 6 and 12 months after the procedure, then once a year, in the absence of symptoms of disease recurrence (progression of dysphonia or dyspnoea), or immediately upon the onset of symptoms of disease recurrence.
5. Obtaining sufficiently large tissue specimens during biopsy is critical for a definitive histological diagnosis of verrucous carcinoma of the larynx. We recommend the use of a diathermy loop as the instrument of choice for the biopsy of verrucous neoplasms in order to obtain a definitive histological diagnosis of VCL in an outpatient setting.
6. Following endoscopic resection of glottic cancer, our recommendations for post-operative follow-up examinations using flexible laryngoscopy are as follows: once a month during the first year after surgery, once every 2 months during the second year, once every 3 months during the third year, once every 6 months during the fourth and fifth years, and once a year after 5 years. In addition, for patients with T2 disease, we recommend cervical ultrasound once every 3 months during the first 2 years after surgery.

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ANNEX 1.

PUBLICATIONS ON WHICH THE AWARD OF THE TITLE OF DOCTOR HABILITATUS BASED ON A SYNTHESIS OF SCIENTIFIC WORKS IS REQUESTED

• Monograph:

Gurău P. Endoscopia flexibilă în diagnosticul și tratamentul leziunilor neoplazice ale laringelui. Chișinău: Tipografia „Bons Offices SRL”; 2025. 143 p. ISBN 978-5-36241-484-9. <https://library.usmf.md/ro/gurau-p-endoscopia-flexibila-diagnosticul-si-tratamentul-leziunilor-neoplazice-ale-laringelui>

• Articles in journals indexed in WoS, SCOPUS and other international databases recognised by ANACEC:

Gurău P, Arnaut O, Sencu E, Sofroni D. Office-based endoscopic surgery for benign, premalignant, and malignant laryngeal lesions. *Egypt J Otolaryngol.* 2025; 41:122. doi: 10.1186/s43163-025-00872-w. (IF Clarivate 0.5)

Gurău P, Arnaut O. Flexible Endoscopic Approach to Glottic Carcinoma: Five-Year Oncological Outcomes. *J Voice.* 2024 Oct 14:S0892-1997(24)00300-X. doi: 10.1016/j.jvoice.2024.09.007. Epub ahead of print. PMID: 39406620. (IF Clarivate 2.4)

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Gurău P. A non-traditional endoscopic approach to laryngeal schwannoma. *Braz J Otorhinolaryngol.* 2024 May-Jun;90(3):101400. doi: 10.1016/j.bjorl.2024.101400. PMID: 38428327. (IF Clarivate 1.8)

Gurău P. Endoscopic approach to hyperplastic laryngeal lesions: a literature review and personal experience. *Egypt J Otolaryngol.* 2023; 39:124. doi: 10.1186/s43163-023-00490-4. (IF Clarivate 0.5)

Gurău P. Laryngeal Papillomatosis: A Non-traditional Flexible Endoscopic Approach. *J Voice.* 2025;39(6):1641-1646. doi: 10.1016/j.jvoice.2023.07.014. PMID: 37684190. (IF Clarivate 2.4)

Gurău P, Arnaut O, Sencu E, Sofroni D. Flexible Endoscopic Laser Surgery for Glottic Carcinoma After Radiotherapy Failure: A First Experience. *Cureus.* 2026;18(3):e106051. doi: 10.7759/cureus.106051. PMID: 41913727. (PubMed)

Gurău P, Sencu E, Balica I. Lipoma of the larynx: fibroendoscopic approach (case report). *Revue de Laryngologie Otologie Rhinologie.* 2016; 137(5): 135-136. ISSN 0035-1334. (SCOPUS)

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• **Articles in peer-reviewed international journals:**

Gurău P. Laserul în chirurgia endoscopică a laringelui. ORL.ro. 2020; 49(4):22-30. doi: 10.26416/ORL.49.4.2020.3974.

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• **Articles in national scientific journals (Category B):**

Gurău P, Vitiuc A, Tâbâră Gh. Utilizarea fibroendoscopiei în chirurgia cancerului glotic: prezentarea primului caz. Arta medica. 2004; 7(4):61-63. ISSN 1810-1852.

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Gurău P, Arnaut O, Sencu E, Sofroni D. Chirurgia prin endoscopie flexibilă laser a cancerului glotic precoce cu afectarea comisurii anterioare. Buletinul Academiei de Științe a Moldovei. Științe medicale. Chișinău, 2024;79(2):109-111. ISSN 1857-0011. doi: 10.52692/1857-0011.2024.2-79.20.

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• **Abstracts/theses in the proceedings of international scientific forums:**

Gurău P, Tirbu V. Fibroendoscopic approach in verrucous carcinoma of the larynx. In: 4th European Congress for Bronchology & Interventional Pulmonology, Belgrade, Serbia, April 27-30, 2017. Abstract Book, OP-17, p.19.

Gurău P. Flexible endoscopic combined diathermy-laser resections in malignant tumors of larynx, trachea and bronchi. In: The 21st World Congress of Bronchology & Interventional Pulmonology, Shanghai, China, November 19-22, 2020. Abstract Book, PO-519, p.414-415.

Gurău P, Arnaut O, Sencu E, Sofroni D. Chirurgia prin endoscopie flexibilă în tratamentul edemului Reinke. În: Conferința Națională de Otorinolaringologie și Chirurgie Cervico-facială cu Participare Internațională, Eforie Nord, România, 28-31 Mai 2025. Caiet Rezumate, p.14-15.

Gurău P, Arnaut O, Sencu E, Sofroni D. Chirurgia prin endoscopie flexibilă în tratamentul polipilor corzilor vocale. În: Conferința Națională de Otorinolaringologie și Chirurgie Cervico-facială cu Participare Internațională. Eforie Nord, România, 28-31 Mai 2025. Caiet Rezumate. p.61-62.

Gurău P. Endoscopia flexibilă intervențională în leziunile neoplazice ale laringelui. În: Al 27-lea Congres Național al Societății Române de Pneumologie, Sinaia, România, 2-6 Noiembrie 2022. Rezumatele lucrărilor, Vol.1, p.140. ISBN: 978-606-8463-76-6.

Гурăу ПП. Гибкая эндоскопия в диагностике и лечении веррукозной карциномы гортани. В: Оториноларингология. 2019; 1-с (2). с. 26-27. ISSN 2528-8253.

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Petru Gurău

ENDOSCOPIA FLEXIBILĂ

ÎN DIAGNOSTICUL ȘI TRATAMENTUL
LEZIUNILOR NEOPLAZICE ALE LARINGELUI

MONOGRAFIE



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RESEARCH

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Office-based endoscopic surgery for benign, premalignant, and malignant laryngeal lesions

Petru Gurău^{1*}, Oleg Arnaut^{2,4}, Eusebiu Sencu³ and Dumitru Sofroni¹

Abstract

Background The available publications concerning office-based flexible endoscopic laryngeal surgery (OBFELS) are mostly dedicated to managing benign and premalignant laryngeal lesions using angiolytic lasers. There is a lack of information about using other lasers and different treatment approaches in OBFELS. There is also a lack of publications related to OBFELS for malignant laryngeal lesions. The objective of the study was to share our experience in OBFELS using Nd:YAG laser, 980/1470 nm diode laser, diathermy snare, and biopsy forceps for benign, premalignant, and malignant laryngeal lesions, and to evaluate the effectiveness of the treatment.

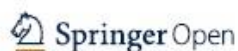
Methods OBFELS was performed in 362 patients from 3 groups: benign lesions (BL) ($n = 285$), represented by nodules, polyps, Reinke's edema (RE), nonspecific granulomas, cysts, and neurofibroma; premalignant lesions ($n = 53$), represented by laryngeal papilloma/papillomatosis (LP), and hyperplastic laryngeal lesions (HLL), including chronic hyperplastic laryngitis with keratosis, leukoplakia, pachydermia, and verrucous neoplasia; and malignant lesions, represented by primary T1-T2 glottic carcinoma ($n = 24$). All endoscopic interventions were performed with spontaneous breathing under topical anesthesia without sedation or with minimal/moderate intravenous sedation/analgesia. The following endoscopic techniques in different combinations were used for lesion eradication: cold surgery by flexible forceps, diathermy snare excision, and laser ablation/vaporization using Nd:YAG laser (1064 nm) or 980 nm diode laser.

Results Complete eradication/removal of visible lesions was obtained in all treated cases. Recurrent lesions were registered in the BL group in 2.8%, in the LP group – in 33.3%, in the HLL group – in 6.9%, and in the glottic carcinoma group – in 4.2% of cases. Larynx preservation was obtained in all the patients, and ultimate disease control by OBFELS alone was achieved in 79.2% of patients with glottic carcinoma.

Conclusions OBFELS using Nd:YAG laser, 980 nm diode laser, diathermy snare, and flexible biopsy forceps can be considered an alternative to traditional OR endoscopic laryngeal surgery for benign, premalignant, and malignant laryngeal lesions in selected patients. The proposed techniques allow for overcoming some limits of previously proposed methods and demonstrate the applicability of OBFELS even for bulky lesions and primary malignant lesions, especially in patients with risks and contraindications for general anesthesia and direct laryngoscopy.

Keywords Office-based laryngeal surgery, Nd:YAG laser, 980 nm diode laser, Benign lesions, Premalignant lesions, Glottic carcinoma

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Background

Office-based laryngeal surgery (OBLS) has been a trend in development in modern laryngology for about 2 decades. According to Zeitels and Burns, office-based laryngeal laser surgery was instituted in 2001 and first discussed at the American Laryngological Association in 2003 [1]. Most of the publications on OBLS of laryngeal lesions are dedicated to using angiolytic lasers: 585 nm pulsed-dye laser (PDL), 532 nm pulsed-potassium-tetanyl-phosphate (KTP) laser, and a new 445 nm blue diode angiolytic laser [2–7]. The available publications concerning OBLS are mostly dedicated to managing benign and premalignant laryngeal lesions, the reported results being comparable to the traditional operating room (OR) laryngeal endoscopic surgery under general anesthesia (GA) [5, 7]. There is a lack of information about using other lasers and different treatment approaches in OBLS. There is also a lack of publications related to OBLS for malignant laryngeal lesions.

The objective of the present study is to share our experience in OBLS using Nd:YAG laser, 980 nm diode laser, diathermy snare, and biopsy forceps for benign, premalignant, and malignant laryngeal lesions, and to evaluate the effectiveness of the treatment.

Methods

This is a retrospective study. Office-based flexible endoscopic laryngeal surgery (OBFELS) was performed (in the time interval from 1992 to 2024) on 362 patients from 3 nosological groups: benign lesions ($n=285$), premalignant lesions ($n=53$), and malignant lesions ($n=24$). Benign lesions (BL) were represented by nodules, polyps, Reinke's edema (RE), nonspecific granulomas, cysts, and neurofibroma. Premalignant lesions were represented by laryngeal papilloma/papillomatosis (LP) and hyperplastic laryngeal lesions (HLL). HLL were classified as follows: chronic hyperplastic laryngitis with keratosis, leukoplakia, pachydermia, and verrucous neoplasia [8]. Malignant lesions were represented by primary glottic carcinoma (T1-T2). Office-based laryngeal surgery for patients with such lesions as vocal nodules, mild Reinke's edema, nonspecific granulomas, and HLL was considered after conservative treatment failure or suspicion of malignancy.

Selection criteria for OBLS were the following: patients with benign, pre-malignant, and malignant (T1-T2 glottic carcinoma) lesions who had risks/contraindications for general anesthesia and/or direct rigid laryngoscopy, who preferred surgery in an office setting, and who could tolerate the awake procedure under topical anesthesia. Patient cooperation (ability to endure the procedure) was appreciated during the diagnostic flexible laryngoscopy with biopsy (if necessary)

performed before the operation. Exclusion criteria for OBLS included compromised airways and poor/unstable cardio-pulmonary condition of the patient.

All the interventions were performed by a single surgeon in the office or hospital-based endoscopy suite. Written informed consent was obtained from the patients. All endoscopic interventions were performed with spontaneous ventilation/breathing under topical anesthesia without sedation or with minimal/moderate intravenous sedation/analgesia (on the patient's demand). Patients were discharged home in a time interval of 1–2 h after completing the procedure.

Patients were operated on under topical anesthesia of the larynx with Lidocaine 2% (10–15 ml) that was instilled through a catheter passed via the working channel of the flexible bronchoscope during phonation, producing "laryngeal gargle". Sometimes (on patient demand), minimal/moderate intravenous sedation/analgesia was applied. Appropriate cardiovascular monitoring and pulse oximetry were assured for such cases.

The main tools used for performing OBLS were a flexible bronchoscope with a 2.2–3.0 mm working channel, a diathermy snare (oval-shaped, size 10–15 mm), a Nd:YAG laser (wavelength 1064 nm), a 980 nm diode laser, and a flexible biopsy forceps (4.5–7.3 mm cup opening).

The patients were preferably operated on in a sitting upright position (Fig. 1). After topical anesthesia of the nasal cavity, pharynx (with 10% Lidocaine spray), and larynx, a flexible bronchoscope was introduced transnasally to the larynx to obtain adequate lesion exposure. Biopsy forceps was used for biopsying a lesion, and removal/eradication of small lesions (1–4 mm). Diathermy snare in cutting mode was used for biopsying verrucous neoplasia, and partial/complete resection of various protruding lesions. Flexible guide-based Nd:YAG laser (1064 nm) or 980 nm diode laser were used for the ablation of different types of lesions in near non-contact continuous mode with 20–40 W power setting for Nd:YAG laser and 20–30 W power setting for 980 nm diode laser (Fig. 2).

Numerical data (age and follow-up period in months) were presented as min–max range, mean \pm standard deviation, median, and interquartile range. Categorical data were presented as absolute and relative frequencies.

The voice outcome was assessed by a scale representing the patient's subjective appreciation of his voice as follows: normal voice, mild dysphonia, moderate dysphonia, and severe dysphonia. Recurrence of the lesions was documented by biopsy or complete removal of the visible lesion with subsequent histological examination of the obtained specimen.



Fig. 1 Diode laser ablation of glottic carcinoma in the office-based setting



Fig. 2 Laser ablation of right vocal fold carcinoma

Results

The selection criteria for the study were met by 362 patients with benign, premalignant, and malignant laryngeal lesions.

Benign lesions

Benign lesions were identified in 285 patients (188 males, 97 females). The age distribution ranged from 16 to 73 years, with a mean age of 44 ± 11.4 and a median of 44 years (IQR = 17). The pathology (Table 1) included

Table 1 Benign lesions treated in an office-based setting

Type of pathology	No (%)
Vocal nodule	38 (13.3%)
Myxoid polyp	61 (21.4%)
Fibrous polyp	34 (11.9%)
Angiomatous polyp	39 (13.7%)
Angiofibrous polyp	70 (24.6%)
Cyst	14 (4.9%)
Nonspecific granuloma	19 (6.7%)
Reinke's edema	9 (3.2%)
Neurofibroma	1 (0.3%)
Totally	285 (100%)

Table 2 The number of treatment sessions necessary for BL eradication

No. of treatment sessions per patient	No. of patients
1	281 (98.6%)
2	3 (1.1%)
3	1 (0.3%)
Mean = 1.0	285 (100%)

vocal nodules, vocal fold polyps, RE, nonspecific granulomas, cysts, and neurofibroma.

The majority of lesions (281 (98.6%)) were localized in the glottic portion of the larynx, and four lesions were localized in the supraglottic portion (ventricular cysts). The size of the lesions varied from 0.2 to 2.5 cm.

Table 3 Endoscopic techniques used for BL eradication

Endoscopic techniques	No. of patients (%)
Cold surgery (by forceps)	92 (32.3%)
Diathermy snare excision	117 (41.1%)
Laser ablation	22 (7.7%)
Cold surgery + Laser ablation	30 (10.5%)
Diathermy snare excision + Cold surgery	6 (2.1%)
Diathermy snare excision + Laser ablation	18 (6.3%)
Totally	285 (100%)

The number of treatment sessions necessary for lesion removal/eradication varied from 1 to 3. The majority of BL (98.6%) were removed in 1 session (Table 2).

For BL eradication, the following endoscopic techniques were used in different combinations: cold surgery by flexible forceps, diathermy snare excision, and laser ablation/vaporization (Table 3).

Complete removal of the visible lesion was obtained in all treated patients. Recurrent lesions were registered in 8/285 cases (2.8%). Recurrent nonspecific granuloma was registered in 6 cases that required repeated successful OBLs. The other 2 cases were represented by vocal fold polyps that recurred, respectively, after 153 and 39 months from surgery and were also successfully removed in an office-based setting.

The follow-up duration for this patient group ranged from 1 to 189 months, with a mean of 10 ± 27.6 months and a median of 3.0 months (IQR = 2 months). Notably, malignant lesions were registered during the follow-up period in 4/285 cases (1.4%) (Table 4).

The majority of patients treated in an office-based setting (94.7%) appreciated their voice after the operation as normal (Table 5). Severe dysphonia persisted in 1 patient with bilateral RE (grade 3) treated by laser ablation.

Laryngeal papilloma/papillomatosis

Twenty-four patients with LP (16 males, 8 females) underwent endoscopic laryngeal surgery in an office-based setting. The age distribution ranged from 19 to 77, with a mean age of 42.2 ± 16.5 years and a median age

Table 5 Voice outcome after OBLs for benign laryngeal lesions

Voice outcome	No. of patients (%)
Normal	270 (94.7%)
Mild dysphonia	5 (1.8%)
Moderate dysphonia	9 (3.2%)
Severe dysphonia	1 (0.3%)
Totally	285 (100%)

Table 6 Extension of the lesion in patients with LP treated in an office-based setting

Affected portion of the larynx	No. of patients (%)
glottic	16 (66.6%)
supraglottic	3 (12.5%)
glottic + subglottic	1 (4.2%)
glottic + supraglottic	3 (12.5%)
glottic + supraglottic + subglottic	1 (4.2%)
Totally	24 (100%)

of 40 (IQR = 27). The glottic portion of the larynx was affected in the majority (87.5%) of patients (Table 6).

The lesion size/extension varied from 0.2 to 3.0 cm. In 22 patients (91.7%), the lesion was eradicated/ablated in 1 session, and in 2 cases, 2 treatment sessions were needed. The following endoscopic techniques, in different combinations, were used for LP eradication: cold surgery by flexible forceps, diathermy snare excision, and laser ablation/vaporization (Table 7).

Complete eradication/ablation of the visible lesion was obtained in all the cases (Fig. 3). Recurrent papillomas were registered in 8/24 patients (33.3%) who needed repeated endoscopic interventions in an office-based setting. The follow-up period without disease recurrence ranged from 2 to 203 months, with a mean of 79.7 ± 74.8 months and a median of 58.5 months (IQR = 129.5) (Table 8).

Malignant transformation of papilloma was registered in 1 case: 2 years after cold eradication of glottic papilloma, a T1a squamous cell carcinoma (G2) was

Table 4 Malignancy developed after OBLs for BL of the larynx

Pathology (size of the lesion)	Treatment for BL	Type of malignancy	Time interval between OBLs and diagnosis of malignancy	Treatment for developed malignancy
Angiofibrous polyp (0.5 cm)	CS + LA	SCC (T1a)	252 months	Successful endoscopic LA
Angiomatous polyp (0.6 cm)	CS	SCC (T1a)	28 months	Successful endoscopic LA
Angiomatous polyp (1.5 cm)	DEX	SCC (T2)	68 months	Successful endoscopic LA
Neurofibroma (1.5 cm)	DEX + LA	SCC (T2)	48 months	Open partial laryngectomy

Abbreviations: CS Cold surgery, LA Laser ablation, DEX Diathermy snare excision, SCC Squamous cell carcinoma

Table 7 Endoscopic techniques used for LP eradication

Endoscopic techniques	No. of patients (%)
Cold surgery (by forceps)	5 (20.8%)
Laser ablation	14 (58.3%)
Cold surgery + Laser ablation	1 (4.2%)
Diathermy snare excision + Laser ablation	3 (12.5%)
Cold surgery + Diathermy snare excision + Laser ablation	1 (4.2%)
Totally	24 (100%)

diagnosed and treated by laser ablation in an office-based setting (Fig. 4).

Concerning voice outcome, 17/24 patients (70.8%) with LP appreciated their postoperative voice as normal, and 7 patients (29.2%) presented moderate dysphonia.

Hyperplastic laryngeal lesions

In-office treatment was performed in 29 patients with HLL (26 males, 3 females). The age distribution ranged from 20 to 77 years, with a mean age of 51 ± 13.4 years and a median of 52 years (IQR= 18). HLL were represented by chronic hyperplastic laryngitis with keratosis (n= 3), leukoplakia (n= 13), pachydermia (n= 12), and verrucous neoplasia (n=1) [8]. Histological examination revealed low-grade dysplasia in 2 cases (6.9%), high-grade dysplasia in 1 case (3.4%), and no dysplasia in 26 cases (89.7%). The glottic portion of the larynx was affected in 26 cases, the glottic and supraglottic portions in 1 case, and the supraglottic portion in 2 cases. Lesion size/extension varied from 0.3 to 2.5 cm. In all the cases, complete eradication/ablation of the visible lesion was performed in 1 treatment session (Fig. 5). The following endoscopic techniques in different combinations were used for HLL eradication: cold surgery by flexible forceps, diathermy snare excision, and laser ablation/vaporization (Table 9).

Recurrent lesions were registered in 2 cases (6.9%), respectively, 3 and 11 months after surgery,

and required repeated in-office laser ablation. The recurrence-free follow-up period ranged from 1 to 266 months, with a mean of 69.9 ± 80.6 months and a median of 25 months (IQR= 134) (Table 10). Malignancy (T2 squamous cell carcinoma) was registered 103 months after surgery in 1 patient (3.4%) who continued to smoke after the first surgical intervention.

Nineteen patients (65.5%) appreciated their postoperative voice as normal, 6 patients (20.7%) presented moderate dysphonia, and 4 patients (13.8%) presented severe dysphonia.

Malignant lesions

Twenty-four patients (23 males, 1 female) with primary T1–T2 glottic carcinoma, aged 38 to 81, underwent OBLs. The mean age was 58.2 ± 10.4 years, with a median of 56.2 years (IQR= 11.4). Histological examination revealed squamous cell carcinoma in 16 cases (66.7%), verrucous carcinoma in 6 cases (25.0%), and spindle cell carcinoma in 2 cases (8.3%). According to the primary tumor stage, 7 patients had T1a stage, 8 patients had T1b stage, 6 patients had T2a stage, and 3 patients had T2b stage (with impaired vocal fold mobility) of the disease. Anterior commissure affection was observed in 15 patients (62.5%). In 20 cases, only endoscopic surgery was applied. In 4 cases (all-T2), postoperative radiation therapy (36-70 Gy) was also offered. In one case (T2a), the patient desired to undergo postoperative radiation therapy (RT) without evidence of persistent/recurrent tumor; in another case (T2a), the reason for offering RT was adverse pathological finding in biopsy fragments from the tumor bed; and in other two cases (T2b), endoscopic surgery was initially planned as a cytoreduction tool for bulky tumors in patients who refused open surgery for increasing chances of successful radiation treatment.

Laser ablation/vaporization of the tumor was performed in all carcinoma cases, being preceded by diathermy snare excision in 12 cases (50%). The number of

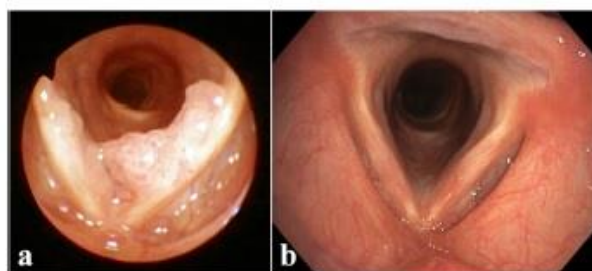


Fig. 3 a Glottic papillomatosis (before OBLs). b Four months after OBLs (DEX + LA) of glottic papillomatosis

Table 8 Follow-up period without disease recurrence in patients with LP after OBLS

The recurrence-free follow-up period after OBLS	No. of patients
Up to 1 year	3
1–3 years	7
3–5 years	2
5–10 years	5
10–15 years	2
15–20 years	5
Totally	24

treatment sessions varied from 1 ($n=13$ (54.2%)) to 3 ($n=1$) (average—1.5).

Tumor recurrence was revealed in 1 case (4.2%) after 10 months from endoscopic laser ablation of T2b glottic carcinoma, and the recurrent tumor was managed by repeated laser ablation in an office-based setting with subsequent postoperative RT. Larynx preservation was obtained in all the patients. Ultimate disease control by OBLS alone was achieved in 19 (79.2%) patients, and the recurrence-free follow-up period from the last organ-sparing intervention ranged from 4 to 270 months, with a mean of 72.5 ± 91.7 months and a median of 16 months

(IQR= 133.5). One-third of the patients (33.3%) were followed up for over 5 years (Table 11).

Fourteen patients presented mild postoperative dysphonia, 5 patients presented moderate dysphonia, and 5 patients presented severe dysphonia.

There were no complications during the operation. All the therapeutic procedures were completed in an office-based setting, without referrals to OR surgery. All treated patients were discharged home 1–2 h after the procedure.

Discussion

Transoral microsurgery (TOMS) under general anesthesia with myorelaxation, being the mainstay in the treatment of laryngeal lesions, beside many indubitable advantages (great cutting precision, possibility to assess margins of resected specimen, etc.) has also some disadvantages, including time delay to diagnosis and treatment due to scheduling, dental damage due to rigid laryngoscopy, and health risks associated to general anesthesia [9].

Office-based laryngeal surgery (OBLS) has been a trend in development in modern laryngology for about 2 decades. According to Zeitels and Burns, office-based laryngeal laser surgery was instituted in 2001 and first discussed at the American Laryngological Association in 2003 [1]. Karatayli-Ozgursoy et al. mentioned as a trend



Fig. 4 a T1a glottic carcinoma diagnosed 2 years after cold eradication of glottic papilloma. b Six months after flexible endoscopic diode laser ablation of glottic carcinoma: no visible lesions

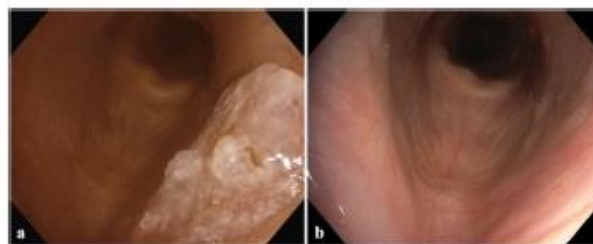


Fig. 5 a Laryngeal leukoplakia (before OBLS). b Five months after laser ablation of laryngeal leukoplakia: no visible lesions

Table 9 Endoscopic techniques used for the eradication of HLL

Endoscopic techniques	No. of patients (%)
Cold surgery (by forceps)	1 (3.4%)
Laser ablation	24 (82.8%)
Cold surgery + Laser ablation	2 (6.9%)
Diathermy snare excision + Laser ablation	2 (6.9%)
Totally	29 (100%)

Table 10 Follow-up period without disease recurrence in patients with HLL after OBLs

The recurrence-free follow-up period after OBLs	No. of patients
Up to 1 year	11
1–3 years	7
3–5 years	1
5–10 years	1
10–15 years	5
15–20 years	3
20–25 years	1
Totally	29

Table 11 The disease-free follow-up period in patients with glottic carcinoma from the last OBLs

The disease-free follow-up period from the last organ-sparing surgery	No. of patients
Up to 1 year	5
1–3 years	10
3–5 years	1
5–10 years	1
10–15 years	2
15–20 years	2
20–25 years	3
Totally	24

transitioning patients with recurrent disease to the office for the treatment with angiolytic lasers after initial operating room surgery [10]. Nowadays, it is estimated that more than 15% of laryngeal operations are carried out in office-based settings, and the number of in-office procedures is growing due to many related benefits [11].

Mentioned advantages of OBLs include lack of hospitalization; more rapid diagnostic process; a minimally invasive therapeutic alternative in patients with contraindications for general anesthesia and inaccessibility of a lesion by rigid endoscopy because of anatomic difficulties (e.g., limited neck extension, dental limitations); avoiding

of risks of general anesthesia and direct laryngoscopy; suitability for patients with comorbidities; inclusion of patients not suitable for general anesthesia; optimal setting for highly recurrent diseases; better visualization of all laryngeal subsites; overcoming the oral tissues that are prone to trauma during direct laryngoscopy; reduced recovery time; minimal morbidity; safety, reduced health risks largely due to avoiding general anesthesia; cost savings; time efficiency, reduction in operating time, patient ability to walk away from the office with no life restriction and even to return to work almost immediately after finishing the procedure, easier planning, short waiting list; ability to assess phonatory outcome in real time; and strong patient’s preference for office-based setting [7, 9, 11–15]. For some patients, in case of high risk for general anesthesia, awake laryngeal surgery can be the only available treatment option [9, 16]. The only absolute contraindication for OBLs is a compromised airway [9]. According to Lahav et al., 90.2% of office-based laser procedures were well tolerated and completed [4]. Office-based procedures under topical anesthesia are known to present significantly less cardiovascular morbidity compared to procedures under general anesthesia [17]. Lahav et al. did not find any interconnections between such comorbidities as hypertension, ischemic heart disease, and chronic obstructive pulmonary disease and in-office laser treatment completion. The authors consider this finding very important because these patients often have an increased risk for general anesthesia and, therefore, may be considered good candidates for OBLs [4]. In a study by Rees et al., the authors mentioned 54 patients who underwent both OBLs and previous OR surgery for the same pathology. In this group, 87% of patients stated they preferred in-office unsedated PDL surgery over surgery in the OR, and 83% of patients reported more comfort with unsedated OBLs than with OR surgery under GA [18]. Rees et al. mentioned more than \$5000 cost savings per case in performing OBLs using PDL for laryngeal papillomatosis [19]. Hospital cost reduction of up to 95% per procedure was mentioned, comparing in-office procedures under topical anesthesia to similar procedures performed under general anesthesia [20].

The benefits of OBLs are most evident for diseases that have a high tendency for recurrence, such as non-specific granulomas, recurrent respiratory papillomatosis (RRP), and HLL (leukoplakia, dysplasia, etc.), that are likely to require multiple interventions [4, 21]. For these patients, avoiding repeated surgeries in the OR under GA is of major importance. Kuet and Pitman mentioned that before the era of OBLs, because of the risks related to general anesthesia and direct laryngoscopy, patients with RRP usually waited until the disease symptoms (dysphonia and dyspnea) were severe enough, enduring

significant chronic morbidity, before deciding to undergo surgery in the OR. Because of the advantages of OBLS (safety, time efficiency, etc.), the threshold for the decision for surgery has been lowered, and patients often prefer to be treated when symptoms are minimal. A follow-up exam and surgery can be performed in a single office visit, and patients can return to their life schedule the same day. Hence, OBLS, being performed for a limited lesion, shifted the treatment paradigm, resulting in decreased morbidity of both OBLS and the disease itself [3].

Rosen et al., in a review publication, mentioned that the term "office-based setting" is also applied for procedures that are performed in a hospital-based endoscopy suite, provided key elements of the office-based treatment concept are maintained [22]. Among a variety of techniques and tools that are applied in OBLS, the use of biopsy forceps, introduced through the working channel of the flexible endoscope, to remove vocal nodules, polyps, and granulomas was mentioned [9]. Most of the publications on OBLS have been dedicated to using two angiolytic lasers: 585 nm pulsed-dye laser (PDL) and 532 nm pulsed-potassium-tetanyl-phosphate (KTP) laser. In 2018, a new 445 nm blue diode angiolytic laser was launched that seems to gradually replace the former two mentioned lasers, demonstrating similar treatment outcomes when compared to the KTP laser [4, 6, 7]. Angiolytic lasers (PDL, KTP, blue laser) are highly absorbed by oxyhemoglobin and cause photocoagulation of sublesional or intralesional microvasculature, with subsequent lesion regression/involution. In the case of subepithelial lesions, the epithelium is not vaporized, which leads to superficial lamina propria (SLP) protection and maintaining the pliability of the vocal folds for better vocal outcomes [1]. Zeitels et al. proposed a 4-level grading scheme for delineating the degree of lesion resolution: 0% to 50%, 51% to 70%, 71% to 99%, and 100% [2]. The available publications concerning OBLS using angiolytic lasers are mostly dedicated to managing benign and premalignant laryngeal lesions.

Benign lesions

Hamdan and Ghanem presented their experience using the blue laser (445 nm) for different vocal fold lesions and reported complete regression of lesions in 50% of cases [23]. In another study, Hamdan et al. reported complete regression after blue laser in-office treatment in 76% of cases (13/17) for vocal fold polyps and in 33% of cases (21/33) for RE [24]. Filauro et al. mentioned comparable efficacy of office-based procedures to the standard microlaryngoscopic approach for vocal fold polyps and RE and documented a complete regression of RE in 85.7% of patients treated with blue laser in the office [7]. Abi

Zeid Daou et al., in a systematic review article on OBLS in vocal fold polyps, mentioned the complete regression rate of vocal fold polyps between 27.6% and 96.8% across different studies and concluded that OBLS is a reliable alternative to classical phonomicrosurgery [25]. Chadwick et al. reported comparable voice outcomes of in-office photoangiolytic KTP laser treatment for vocal fold polyps to traditional excision using transoral microlaryngoscopy in the OR regardless of polyp size [5]. There are also proposals for using an angiolytic laser in combination with flexible endoscopic forceps for removing vocal fold polyps and granulomas to achieve an earlier therapeutic effect [26, 27].

Hyperplastic laryngeal lesions (HLL)

Koufman et al. reported that 80% of patients (20/25) with glottic leukoplakia did not require further treatment after PDL treatment [13]. Zeitels et al. reported 75–100% lesion regression in 62% of 29 patients with glottic dysplasia using KTP laser [2]. Hamdan et al. reported the first case series on vocal fold leukoplakia (10 patients and 12 lesions) treated with blue laser in an office-based setting, mentioning complete lesion regression in 75% of cases (9/12) [28].

Laryngeal papillomatosis (LP)

The goal of surgery for LP is to reduce disease severity, improve voice quality, and maintain a patient airway, the unpredictable recurring and remitting natural history of the disease being a challenge for any study of LP treatment efficacy [3]. Photoangiolytic (PDL, KTP) laser treatment was shown to result in disease regression and improvement of voice quality [3]. Del Signore et al. pointed out that 50% of patients with LP treated with angiolytic lasers (PDL or KTP) needed follow-up treatments [29]. Mao et al. reported their experience using KTP laser in an office-based setting for LP with complete disease resolution in 66.7% of cases with follow-up ranging from 13 to 81 months [30].

Some authors consider that premalignant recurrent lesions, such as papilloma and leukoplakia/dysplasia, should be initially treated in the operating room under general anesthesia for biopsy in order not to omit carcinoma [12, 31]. On the other hand, Omori et al. consider that suspension laryngoscopy under general anesthesia is too invasive to be used only for a biopsy of the laryngeal lesion [32].

A disadvantage of photoangiolytic laser treatment is the lack of a clear endpoint, resulting in suboptimal treatment that requires repeated unplanned surgeries in about 20% of cases [29]. The treatment strategy using angiolytic lasers is aimed at obtaining lesion involution/regression rather than obtaining immediate lesion removal/ablation.

Lesion regression can take several weeks (4–5 weeks or more) [5, 33]. Hence, some authors stated that bulky benign lesions, such as Reinke's edema, are not suitable for OBLS using angiolytic laser because of the risk of airway obstruction and recommended OR surgery under GA for these cases [7, 33]. Lahav et al. also mentioned that bulky lesions (papillomas) should be carefully considered for in-office treatment, as it may be difficult to deliver enough laser energy to address the lesion [4]. Bar et al. mentioned limited working time after local anesthesia of the larynx as a limitation of in-office procedures. Hence, if a lesion requires longer operative time or the patient is not compliant enough, surgeons may not have enough time to complete the treatment [11].

There is a lack of information about using other types of lasers and different treatment approaches in OBLS for neoplastic laryngeal lesions. In contrast to many researchers who reported treatment results as a percentage of regression of the lesion, Wellenstein et al. consider that the goal of in-office treatment, except for LP, should be complete removal of the lesion to avoid additional treatment and to be a valid alternative to surgery in the OR [15]. The authors presented their experience using CO₂ laser in an outpatient setting in 27 patients with benign and premalignant laryngeal lesions and mentioned that 66% of the treated patients, including 63% of patients with leukoplakia/hyperkeratosis (10/16), did not have residual/recurrent disease and did not require further treatment [15]. Hu et al. reported complete remission in 82% of patients with leukoplakia (9/11) treated with CO₂ laser in an office-based setting [34]. There is very scarce information on using thulium laser in OBLS [13, 35, 36]. As an alternative to photoangiolysis with subsequent lesion regression, vaporization of the lesion using KTP laser, CO₂ laser, and thulium laser in an office-based setting was reported [4, 34, 36].

Malignant laryngeal lesions

There is a lack of publications related to OBLS for malignant laryngeal lesions. Wellenstein et al., in a review article, stated the absence of studies on OBLS for glottic carcinoma and mentioned that the oncological effectiveness of OBLS remains unknown [9]. In another study, Wellenstein et al. admitted that in patients with small (T1a) glottic carcinoma with severe comorbidities or an inaccessible lesion during rigid microlaryngoscopy, OBLS could be an alternative [15]. Lahav et al., in an article analyzing 5-year outcomes of OBLS using KTP laser for different laryngeal pathologies, mentioned a group of patients with prior malignant lesions previously treated in the OR under GA ($n=30$) that underwent in-office laser procedures for suspected residual/recurrent lesions. The authors stated that establishing the role of in-office

laser surgery in the oncologic setting is challenging and suggested that in-office procedures should be avoided in patients who failed radiation therapy and in patients with anterior commissure disease [4]. Hamdan and Ghanem stated that they do not advocate in-office blue laser therapy in laryngeal cancer until a large prospective study is conducted [23]. Lechien et al. stated that using KTP laser for malignant laryngeal lesions is still controversial [21]. Wellenstein et al. mentioned the lack of studies comparing the effectiveness of different lasers for specific laryngeal lesions [9].

In accessible English literature, we have not found any references on using Nd:YAG laser, 980 nm diode laser, and diathermy snare in OBLS. We have also not come across any studies related to treating primary glottic carcinoma in an office-based setting. To our knowledge, this is the first study that presents a series of patients with primary glottic carcinoma treated in an outpatient setting ($n=24$), including 79.2% of patients followed up over a year, and 33.3% of patients followed up over 5 years.

We share the above-mentioned opinion of Wellenstein et al. [15] and consider complete removal/eradication of the visible lesion (even for LP) as a goal of the office-based treatment. As shown in the previous section, we used biopsy forceps for cold eradication/removal of laryngeal lesions in 138/362 cases (38%) (for BL – in 44.9%, for LP – in 29.2%, and for HLL – in 10.3%). We applied diathermy snare excision for treating various types of lesions in 159/362 cases (43.9%) (for BL – in 49.5%, for LP – in 16.7%, for HLL – in 6.9%, and for glottic carcinoma – in 50%). In our opinion, using diathermy snare excision allows for a significant shortening of operative time, which is very important for increasing treatment completion rate [11, 22]. Another advantage of this technique is the possibility to apply OBLS for bulky lesions, such as advanced RE, cysts, bulky papillomas, etc., which is one of the main limitations of traditional office-based nonablative techniques, and to increase procedure safety (Fig. 6). We find the diathermy snare particularly useful for establishing the diagnosis of verrucous carcinoma in an office-based setting because of a thick layer of keratin on the tumor surface and major difficulties in obtaining adequate biopsy specimens by traditional forceps biopsy [37]. Laser vaporization of the laryngeal lesion was applied, mainly for treating premalignant and malignant lesions (for LP—in 79.2% of cases, for HLL – in 96.6% of cases, and for glottic carcinoma – in 100% of cases). Nd:YAG laser has been successfully used for many years in interventional bronchoscopy but has not gained wide acceptance in laryngology, mainly because of concerns related to its higher, compared to other lasers, penetration depth, and collateral thermal damage of tissues [22]. We applied laser vaporization for

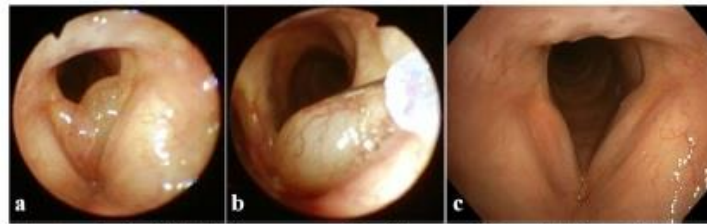


Fig. 6 **a** Bilateral Reinke’s edema (before OBLs). **b** Diathermy snare excision of the polypoid lesion of the left vocal fold. **c** Three months after diathermy snare excision of RE

BL in 24.6% of cases and as a main tool, only in 7.7% of cases. Our policy is to use the laser as a main/first-line tool only for flat, extended lesions. Whenever possible, we prefer to use the laser in combination with other techniques (prior cold removal by forceps or diathermy snare excision) as a second-line tool for vaporizing only the residual lesion. This approach prevents transmitting large amounts of laser energy to the treated tissue and, therefore, reduces the risk of collateral tissue injury. In treating malignant lesions, we consider the increased penetration depth of a laser as an advantage that allows good vessel coagulation for better hemostasis and vaporization of large amounts of tissue for efficient debulking. We used the Nd:YAG laser for most of our premalignant and malignant cases. Recently (from 2022), we started to use the 980 nm diode laser that has replaced the Nd:YAG laser in our office-based practice. The 980 nm diode laser is equally absorbed in oxyhemoglobin and water, has excellent coagulation properties, and allows the vaporization of large amounts of tissue. We applied the 980 nm diode laser in 20 patients (LP—2, HLL—4, glottic carcinoma—14). From our experience, with appropriate settings, the 980 nm diode laser has a similar therapeutic effect to the Nd:YAG laser. The laser ablation technique’s disadvantage is the impossibility of assessing the margins of the resected specimen. However, close follow-up and the “wait and see” strategy for early detection of possible tumor recurrence can partially compensate for this.

We find the obtained results encouraging and comparable with the possibilities of traditional OR surgery in all three groups of patients. Therefore, we share the opinion of Wellenstein et al. [9] that OBLs is the future for rapid medical diagnosis and treatment, with minimal health risks for patients.

Limitations of the study

As limitations of the study, we mention the retrospective nature of the study, the lack of a control group, the relatively small number of patients with premalignant and

malignant lesions, a relatively short period of follow-up for some patients, and the lack of either objective measurements or thorough subjective measurements on voice quality (e.g., VHI score) that should be further evaluated.

Conclusions

OBLs using Nd:YAG laser, 980 nm diode laser, diathermy snare, and flexible biopsy forceps can be considered as an alternative to traditional OR endoscopic laryngeal surgery for benign, premalignant, and malignant laryngeal lesions in selected patients. The proposed techniques allow for overcoming some limits of previously proposed methods and demonstrate the applicability of OBLs even for bulky lesions and primary malignant lesions, especially in patients with risks and contraindications for general anesthesia and direct laryngoscopy. Large prospective studies, including a large number of patients with longer follow-up periods, are worthwhile for validating the described approach and categorical conclusions.

Abbreviations

BL	Benign lesions
CS	Cold surgery
DEX	Diathermy snare excision
GA	General anesthesia
HLL	Hyperplastic laryngeal lesions
LA	Laser ablation
LP	Laryngeal papilloma/papillomatosis
OBFLS	Office-based flexible endoscopic laryngeal surgery
OBLs	Office-based laryngeal surgery
OR	Operating room
RE	Reinke’s edema
SCC	Squamous cell carcinoma
SLP	Superficial lamina propria

Authors’ contributions

PG contributed to the study conception and design, material preparation, data collection, analysis and interpretation, and the first draft of the manuscript. OA, ES, and DS contributed to study design, data analysis and interpretation. All the authors approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations**Ethics approval and consent to participate statement**

This study has been granted an exemption from requiring ethics approval by the Institutional Ethics Committee of "Nicolae Testemițanu" State University of Medicine and Pharmacy in view of the retrospective nature of the study and all the performed procedures being part of routine care. The research was conducted ethically, with all study procedures performed in accordance with the requirements of the World Medical Association's Declaration of Helsinki. This study has been granted an exemption from requiring written informed consent from participants in the study by the Institutional Ethics Committee of "Nicolae Testemițanu" State University of Medicine and Pharmacy.

Consent for publication

Written informed consent for publication was obtained from the participants whose images are included in the manuscript.

Competing interests

The authors declare no competing interests.

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Flexible Endoscopic Approach to Glottic Carcinoma: Five-Year Oncological Outcomes

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Summary: Objective. The objective of this study was to demonstrate the long-term oncologic efficacy of flexible endoscopic laryngeal surgery (FELS) in treating T1-T2 glottic carcinoma.

Methods. From 134 patients who underwent FELS, 90 patients (males—82, females—8), aged 18-83 (mean—56.9 ± 10.7) with early glottic carcinoma (T1a—27, T1b—24, and T2—39) were included in the study. Fifty-seven patients (63.3%) underwent FELS under local anesthesia with spontaneous ventilation, the rest of the patients were operated on under general anesthesia with superimposed high-frequency jet ventilation (SHFJV). Tumor ablation by Nd:YAG laser was performed in all the cases, preceded by diathermy snare excision in one-third of cases. In 20 of the T2 cases, adjuvant radiotherapy (RT) was performed.

Results. Five-year overall survival and ultimate disease control, including salvage treatment, was obtained in 82/90 patients (91.1%), cure with larynx preservation—in 88.9% of cases, disease-free survival—in 83.3% of cases, and ultimate local control with FELS alone—in 86.7% of cases. The best 5-year oncological results were obtained in the T1a group of treated patients, all the patients being alive and free of disease with the preserved larynx due to FELS alone. There was no evidence of better oncological results by FELS under general anesthesia with SHFJV over FELS under local anesthesia with spontaneous ventilation. Anterior commissure (AC) involvement worsened the treatment results. Adjuvant RT did not demonstrate an improvement of oncological results in the T2 group of patients.

Conclusions. FELS demonstrates oncological outcomes that are comparable to RT and transoral laser microsurgery and can be considered an oncologically efficient method of treatment of T1-T2 glottic carcinoma. Awake FELS is not inferior to FELS under general anesthesia with SHFJV concerning oncological efficacy. More studies on a bigger clinical material are necessary for definitive conclusions concerning the impact of AC affection and adjuvant RT on the oncological results.

Key Words: Glottic carcinoma—Nd:YAG laser—Flexible endoscopy—Endoscopic laser surgery—Office-based laryngeal surgery.

INTRODUCTION

Larynx carcinomas represent about 30-50% of all head and neck cancers.¹ About 75% of laryngeal carcinomas are confined to the glottic region.^{2,3} The majority of patients (75-80%) present with early glottic carcinoma.³ Early glottic carcinoma is usually defined as Tis, T1, and T2a disease (with unimpaired vocal cord mobility).⁴⁻⁶

Open partial laryngectomy (OPL), radiotherapy (RT), and transoral laser microsurgery (TOLMS) with CO₂ laser showed comparable oncological outcomes in the treatment of early glottic carcinoma.⁷ Nowadays, OPL is falling out of favor and is performed less and less for early glottic carcinoma, mainly because of high morbidity, and is reserved for more advanced disease.⁸⁻¹⁰ External beam radiation (EBR) and TOLMS with CO₂ laser are the main treatment methods

of T1-T2 glottic carcinoma, and the controversy between these two methods continues. The choice of treatment strategy varies among countries and institutions and largely depends on the surgeon and patient's preference and the availability of the equipment. The shortcomings of RT are the long duration of the treatment, increased costs, related complications (hypothyroidism, carotid artery narrowing, laryngeal chondronecrosis, and xerostomia), induction of second malignancy in the radiation area, and the impossibility of repeated EBR for recurrent or new primary head and neck malignancy.¹¹⁻¹⁴ TOLMS that has replaced OPL as the primary surgical treatment of early glottic carcinoma also has limitations, mainly related to difficult anatomy and inadequate lesion exposure, and also due to mandatory larynx suspension and general anesthesia with myorelaxation that is risky or contraindicated for some categories of patients (eg, tooth mobility or dental prosthetic work in the anterior maxillary region, ischemic cardiovascular disease).^{4,6,9,11,15-17}

Flexible endoscopic laryngeal surgery (FELS) could potentially overcome some of the abovementioned limitations of TOLMS and could be an alternative for patients who prefer office-based surgery.

The objective of this study was to evaluate the long-term oncologic efficacy of FELS in the treatment of T1-T2 glottic carcinoma and its relationship with tumor stage/extension, anterior commissure (AC) involvement, method of anesthesia/ventilation, and adjuvant treatment application.

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MATERIALS AND METHODS

This paper was approved by the Institutional Ethical Committee of “Timofei Moşneaga” Republican Clinical Hospital (Ref. N° 07/2023). This is a retrospective study. FELS was performed on 134 patients with T1-T2 glottic carcinoma in the period from 1993 to 2023. All surgical procedures were performed by a single surgeon. Written informed consent was obtained from the patients. The following selection criteria were used for the study: (1) consecutive patients with T1-T2 N0, M0 glottic carcinoma without impairment of vocal cord mobility, (2) the follow-up period of 5 years. For this reason, 44 patients were excluded from the study (Figure 1): 22 patients were under observation less than 5 years after the surgery, seven patients were lost to follow-up before 5 years from the surgery (<1 year—1, 1-2 years—2, 2-3 years—1, 3-4 years—2, 4-5 years—1), and 15 patients died from unrelated reasons before 5 years of follow-up (<1 year—2, 1-2 years—1, 2-3 years—6, 3-4 years—4, 4-5 years—2).

FELS was performed using a therapeutic flexible bronchoscope with a 2.6- to 3.0-mm working channel, flexible guide-based Nd:YAG laser (wavelength—1064 nm), a diathermy snare, and flexible biopsy forceps. All

endoscopic accessories were delivered to the target lesion through the working channel of the flexible bronchoscope. When the intervention was performed with spontaneous ventilation under local anesthesia and mild/moderate intravenous sedation, patients were treated in a sitting upright position. A flexible bronchoscope was introduced transnasally to the larynx. Topical anesthesia of the larynx mucosa was performed with Lidocaine 2% instilled during phonation, producing a laryngeal gargle. Photoablation of flat and infiltrative lesions was performed in continuous near-noncontact mode with power settings of 20-40 W. In some cases, diathermy snare excision of the bulky exophytic component of the tumor was performed before laser ablation (Figure 2). When necessary, repeated treatment sessions were performed at intervals of 2-7 days. Control biopsy from the tumor bed was performed at follow-up flexible laryngoscopy only in case of suspicion of persistent/recurrent tumor. When the intervention was performed under general anesthesia with superimposed high-frequency jet ventilation (SHFJV), the flexible bronchoscope together with accessories was introduced through the rigid suspensive jet laryngoscope (“Carl Reiner,” Austria). Awake procedures with spontaneous ventilation were

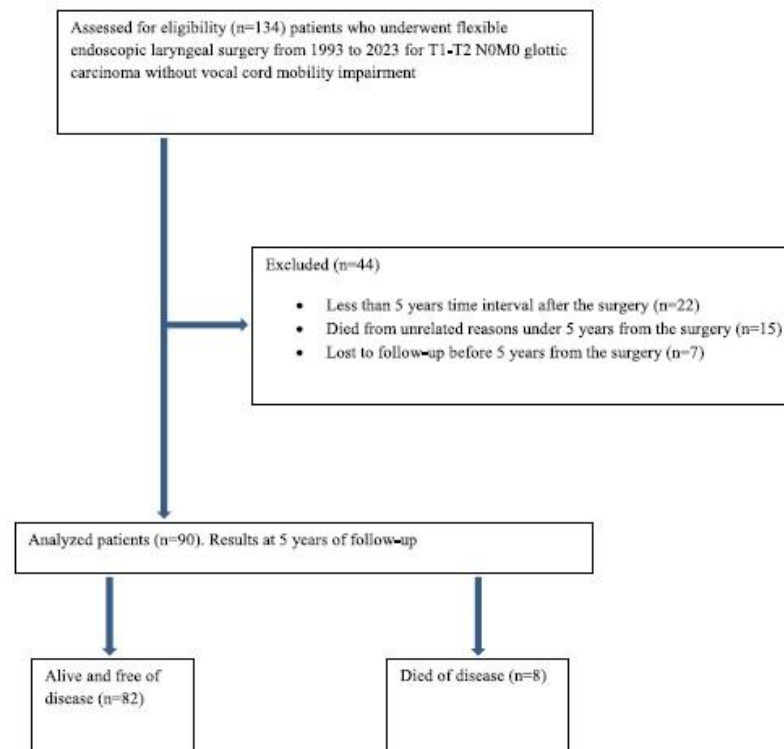


FIGURE 1. Inclusion and exclusion criteria for study participants and outcome summary.



FIGURE 2. FELS for glottic carcinoma. **A.** Initial tumor appearance. **B.** Diathermy snare excision. **C.** Laser ablation. **D.** Four months after endoscopic treatment.

chosen in cases of contraindications or major risk for general anesthesia with myorelaxation and/or transoral microsurgery, the patient's desire to undergo an awake endoscopic surgery, and patient compliance and ability to tolerate the awake procedure. The grade of patient compliance was estimated before the surgery during the diagnostic flexible laryngoscopy with a biopsy of the lesion by flexible forceps.

The data were recorded using Microsoft Office Excel 2007 (Redmond, WA). The data analysis was performed using the open-source programming tools RStudio (<https://www.rstudio.com/>) and Python (<https://www.python.org/>), ensuring the reproducibility of the statistical analysis. For the numeric variables, the five basic indicators were estimated: the mean value with standard deviation, the median value with interquartile range, the minimum value, and the maximum value, supplemented by 95% CI for the mean, these indicators being part of the descriptive statistics, either for the examined cohort or for the groups formed in the comparative evaluation of the examined groups. The comparative evaluation for numeric variables was performed using nonparametric tests depending on the number of groups and relationships between the groups (the Wilcoxon-Mann-Whitney test for dependent and independent groups or the Kruskal-Wallis test for independent groups, with multiple comparisons and Holm corrections being applied when necessary). For qualitative variables, relative frequencies were estimated, supplemented with 95% confidence intervals as well as absolute frequencies. Hypothesis testing for categorical data was performed using Pearson's chi-square test, Monte Carlo variant (100,000 samples). For all the statistical tests described above, the threshold value (α) was considered to be 0.05.

The following 5-year oncological outcomes of FELS were analyzed:

- Overall survival (OS);
- Ultimate disease control, including salvage treatment (UDC);
- Disease-free survival (DFS)/disease control without recurrence: the endpoint for DFS was the date of the first locoregional recurrence;
- Local control (LC): the disappearance of the primary tumor and regional lymph node metastases without

any locoregional recurrence; the endpoint for LC was the date of the first locoregional recurrence;

- Local recurrence (LRc): LRc included recurrent primary tumors (revealed > 6 months after the treatment) and persistent primary tumors (revealed < 6 months after the treatment);
- Death of disease (DD);
- Cure with larynx preservation (CLP);
- Ultimate disease control with FELS alone (UDC FELS).

The voice outcome after the treatment was assessed by scoring on a scale representing the patient's appreciation as follows: satisfactory voice/mild dysphonia, moderate dysphonia, and severe dysphonia.

RESULTS

Ninety patients met the selection criteria for the study (Figure 1): males ($n = 82$), and females ($n = 8$), aged 18–83 years (mean 56.9 ± 10.7 years). The histological structure of the tumors was represented by squamous cell carcinoma—71 (78.9%), verrucous carcinoma—15 (16.7%), hybrid verrucous carcinoma—2 (2.2%), and spindle cell carcinoma—2 (2.2%). Primary tumors were registered in 84 (93.3%) cases, and six patients (6.7%) presented with recurrent ($n = 3$) or persistent ($n = 3$) tumors after RT failure. According to the tumor extent, 27 patients (30.0%) had T1a stage, 24 patients (26.7%)—T1b stage (vocal fold carcinoma with AC involvement was considered as T1b stage), and 39 patients (43.3%)—T2 stage of disease (due to supraglottic or/and subglottic extension of the tumor without impairment of vocal cord mobility). The AC involvement was registered in 60 cases (66.7%).

In 70 cases (77.8%), only endoscopic treatment was applied, and in 20 cases (all of them—T2), postoperative narrow-field RT was also offered. The reasons for offering adjuvant RT for a part of T2 tumors were the following: (1) a large infiltrative tumor with extension to the AC (FELS was initially considered as a means of cytoreduction for increasing the efficiency of EBR), (2) lack of surgeon's confidence concerning oncological adequacy of the ablation, and (3) adverse pathological findings in biopsy fragments from tumor bed.

The following endoscopic techniques were applied: Nd:YAG laser ablation as a single technique—in 60 (66.7%) cases, and laser ablation preceded by diathermy snare excision of the tumor—in 30 (33.3%) cases. Awake interventions with spontaneous ventilation were performed in 57 (63.3%) patients, and general anesthesia with SHFJV was used in 33 (36.7%) cases.

There were no complications during or after FELS interventions. Five-year OS and ultimate disease control, including salvage treatment, was obtained in 82/90 patients (91.1%). Cure without recurrence (LC)/DFS was achieved in 75 cases (83.3%). Primary tumor recurrence/persistence was registered in 13 (14.4%) cases. In 11/13 (84.6%) cases, disease recurrence occurred during 2 years after surgery and in two cases—after 4 years. Successful salvage treatment for recurrent disease was registered in 7/13 (53.8%) patients: three patients underwent repeated FELS, salvage RT was offered to one patient, OPL was performed in one case, and two patients underwent total laryngectomy. Death of disease was registered in 8/90 cases (8.9%). Primary tumor progression was observed in six of these cases and regional metastatic disease without recurrence of the primary tumor—in the other two cases. Cure with larynx preservation was obtained in 80/90 (88.9%) cases. Ultimate disease control with FELS alone (without salvage RT or/and open surgery) was achieved in 78/90 (86.7%) patients.

The best results were obtained in the T1a group of treated patients (all the patients were alive, free of disease with the preserved larynx), followed by the T1b and T2 groups (Table 1). AC involvement worsened the treatment results, though the obtained data did not reach the statistical significance (Table 2).

General anesthesia with myorelaxation and SHFJV did not show any advantage over local anesthesia with spontaneous ventilation concerning oncological outcomes (Table 3).

Our expectation concerning the combination of FELS with adjuvant RT for T2 lesions was to reach better oncological outcomes than with FELS alone, but the obtained data did not support this hypothesis. The results in the group with combined treatment appeared to be even a little bit worse than in the group treated by FELS alone, to mention UDC/OS and DD (Tables 4 and 5).

The voice outcome mainly depended on the tumor extent and, particularly, on the AC involvement that impaired the quality of the voice. In the majority of patients with T1a lesions (77.8%), a satisfactory voice quality/mild dysphonia was registered (Table 6). None of the follow-up patients with preserved larynx had regrets about their treatment choice, regardless of the voice quality.

DISCUSSION

Nowadays, there is no consensus about the primary treatment approach to early glottic carcinoma. The choice of treatment method varies among countries and institutions

TABLE 1.
Five-Year Results of Glottic Carcinoma Treatment, Related to Tumor Stage

Results	Overall (T1-T2), n = 90	95% CI	T1a, n = 27	95% CI	T1b, n = 24	95% CI	T2, n = 39	95% CI	Statistic test	P value *
UDC/OS	82 (91.1%)	85%, 97%	27 (100.0%)	100%, 100%	23 (95.8%)	88%, 104%	32 (82.1%)	70%, 94%	7.2	0.027
LC/DFS	75 (83.3%)	76%, 91%	25 (92.6%)	83%, 102%	21 (87.5%)	74%, 101%	29 (74.4%)	61%, 88%	4.2	0.12
UDC FELS	78 (86.7%)	80%, 94%	26 (96.3%)	89%, 103%	22 (91.7%)	81%, 103%	30 (76.9%)	64%, 90%	5.9	0.053
CLP	80 (88.9%)	82%, 95%	27 (100.0%)	100%, 100%	22 (91.7%)	81%, 103%	31 (79.5%)	67%, 92%	7.1	0.029
DD	8 (8.9%)	3.0%, 15%	0 (0.0%)	0.00%, 0.00%	1 (4.2%)	— 3.8%, 12%	7 (17.9%)	5.9%, 30%	7.2	0.027
LRc	13 (14.4%)	7.2%, 22%	2 (7.4%)	— 2.5%, 17%	3 (12.5%)	— 0.73%, 26%	8 (20.5%)	7.8%, 33%	2.3	0.3

Abbreviations: CI, confidence interval; CLP, cure with larynx preservation; DD, death of disease; DFS, disease-free survival; LC, local control; LRc, local recurrence; n, number of patients; OS, overall survival; UDC, ultimate disease control; UDC FELS, ultimate disease control with FELS alone.
* Pearson's chi-squared test.

TABLE 2.
Five-Year Results of Glottic Carcinoma Treatment, Related to Anterior Commissure (AC) Involvement

Results	Overall, n = 90	95% CI	No AC involvement, n = 30	95% CI	AC involvement, n = 60	95% CI	Statistic test	P value*
UDC/OS	82 (91.1%)	85%, 97%	29 (96.7%)	90%, 103%	53 (88.3%)	80%, 96%	0.84	0.4
LC/DFS	75 (83.3%)	76%, 91%	27 (90.0%)	79%, 101%	48 (80.0%)	70%, 90%	0.81	0.4
UDC FELS	78 (86.7%)	80%, 94%	28 (93.3%)	84%, 102%	50 (83.3%)	74%, 93%	0.97	0.3
CLP	80 (88.9%)	82%, 95%	29 (96.7%)	90%, 103%	51 (85.0%)	76%, 94%	1.7	0.2
DD	8 (8.9%)	3.0%, 15%	1 (3.3%)	- 3.1%, 9.8%	7 (11.7%)	3.5%, 20%	0.84	0.4
LRc	13 (14.4%)	7.2%, 22%	2 (6.7%)	- 2.3%, 16%	11 (18.3%)	8.5%, 28%	1.4	0.2

Abbreviations: CI, confidence interval; CLP, cure with larynx preservation; DD, death of disease; DFS, disease-free survival; LC, local control; LRc, local recurrence; n, number of patients; OS, overall survival; UDC, ultimate disease control; UDC FELS, ultimate disease control with FELS alone.
* Pearson's chi-squared test.

TABLE 3.
Five-Year Results of Glottic Carcinoma Treatment, Related to Method of Anesthesia/Ventilation

Results	Overall, n = 90	95% CI	General anesthesia/ SHFJV, n = 33	95% CI	Local anesthesia/Spontaneous ventilation, n = 57	95% CI	Statistic test	P value*
UDC/OS	82 (91.1%)	85%, 97%	29 (87.9%)	77%, 99%	53 (93.0%)	86%, 100%	0.19	0.7
LC/DFS	75 (83.3%)	76%, 91%	28 (84.8%)	73%, 97%	47 (82.5%)	73%, 92%	0.00	> 0.9
UDC FELS	78 (86.7%)	80%, 94%	28 (84.8%)	73%, 97%	50 (87.7%)	79%, 96%	0.00	> 0.9
CLP	80 (88.9%)	82%, 95%	28 (84.8%)	73%, 97%	52 (91.2%)	84%, 99%	0.34	0.6
DD	8 (8.9%)	3.0%, 15%	4 (12.1%)	0.99%, 23%	4 (7.0%)	0.39%, 14%	0.19	0.7
LRc	13 (14.4%)	7.2%, 22%	5 (15.2%)	2.9%, 27%	8 (14.0%)	5.0%, 23%	0.00	> 0.9

Abbreviations: CI, confidence interval; CLP, cure with larynx preservation; DD, death of disease; DFS, disease-free survival; LC, local control; LRc, local recurrence; n, number of patients; OS, overall survival; SHFJV, superimposed high-frequency jet ventilation; UDC, ultimate disease control; UDC FELS, ultimate disease control with FELS alone.
* Pearson's chi-squared test.

TABLE 4.
Five-Year Results of T1-T2 Glottic Carcinoma Management, Related to Method of Treatment

Results	Overall (T1-T2), n = 90	95% CI	FELS, n = 70	95% CI	FELS+RT, n = 20	95% CI	Statistic test	P value*
UDC/OS	82 (91.1%)	85%, 97%	67 (95.7%)	91%, 100%	15 (75.0%)	56%, 94%	5.9	0.015
LC/DFS	75 (83.3%)	76%, 91%	61 (87.1%)	79%, 95%	14 (70.0%)	50%, 90%	2.2	0.14
UDC FELS	78 (86.7%)	80%, 94%	63 (90.0%)	83%, 97%	15 (75.0%)	56%, 94%	1.9	0.2
CLP	80 (88.9%)	82%, 95%	65 (92.9%)	87%, 99%	15 (75.0%)	56%, 94%	3.4	0.066
DD	8 (8.9%)	3.0%, 15%	3 (4.3%)	—	5 (25.0%)	6.0%, 44%	5.9	0.015
LRc	13 (14.4%)	7.2%, 22%	8 (11.4%)	4.0%, 19%	5 (25.0%)	6.0%, 44%	1.4	0.2

Abbreviations: CI, confidence interval; CLP, cure with larynx preservation; DD, death of disease; DFS, disease-free survival; LC, local control; LRc, local recurrence; n, number of patients; OS, overall survival; UDC, ultimate disease control; UDC FELS, ultimate disease control with FELS alone.
* Pearson's chi-squared test.

and considerably depends on the surgeon and patient's preference and the availability of the equipment. The rate of occult neck metastases for early glottic cancer is less than 10%, and it is now generally agreed that prophylactic treatment of the neck is not necessary if the tumor is classified radiologically as N0.⁹

Radiation therapy, TOLMS, and OPL demonstrate high and comparable cure rates,^{7,18} but all the abovementioned treatment methods have shortcomings. In the selection of treatment modality, several factors are taken into consideration: treatment duration, treatment cost, general medical condition of the patient, posttreatment voice outcome, preservation of future treatment options, and patient's preference for radiation or surgery.^{7,18}

OPL results in local control of 91-98% for T1 glottic carcinoma and 84-86% for T2 lesions.⁴ The shortcomings of OPL include (1) major surgical trauma, implying cutting normal anatomic structures (muscles, nerves, vessels, and cartilages) and resulting in postoperative pain and edema; (2) temporary tracheostomy (5-18 days); (3) temporary nasogastric tube placement due to swallowing impairment and aspiration episodes; (4) long hospitalization time (22-35 days); (5) poor postsurgical voice quality; (6) high rates (up to 51%) of postoperative complications, many severe (laryngeal stenosis, pneumonia, and perioperative deaths).^{4,7,19,20} Because of the abovementioned reasons, OPL presently is falling out of favor and is performed less and less for early glottic carcinoma, and is reserved for more advanced disease.⁸⁻¹⁰

Radiation therapy is still preferred for early carcinoma treatment in many institutions, demonstrating 80-90% cure rates for Tis-T1 glottic lesions.²¹ The drawbacks of RT include (1) long duration of treatment (6 weeks), associated with increased medical costs (RT is 2-15.5 times more costly than TOLMS) and travel commitments^{11,12,20,22,23}; (2) radioresistance of some tumors (even small lesions)²¹; (3) risk (up to 17%) of serious long-term complications (xerostomia, hypothyroidism, skin and salivary gland changes, persistent glottic edema and erythema, cervical myelitis, accelerated carotid artery stenosis, and laryngeal chondronecrosis)^{9,13,14,24}; (4) risk of development of a second malignancy, induced by radiation, especially in younger patients^{1,9,12,25-27}; (5) reduced efficiency in bulky tumors^{21,28}; (6) reduced efficiency in AC involvement^{21,28}; (7) reduced efficiency in verrucous carcinoma²¹ and risk of anaplastic transformation of this type of tumor²⁹; (8) impossibility of reusing RT in case of recurrent glottic carcinoma or new primary tumor in head and neck area that can occur in up to 20% of treated patients, limiting further treatment options¹¹; (9) difficult and delayed diagnosis of persistent or recurrent tumors due to persistent postradiation edema^{1,24}; (10) difficult salvage endoscopic laser resection in an irradiated larynx,³⁰ resulting in high rate (75%) of total laryngectomy in case of radiation failure²² and worse larynx preservation rate, compared with primary endoscopic surgery.^{8,16,24,31-33} Thus, RT is by far not an ideal primary treatment modality for early glottic carcinoma, and for T1is and T1a tumors, it was

TABLE 5.
Five-Year Results of T2 Glottic Carcinoma Management, Related to Method of Treatment

Results	Overall (T2), n = 39	95% CI	FELS, n = 19	95% CI	FELS+RT, n = 20	95% CI	Statistic test	P value*
UDC/OS	32 (82.1%)	70%, 94%	17 (89.5%)	76%, 103%	15 (75.0%)	56%, 94%	0.58	0.4
LC/DFS	29 (74.4%)	61%, 88%	15 (78.9%)	61%, 97%	14 (70.0%)	50%, 90%	0.07	0.8
UDC FELS	30 (76.9%)	64%, 90%	15 (78.9%)	61%, 97%	15 (75.0%)	56%, 94%	0.00	> 0.9
CLP	31 (79.5%)	67%, 92%	16 (84.2%)	68%, 101%	15 (75.0%)	56%, 94%	0.10	0.8
DD	7 (17.9%)	5.9%, 30%	2 (10.5%)	– 3.3%, 24%	5 (25.0%)	6.0%, 44%	0.58	0.4
LRc	8 (20.5%)	7.8%, 33%	3 (15.8%)	– 0.61%, 32%	5 (25.0%)	6.0%, 44%	0.10	0.8

Abbreviations: CI, confidence interval; CLP, cure with larynx preservation; DD, death of disease; DFS, disease-free survival; LC, local control; LRc, local recurrence; n, number of patients; OS, overall survival; UDC, ultimate disease control; UDC FELS, ultimate disease control with FELS alone.

* Pearson's chi-squared test.

suggested (even by radiation oncologists) that RT should be saved for situations of failure of all surgical options.⁹

Transoral CO₂ laser microsurgery is considered the gold standard of surgical management of early glottic carcinoma that replaced OPL as the primary treatment modality.^{6,34,35} The advantages of TOLMS include (1) limited surgical trauma and preservation of cartilaginous skeleton integrity^{7,36}; (2) avoidance of tracheotomy^{7,36}; (3) short duration of treatment with no or minimal hospitalization period^{7,37,38}; (4) easier and earlier detection of recurrent tumors than after RT and OPL^{5,37}; (5) uncommonness of complications other than persisting dysphonia³⁷; (6) smaller costs (50% or less) compared with RT and OPL^{5,7,12,20,22,23,39,40}; (7) possibility to be repeated and availability/preservation of all salvage treatment options in case of recurrent or second primary tumor, resulting in better larynx preservation rate, compared with RT.^{6-8,11,16,24,32,33,38,41} Vaculik et al in a systematic review and meta-analysis of T1 glottic cancer treatment outcomes state that with TOLMS, patients are approximately six times more likely to preserve their larynx than those treated with RT.⁸

With the advent of fiber-based laser technologies, other types of lasers, besides CO₂ laser, have been used for early carcinoma treatment in the last two decades. In a review article, Karkos et al present the advantages of 980-nm diode laser transoral microsurgery over traditional CO₂ laser microsurgery, such as the improved access to distant, angled, and difficult-to-reach regions, like the AC, due to its flexible fiber, mentioning similar oncological outcomes between 980-nm diode and CO₂ laser systems.³⁵ In recent years, laser ablation, using a fiber-based 532-nm KTP laser, has been proposed for early carcinoma management as an alternative to laser resection.^{3,18,34,42-45} This technique allows better preservation of the vocal fold's architecture and function. Similar to CO₂ laser resection, oncological outcomes and improved voice outcomes are mentioned.^{34,42,45}

TOLMS also has limitations: (1) endoscopic exposure of the lesion is not possible in some cases because of difficult anatomy (short neck, insufficient neck extension, large

tongue base, prominent incisors, retrognathism, temporomandibular joint ankylosis/reduced mouth opening, etc), resulting either in aborted procedure or inadequate resection; (2) possibility of tooth damage in case of tooth mobility or dental prosthetic work in the anterior maxillary region, associated with additional health problems and costs for the patient; (3) patients with ischemic cardiovascular disease may not tolerate the prolonged laryngoscopic suspension that stimulates the vagus nerve and may produce cardiac arrhythmia or silent myocardial infarction; (4) risks of general anesthesia with myorelaxation, related to patient comorbidities.^{4,6,9,11,15-17}

van Loon et al, as a result of an investigation of treatment preferences in patients with early glottic carcinoma who were given a choice between TOLMS and RT, found that 168/175 patients (96%) chose TOLMS, mainly because of shorter treatment duration and more treatment options in case of recurrence.³⁰

Office-based laryngeal surgery (OBLS) under local anesthesia with spontaneous ventilation using flexible endoscopes has become popular in recent years for the management of benign and premalignant lesions, opening a new era in laryngology and demonstrating some advantages over conventional TOLMS, including avoidance of risks of general anesthesia with myorelaxation and larynx suspension, economy of time, and lower costs.⁴⁶⁻⁵² Patients seem to prefer the awake OBLS under local anesthesia over TOLMS in the operating room (OR). Rees et al report that the majority (87%) of patients who underwent both, OR TOLMS and awake OBLS for the same pathosis, preferred the awake procedure, and 83% of these patients found OBLS more comfortable than TOLMS in OR.⁵³

FELS can overcome the abovementioned limitations of TOLMS and could be an alternative for patients who prefer OBLS. Lai et al were the first in English literature who report performing awake flexible endoscopic Nd:YAG laser treatment for early glottic carcinoma under local anesthesia. The authors present 27 patients with Tis-T1 glottic lesions who were followed up for 3 to 7 years, the

TABLE 6.
Five-Year Voice Outcome in the Group of Cured Patients with Preserved Larynx (n = 80)

Stage	T1a, n = 27	95% CI	T1b, n = 22	95% CI	T2, n = 31	95% CI	Statistic test	P value*
Overall (T1-T2), n = 80	21 (77.8%)	62%, 93%	5 (22.7%)	5.2%, 40%	8 (25.8%)	10%, 41%	27	< 0.001
Voice quality Satisfactory/Mild dysphonia	3 (11.1%)	- 0.74%, 23%	11 (50.0%)	29%, 71%	7 (22.6%)	7.9%, 37%		
Moderate dysphonia	3 (11.1%)	- 0.74%, 23%	6 (27.3%)	8.7%, 46%	16 (51.6%)	34%, 68%		
Severe dysphonia								

Abbreviations: CI, confidence interval; n, number of patients.
* Pearson's chi-squared test.

estimated cure rate being 85.2%.⁵⁴ In a review article, Wellenstein et al mention the lack of studies related to OBLs for early glottic cancer.⁵⁵ To our knowledge, to date, this study presents the largest series of patients, treated by FELS and followed up for 5 years after surgery.

We state that 5-year oncological outcomes of FELS, presented in this study, are comparable with published long-term results obtained by TOLMS and RT (Table 7).

The management of glottic carcinoma involving the AC is controversial.^{6,66} Despite therapeutic modality (RT, OPL, and TOLMS), tumor affection of the AC (particularly for infiltrating and ulcerating tumors) is considered a poor prognostic factor, and the recurrence rate up to 70% is mentioned.^{1,9,21,24,28,69} At the point of attachment of the vocal cords to the thyroid cartilage by Broyles' ligament, there is no perichondrium, so some authors consider this place as a weak point that favors tumor invasion of the cartilage, transforming a T1 tumor into a T4.^{1,6} Lesions affecting the AC are often understaged, the involvement of the thyroid cartilage being missed, resulting in treatment of T3-T4 lesions as T1-T2 with consequently poor outcomes.⁴ In some publications, tumor extension to the AC is considered as a contraindication to endoscopic management.^{4,17} Conversely, others consider Broyles' ligament as a protection for the cartilage and point at the negative impact of the AC involvement only for T2 tumors crossing the AC in the vertical plane.^{6,12,41} The higher recurrence rate for infiltrating and ulcerating tumors is considered to be related to deep superior and inferior extensions along the inner perichondrium of the thyroid cartilage.⁹ Shvero et al state that in case of tumor involvement of the AC, laser resection must include the AC until the thyroid cartilage, at least 0.5 cm of the subglottic area, and the anterior third of the other vocal fold.³⁹ Stephenson and Fagan recommend TOLMS with adjuvant RT for the primary treatment of glottic carcinoma with AC involvement in patients with adverse pathological findings (positive or uncertain margins).⁷⁰

In our series, patients with tumor extension to the AC showed worse oncological outcomes, compared to those without extension (Table 2), especially concerning local recurrence rate (18.3% vs 6.6%), though we could not demonstrate the statistical significance of our results due to insufficient number of observations. We consider that oncological outcome is more important than voice outcome in patients with glottic carcinoma, so sparing the AC during surgery to achieve a better voice quality is not relevant for this category of patients because of the high risk of persistent tumor. Tumor affection of the AC was also one of the main reasons for offering the adjuvant RT for a part of patients with T2 disease, but our data have not supported the supposition that postoperative RT could improve the oncological outcomes (Tables 4 and 5). Surprisingly, the results in the group with combined treatment (FELS and postoperative RT) appeared to be even a little bit worse than in the group treated by FELS alone, to mention UDC/OS (75.0% vs 89.5%) and DD (25.0% vs 10.5%) for the T2

TABLE 7.
Five-Year Results of FELS for Glottic Carcinoma, Compared with Historical Results of TOLMS and RT (From the Literature)

Results	FELS (Our results)	TOLMS (From the literature)	RT (From the literature)
UDC, including salvage treatment	For T1 and T2 disease, respectively: 98.0% (T1a—100%, T1b—95.8%) and 82.1%.	For T1 disease: 97% (Eckel), ⁵⁶ 96% (Zeitels and Burns) ¹⁸ ; for T2 disease: 80% (Zeitels and Burns). ¹⁸	For T1 disease: 98% (Pelliteri et al). ⁵⁷
LC/DFS	For T1 and T2 disease, respectively: 90.2% (T1a—92.6%, T1b—87.5%) and 74.4%.	For T1 disease: 85% (Peretti et al), ⁴¹ 86.3% (Eckel), ⁵⁶ 85-87% (Sjögren) ⁵ ; for T1a disease: 76.1% (Canis et al), ⁵⁸ 92.3% (Lee et al), ⁵⁹ 93.1% (Djukic et al) ⁶⁰ ; for T1b disease: 74.1% (Lee et al), ⁵⁹ 75% (Alkan et al), ¹ 77% (Gioacchini et al), ² 55.6% (Djukic et al) ⁶⁰ ; for T2 disease: 72.7% (Lee et al), ⁵⁹ 66-82% (Sjögren), ⁵ 59% (Peretti et al), ⁵¹ 77.3% (Warner et al), ⁶² 75.4% (Campo et al). ¹⁰	For T1 disease: 85-88% (Motta et al), ²⁰ 93% (Pelliteri et al), ⁵⁷ 88% (Jørgensen et al) ⁶³ ; for T1a disease: 94% (Khan et al) ⁶⁴ ; for T1b disease: 87% (Gioacchini et al), ² 83% (Khan et al) ⁶⁴ ; for T2 disease: 70-73% (Motta et al), ²⁰ 73% (Pelliteri et al), ⁵⁷ 67% (Jørgensen et al), ⁶³ 18% (Eckel), ⁵⁶ 77% (de Ridder et al), ⁵⁶ 75.8% (Warner et al), ⁶² 75.6% (Campo et al). ¹⁰
UDC with endoscopic surgery alone	For T1 and T2 disease, respectively: 94.1% (T1a—96.3%, T1b—91.7%) and 76.9%.	For T1 disease: 87% (Peretti et al), ⁵ 90% (Peretti et al), ⁴¹ 93-95% (Sjögren) ⁵ ; for T1a disease: 94% (Gallo et al), ³⁸ 98% (Lee et al), ⁵⁹ 98% (Chiesa-Estomba et al) ⁶⁶ ; for T1b disease: 91% (Gallo et al), ³⁸ 83.3% (Lee et al), ⁵⁹ 90% (Chiesa-Estomba et al) ⁶⁶ ; for T2 disease: 81.8% (Lee et al), ⁵⁹ 79-86% (Sjögren), ⁵ 76% (Peretti et al). ⁵¹	NA
CLP	For T1 and T2 disease, respectively: 96.1% (T1a—100%, T1b—91.7%) and 79.5%.	For T1 disease: 91.7% (Eckel), ⁵⁶ 99% (Zeitels and Burns), ¹⁸ 94-98% (Sjögren) ⁵ ; for T1a disease: 97.3% (Canis et al), ⁵⁸ 95% (Schrijvers et al) ³¹ ; for T2 disease: 80% (Zeitels and Burns), ¹⁸ 82-95% (Sjögren), ⁵ 88.8% (Hendriksma et al), ³³ 84% (Peretti et al). ⁵¹	For T1a disease: 77% (Schrijvers et al) ³¹ ; for T2 disease: 60.4% (Furusaka et al). ⁶⁷
DD	For T1 and T2 disease, respectively: 2.0% (T1a—0%, T1b—4.2%) and 17.9%.	For T1 disease: 1.5% (Wolfensberger and Dort). ²⁷	NA
LRc	For T1 and T2 disease, respectively: 9.8% (T1a—7.4%, T1b—12.5%) and 20.5%.	For T1 glottic disease: 11.2% (Eckel), ⁵⁶ 12.3% (Thomas et al), ¹⁷ 12.9% (Brandenburg), ²² 14% (Wolfensberger and Dort), ²⁷ 18% (Peretti et al) ⁵ ; for T2 disease: 26% (Peretti et al). ⁵	For T1 lesions: 16% (Brandenburg) ²² ; for T1a lesions: 14% (Schwaab et al) ⁶⁸ ; for T1b lesions: 16% (Schwaab et al) ⁶⁸ ; for T2 lesions: 36% (Schwaab et al). ⁶⁸

disease group, and UDC/OS (75.0% vs 95.7%) and DD (25.0% vs 4.3%) for the whole group ($P=0.015$). Our data support the data by Djukic et al who stated lower OS and disease-specific survival in patients who underwent post-operative RT, compared to those who were treated only by TOLMS.⁶⁰ More clinical data are needed to clarify this issue.

The limitations of our study are the following: the retrospective nature of the study, the lack of a control group

to compare our results (TOLMS and/or RT), and the lack of a thorough voice outcome assessment that would be useful for a follow-up study, though it was not the purpose of the present study. We decided to focus our study on oncological outcomes, but we also present the available data concerning functional outcomes (Table 6).

Concerning posttreatment voice outcome, both RT and TOLMS may produce an abnormal voice. Impairment of voice quality after RT is caused by edema, stiffness,

scarring, and atrophy. Voice quality after TOLMS can be reduced because of scarring of the operated vocal cord or glottis incompetence related to the depth of excision.⁴¹ The advantage of one method over another is still debatable. Greulich et al in a systematic review and meta-analysis, revealed no clinically significant difference in voice outcomes between RT and TOLMS.⁷¹ Brandenburg states that the size and location of the tumor may have a greater impact on the voice quality than the selected treatment modality (eg, AC involvement will result in poor voice outcome, regardless of the treatment modality used).²² Functional deficits are often considered to be acceptable in early glottic cancer.³⁴

Our data confirm that tumor extension has a statistically significant impact on voice quality (Table 6). Satisfactory voice/mild dysphonia was registered in 77.8% of the patients with T1 disease, whereas more than half of the patients with T2 disease postoperatively had severe dysphonia.

The limitation of tumor ablation versus resection is the impossibility of histologic examination of the margins of the resected specimen. The clinical value of positive resection margins is still debatable. It is generally accepted that a part of patients with positive margins after TOLMS for glottic carcinoma will not develop a recurrence, and the relationship between the status of resection margins and tumor recurrence is unclear.^{6,66} The assessment of histological specimens after laser excision is problematic because of carbonization and shrinking of the specimens.^{7,66} There is no unanimity among specialists concerning positive resection margins. Some authors consider that, in case of margin positivity, additional treatment should always be offered.⁷² Others advocate the “wait and see” strategy.^{6,73} Sigston et al state that 84% of their patients with positive resection margins would have received unnecessary additional treatment without the “wait and see” strategy.⁷³ Aluffi Valetti et al report that in 83% of patients with positive margins that were surgically re-excised, no residual carcinoma was detected.⁷⁴ Bertino et al consider that if surgical margins are clearly free of tumor during the surgical procedure, second treatment can be avoided even if histological specimens are positive.⁷ Lee et al report that oncological outcomes in margin-positive cases did not differ significantly from those of margin-negative cases, and suggest that the identification of surgical margin by an experienced surgeon may be trusted and considered more clinically predictive than a histologic assessment.⁵⁹ We support and practice the abovementioned “wait and see” strategy, taking into consideration the accessibility of the glottic region for visual examination, and do not routinely perform biopsy from the tumor bed, unless a persistent/recurrent lesion is suspected during follow-up laryngoscopy. The importance of patient cooperation and closely scheduled follow-up flexible laryngoscopy exams cannot be overemphasized for early detection of potential tumor recurrence. Thus, our recommendations for post-operative follow-up flexible laryngoscopy exams are as follows: once a month during the first year after surgery, once in 2 months during the second year, once in 3 months

during the third year, once in 6 months during the fourth and fifth year, and once a year after 5 years. In addition, for patients with T2 disease, we recommend a neck ultrasound exam once in 3 months during the first 2 years after the surgery.

CONCLUSIONS

FELS demonstrates oncological outcomes that are comparable to RT and TOLMS and can be considered an oncologically efficient method of treatment of T1-T2 glottic carcinoma.

Awake FELS is not inferior to FELS under general anesthesia with SHFJV concerning oncological efficacy and can be recommended for office-based management of early glottic carcinoma, especially for T1a lesions.

More studies on a bigger clinical material are necessary for definitive conclusions concerning the impact of AC affection and adjuvant RT on the oncological results.

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Declaration of Competing Interest

We declare that we have no competing interests in relation to the work.

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Flexible endoscopic laser surgery for early glottic carcinoma

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ABSTRACT

Objective: Flexible endoscopic laser surgery (FELS) is able to overcome some limitations of traditional transoral CO₂ laser surgery. The objective of this study was to assess the efficacy of FELS in the treatment of T1-T2 glottic carcinoma.

Method: We applied FELS for 120 patients with T1-T2 glottic carcinoma. Tumour ablation was performed with Nd:YAG laser. In 76 (63.3%) cases the intervention was performed under local anesthesia. Twenty nine (24.2%) patients (T1b - 2, T2-27) underwent postoperative radiation therapy (RT).

Results: Successful treatment, with local control and larynx preservation, was obtained in 106 cases (88.3%), with mean follow-up of 6.4 years. More than 50% of the patients were followed-up over 5 years.

Conclusions: FELS can be proposed as an alternative treatment method for patients with early glottic carcinoma. The advantages of the method include: possibility of applying treatment under local anesthesia, that allows avoiding of general anesthesia and its related risks; applicability to patients with contraindications to general anesthesia and patients with anatomic particularities, that make transoral microsurgery impossible, allowing avoidance of the laryngofissure and tracheotomy.

1. Introduction

Laryngeal cancer accounts for approximately 30–40% of malignant head and neck tumours and up to 2.5% of all malignancies of the human body. The glottic region being affected most frequently – approximately in 60% of cases [1].

There is no clear definition for early glottic carcinoma. Some authors include in this definition Tis, T1a and T1b stages [2]. Others include also T2 lesions [3].

Tumour spread into cervical lymph nodes in T1 glottic lesion is rare – under 1% of cases [2].

Transoral laser microsurgery (TLMS) with CO₂ laser, being the most popular surgical method for treatment of early glottic carcinoma at present, has some limitations and cannot be applicable in all the cases. Flexible endoscopic laser surgery (FELS), keeping the advantages of TLMS, is capable to overcome some limitations of traditional transoral laser surgery, being applicable in situations of difficult anatomy and in patients with major risk for general anesthesia.

The objective of this study was to evaluate the efficacy of FELS in the treatment of T1-T2 glottic carcinoma.

2. Materials and methods

This manuscript was approved by Institutional Ethical Committee of “Timofei Moşneaga” Republican Clinical Hospital (Ref. No 36).

We applied FELS for 120 patients with T1-T2 glottic carcinoma in the time period from 1993 to 2019. Written informed consent was obtained from the patients. All the interventions were performed by a single surgeon. Patients age varied from 18 to 83 years, men - 112, women - 8. According to the stage of the tumour, patients were categorized as follows: T1a- 34 (28.3%), T1b- 32 (26.7%), T2-54(45.0%). Morphology of the tumours was as follows: squamous cell carcinoma - 92 (76.6%), verrucous carcinomas - 20 (16.7%), hybrid form of verrucous carcinoma 4 (3.3%), spindle cell carcinoma - 2 (1.7%), carcinosarcoma - 2 (1.7%). Primary tumours were registered in 112 cases (93.3%), and in 8 cases (6.7%) there were persistent or recurrent post radiotherapy tumours. After tumour biopsy and histologic confirmation of tumour nature, endoscopic tumour ablation with Nd:YAG laser (1064 nm wavelength) was performed in 77 cases. In 43 cases laser ablation was preceded by diathermy snare excision of the exophytic component of the tumour. The number of treatment sessions varied from 1 to 9 (mean, 1.6) (Table 1). In 76 (63.3%) cases the intervention was performed under local anesthesia and intravenous sedation, with spontaneous respiration. In 44 cases

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Table 1
Number of treatment sessions, applied for endoscopic tumour eradication.

No. treatment sessions	No. patients
1	79
2	27
3	6
4	3
5	3
6	1
9	1
Mean - 1.6	120 (100%)



Fig. 1. Exophytic tumour, broadly implanted, affects the mid third of the right vocal fold.



Fig. 2. Diathermy snare excision of the exophytic component of the tumour.

(36.7%) a suspension laryngoscopy under general anesthesia with high frequency jet ventilation (HFJV) was used, in combination with flexible endoscopy. In 91 cases (75.8%) only endoscopic treatment was applied, and 29 (24.2%) patients (T1b - 2, T2-27) underwent postoperative radiation therapy (RT).

2.1. Surgical technique

When procedures are performed under local anesthesia, patients are treated in the up-right sitting position. Flexible therapeutic



Fig. 3. Tumour ablation with Nd:YAG laser.

bronchoscope (working channel - 2.8 mm) is introduced transnasally, after local anesthesia with Lidocaine spray 10%. For larynx anesthesia, Lidocaine 2% is instilled in the larynx by a catheter, introduced via working channel of the bronchoscope. When a prominent exophytic component of the tumour is present (Fig. 1), this is resected by diathermy snare, introduced via working channel of the bronchoscope (Fig. 2). The excision is performed in cutting setting. Flexible guide of the Nd:YAG laser (1064 nm) is introduced through the working channel of the bronchoscope for tumour ablation, that is done in continuous irradiation mode, the power being set up to 40 W (Fig. 3). When interventions are done under general anesthesia with HFJV, the flexible bronchoscope together with laser guide or diathermy snare is introduced through the rigid suspensive laryngoscope. When necessary, multiple treatment sessions are performed with 2-7 days time interval.

3. Results

The initial treatment was efficient (lack of recurrent or persistent tumour) in 98 cases (81.7%). Although it's known, that Nd:YAG laser has deeper penetration and produces more thermal damage in vocal fold tissue, than CO₂ laser, no excessive scarring was observed after laser procedures. Voice outcome was assessed as satisfactory by all the patients with T1a lesions. Severe hoarseness was observed only in patients with anterior commissure and contralateral vocal fold involvement. Poor voice outcome in this category of patients was anticipated and accepted by the patients, oncological outcome being a priority in these cases.

Persistent tumour or local recurrence was registered (in the period of 1 to 48 months, mean - 9.5 months) in 19 cases (15.3%), from which in 8 cases local control with organ preservation was obtained by repeated endoscopic intervention (4 cases), FELS combined with postoperative RT (3 cases) and open partial laryngectomy (1 case). In other 11 cases local control was not obtained (patients underwent either total laryngectomy or palliative treatment).

Tumour progression by regional lymph node metastasizing was registered in 3 cases (2.5%), all these patients died of disease.

Table 2
Follow-up without recurrence after treatment.

Follow-up without recurrence after treatment	(n - 106)
Up to 1 year	6 (5.7%)
1-3 years	27 (25.5%)
3-5 years	19 (17.9%)
Over 5 years	54 (50.9%)
Mean - 77 months (6.4 years)	

Table 3
Results of glottic carcinoma treatment, related to tumour stage and previous treatment.

Tumour stage (T) and previous treatment	Locoregional recurrence	Cure rate
Primary tumour T1a (n = 33)	1 (3.0%)	100%
Primary tumour T1b (n = 31)	5 (16.1%)	90.3%
Primary tumour T2 (n = 48)	12 (25.0%)	85.4%
Persistent or recurrent tumour after RT - T1 (n = 2)	0	100%
Persistent or recurrent tumour after RT - T2 (n = 6)	4 (66.7%)	33.3%

Successful treatment after initial or repeated treatment, with local control and larynx preservation, was obtained in 106 cases (88.3%), with follow-up range from 1 to 259 months, mean – 77 months (6.4 years). More than 50% of the patients were followed-up over 5 years (Table 2). Death of unrelated reasons was registered in 32 cases.

In the group of primary patients with T1a lesion, that underwent only FELS, local recurrence was observed in 1 case (3.0%), local control with larynx preservation and cure rate in this group was 100% (Table 3). In the group of primary patients with T1b lesion, local recurrence was observed in 16.1%, and cure rate in this group was 90.3%. In the group of patients with persistent or recurrent tumour after RT, with T2 lesion, locoregional recurrence was registered in 66.7%, cure rate in this group was only 33.3%.

4. Discussion

The priority of surgery or radiation therapy, as primary treatment approach for early glottic carcinoma, remains a subject of continuous debate. Both methods demonstrated good oncologic and functional results. The choice of the method depends on the experience and preference of the specialists, as well as preference of the patient, and varies among countries, institutions and specialists.

4.1. Radiation therapy

Tumours in T1 stadium are still today often submitted to RT. Cure rate after RT for Tis-T1 lesions is 80–90% [4]. In 10–20% of T1 lesions RT fails [5].

It was demonstrated, that larynx preservation rate after RT is worse, compared to surgery [6–8].

McGuirt W.F. et al. [9] did not find statistically significant differences in voice quality after RT, compared to laser surgery [9].

Efficiency of RT is highly related to tumour size. The greater the tumour bulk, the less well the lesion will do with RT [5].

For T2 lesions, local control rate of only 18% have been reported with RT, and a 40% local failure rate following transoral laser surgery (TLS) have been reported [10].

Using RT for early glottic carcinoma, impedes using it afterwards for a recurrent tumour or another primary tumour. These tumours can appear in the head and neck region in up to 20% of treated patients and can even induce carcinogenesis in atypical epithelium. In case of tumour recurrence, the only curative option is “salvage surgery”, that means a partial or total laryngectomy. When RT fails, 75% of surgical salvages require total laryngectomy. Another disadvantage of RT is long duration of the treatment (six weeks with five sessions a week), that brings additional medical costs and an increased burden of travel commitments [11–13].

Neck radiation is associated with serious complications: hypothyroidism, xerostomia, accelerated carotid artery narrowing, skin and salivary glands changes, persistent glottis erythema, necrosis of larynx cartilages [14–17].

There are reports concerning developing of a second malignancy, induced by RT of larynx carcinoma [18–21].

The above-mentioned data explain concerns of many specialists about using RT as a first line treatment for glottic carcinoma, especially in young patients.

4.2. Open surgery

Open partial laryngectomy assures local control in 91–90% for T1 and 84–86% for T2 glottic lesions [15].

During open surgery for glottic tumour exposure by external approach, normal anatomic structures are cut or resected. These include muscles, nerves, vessels and cartilages, resulting in postoperative pain and edema, that always requires a temporary tracheostomy (5–18 days). Deglutition impairment and aspiration episodes in postoperative period are common and require nasogastric tube placement for 15–16 days. Scar airway stenoses are common and often lead to unpredictable functional results. Hospital stay is long (22–35 days) [15,22,23]. All these limitations of the open approach led to efforts for developing of endoscopic techniques for treatment of glottic carcinoma.

4.3. Transoral laser surgery

Transoral laser microsurgery was first introduced in 1972 by Strong and Jako, when they coupled CO2 laser to a surgical microscope [3]. TLMS is based on following the actual tumour spread itself, resecting only the involved tissue and structures using narrow margins to spare unaffected structures and therefore improve functional results. The overwhelming majority of surgeons use the CO2 laser for TLMS [3]. Lee H.S. et al. [24] reviewed a single surgeon’s experience with TLMS for 118 patients with T1-T2 glottic lesions and found, that at 5 years, disease-free and overall survival rates of 87.9% and 92.2% were comparable to data reported for large cohorts treated with RT [24]. Feng Y. et al. [25] in a large meta-analysis, including 11 studies and 1135 patients with T1-T2 glottic carcinoma, demonstrated no significant difference in cure rates between TLMS and RT [25].

Among advantages of TLMS compared to RT and open surgery are mentioned [2,10,11,13,23,26,27]:

- Only 1–2 treatment sessions;
- Shorter hospital stay: the intervention requires hospitalization for 1 to a few days. There is a huge contrast between time spent recuperating from laser surgery and the time required for a full course of RT (5–6 weeks) or open surgery (4–8 weeks);
- Favorable cost-effectiveness ratio: TLMS demands much less costs (approximately 50%), compared to RT or open surgery;
- Reduced morbidity and less side effects: postoperative pain is minimal, integrity of cartilaginous skeleton and deglutition are not affected, patient begins oral feeding on the second day after surgery, the tracheostomy is not necessary, thus, the quality of life is unaltered;
- Quality of voice is good as long as the anterior commissure is not involved;
- Residual or recurrent tumour can be detected earlier than it can after open surgery or RT;
- Laser resection can be applied repeatedly, in contrast to RT or open surgery, and does not preclude further treatment: if the lesion recurs or another primary tumour appears, treatment options with larynx preservation (TLMS, RT, open partial laryngectomy) remain still available, that contributes to high larynx preservation rate. This is important because a second primary tumour in the head and neck region may occur in up to 20% of treated patients. If RT fails, 75% of the patients need total laryngectomy. In contrast, only 1.5% of patients with early glottic cancer, initially treated with endoscopic laser surgery eventually need total laryngectomy. The importance of meticulous follow-up of these patients for early detection of tumour recurrence is mentioned.

TLMS has also some disadvantages and limitations. Endoscopic exposure of the lesion is not possible in all cases because of anatomic difficulties (short neck, prominent incisors, large tongue base, short mandible, reduced mouth opening, cervical pathology). This makes maneuvering of the endoscope problematic resulting in either an aborted procedure or inadequate oncologic resection. Furthermore, patients with ischemic cardiovascular disease may not withstand the prolonged laryngoscopic suspension which stimulates the vagus nerve and may produce cardiac arrhythmia or silent myocardial infarction [3,28,29].

Anterior commissure is not easily accessible endoscopically and as a result lesions of this area are often understaged. The involvement of the thyroid cartilage is often missed or misjudged, with the result that true T4 lesion may be treated as T2 with consequently poor results. Therefore, many specialists do not recommend the use of endoscopic laser surgery for lesions of the anterior commissure [15]. Hod R. et al. [30] suggest for patients with short neck or anterior commissure involvement a laryngofissure procedure, followed by laser cordectomy [30]. Peretti G. et al. [31] mention, that tumours confined to the level of the glottis with mobile vocal cords are not deeply invasive and do not penetrate the underlying thyroid cartilage, which is protected by the fibroelastic tissue of Broyle's ligament. In contrast, anterior glottic lesions spreading to the base of epiglottis and/or the subglottis invade the thyroid cartilage in almost every case. The authors recommend that endoscopic treatment should be limited to selected cases of anterior commissure cancer, superficially spreading at the level of the glottis without extension to the supraglottis or subglottis [31].

Although transoral CO2 laser microsurgery is the most popular surgical method of treatment of early glottic carcinoma at present, it is sometimes difficult or impossible. Given this, studying and mastering the alternative endoscopic techniques seems reasonable.

4.4. Flexible endoscopic laser surgery

With the advent of flexible endoscopy and possibility to transmit the laser beam via flexible guide, the diagnosis and treatment of premalignant lesions in outpatient setting under local anesthesia began to develop. Several advantages of this approach are mentioned, with the most common including: avoiding risk of general anesthesia, cost-effectiveness and time saving [32,33].

In saying this, the use of flexible endoscopy for glottic carcinoma treatment is poorly reflected in the literature. In accessible English literature we have found a single reference concerning using of Nd:YAG laser under local anesthesia in 34 patients with Tis and T1 glottic carcinoma, with a cure rate of 85.2% being reported [34]. Therefore, to our knowledge, the present material (120 patients, that underwent FELS, from which more than 50% were followed-up over 5 years) is the largest series presented in the literature to date. Cure rate after only the initial treatment was 81.7%, and together with "salvage" therapy after the appearance of recurrent tumour – 88.3%. This is comparable with results obtained by traditional treatment modalities for glottic carcinoma (RT, open surgery, TLMS). FELS, keeping the advantages of TLMS, is capable to overcome some limitations of traditional transoral laser surgery, being applicable in situations of difficult anatomy (short neck, temporomandibular joint ankylosis, insufficient exposure of the anterior commissure etc.) and in patients with major risk for general anesthesia. A disadvantage of endoscopic tumour ablation with Nd:YAG laser is the impossibility to examine the margins of the resected tumour. However, this can be partially compensated for by multiple biopsy from the bed of the eradicated tumour. There is a controversy in the literature regarding the importance of the examination of margins of the resected tumour. Ansarin M. et al. [35] state that, if positive margins are found, additional treatment should always be given, margins being considered free if the distance to disease is at least 1 mm [35]. From the other part, Sjögren E. V. [3] mention, that in TLMS of early glottic carcinoma, it is generally accepted, that a proportion of patients with positive margins will not develop a recurrence, and the relationship between resection margin



Fig. 4. Endoscopic follow-up 1 year after tumour ablation. No signs of tumour recurrence are detected.

status and relapse rate is still unclear [3]. Some authors advocate a "wait and see" policy. Sigston E. et al. [8] state, that there are no convincing data to suggest, that the ultimate outcome is significantly altered by further immediate treatment. The authors, advocating "wait and see" policy, mention, that because of the readily accessible localization of glottic cancers, qualitative visual follow-up is adequate for monitoring patients. The authors conclude that 84% of their patients with positive surgical margins would potentially have received unnecessary additional treatment without this "wait and see" policy [8].

We consider that close follow-up of the patients after FELS permits early detection of possible tumour recurrences and application of adequate additional treatment for organ preservation. We recommend the following follow-up schedule for patients after FELS: first year after intervention – monthly; second year – once in 2 months; third year – once in 3 months; fourth and fifth year – once in 6 months; after 5 years – once a year (Fig. 4).

5. Conclusions

Our conclusions are as follows:

1. FELS is an efficient and feasible method, that can be proposed as an alternative treatment method for patients with early glottic carcinoma, provided close endoscopic follow-up. The advantages of the method that deserve mentioning are:
 - possibility of applying treatment under local anesthesia, that allows avoiding of general anesthesia and its related risks;
 - applicability to patients with contraindications to general anesthesia and patients with anatomic particularities, that make transoral microsurgery impossible, allowing avoidance of the laryngofissure and tracheotomy.
2. The best results can be obtained in primary T1a glottic carcinoma, the local control and cure rate being, by our data, 100%.
3. The most reserved prognosis can be attributed to the category of patients with persistent or recurrent post radiotherapy tumour with T2 extension, cure rate being, by our data, 33.3%.
4. Additional studies on a larger material are necessary, to clarify, if postoperative RT can improve cure rate in T2 lesions.

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Declaration of competing interest

None.

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Awake endoscopic laser surgery for early glottic carcinoma

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Abstract

The objective of this study was to demonstrate the oncologic efficacy of awake endoscopic laryngeal surgery in the treatment of T1-T2 glottic carcinoma. This is a retrospective study. Seventy-one patients with early glottic carcinoma (T1a- 26, T1b- 18, T2- 27) who underwent awake flexible endoscopic laryngeal surgery under local anesthesia and mild intravenous sedation were included in the study. In 64 cases (90.1%) only endoscopic tumor ablation by Nd:YAG laser (in 32.4% of cases being preceded by diathermy snare excision) was performed, and in 7 T2 cases postoperative radiotherapy was also offered. There were no complications during or after the endoscopic surgery. Ultimate control of disease, including salvage treatment, was obtained in 67 patients (94.4%). Cure without recurrence was achieved in 60 cases (84.5%). Local control without salvage radiotherapy or/and open surgery was achieved in 64 (90.1%) patients. Larynx preservation was obtained in 66 (93.0%) cases. At 5 years from the beginning of endoscopic treatment, 74.6% of the patients were alive and free of disease. The best results were obtained in the T1a group of treated patients, all the patients being free of disease with the preserved larynx. Awake endoscopic laryngeal surgery is a safe and oncologically efficient method of treatment of early glottic carcinoma that can be considered as an alternative to the traditional approach, primarily, for patients with risks/contraindications for radiotherapy, general anesthesia, and transoral microsurgery, and also for the patients who prefer to avoid general anesthesia with its related risks and would rather choose office-based laryngeal surgery.

Keywords Glottic Carcinoma · Nd:YAG Laser · Flexible endoscopy · Awake endoscopic surgery

Introduction

Carcinoma of the larynx represents about 30–40% of head and neck malignancies [1]. The glottic part of the larynx is affected in approximately 60% of cases [1, 2]. The definition of early glottic carcinoma is not unanimous. Some experts define it as early glottic cancer only Tis, T1a, and T1b stages [3]. Other authors also consider the T2 stage as early carcinoma [4]. The regional lymph node involvement in T1 glottic cancer is rare (under 1%) [3].

Radiotherapy, open surgery, and transoral CO₂ laser microsurgery have comparable oncological efficacy in the treatment of early glottic carcinoma, but all the above-mentioned methods have shortcomings. Some of

the known drawbacks of radiotherapy are the impossibility of reusing radiation for a recurrent or another primary tumor; long treatment duration with associated increased costs; related complications (xerostomia, accelerated carotid artery narrowing, hypothyroidism, laryngeal chondronecrosis, etc.); induction of second malignancy in the head and neck region [5–8]. Reported open surgery disadvantages are: cutting/resection of normal anatomic structures; temporary tracheostomy; swallowing impairment in the postoperative period; common development of cicatricial airway stenosis after the surgery; long hospitalization period [9, 10]. Nowadays, transoral CO₂ laser microsurgery is the mainstay in the surgical treatment of glottic carcinoma, nevertheless, this method also has limitations, mostly, due to anatomic particularities (temporomandibular joint ankylosis, short mandible, large tongue base, insufficient neck extension, etc.) that cause inadequate lesion exposure, and contraindications for general anesthesia [4, 11, 12].

Office-based laryngeal surgery is an evolving trend in modern laryngology that is successfully used in the

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management of benign and premalignant laryngeal lesions, and is preferred by the majority of patients [13], but is rarely practiced for the treatment of glottic carcinoma. Awake flexible endoscopic laryngeal surgery has the potential to overcome the limitations of transoral CO₂ laser microsurgery, but it is still unclear if this method is oncologically effective and safe for the patients. The objective of this study was to demonstrate the safety and oncologic efficacy of awake endoscopic laryngeal surgery (AELS) in the treatment of T1-T2 glottic carcinoma.

Materials and methods

This manuscript was approved by the Institutional Ethics Committee of “Timofei Moşneaga” Republican Clinical Hospital. This is a retrospective study. We performed flexible endoscopic laryngeal surgery (FELS) on 124 patients with T1-T2 glottic carcinoma in the period from 1993 to 2022. All surgical procedures were performed by a single surgeon who has skills in interventional bronchoscopy. In 77 cases (62.1%) interventions were performed as awake procedures under local anesthesia and mild intravenous sedation. Written informed consent was obtained from the patients. Selection criteria for the study were the following: (1) consecutive patients with T1-T2, N0, M0 glottic carcinoma without vocal cord mobility impairment, (2) time interval of at least 5 years after the endoscopic treatment, and (3) at least 2 years of the follow-up period (i.e. patients who met the first two criteria, but were not lost to follow-up and did not die from unrelated reasons before 2 years of the follow-up period). For this reason, 6 patients were excluded from the study (1 patient was under observation for 18 months, 2 patients died from unrelated reasons before 2 years of follow-up, and 3 patients were lost to follow-up before 2 years from the surgery (Fig. 1).

The first awake intervention for glottic carcinoma was performed on 10.03.1993. At that time, the clinic did not have either a CO₂ laser or surgical microscope. The only available options for patients with glottic cancer were either radiotherapy or open surgery. Having some experience in using Nd:YAG laser through the flexible bronchoscope for endoscopic ablation of tracheobronchial tumors, we proposed these tools for the ablation of glottic tumors. The patients were informed about awake endoscopic surgery as an alternative to radiotherapy and open surgery, and the preserved availability of both above-mentioned methods in case of endoscopic approach failure. Many patients readily accepted the proposed alternative. Patient cooperation is critical during awake endoscopic procedures. The grade of patient compliance

is estimated during the diagnostic flexible laryngoscopy with tumor biopsy by flexible forceps. Selection criteria for the awake endoscopic surgery were: contraindications or major risk for general anesthesia and/or transoral microsurgery, predominantly due to anatomical particularities (short neck, insufficient head extension, temporomandibular joint ankylosis, poor anterior commissure exposure, etc.), the patient desire to undergo an awake endoscopic surgery, and patient compliance and ability to tolerate the procedure. The cases with many treatment sessions are related to the above-mentioned period of lack of equipment for transoral laser surgery.

For AELS we used a therapeutic flexible bronchoscope with a 2.6-3.0 mm working channel (models: BF-1T10, BF-TE2, BF-1T60 (“Olympus”, Japan)), flexible guide-based Nd:YAG laser (wavelength: 1064 nm, model: LTN-102 (Russia)), a diathermy snare (oval-shaped, size 10–15 mm (“Micro-Tech”, China)), and flexible biopsy forceps (4.5 mm cup opening (“Micro-Tech”, China)). The accessories (laser guide, forceps, diathermy snare) were delivered to the target lesion through the working channel of the bronchoscope. Patients were treated in sitting up-right position. After mild intravenous sedation and local anesthesia of the nasal and pharyngeal mucosa with Lidocaine spray 10% (“Egis Pharmaceuticals”, Hungary), the bronchoscope was introduced transnasally to the laryngeal aditus. Laryngeal mucosa was anesthetized with Lidocaine 2% instilled through a catheter (model: PR-2B (“Olympus”, Japan)), inserted in the working channel of the bronchoscope, during phonation, producing a laryngeal gargle. Flat and infiltrative lesions were ablated by laser in continuous near non-contact mode, the power being set up to 40 W. In the presence of a bulky exophytic component of the tumor, diathermy snare excision was performed in some cases, and the laser was applied as a second-line tool for the ablation of the residual lesion (Fig. 2). When necessary, repeated sessions of AELS were performed with a time interval of 2–7 days. Control biopsy from the tumor bed was not performed routinely immediately after the intervention, but was performed at follow-up flexible laryngoscopic exams only in case of suspicion of persistent/ recurrent tumor.

The data were recorded and analyzed using Microsoft Office Excel 2007 (Redmond, WA, USA) and SPSS version 20.0 (IBM, Armonk, NY, USA).

Results

According to the selection criteria, 71 patients were eligible for the study (males- 65, females- 6). The age of the patients varied from 18 to 83 years (mean – 56.8 ± 11.6

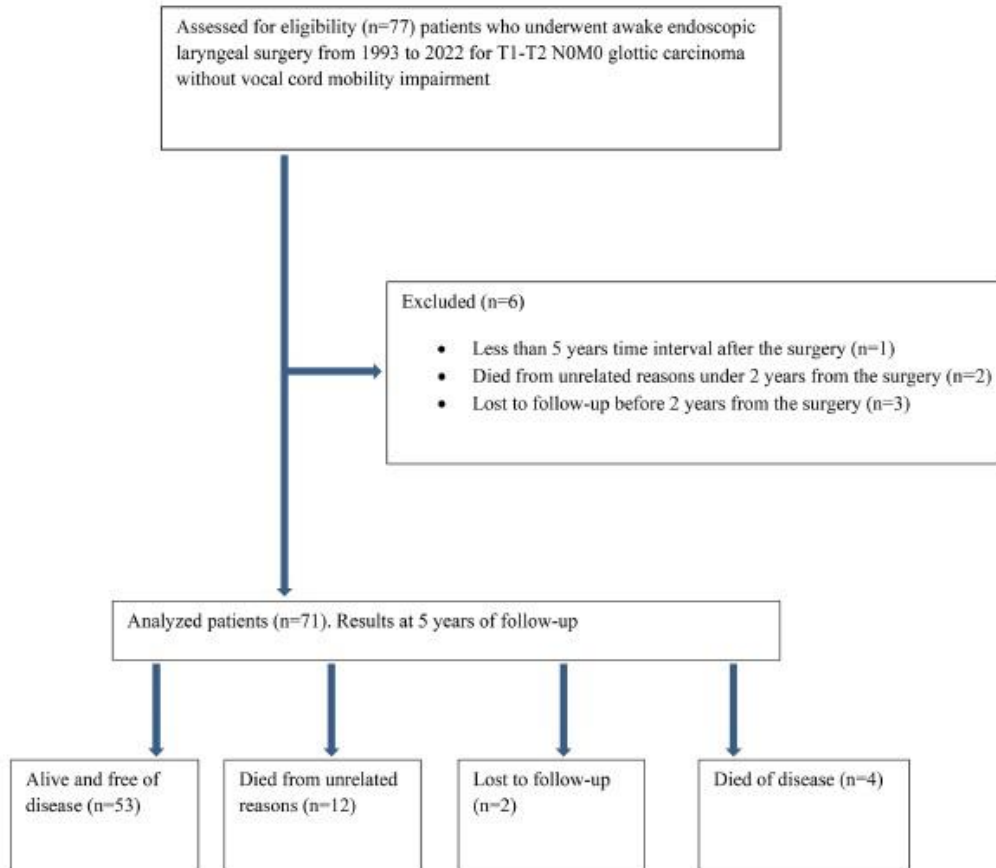


Fig. 1 Inclusion and exclusion criteria for study participants and outcome summary

years). The histological structure of the tumors was as follows: squamous cell carcinoma-54, verrucous carcinoma-13, hybrid verrucous carcinoma-1, and spindle cell carcinoma-3. In 67 (94.4%) cases we dealt with primary tumors and in 4 cases (5.6%) patients presented with recurrent (2) or persistent (2) tumors after radiotherapy. According to the tumor extent, 26 patients (36.6%) had T1a stage, 18 patients (25.4%) - T1b stage (vocal fold carcinoma with anterior commissure involvement was considered as T1b stage), and 27 patients (38.0%) - T2 stage of disease (due to supraglottic or/and subglottic extension of the tumor without impairment of vocal cord mobility). The anterior commissure involvement was in 42 cases (59.2%). In 64 cases (90.1%) only endoscopic treatment was applied, and in 7 cases (all of them - T2)

postoperative radiotherapy was also offered. The following endoscopic techniques were applied: Nd:YAG laser ablation as a single technique - in 48 (67.6%) cases, and laser ablation preceded by diathermy snare excision of the tumor - in 23 (32.4%) cases. The number of treatment sessions varied from 1 to 9 (mean - 1.9). In 34 (47.9%) cases treatment was realized in one session.

There were no complications during or after the endoscopic surgery. No patients had swallowing problems. Ultimate control of disease, including salvage treatment, was obtained in 67 patients (94.4%). Cure without recurrence was achieved in 60 cases (84.5%). Recurrent disease with successful salvage treatment was registered in 7 patients. In 6 (85.7%) cases disease recurrence occurred during 2 years after surgery and in 1 case - after

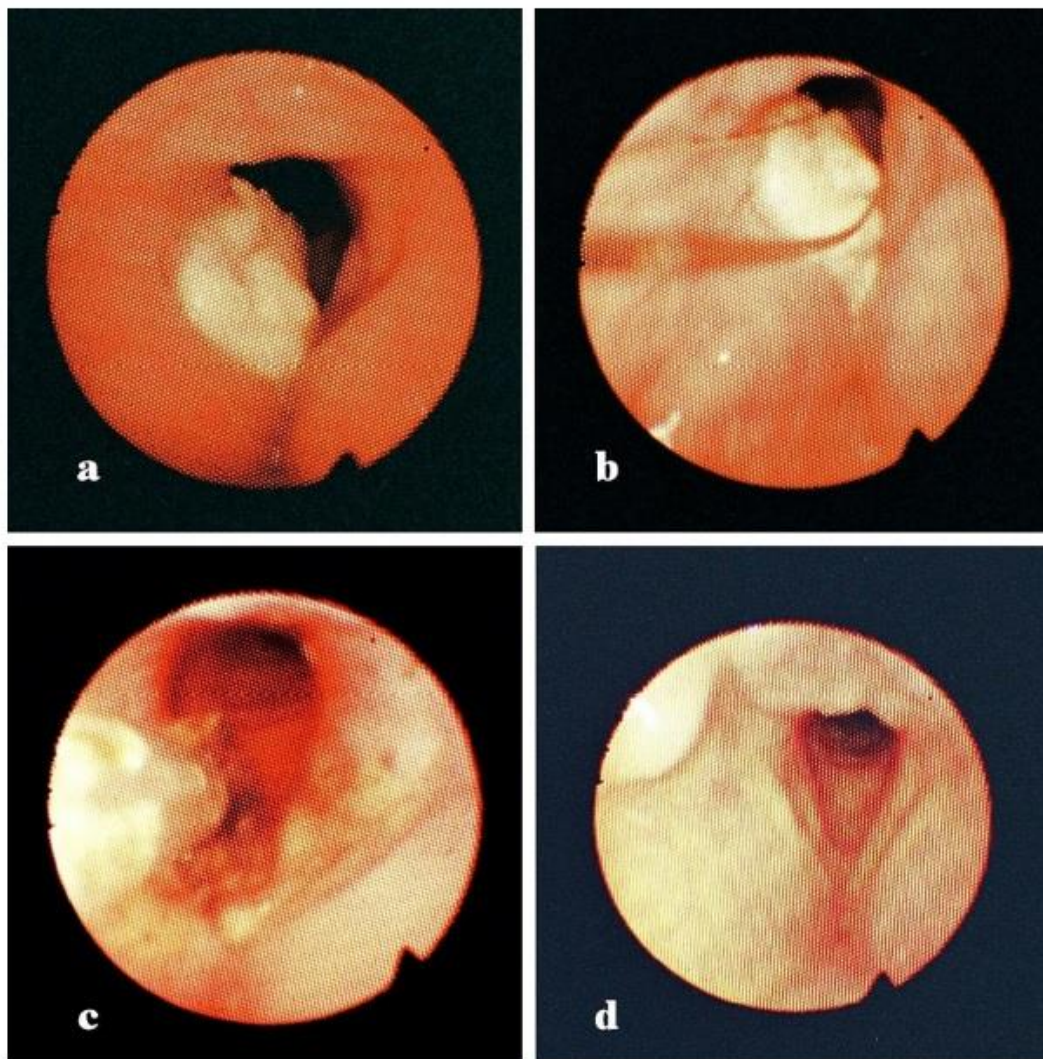


Fig. 2 Verrucous carcinoma of the glottis (T2). **a:** before the treatment; **b:** diathermy snare excision; **c:** Nd:YAG laser ablation; **d:** two years after endoscopic surgery

4 years. From 7 patients with recurrent disease, 4 patients underwent repeated FELS, salvage radiotherapy (RT) was offered to 1 patient, open partial laryngectomy was performed in 1 case, and 1 patient underwent total laryngectomy. Local control (LC) without salvage RT or/and open surgery was achieved in 64 (90.1%) patients. Larynx preservation (LP) was obtained in 66 (93.0%) cases. In the time interval from 2 up to 5 years after endoscopic surgery, 12 patients died of unrelated reasons and

2 patients were lost to follow-up. Death of disease was registered in 4 cases (5.6%). Primary tumor progression was observed in 2 of these cases and regional metastatic disease without recurrence of the primary tumor- in the other 2 cases. At 5 years from the beginning of endoscopic treatment, 53 patients (74.6%) were alive and free of disease (Table 1). The best results were obtained in the T1a group of treated patients, all the patients being free of disease with the preserved larynx (Table 2). In the

Table 1 Results at 5 years from the beginning of endoscopic treatment of glottic carcinoma

Result at 5 years of follow-up	No. patients (%)
Alive and free of disease	53 (74.6%)
Died of unrelated reasons (2–5 years of follow-up period)	12 (16.9%)
Lost to follow-up (2–5 years of follow-up period)	2 (2.8%)
Died of disease	4 (5.6%)
Totally	71 (100%)

Table 2 Results of glottic carcinoma treatment, related to tumor stage

Results	T1a (26)	T1b (18)	T2 (27)	Totally (71)	χ^2	P-value
Cure (free of disease)	26/26 (100%)	17/18 (94.4%)	24/27 (88.9%)	67/71 (94.4%)	3.08	> 0.05
Cure without recurrence	24/26 (92.3%)	15/18 (83.3%)	21/27 (77.8%)	60/71 (84.5%)	2.16	> 0.05
Cure without salvage RT and/or open surgery	25/26 (96.2%)	16/18 (88.9%)	23/27 (85.2%)	64/71 (90.1%)	1.84	> 0.05
Cure with larynx preservation	26/26 (100%)	16/18 (88.9%)	24/27 (88.9%)	66/71 (93.0%)	3.11	> 0.05
Death of disease	0/26 (0%)	1/18 (5.6%)	3/27 (11.1%)	4/71 (5.6%)	3.08	> 0.05

Table 3 Follow-up period in the group of cured patients

Follow-up period	No. patients
2–3 years	6
3–5 years	8
5–10 years	22
10–15 years	18
15–20 years	9
20–25 years	3
> 25 years	1
Mean = 10 years	Totally = 67

group of cured patients (67), 53 (79.1%) patients were followed up for more than 5 years (Table 3). The mean follow-up period in this group was 120 months. In the group of patients that were cured with larynx preservation (66), satisfactory long-term voice outcome/ mild dysphonia was registered in 27 cases (40.9%), moderate dysphonia – in 18 cases (27.3%), and severe dysphonia – in 21 cases (31.8%). Mild dysphonia was predominant in the T1a subgroup (88.5%), moderate dysphonia – in the T1b subgroup (62.5%), and severe dysphonia – in the T2 subgroup (58.3%) (Table 4).

Discussion

The treatment approach to early glottic carcinoma is still debatable. Radiation therapy, open surgery, and endoscopic surgery demonstrate similar oncological results and the treatment approach is largely dependent on institutional traditions, specialists preferences, and equipment availability.

Endoscopic laser surgery as primary treatment is attractive, particularly, because it leaves more salvage options in case of initial treatment failure and the future appearance of a new malignancy in the head and neck region [3, 14, 15]. Nowadays, transoral CO₂ laser microsurgery is the most used surgical method for glottic carcinoma management, being considered the gold standard [14, 16]. In the recent 2 decades, due to the development of fiber-based laser technology, other types of lasers, such as PDL, KTP, Thulium, Nd:YAG, and diode, have been also used in laryngology. Karkos et al., in a review article, report that 980 nm diode laser microsurgery has similar oncologic results, compared to CO₂ laser, mentioning improved access to difficult-to-reach areas, such as the anterior commissure [14].

Laser ablation, as an alternative to laser resection, has been gaining popularity in recent years. There are publications related to glottic carcinoma ablation by transoral microsurgery using fiber-based lasers (mainly, KTP laser) [15–22]. Zeitels et al., using KTP laser as an ablation tool, demonstrated comparable oncological results to CO₂ laser resection in the treatment of early glottic carcinoma [15]. Supphah et al., in a systematic review, also mention similar oncological outcomes of KTP laser ablation to CO₂ laser resection, mentioning improved voice outcomes [22].

Office-based awake laryngeal surgery is a developing trend in modern laryngology that has gained popularity in recent years, offering such advantages as avoidance of general anesthesia risks, cost-effectiveness, and time economy, but available publications include, mostly, small series related to benign and premalignant lesions management [23–29]. Office-based awake laryngeal

Table 4 Long-term voice outcome in the group of cured patients with preserved larynx

Voice quality	T1a (26)	T1b (16)	T2 (24)	Totally (66)	χ^2	P-value
Satisfactory/ mild dysphonia	23/26 (88.5%)	1/16 (6.2%)	3/24 (12.5%)	27/66 (40.9%)	46.41	< 0.01
Moderate dysphonia	1/26 (3.8%)	10/16 (62.5%)	7/24 (29.2%)	18/66 (27.3%)		
Severe dysphonia	2/26 (7.7%)	5/16 (31.3%)	14/24 (58.3%)	21/66 (31.8%)		

surgery seems to be preferred by the majority of patients. In the study by Rees et al. (2006), the authors mention that the vast majority (87%) of 54 patients with aerodigestive tract lesions who underwent both, operating room laser surgery under general anesthesia and office-based awake laser surgery for the same pathosis, preferred awake procedure, and 83% of these patients found the in-office unsedated treatment more comfortable than the surgery in the operating room [13].

Awake flexible endoscopic laryngeal surgery permits overcoming such limitations of traditional transoral CO₂ laser microsurgical approach as difficult anatomy and a major risk for general anesthesia, but there is a lack of publications relating to awake laryngeal surgery for glottic cancer. Lai et al. (2001) for the first time in English literature reported performing awake fiberoptic laryngoscopic laser treatment for early glottic carcinoma. The authors presented their experience of using Nd:YAG laser under local anesthesia in 34 patients with Tis and T1 glottic carcinoma, with a cure rate of 85.2% [30]. Wellenstein et al. (2018), in a review article, state the absence of studies related to office-based laser surgery for early glottic carcinoma [31]. Lechien et al. (2021), in a systematic review article, mention that the use of KTP laser in the office for malignant lesions is controversial [21]. We have not found in accessible English literature any other studies related to AELS for glottic carcinoma. To our knowledge, this manuscript presents the largest series of glottic carcinoma patients, treated by awake laryngeal surgery using Nd:YAG laser, with long-term follow-up. The obtained results (overall LC rate of 94.4%, LC without salvage RT or/and open surgery of 90.1%, and LP rate of 93.0%) are comparable with those obtained by radiotherapy [32–35], open surgery [36], and transoral CO₂ laser microsurgery [37, 38]. The results, obtained in the T1a subgroup of patients (overall LC rate of 100%, LC without salvage RT or/and open surgery of 96.2%, and LP rate of 100%) are particularly encouraging. The limitations of this study are the lack of a thorough voice outcome assessment and a comparison of pre and post-treatment voice outcomes that would be useful for a follow-up study. Future studies could also compare the relative voice improvements after different oncologic treatments. Concerning the voice outcome, it mostly depended on the tumor extent and, particularly, on the anterior commissure involvement that worsened the voice quality. None of the follow-up patients had regrets about their treatment choice regardless of the voice quality, being grateful for their disease-free survival and organ preservation. The cases with tumor affection of the anterior commissure are challenging for endoscopic treatment. The thyroid cartilage involvement is often

missed, and, as a result, these tumors are often understaged, with T3 and T4 tumors being treated as T1b and T2. Taking this into account, a part of specialists do not recommend endoscopic laser surgery for tumors involving the anterior commissure [36]. As the anterior commissure involvement was registered in the majority of the patients, included in our study (59.2%), we did not expect a great voice outcome in this subgroup of patients. We consider sparing the anterior commissure during surgery for obtaining a better voice outcome not relevant in patients with glottic carcinoma because it is related to an increased risk of a persistent tumor, so oncological outcome should be a priority. The limitation of ablative techniques is the absence of tumor resection margins that could be examined histologically. This drawback can be compensated by a control biopsy from the tumor bed [16, 19] and a “wait and see” strategy, taking into consideration the accessibility of the glottic region for visual examination [39]. Patient cooperation and closely scheduled follow-up flexible laryngoscopy exams can ensure early detection of potential tumor recurrence. According to our follow-up protocol, we recommend office flexible laryngoscopy once a month during the first year after surgery, once in 2 months during the second year, once in 3 months during the third year, once in 6 months during the fourth and fifth year, and once a year after 5 years. In T2 disease, we also recommend neck ultrasonography once in 3 months during the first two years after the surgery.

Conclusion

Awake endoscopic laryngeal surgery is a safe and oncologically efficient method of treatment of early glottic carcinoma that can be considered as an alternative to the traditional approach, primarily, for patients with risks/contraindications for radiotherapy, general anesthesia, and transoral microsurgery, and also for the patients who prefer to avoid general anesthesia with its related risks and would rather choose office-based laryngeal surgery.

Author contributions The author (PG) contributed to the study conception and design, material preparation, data collection and analysis, the first draft of the manuscript and approval of the final manuscript.

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Data availability The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request. The author has full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Declarations

Conflict of interest There are no relevant financial or non-financial interests to disclose.

Ethical approval This manuscript was approved by the Institutional Ethics Committee of “Timofei Mo’neaga” Republican Clinical Hospital (Ref. No 3/23). The research was conducted ethically, with all study procedures performed in accordance with the requirements of the World Medical Association’s Declaration of Helsinki.

Informed consent This study has been granted an exemption from requiring written informed consent from participants in the study by the Institutional Ethics Committee of “Timofei Mo’neaga” Republican Clinical Hospital in view of the retrospective nature of the study.

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Flexible endoscopic approach to verrucous carcinoma of the larynx

1 | INTRODUCTION

Verrucous carcinoma of the larynx (VCL) is a rare form of larynx cancer, which accounts for 1–4% of all malignant laryngeal neoplasms,^{1–4} and frequently causes problems in diagnosis and choice of the right treatment strategy. Diagnosis is difficult because the tumour appears macroscopically 'malignant' and microscopically 'benign'.⁵ The presence of the thick layer of keratin on the tumour surface creates major obstacles for obtaining an adequate biopsy material, which frequently results in inadequate traditional biopsy and inconclusive histologic response. As a consequence, the tumour is usually interpreted as benign, and the adequate treatment is delayed. Although currently there is no consensus regarding the treatment strategy to VCL, surgery is regarded as the first choice in an overwhelming majority of cases. Surgical interventions can be performed via an open approach, including laryngofissure, partial or total laryngectomy, and transoral CO₂ laser microsurgery. Flexible endoscopic laser surgery (FELS) can help overcome some limitations of traditional transoral laser surgery, being applicable in situations of difficult anatomy and in patients with major risk for general anaesthesia. The objective of this study was to assess the effectiveness of the flexible endoscopic approach for diagnosis and treatment of glottic verrucous carcinoma.

2 | METHODS

2.1 | Ethical considerations

This study was approved by the Institutional Review Board of 'Timofei Mosneaga' Republican Clinical Hospital.

2.2 | Participants

The study group consisted of 24 patients with glottic verrucous carcinoma, treated by a single surgeon by flexible endoscopic laser surgery between 1993 and 2019. Written informed consent was obtained from the patients. All the patients in the examined group were male, aged 38 to 80 (mean age 58) years. In all cases, the tumour affected the glottic region of the larynx. According to the stage of the

tumour, patients were categorised as follows: T1a- 7 (29.2%), T1b- 5 (20.8%) and T2- 12 (50.0%). Biopsy by forceps, introduced through the working channel of the flexible bronchoscope, in 22 of 24 cases (92%) was inconclusive. Received histologic responses were mainly 'leukoplakia', 'pachydermia', 'hyperkeratosis' and 'papilloma'. In order to obtain an adequate biopsy specimen for histologic confirmation of the nature of tumour, flexible endoscopic snare diathermy excision under local anaesthesia with lidocaine 2% was used. After histological confirmation of the nature of the tumour, flexible endoscopic LASER ablation (FELA) of the tumour was performed with Nd:YAG laser and a therapeutic flexible bronchoscope. The number of treatment sessions varied from 1 to 9 (mean - 2.1). In 14 cases (58.3%) tumour eradication was obtained in 1 session. In 14 cases, intervention was performed by flexible endoscopy, under local anaesthesia and intravenous sedation, with spontaneous respiration. In 10 cases, a suspension laryngoscopy under general anaesthesia with high-frequency jet ventilation (HFJV) was used in combination with flexible endoscopy because of either patient preference or surgical preference due to the size of the tumour. One patient (T2 hybrid form of VC) underwent post-operative radiation therapy (RT).

2.3 | Surgical technique

When procedures were done under local anaesthesia, patients were treated while sitting in the upright position. A therapeutic bronchoscope (2.8 mm working channel) was passed transnasally after giving topical anaesthesia with 10% lidocaine spray. For laryngeal anaesthesia, 2% lidocaine was dripped on the larynx through a catheter, which was passed through the working channel of the flexible bronchoscope. For the biopsy of the tumour, diathermy snare was passed through the working channel of the bronchoscope. Excision was performed in the cutting setting. An Nd:YAG laser (1064 nm) with flexible laser fibre was passed through the working channel of the bronchoscope for tumour ablation. The laser was set to a continuous wave mode with up to 40 W energy delivery. When interventions were done under general anaesthesia with HFJV, a therapeutic flexible bronchoscope together with laser guide or diathermy snare was passed through the rigid suspensive laryngoscope. When multiple treatment sessions were performed, intervals between sessions varied from 2 to 7 days.

3 | RESULTS

Local control was obtained in 22 cases (92%). In 19 cases (79%), no recurrence was revealed (Table 1). The average period of observation without recurrence in this group was 70 (range: 12–193) months. Persistent or recurrent tumours were registered in 5 cases (21%), and in 3 of them, local control with organ preservation was obtained by repeated FELS (2 cases) and open surgery (1 case). In 2 cases, patients underwent total laryngectomy (in both cases, the hybrid form of VCL was revealed). One patient died of tumour progression.

4 | DISCUSSION

4.1 | Diagnosis

VCL is characterised by discrepancy between macroscopic and microscopic appearances of the tumour, which means that tumour appeared macroscopically 'malignant' and microscopically 'benign'.⁵ If the clinician does not suspect a VCL and performs a routine biopsy of the tumour, as a rule, the histologic response will be 'benign', such as 'epithelial hyperplasia with keratosis, parakeratosis and acantosis' or 'papilloma'. The pathologist, without being guided and sensibilised by the clinician, will not give a conclusive response of VCL just based on the biopsy specimen. As a consequence, VCL is frequently underdiagnosed, resulting in late diagnosis in an advanced stage, inadequate treatment and unfavourable prognosis for the patient. Orvidas et al. (1997) report a high rate (52%) of wrong initial diagnosis of VCL, the lesion being catalogued as benign with a higher incidence of total laryngectomies in the group of patients with initial wrong diagnosis.⁶ The diagnosis of VCL is always clinicopathological, and macroscopic findings need correlation with microscopic findings,

Key points

- Close cooperation between the clinician and pathologist is vital for correct diagnosis of verrucous carcinoma of the larynx.
- Obtaining a large biopsy specimen is critical for conclusive histologic response for the diagnosis of verrucous carcinoma of the larynx. A conventional biopsy is often inadequate.
- Diathermy snare excision through the flexible endoscope allows performing an adequate biopsy, under local anaesthesia, in the outpatient setting.
- Transoral microsurgery is not possible in some patients, due to anatomic particularities and comorbidities.
- Flexible endoscopic laser surgery can be a valid treatment alternative for patients with verrucous carcinoma of the larynx, which allows avoidance of general anaesthesia, laryngofissure and tracheotomy.

which demands a high competency of both the laryngologist and pathologist and good communication between them for obtaining a correct diagnosis.^{5,6}

Conclusive histologic diagnosis demands obtaining large enough tissue fragments, including an epithelial-stromal interface, which would allow examination of the whole epithelial thickness and the adjacent stromal tissue (Figure 1). This is a difficult task, due to the thick keratin layer on the tumour surface and hard tumour consistency, and requires a special effort from the clinician, which usually is not necessary in case of biopsy of papilloma or typical SCC. Damm et al. (1997) report that biopsy specimens, obtained during transoral microlaryngoscopy, did not suffice for a

No recurrence	19 (79.2%)	Follow-up: 12–193 months (average=70 months)
Persistent or recurrent tumour	5 (20.8%)	<ol style="list-style-type: none"> 1. T2(VC): Recurrence after 4 months →FELS →48 months (4 years) without recurrence 2. T1a (VC): Recurrence after 4 years →open surgery (laryngofissure+tumour resection) →96 months (8 years) without recurrence 3. T1b(hybrid VC): Persistent tumour after 2 months →repeated FELS+RT(50 Gy) → Recurrence after 4 months after FELS→repeated FELS→2 months without recurrence 4. T2(hybrid VC): Recurrence after 4 months (keratinized SCC) → RT (60 Gy) → tumour progression →total laryngectomy 5 months after RT →23 months without recurrence 5. T2(hybrid VC): Persistent tumour, revealed by control biopsy after 4th session of FELS (nonkeratinised SCC) → total laryngectomy →death after 7 months

TABLE 1 Treatment results of VCL by FELS

FIGURE 1 Biopsy of VCL: (A) Inadequate biopsy by forceps; (B) adequate biopsy by diathermy snare excision

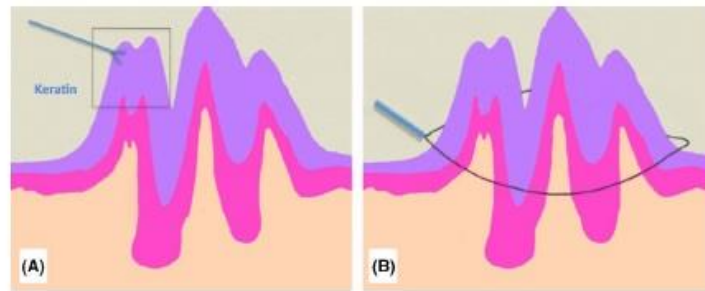
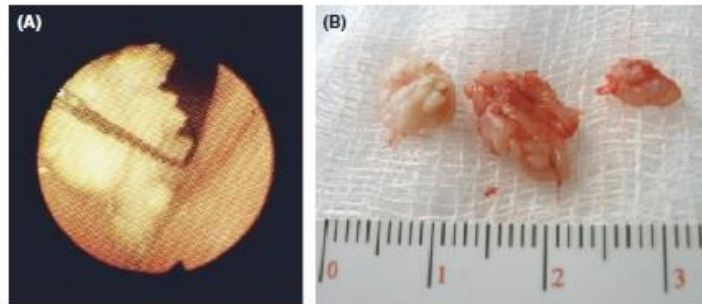


FIGURE 2 (A) Biopsy of VCL by diathermy snare excision; (B) tumour fragments obtained following biopsy by diathermy snare excision



proper diagnosis in 40% of cases, arguing for necessity of multiple biopsy specimens.⁷

We applied transnasal flexible endoscopy under local anaesthesia, with tumour biopsy by diathermy snare excision (Figure 2). This method allows obtaining large enough tumour fragments for a conclusive histopathologic diagnosis and performing the biopsy in the outpatient setting, avoiding general anaesthesia.

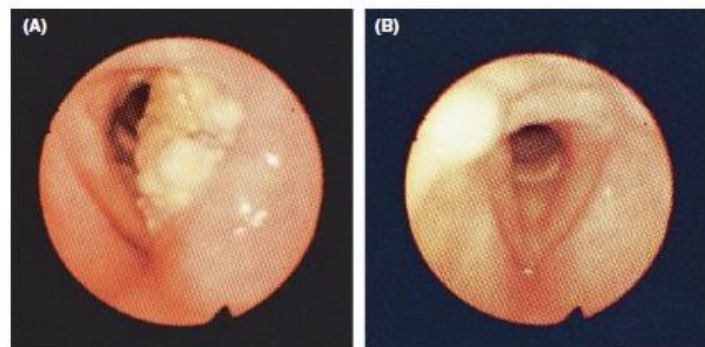
4.2 | Treatment

Due to the rarity of VCL, existent publications mainly are limited to case reports and small case series; hence, a definitive treatment strategy, at present, does not exist. From the date of first tumour

description till the present, management strategies of VCL remain a subject of continuous discussions. Surgical resection is the principal method of treatment for VCL at present, providing local control in 80% of cases.^{4,6} Application of RT in the treatment of VCL is controversial and is reserved, mainly for lesions that cannot be resected with sparing of larynx function, recurrent tumours, persistent tumours and hybrid tumours.^{3,8,9}

There are some publications concerning CO₂ laser application in endoscopic surgery for VCL with encouraging results.^{7,8} Transoral CO₂ laser microsurgery is possible in the majority of cases, but some disadvantages of the method are mentioned, specifically problems manoeuvring the endoscope in patients with a short neck or cervical pathology, and the risk that the surgeon will not be able to visualise the anterior commissure and that surgery will therefore not be as

FIGURE 3 (A) VCL: exophytic tumour, broadly implanted, with the tuberos surface, whitish colour, affects the left vocal fold, anterior commissure, with subglottic and supraglottic involvement; (B) three years after Nd:YAG laser ablation: no signs of tumour recurrence, laryngeal mucosa with no visible lesions



radical as it should be. In patients with short neck or anterior commissure involvement, the authors suggest a laryngofissure procedure followed by laser cordectomy.⁸

In accessible English literature, we did not find any references, concerning flexible endoscopic surgery for VCL. According to our experience, FELS for VCL demonstrates similar results, compared with traditional transoral CO₂ laser surgery, and allows overcoming difficulties that are encountered in patients with cervical problems or anterior commissure involvement, avoiding the laryngofissure and tracheotomy. Less aggressive biologic behaviour of VCL than typical SCC often allows performing of a sparing tumour ablation by FELS, even in bulky tumours that obstruct the laryngeal lumen (Figure 3).

5 | CONCLUSIONS

Close cooperation between the clinician and pathologist is vital for correct diagnosis of VCL. Obtaining a large biopsy specimen is critical for conclusive histologic response. Diathermy snare excision through the flexible endoscope allows performing an adequate biopsy under local anaesthesia in the outpatient setting. FELS can be a valid treatment alternative for patients with VCL, provided close endoscopic monitoring is assured. Some advantages of the method deserve to be emphasised: FELS can be performed under local anaesthesia, which allows avoiding general anaesthesia and its related risks, and applicability to patients with contraindications to general anaesthesia and patients with anatomic particularities, which make transoral microsurgery impossible (short mandible, lack of cervical extension, temporomandibular joint ankylosis, inadequate exposure of the anterior commissure).

KEYWORDS


flexible endoscopy, larynx, Nd:YAG laser, verrucous carcinoma

CONFLICT OF INTEREST

There are no conflicts of interest regarding this publication.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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CASE STUDY

Endoscopic ablation for glottic cancer in a patient with temporomandibular joint ankylosis



Ablación endoscópica del cáncer de glotis en un paciente con anquilosis de la articulación temporomandibular

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Case report

A 75-year-old man, nonsmoker, presented with a 3-month history of moderate progressive hoarseness.

Fiberoptic laryngoscopy demonstrated an exophytic flattened tuberos tumor with a rose-colored surface, affecting the whole right vocal fold (Fig. 1). Biopsy of the tumor was performed. The histologic exam revealed squamous cell keratinizing carcinoma (G2). No evidence of cervical lymphadenopathy was found either by palpation or ultrasound.

As accompanying diseases, the patient had temporomandibular joint ankylosis, limited head extension and an aggravated cardiologic status (arterial hypertension gr II, very high added risk; ischemic and hypertensive cardiopathy with impaired diastolic function of the left ventricle; mitral valve regurgitation gr II, tricuspid valve regurgitation gr II, pulmonary valve regurgitation gr I; moderate

pulmonary hypertension; long-standing persistent atrial fibrillation; high thromboembolic risk (CHADS2 - 3 p); moderate hemorrhagic risk (HAS-BLED - 1 p); CHF II NYHA).

Radiotherapy was not considered as the best treatment option for the patient because of an aggravated cardiologic status and potential adverse effects. Taking into consideration the limited tumor extent (T1aN0M0), contraindication for transoral laser surgery and major risk for general anesthesia, flexible endoscopic management of the tumor was proposed as the method of choice. Informed consent was obtained from the patient.

The patient was treated in the sitting upright position. Intravenous sedation with Propofol was applied. After local topical anesthesia with 10% Lidocaine spray, flexible therapeutic bronchoscope (working channel - 2.8 mm) was introduced transnasally to obtain good exposure of the glottis. For larynx anesthesia, 2% Lidocaine solution was instilled in the larynx by a catheter, introduced via the working channel of the bronchoscope. The flexible guide of the Nd:YAG laser (1064 nm) was introduced through the working channel of the bronchoscope for tumor ablation, that was done

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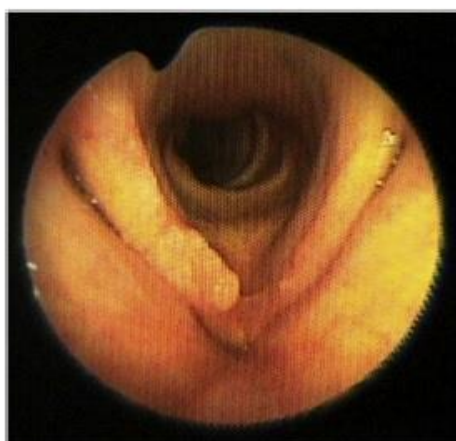


Figure 1 Exophytic flattened tuberosity tumor with rose-coloured surface, affecting the whole right vocal fold.

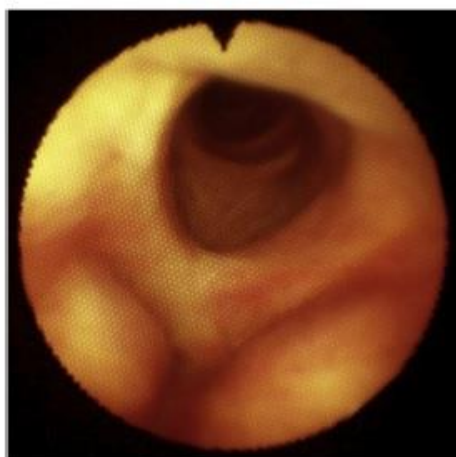


Figure 2 34 months after operation: no evidence of tumor recurrence.

in continuous irradiation mode, the power being set up to 40W. Postablation biopsies from the margins of the tissue defect were negative. The patient was discharged from the hospital 2 days later.

Follow-up flexible endoscopic exams in 2, 4, 7, 13 and 34 months after operation didn't reveal any evidence of recurrence of the laryngeal tumor (Fig.2). As a result of healing process of the postoperative wound, a scar deformation of the glottis with synechia formation in the region of the anterior commissure appeared, associated with severe dysphonia. Such a result was expected due to proximity of the tumor to the anterior commissure. No evidence of cervical lymphadenopathy was found.

Discussion

The available treatment opportunities for early glottic carcinoma, having comparable oncological outcomes, also have some limitations and contraindications.

Radiation therapy, being preferred by some authors as first-line choice, is related to worse organ preservation rate compared to surgery and contains the risk of some complications, that could affect quality of life of the patient (xerostomia, local edema, hypothyroidism, accelerated carotid artery narrowing, skin and salivary changes, limitation of neck movement, chondronecrosis, risk of second malignancy in the area of radiation, etc.).¹ Open surgery is related to increased morbidity, temporary tracheostomy, longer hospitalization time and higher costs.² Transoral CO₂ laser microsurgery has some advantages over radiotherapy and open surgery: lower morbidity, shorter treatment and hospitalization time, less damage to healthy tissues compared to those of radiotherapy, superior functional results compared to those of open surgery.³ Another approach, laser ablation by angiolytic lasers instead of laser resection, was proposed by Zeitels et al.⁴ The technique, using 585nm pulsed-dye laser (PDL) or pulsed-KTP laser (532 nm), allows tumor ablation to the level just beneath the tumor, resulting in maximal sparing of underlying normal tissue. Authors of some recent publications state that KTP laser ablation has similar oncological outcome and appears to be superior in terms of voice outcome compared to CO₂ laser resection.^{5,6} Meanwhile, Lahav et al. state that it is still not clear which factor is more important for better vocal outcome, the type of laser or surgical technique.⁵ There is a very limited experience of using diode lasers, that deliver the energy through a fiber guide, for glottic cancer treatment. Similar oncologic outcome and survival rate of diode laser (810 and 980nm), compared to CO₂ laser transoral microsurgery, are mentioned.⁷ The advantages of diode lasers are: portability, lower cost, easier setup, better coagulation and hemostatic effect, better access to distant and angled areas not easily reached with the direct straight beam of the CO₂ laser. Proposed techniques imply transoral microsurgery and continuous wave radiation in contact or near contact mode, using a laryngeal handpiece.⁷

Transoral laser microsurgery has also some limitations: short neck, large tongue base, poor exposure of the anterior commissure in some patients, reduced mouth opening, retrognathism, impaired cervical mobility and associated risk of general anesthesia.⁸ With the advent of flexible endoscopy and possibility to transmit the laser beam via a flexible guide, minimally invasive surgery under local anesthesia became attractive. The concept of office-based laryngeal surgery has evolved in the utilization of 2 types of angiolytic lasers: 585 nm pulsed-dye laser (PDL) and pulsed-KTP laser (532 nm).⁹ The techniques, used in office-based endolaryngeal surgery with these 2 types of lasers, are focused more on the induction of lesion regression, rather than on complete lesion ablation, and have not become popular for the treatment of glottic cancer.

In accessible English literature we have found only one article dedicated to flexible endoscopic Nd:YAG laser surgery of early glottic carcinoma,¹⁰ and no references concerning a flexible endoscopic approach in treatment of the

glottic carcinoma in a patient with temporomandibular joint ankylosis. We used the Nd:YAG laser as the only available option to transfer the laser beam through the flexible guide, using the flexible endoscope. We do not consider formation of the synechia in the region of the anterior commissure as a complication of the procedure, because the priority of the intervention was the complete ablation of the tumor and minimizing the risk of positive margins and not the voice quality. The patient was aware about this strategy and gave his written informed consent.

Flexible endoscopic laser surgery is a method that allows complete eradication of the tumor, avoiding the risk related to radiation therapy and general anesthesia. The impossibility of histologic exam of the margins of the resected specimen is a limitation of the technique, that can be compensated partially by multiple biopsies from the margins and the bottom of the tissue defect following photovaporization and close follow-up in short time intervals, that permits early detection of recurrence.

Conclusion

The obtained results demonstrate that, in some cases, related to anatomic particularities (e.g. temporomandibular joint ankylosis, limited head extension etc.) and major risk for general anesthesia, transnasal flexible endoscopy with laser vaporization under local anesthesia can be a reasonable alternative for performing a minimally invasive intervention for early glottic carcinoma. The method deserves future studies based on big clinical material.

Author's contribution

All authors contributed intellectually to the development of the work, qualify as authorship and have approved the final version. The authors declare that the work is original and has not been previously published or is under review by any other journal.

Informed consent

Informed consent was obtained from the patient included in the study.

Copyright transfer

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Conflict of interest

The authors have no conflicts of interest to declare.

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Flexible Endoscopic Surgery for Benign Nonepithelial Lesions of the Larynx

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Abstract

Aims The traditional approach for the management of benign laryngeal lesions is transoral microsurgery. In cases of anatomic particularities, such as insufficient cervical extension, short mandible, temporomandibular joint ankylosis etc., and contraindications for general anesthesia, transoral microsurgery is not possible. In such cases transnasal flexible endoscopic surgery under local anesthesia can be a relevant alternative. The purpose of the study was to assess the possibilities of flexible endoscopic management of benign nonepithelial lesions of the larynx.

Materials and methods Flexible endoscopic surgical interventions were performed on 315 patients with different benign nonepithelial lesions of the larynx. The larynx pathology was represented by following lesions: myxoid polyp, polypoid degeneration of vocal folds, fibrous polyp, angiofibrous polyp, angiomatous polyp, nonspecific granuloma, cyst, lipoma, neurofibroma and amyloidosis. In 97,8% of the cases interventions were performed under local anesthesia with spontaneous respiration. In 88,6% of the cases interventions were performed as outpatient procedures.

Results In all the cases the expected result was obtained – complete ablation of the visible lesion. In 7 cases repeated interventions were performed for recurrent lesions.

Conclusion Flexible endoscopic surgery is an efficient method for the treatment of benign nonepithelial lesions of the larynx, that offers a relevant therapeutic alternative, especially for the patients who have contraindications for general anesthesia or transoral microsurgery. The advantages of the method, worthy of mentioning, are positive economic effect and time economy, the intervention being possible in an outpatient setting for the majority of patients.

Keywords Benign lesions · Larynx · Endoscopic surgery · Flexible endoscopy

Introduction

Minimally invasive interventions for benign neoplastic lesions of the larynx present clinical interest in view of obtaining a radical curative outcome with minimal trauma. The traditional approach for the management of benign laryngeal lesions is transoral microsurgery, that has been successfully used for several decades. In cases of anatomic particularities, such as insufficient cervical extension, short

mandible, temporomandibular joint ankylosis etc., and contraindications for general anesthesia, transoral microsurgery is not possible. In such instances transnasal flexible endoscopic surgery under local anesthesia can be a relevant alternative. The purpose of the study was to assess the possibilities of flexible endoscopic management of benign nonepithelial lesions of the larynx.

Materials and Methods

This is a retrospective study. Flexible endoscopic surgical interventions were performed on 315 patients with different benign nonepithelial lesions of the larynx. The surgeon who performed the procedures has experience in interventional bronchology and applied some skills in flexible bronchoscopy for the surgical interferences on the larynx. The interventions were performed in challenging cases for patients

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Table 1 Ablative techniques for benign nonepithelial laryngeal lesions

Ablative techniques	Nr. Patients
Cold surgery (by forceps)	92
Diathermy excision (by snare)	118
Laser ablation	31
Cold surgery + Laser ablation	39
Diathermy excision + Cold surgery	6
Diathermy excision + Laser ablation	29
Totally	315

Table 2 Number of treatment sessions necessary for lesion eradication

Nr. Treatment sessions	Nr. Patients
1	305
2	8
3	1
4	1
Average	1,04

who were not fit for conventional oral micro-laryngoscopy and also in some non-challenging cases to understand the feasibility of the new technique. Patient's preference to avoid general anesthesia and to undergo the operation in an outpatient setting was also taken into consideration. Informed consent was obtained from all the patients. The larynx pathology was represented by the following lesions: myxoid polyp (103), polypoid degeneration of vocal folds (Reinke's edema) (14), fibrous polyp (39), angiofibrous polyp (76), angiomatous polyp (38), nonspecific granuloma (24), cyst (18), lipoma (1), neurofibroma (1) and amyloidosis (1).

Endoscopic interventions were performed with a flexible therapeutic bronchoscope (working channel – 2,8 mm). In 308 cases (97,8%) surgeries were performed under local anesthesia with spontaneous respiration and in 7 cases (2,2%) we used general anesthesia with high frequency jet ventilation, the flexible endoscope being introduced through the rigid suspensive laryngoscope. In 278 cases (88,6%) the interventions were performed as outpatient procedures.

The following ablative techniques were used to treat laryngeal lesions (shown in Table 1): cold surgery with flexible forceps, diathermy snare excision, Nd:YAG laser ablation and combined techniques.

The number of treatment sessions varied from 1 to 4 (shown in Table 2). In 96,8% of cases the treatment was done in one session.

When the procedure is performed under local anesthesia, patients are treated in the sitting upright position. The flexible therapeutic bronchoscope is introduced transnasally after local topical anesthesia with 10% Lidocaine spray. For larynx anesthesia, 2% Lidocaine solution (10–15 ml) is instilled in the larynx by a catheter, introduced via the working channel of the bronchoscope. Small lesions (1–4 mm) ablation is performed by cold surgery using flexible forceps, introduced through the working channel of the flexible endoscope (shown in Fig. 1a - b). More bulky lesions with a prominent exophytic component are resected by diathermy snare, introduced through the working channel of the bronchoscope (shown in Fig. 2a - c). The excision is done in cutting mode. The Nd:YAG laser (1064 nm) is used, if necessary, after diathermy resection, for the ablation of

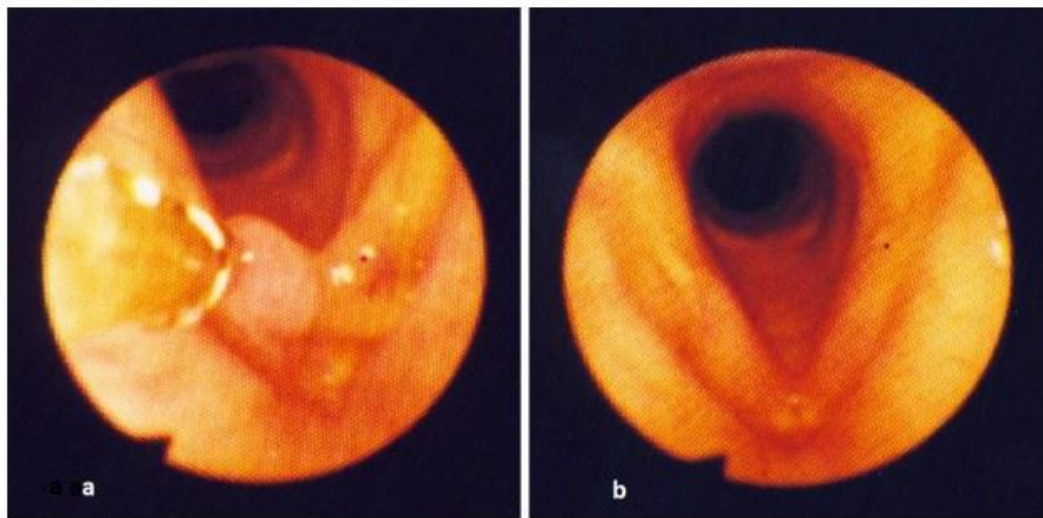


Fig. 1 a: Myxoid polyps of vocal cords: polypoid lesions located in the anterior third of both vocal cords on their free margin, with smooth surface and elastic consistence. Cold ablation by flexible forceps; b: Endoscopic view in 2 months after the ablation of vocal polyps

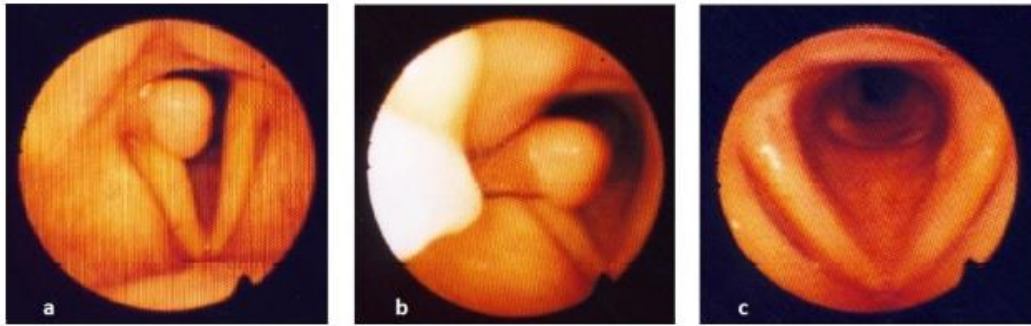


Fig. 2 a: Vocal process granuloma of the right vocal cord: polypoid mass on a large implantation base, with regular shape, smooth surface and hard consistence, located in posterior third of the right vocal fold;

b: Diathermy snare placement at the base of the polypoid lesion; c: Endoscopic view in 3 months after endoscopic resection of the granulomatous polyp of the right vocal cord: absence of the residual lesion

the residual lesion or as a main tool for the ablation of flat lesions. The flexible guide of the Nd:YAG laser is introduced through the working channel of the bronchoscope for the ablation of the lesion, which is done in continuous irradiation mode, the power being set up to 40 W. In patients with advanced grades (3 or 4) of Reinke's edema the polypoid lesions are entrapped in the diathermy snare, that is fixed at their base with subsequent resection. Superficial lesions (grade 1 or 2) are usually stripped by jumbo flexible forceps, introduced through the working channel of the bronchoscope. Good cooperation with the patient is needed during the procedure. When the lesion is resected, the patient is asked to cough out the resected specimen that is subsequently collected for the histologic examination. No patients had aspiration of resected specimen, some patients swallowed the specimen. In case of aspiration of the specimen in the tracheobronchial tree, it can be easily extracted as a foreign body. In case the histological examination is important and the specimen is swallowed, it is possible to find and extract it using flexible upper digestive endoscopy. The unседated procedures are usually well tolerated by the patients when thorough anesthesia of the vocal cords during fonation and also the anesthesia of the main carina are performed. In cases, when patients can not control their reflexes, the solution is an additional intravenous sedation and, if it doesn't work, general anesthesia with high frequency jet ventilation (HFJV) can be used, but it happens quite rarely. When interventions are done under general anesthesia with HFJV, the flexible bronchoscope together with the laser guide, forceps or diathermy snare is introduced through the rigid suspensive laryngoscope. When necessary, multiple treatment sessions are performed with 2–7 day intervals.

Results

In all treated patients the expected result was obtained – complete ablation of the visible lesion. In 7 cases repeated interventions were performed for recurrent lesions: non-specific granuloma – 6 from 24 cases (25%) (time interval of 1 to 6 months), angiofibrous polyp – 1 from 76 cases (1,3%). In 3 from 315 patients with benign nonepithelial lesions (0,95%) afterwards squamous cell carcinoma was diagnosed. In one case of neurofibroma of the vocal cord, carcinoma (T2) was revealed in the region of the ablated tumor in 4 years after the operation. In one case of angiofibrous polyp, carcinoma (T2) was revealed on the ipsilateral vocal cord after 5 years and 8 months from the operation, and in one case of angiofibrous polyp, carcinoma (T1a) was diagnosed on the contralateral vocal cord after 2 years and 4 months from the intervention. The follow-up period after successful treatment varied from 1 to 72 months. After the treatment, the functional results were assessed in accordance with the patient's subjective evaluation. All the patients with polyps, cysts, granulomas of the vocal cords evaluated their voice after the intervention as satisfactory. In the patients with polypoid degeneration of the vocal cords (Reinke' edema) after the intervention the voice improved, 5 from 14 patients (25,7%) evaluated their voice as satisfactory, 5 patients (35,7%) had mild dysphonia, and 4 patients (28,6%) had moderate dysphonia.

Discussion

The conventional approach to the management of benign laryngeal lesions is transoral microsurgery that has been used successfully for several decades [1–5]. A special merit in the development of this method is attributed to O. Kleinsasser [1–3]. The use of lasers revolutionized endolaryngeal

surgery. In 1972 M.S. Strong and G.J. Jako for the first time published their experience of using CO₂ laser in the treatment of different neoplastic lesions of the larynx [6]. So far, CO₂ laser is the most utilized type of laser in endolaryngeal surgery, which has the following advantages over cold surgery (Remacle M. et al., 1999, Chureshkin D.G. et al., 1990): high precision, reduced bleeding, minor reactive phenomena in the larynx, good functional results [7, 8].

With the advent of flexible endoscopy and possibility to transmit the laser beam via a flexible guide, minimally invasive surgery in an outpatient setting under local anesthesia became attractive. Zeitels S.M. and Burns J.A. (2007), mention in a review article, that the concept of office-based laryngeal surgery, instituted in 2001 and discussed for the first time at the American Laryngological Association in 2003, has evolved in the utilization of 2 types of angiolytic lasers: 585 nm pulsed-dye laser (PDL) and pulsed-KTP laser (532 nm) [9]. Currently, office-based surgical interventions are part of an evolving trend in modern laryngology, that have as advantages minimal invasiveness, reduced costs, avoiding general anesthesia and the possibility of real time monitoring of the vocal function during the surgery [10].

The majority of techniques, used in office-based endolaryngeal surgery, are focused more on the induction of lesion regression, rather than on complete lesion ablation. Due to delayed lesion regression, the final result of the treatment is expected in 4–5 weeks and more, and bigger polyps need repeated procedures. In bulky lesions these nonablative techniques, using angiolytic lasers, are not recommended, because of the risk of airway obstruction in the postoperative period [11]. The techniques of ablation for polyps and granulomas of vocal cords, combining KTP laser with cold surgery, using flexible forceps, are also described [10, 12]. The polypectomy with flexible forceps, preceded by application of KTP laser, results in more rapid therapeutic effect, than using the laser alone [10]. Other types of lasers are rarely used in office-based clinical practice. In an article published in 2017, Hu H.C. et al. [13] present a series of 40 patients with benign laryngeal lesions (including 10 patients with benign nonepithelial lesions of vocal cords), treated by CO₂ laser, transmitted through the flexible guide, in an outpatient setting, by photovaporization, with encouraging results. There is a very limited experience of using diode lasers, including, in an outpatient setting, for treating benign laryngeal lesions, the authors mentioning the efficacy of the method (Arroyo H.H. et al., 2016; Karasu M.F. et al., 2014; Hwang S.M. et al., 2015) [14–16]. The Nd:YAG laser (1064 nm), a very popular tool in interventional bronchology, is rarely used in laryngology. The caution of the specialists concerning this type of laser can be explained by the fact, that the cutting precision of Nd:YAG laser is smaller and the penetration capacity into biological tissue is

bigger than for other types of lasers, resulting in a concern about the potential excessive thermal injury to adjacent tissues. Poddubnyi B.K. et al., (2006) present the experience of using Nd:YAG laser under local anesthesia for treating 205 patients with benign laryngeal neoplasms, mentioning the feasibility and efficacy of the method [17]. We consider, that the thermal effect of the Nd:YAG laser can be minimized by using the laser as a second-line tool, in combination with cold surgery or diathermy excision, vaporizing only the residual lesion.

Although flexible endoscopic surgery under local anesthesia is not as precise as transoral microsurgery, the method, nevertheless, looks attractive due to a reduced intervention risk for the patients, especially for those with comorbidities, decreased costs and time savings, allowing the patients to keep the comfortable tempo of life. Flexible endoscopic surgery deserves to be considered also because of patients preferences, a lot of them preferring to avoid general anesthesia.

We consider flexible endoscopic surgery as an efficient method for the treatment of benign nonepithelial lesions of the larynx, which offers a relevant therapeutic alternative, especially for the patients who have contraindications for general anesthesia or transoral microsurgery. The advantages of the method, worthy of mentioning, are positive economic effect and time economy, the intervention being possible in an outpatient setting for the majority of patients. Although carcinoma incidence after endoscopic surgery for benign nonepithelial lesions is low (under 1%, by our data), we recommend endoscopic monitoring of the patients at least once a year for 5 years after the intervention.

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Author's Contribution All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Petru Gurău, Eusebiu Sencu and Sergiu Vetrician. The first draft of the manuscript was written by Petru Gurău and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Declarations

Competing Interests The authors have no relevant financial or non-financial interest to disclose.

Ethics Approval This study has been granted an exemption from requiring ethics approval by Institutional Ethics Committee of „Timofei

Moşneaga” Republican Clinical Hospital.

Consent Statement This study has been granted an exemption from requiring written informed consent from participants in the study by Institutional Ethics Committee of „Timofei Moşneaga” Republican Clinical Hospital.

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Key Message Flexible endoscopic surgery for benign nonepithelial lesions of the larynx is a relevant therapeutic alternative for patients, who have contraindications for general anesthesia or transoral microsurgery and for patients, who prefer office-based unsedated larynx surgery.

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CASE REPORT

A non-traditional endoscopic approach to laryngeal schwannoma

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Introduction

Laryngeal schwannomas are rare benign nerve sheath tumors that represent up to 1.5% of all benign laryngeal tumors.¹ All laryngeal schwannomas are encapsulated submucosal tumors that arise predominantly in the supraglottis¹ and originate mostly from the internal branch of the superior laryngeal nerve.^{1,2} The symptoms usually develop over years and include hoarseness/dysphonia, inspiratory dyspnea, and foreign body sensation during swallowing.² The diagnosis is based, mainly, on flexible laryngoscopy, imaging techniques, and histological exam.

A case of non-typically located laryngeal schwannoma is reported below, and a non-traditional endoscopic approach to treating obstructive laryngeal schwannoma as a means of avoidance of external surgical approach and minimizing of surgical trauma is discussed.

Case report

A 29-year-old man presented with a 12-year history of progressive hoarseness and inspiratory dyspnea. Six years ago, the patient was consulted in another hospital, a larynx tumor

was detected, and open laryngeal surgery was proposed, but the patient rejected the operation.

Computed tomography examination with contrast showed a broad-based hypodense mass, emerging from the posterior and right lateral wall of the larynx, with dimensions of 3.6 × 1.8 × 1.6 cm, occupying all three parts of the larynx and obstructing approximately 80% of the laryngeal lumen, without signs of erosion of the adjacent cricoid cartilage (Fig. 1).

Flexible laryngoscopy revealed on the posterior laryngeal wall an exophytic broad-based tumor, with irregular shape and hard-elastic consistency, the surface being smooth and glossy with accentuated vascular pattern, with approximate dimensions of 4.0 × 2.0 × 2.0 cm, that considerably obstructed the lumen of supraglottic, glottic and subglottic parts of the larynx. The superior margin of the tumor was appreciated 0.3 cm above the upper margin of the arytenoids, and the inferior margin of the tumor was appreciated 1.5 cm below the vocal cords. The endoscopic appearance was suggestive of a benign non-epithelial laryngeal tumor (Fig. 2a-c).

Endoscopic management was selected as the first-line approach for this case. Written informed consent was obtained from the patient. After preventive tracheostomy, direct suspension rigid laryngoscopy combined with flexible laryngoscopy using a therapeutic flexible bronchoscope under superimposed high-frequency jet ventilation was per-

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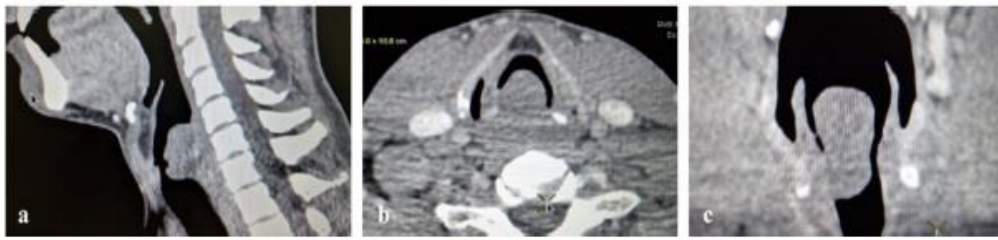


Figure 1 Computed tomography image of laryngeal schwannoma. (a) Sagittal view; (b) axial view; (c) coronal view.

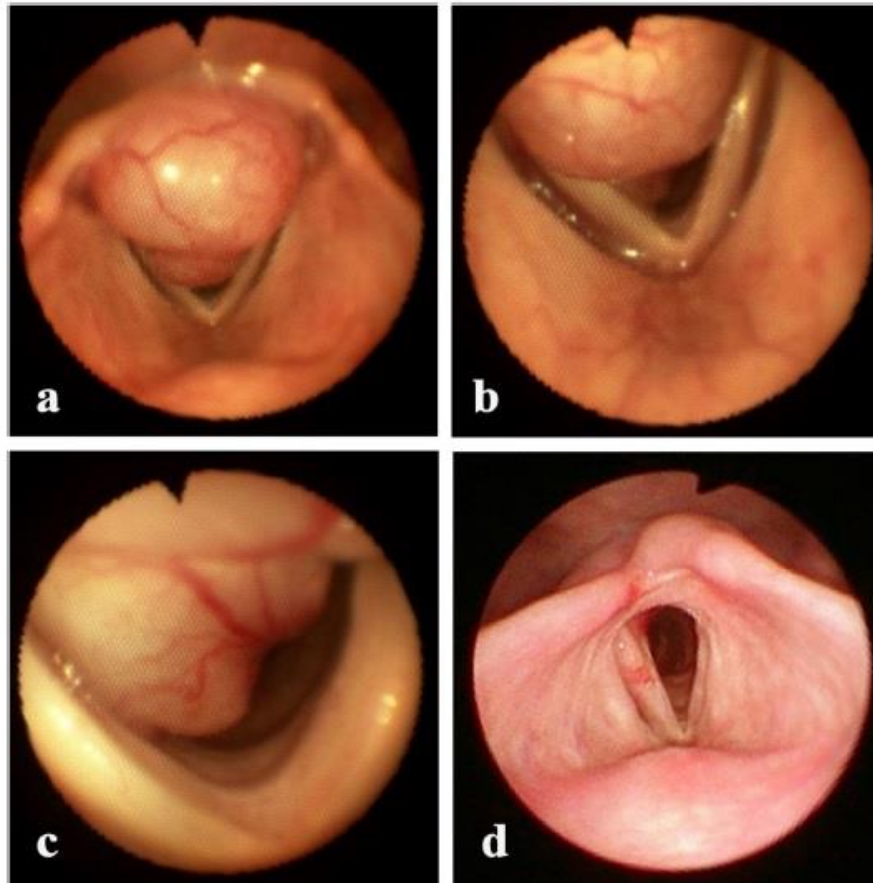


Figure 2 Endoscopic appearance of laryngeal schwannoma. (a) Supraglottic portion; (b) glottic portion; (c) subglottic portion; (d) 7-months after surgery: no visible laryngeal tumor.

formed. Initially, incisions using a 980/1470 nm diode laser (20 W) were made at the upper and lower (via tracheotomy orifice) margins of the tumor base, the flexible laser guide being introduced through the working channel of the flexible

bronchoscope. In the following step, cold resection/coring out of the tumor by the bevel of the rigid bronchoscope was performed. A minor bleeding/oozing was encountered after cold resection. Finally, laser coagulation of the bleeding sur-

face and vaporization of tumor remnants was performed at the base and margins of the tumor bed. The patient was decannulated 3 days later and discharged home on the fifth postoperative day. The histological exam revealed a schwannoma.

Flexible laryngoscopy, performed 7-months after the operation, showed no tumor recurrence, free laryngeal lumen, and minor scar changes of the mucosa of the posterior wall of the larynx (Fig. 2d). The patient's voice and respiration were completely restored.

Discussion

The larynx is an extremely rare location for schwannomas. Approximately 130 cases had been reported in the literature up to 1993.²

The most common laryngeal schwannoma is located in the false vocal folds (45.8%), followed by the aryepiglottic folds (33.3%), less frequently it arises from the true vocal folds (16.7%), epiglottis (9.7%), subglottis (5.6%) and postcricoid area (4.1%).³ Typical finding on laryngoscopy is a round submucosal bulge in the region of the false vocal fold or aryepiglottic fold.¹

Surgery is the mainstay for the treatment of laryngeal schwannomas. Transoral surgery is recommended for small and pedunculated lesions and an external approach (lateral pharyngotomy, lateral thyrotomy, or laryngofissure) is recommended for large obstructive tumors.^{1,3} The prognosis after complete surgical excision of the tumor is, generally, good. Recurrent/persistent lesions after surgery are encountered in about 17% of non-pedunculated tumors with no statistically significant difference between endoscopic and open procedures.³

There is no consensus about follow-up after surgery for laryngeal schwannoma. Tulli et al. mention in the most comprehensive review on laryngeal schwannoma that recurrent disease in almost all patients was identified within 3-months of surgery and suggest performing flexible laryngoscopy every 3-months for the first year and then annually for at least 2-years after surgery.³

Concerning the presented case, a strong desire of the patient to avoid open laryngeal surgery was primarily taken into consideration (six years before the patient rejected an open surgery proposal). The surgeon who performed the intervention has experience in interventional bronchoscopy and applied some techniques used in interventional bronchoscopy for the described case. It is not uncommon to treat endotracheal and endobronchial tumors using fiber-based lasers and to resect them by coring using a rigid bronchoscope,⁴ but we have not found in the literature any descriptions of using such a technique in endolaryngeal surgery.

Summarizing the particularities of the presented case, we would like to mention the following reasons that make it, in our opinion, a special one:

- Tumor location was not typical: the broad-based tumor was arising from the posterior wall of the larynx (on the cricoid cartilage and interarytenoid fold);

- Tumor extension was not typical: the tumor occupied all three parts of the larynx: supraglottis, glottis, and subglottis;
- Tumor dimensions were not typical: approximately, 4.0 cm in its largest dimension;
- The therapeutic approach was not typical: we have not found in the accessible literature a description of an endoscopic approach to the broad-based tumor with such dimensions affecting subglottis (normally, an external approach is chosen in such cases);
- The tools that were used for resolving this case were not typical: flexible bronchoscope, diode laser, and rigid bronchoscope.

Conclusion

The presented case demonstrates that even big obstructive laryngeal schwannomas, that affect all three parts of the larynx, can be successfully eradicated by endoscopic surgery in selected cases, combining such tools as flexible bronchoscope, laser, and rigid bronchoscope, provided the absence of extraluminal growth of the tumor. The described technique could add to the diversity of approaches in the management of this rare entity.

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Consent statement

Informed consent was obtained from the patient for the publication of this case report.

Ethics approval statement

This manuscript was approved by the "Timofei Moşneaga" Republican Clinical Hospital Institutional Ethics Committee. The research was conducted ethically, with all study procedures performed in accordance with the requirements of the World Medical Association's Declaration of Helsinki. Patient's data are not identifiable. The patient did not receive any stipend for participation in the study.

Data and materials availability statement

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Conflicts of interest

The author declares no conflicts of interest.

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REVIEW ARTICLE

Open Access



Endoscopic approach to hyperplastic laryngeal lesions: a literature review and personal experience

Petru Gurău^{1*}

Abstract

Background Presently, there is a lot of confusion in the identification and classification and no consensus regarding the management of hyperplastic laryngeal lesions (HLL). Conventional transoral microsurgery has some drawbacks and is not always possible. The purpose of the study was to identify criteria for preoperative detection of HLL with high malignant potential and to assess the effectiveness of flexible endoscopic surgery (FES) in the management of HLL.

Methods A review of relevant English literature and a retrospective review of medical records of 37 patients with HLL, treated by FES, was performed.

Results Endoscopic and histologic features of HLL are discussed. An endoscopic classification of HLL is proposed: chronic hyperplastic laryngitis (CHL), chronic hyperplastic laryngitis with keratosis (CHLK), leukoplakia, pachydermia, and verrucous neoplasia. The role of FES using different tools in the diagnosis and management of HLL is presented. We applied flexible endoscopic laryngeal surgery (FELS) for 37 patients (ages, from 20 to 77 years, men 34, women 3) with the following types of HLL: CHLK 5, leukoplakia 18, pachydermia 12, verrucous neoplasia 2. Tracheostomy was offered in 1 case of obstructive verrucous neoplasia with subsequent decanulation after successful endoscopic management.

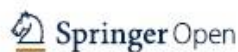
According to the data from the literature and our own observations, the following criteria seem to point to a HLL with high malignant potential: verrucous neoplasia, pachydermia, a lesion affecting more than a half of the vocal fold, mucosal hyperemia, high-grade dysplasia in biopsy samples.

The expected result (total eradication of the visible lesion) was obtained in all of our cases (mean follow-up period 76 months). Invasive carcinoma developed subsequently in 2 patients that continued to smoke after surgery. All the patients that could be followed-up stated an improvement of their voice after surgery.

Conclusion The following criteria can be used for preoperative detection of HLL with high malignant potential: verrucous neoplasia, pachydermia, a lesion affecting more than a half of the vocal fold, mucosal hyperemia, high-grade dysplasia in biopsy samples. Flexible endoscopic surgery, preceded by large flexible forceps biopsy, is a good alternative for HLL management. Diathermy snare is a useful tool for the diagnosis and first-line treatment in selected patients.

Keywords Hyperplastic laryngeal lesions, Endoscopy, Office-based laryngeal surgery

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Background

There is a lot of confusion in the identification and clinicopathological classification of hyperplastic laryngeal lesions (HLL) [1–4]. The variety of classifications of squamous intraepithelial lesions (SIL) reflects discrepancies among laryngologists and pathologists concerning classification, clinical and pathologic diagnosis, prognosis, and management of these lesions. An appropriate classification and unified terminology that would permit reproducible interpretation of HLL, would reflect biological behavior of SIL, and would divide lesions of high malignant potential from those of low malignant potential, seems to be desirable, because it would result in a rational management of the disease. It is important to identify some endoscopic criteria that would guide the clinician in preoperative detection of lesions of high malignant potential. This would contribute to the selection of a rational strategy of treatment and monitoring of the patients with HLL.

Materials and methods

A review of relevant English literature, based on the search in PubMed, Hinari, and Google Scholar databases, was made, using such search terms as hyperplastic laryngeal lesions, precancerous laryngeal lesions, premalignant laryngeal lesions, laryngeal leukoplakia, laryngeal dysplasia, verrucous lesions of the larynx, larynx endoscopy, office-based laryngeal surgery, endoscopic laser surgery of the larynx, and laser ablation of glottic neoplasms.

Additionally, our experience from performing more than 10 000 diagnostic flexible laryngoscopy procedures was used in this manuscript, and a retrospective review of medical records of the patients with HLL, treated by a single surgeon between 1993 and 2022, was performed.

Flexible endoscopic laryngeal surgery (FELS) was applied for 37 patients (ages, from 20 to 77 years, men 34, women 3) with HLL. Written informed consent was obtained from the patients. Thirty-three out of 37 patients (89.2%) underwent surgery under topical anesthesia and 4 patients—under general anesthesia with superimposed high frequency jet ventilation (SHFJV). Twenty-two patients (59.5%) were operated on in an outpatient setting. The desire to be operated on under topical anesthesia and ability to tolerate the procedure were the main criteria for patients selection for unsedated procedures. Tracheostomy was offered in 1 case of obstructive lesion with subsequent decanulation after successful endoscopic management. A flexible therapeutic bronchoscope with a large working channel (2.8 mm), inserted transnasally, was used to perform unsedated procedures. The necessary accessories (biopsy forceps, diathermy snare, flexible laser guide) were brought to

the lesion, being introduced via the working channel of the endoscope. For interventions performed under general anesthesia, the flexible bronchoscope together with accessories was introduced through the rigid suspended jet laryngoscope. The following types of interventions were used: cold eradication by large/jumbo biopsy forceps (7.3 mm cup opening)—1 case, Nd:YAG laser (1064 nm) ablation—33, laser vaporization preceded by diathermy snare resection—3.

Diagnostic flexible laryngoscopy (FLS) is performed under topical anesthesia. Upright sitting position of the patient is preferred. After topical anesthesia of the nasal cavity and the pharynx with 10% Lidocaine spray, the flexible bronchoscope is introduced transnasally close to the larynx. After that, 2% Lidocaine solution (10–15 ml) is instilled onto the larynx during phonation, producing laryngeal gargle, by a catheter placed through the working channel of the bronchoscope. After thorough visual examination of the larynx, the biopsy of the visible lesion is taken using flexible biopsy forceps that is introduced through the working channel of the endoscope. Sometimes, in the presence of a prominent exophytic component, a diathermy snare resection in cutting mode is performed for obtaining of a large biopsy specimen.

FELS is always preceded by diagnostic FLS. Good cooperation with the patient is essential during awake FELS. The grade of patient compliance is estimated during diagnostic FLS procedure. The same technique of topical anesthesia as for diagnostic FLS is used. Small lesions (1–4 mm) can be eradicated by a cold manner using biopsy forceps. The Nd:YAG laser (1064 nm) is used as a main tool for flexible endoscopic surgery (FES) of HLL. Laser coagulation or/and vaporization of the visible lesion is performed in a targeted manner using continuous non-contact irradiation mode, the power being set from 20 W up to 40 W. When prominent exophytic component of a lesion is present, we prefer to resect it by diathermy snare in cutting mode and to use the laser as a second-line tool. This technique allows faster debulking, shortens the operation time and reduces collateral thermal damage to adjacent tissues. Immediately after snare resection of the lesion, the patient is called to cough it out for subsequent histologic examination. In case of accidental aspiration of resected specimen into the tracheobronchial tree it could be easily extracted using flexible bronchoscope, forceps and aspiration force. In cases of extensive and obstructing lesions we recommend general anesthesia, provided there are no contraindications for general anesthesia and transoral surgery.

Etiology of HLL

Smoking, especially, being associated with chronic alcohol abuse, is considered the most important factor in the

occurrence of epithelial abnormalities in premalignant and malignant laryngeal lesions. A direct correlation between cancer development risk and smoking duration was revealed: every 5 years of smoking increases the risk of cancer by 23%, and additional daily alcohol consumption increases the risk of cancer by 17% [5]. Gastroesophageal reflux disease (GERD) is also considered a risk factor in laryngeal carcinogenesis [5]. Some industrial harmful agents (wood and metal dust etc.), vocal abuse and nutrition deficiency of vitamins are mentioned as risk factors [6]. The role of human papillomavirus (HPV) in etiology of SIL is not proven [7].

Pathologic epithelial changes in HLL

Clinical and histopathological terminology in characterization of SIL will be discussed separately, because there is not a predictable correlation between them. Identification of some endoscopic criteria that would guide the clinician in preoperative detection of lesions of high malignant potential would be very useful.

Clinical/endoscopic features

There is a lot of ambiguity in the description, interpretation and classification of some laryngeal epithelial lesions with malignant potential. Oloza mentions chronic hyperplastic laryngitis with keratosis and papilloma of the adults as mandatory precancerous conditions [1]. Some authors use the term "pachydermia" to describe a pebbled keratosis of the posterior glottis [2]. Gallo et al. [3] suggest limitation of the clinical appearance of premalignant laryngeal lesions to three types: (1) leukoplakia (synonym of keratosis)—a white/whitish keratotic area; erythroplakia—red/reddish mucosal area; (3) erythrokeratosis—a mixed lesion (alternating of leukoplakia and erythroplakia zones). The term of leukoplakia implies epithelium thickening and the term of erythroplakia implies thinning of the epithelium. Ferlito et al. mention the following terminology for characterizing proliferative epithelial lesions: leukoplakia (any white lesion on the mucosa that cannot be wiped off or ascribed to a specific condition (e.g., Candidal infection); erythroplakia (any reddish plaque on the mucosa, invasive carcinoma being present in a substantial number of biopsies); erythroleukoplakia (mixed lesions that combine zones of leukoplakia and erythroplakia); pachydermia (indicates extensive thickening of the mucosa) [4]. Chen et al. proposed the classification of leukoplakia, based on the macroscopic appearance, into three types: (1) flat and smooth, (2) elevated and smooth, and (3) rough type (elevated lesion with wrinkled surface). Analyzing the correlation of endoscopic appearance and histologic appearance in a group of 375 patients with leukoplakia who underwent

CO₂ laser excision of the lesion, the authors stated the absence of dysplasia in those 3 macroscopic types, respectively, in 68%, 13%, and 1%, and the presence of carcinoma—in 0%, 5.2% and 30.6% [8]. Li et al. proposed a similar classification of leukoplakia: (1) smooth flat, (2) smooth hypertrophic, and (3) rough lesions (irregular, grained or verrucous appearance). The authors specify that no patients (0%) with smooth flat lesions manifested high-grade dysplasia; in smooth hypertrophy group severe dysplasia and carcinoma were found in 28.1%; and 87.8% of rough lesions were represented morphologically as severe dysplasia or carcinoma [9]. Some authors state that the term "keratosis" is purely histological [10]. We agree with the experts who use this term in clinical interpretations. Based on personal experience, we can state that, if the clinician performs a biopsy from a white flat or elevated laryngeal lesion, it is very unlikely to not obtain keratosis in histological response.

Analyzing the macroscopic appearance of HLL, we use and propose the following endoscopic/clinical classification that we consider relevant:

1. Chronic hyperplastic laryngitis (CHL): vocal folds are thickened, the mucosa is hypertrophied, the surface is irregular or plicated, the exposure of laryngeal ventricles is reduced. Mucosal hypertrophy can involve also laryngeal ventricles (being manifested as focal prolapse of ventricular mucosa into the lumen), interarytenoid space and vestibular folds. In case of pronounced hypertrophy of vocal and vestibular folds, laryngeal lumen may become narrowed, leading to stridor. It is important to mention the diffuse and symmetric character of epithelial changes that uniformly affect both hemilarynxes;
2. Chronic hyperplastic laryngitis with keratosis (CHLK): flake-like whitish semitransparent focal deposits with indistinct contour that adhere to hypertrophied mucosa (Fig. 1);
3. Leukoplakia: a flat lesion with white membranous patch appearance, with smooth or irregular surface and well-defined or indistinct contour. The lesion can be solitary or multifocal (several separate or confluent foci) (Fig. 2);
4. Pachydermia: an elevated lesion with well-defined white plaque appearance, with smooth, irregular, granular, or rugous surface and hard consistence (Fig. 3);
5. Verrucous neoplasia: an exophytic tumor-like white lesion with a broad base, tuberous or papillary/warty surface with villiform projections and hard consistence. Endoscopic appearance frequently resembles sheep fur (Fig. 4).

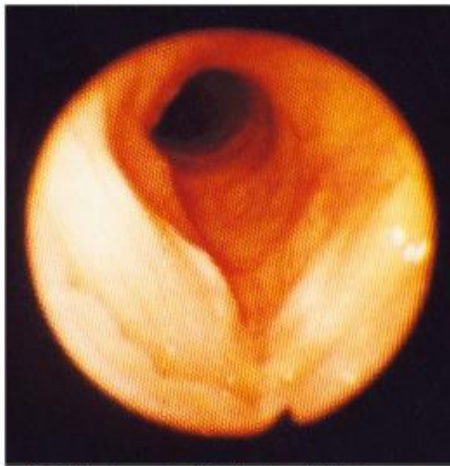


Fig. 1 CHLK: In the anterior third of both vocal folds there are flake-like whitish semitransparent focal deposits with indistinct contour that adhere to hypertrophied mucosa



Fig. 3 Pachydermia of the interarytenoid space: an elevated lesion with well-defined white plaque appearance affects the interarytenoid area of the larynx



Fig. 2 Glottic leukoplakia: a flat lesion with white membranous patch appearance affects the anterior third of the left vocal fold

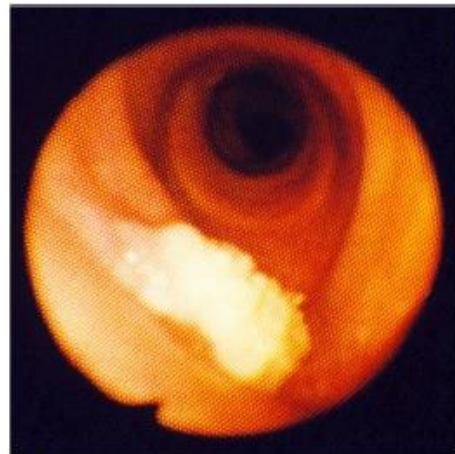


Fig. 4 Verrucous neoplasia: an exophytic tumor-like white lesion with a broad base, warty surface with villiform projections affects anterior two thirds of the right vocal fold

Summarizing shortly the above-mentioned classification of HLL, we would focus on the following main features: CHL—barely symmetric diffuse hypertrophy;

CHLK—flake-like focal white deposits; leukoplakia—a flat well-defined white lesion; pachydermia—an elevated white lesion; verrucous neoplasia—a tumor-like warty white lesion.

The discrepancies that appear in clinical classifications can be explained by the fact that the same lesion may be perceived, interpreted and named differently by different specialists. Analyzing the data from literature, we conclude that "leukoplakia" in our interpretation, corresponds to "flat and smooth leukoplakia" described by Chen et al. [8], "pachydermia" in our interpretation, is similar to "elevated and smooth type of leukoplakia" and "rough type of leukoplakia" according to Chen et al. [8] and "verrucous neoplasia" in our interpretation, corresponds to "keratinizing/hyperkeratotic papilloma" described by Utoza [1] and partially to "rough leukoplakic lesion" described by Li et al. [9]. We believe that behind such terms as "hyperkeratosis", "rough type of leukoplakia", "hyperkeratotic papilloma", "white papilloma", in a substantial proportion of cases could be, actually, verrucous carcinoma that is difficult to diagnose due to a massive layer of keratin on the lesion surface and a high degree of tumor cells differentiation. As a result, a conventional biopsy by forceps, as a rule, is not informative, being followed by an inconclusive histologic response [11]. We promote the mentioned presumption based on the fact that papilloma of the adults is considered a mandatory precancerous condition by some authors with up to 25% malignization rate [1], whereas more recent data demonstrate that the rate of malignant transformation of laryngeal papilloma is up to 4% [12]. For this reason, in our opinion, the term "verrucous neoplasia" is more appropriate for this type of lesion. The benign or malignant nature of this type of lesion can be established only histologically after a thorough examination of the whole lesion or, at least, of a large enough fragment of it, so that the pathologist could examine not only the epithelium, but the stromal component of the lesion as well.

After performing more than 10 000 flexible laryngoscopy procedures, we have never considered acceptable to interpret a lesion as "erythroplakia" or "erythroleukoplakia". After analyzing the interpretation of these lesions in selective literature, we found a confusion: some authors interpret erythroplakia as a sign of epithelium thinning [3], whereas others present it as a hyperplastic lesion with reddish plaque appearance [4]. Taking into consideration mentioning the substantial proportion of invasive carcinoma presence in biopsy specimens, obtained from these lesions [4], most probably, we described these red mucosal areas as hyperemia and defined these lesions as carcinomas in our endoscopic reports.

Gale et al. state that precancerous lesions have no specific macroscopic appearance and none of laryngoscopic features can be considered as reliably diagnostic of precancerous lesions [13]. However, according to the data presented by Chen et al. [8] and Li et al. [9], the presence of dysplasia and carcinoma in a white lesion increases

in proportion as the lesion becomes more elevated and its surface becomes more irregular. Li et al. state a high correlation between the macroscopic appearance of the lesion and its degree of dysplasia [9]. A close correlation between the presence of vocal fold hyperemia and high-risk leukoplakia was stated by Fang et al. [14] and Li et al. [15]. The authors consider that mucosal hyperemia/redness predicts malignant potential of vocal fold leukoplakia. Taking into account the mentioned data, we consider that biopsy, performed during flexible laryngoscopy by large/jumbo biopsy forceps, is an adequate approach when dealing with leukoplakia (flat lesion), but in case of pachydermia (elevated lesion) or verrucous neoplasia (exophytic tumor-like lesion), a biopsy by total or subtotal excision of the lesion, that would result in a conclusive histologic response, is preferable. We performed endoscopic ablation in 26 cases of verrucous neoplasia, from which in 24 cases (92%) verrucous carcinoma was established (these cases are not discussed in detail within present publication), and in 2 cases the malignant nature of the lesion was not confirmed histologically. In 22 of 24 cases (92%) of verrucous carcinoma histologic confirmation of the diagnosis was possible only after partial diathermy snare excision of the lesion. We admit the possibility of verrucous carcinoma presence also in the cases when malignancy was not confirmed, because lesion ablation in those cases was performed after biopsy of the lesion by forceps. Presently, we perform the eradication of the verrucous neoplasia only after receiving a conclusive histologic response as a result of obtaining large enough tissue fragments by diathermy snare in order to not omit carcinoma. Hence, based on our experience, the endoscopic appearance of verrucous neoplasia raises a high suspicion for malignancy.

Histopathologic features

After biopsy or resection of a laryngeal lesion, one can come across several phenomena in histological reports: hyperplasia, akantosis, keratosis, parakeratosis, dyskeratosis, atypia, dysplasia, carcinoma in situ, invasive carcinoma, etc. There are more than 20 classifications of SIL of the larynx [4]. In 1923, Jackson introduced the concept of premalignant laryngeal lesion and presented a case series of larynx carcinoma in association with keratosis [16]. In 1963, Kleinsasser proposed the first classification for premalignant laryngeal lesions: (1) simple squamous cell hyperplasia, (2) hyperplasia with atypia, and (3) carcinoma in situ (CIS) [17]. Friedman introduced the term "laryngeal intraepithelial neoplasia" (LIN), considering different stages of dysplastic progression within the epithelium [18]. Gallo et al. classify keratosis into four groups: (1) keratosis without dysplasia, (2) keratosis with mild dysplasia

(LIN1), (3) keratosis with moderate dysplasia (LIN2), and (4) keratosis with severe dysplasia or CIS (LIN3) [3]. Ferlito et al. (2012) mention three grades of dysplasia: (1) mild dysplasia (LIN1), (2) moderate dysplasia (LIN2), (3) severe dysplasia and CIS LIN3 [4]. The Ljubljana classification of hyperplastic laryngeal lesions accepts four categories of lesions: (1) simple hyperplasia; (2) abnormal hyperplasia; (3) atypical hyperplasia; (4) carcinoma in situ. First two categories are considered benign, third category—potentially malignant and fourth category—actually malignant [13]. The World Health Organization (WHO) 2005 classification includes three grading systems: (1) the dysplasia system, (2) the squamous intraepithelial neoplasia (SIN) system, and (3) the Ljubljana classification [19]. The experts recognized the presence of a subjectivism element in grading of laryngeal dysplasia by pathologists that generates discrepancies in diagnosis of laryngeal dysplasia, even using the same classification system. Different grades of dysplasia can be attributed by different pathologists in the evaluation of the same case. Also, there is a possibility to evaluate differently the same intricate case by the same pathologist after a period of time [20]. Discouraging results of appreciating the variability of histological interpretations according to the WHO 2005 classification, that were declared by many groups of experts, led to development of unified morphological criteria of SIL, that are reflected in the new WHO 2017 classification of SIL [21], that divides SIL into two or three categories: (1) low-grade dysplasia/SIL (includes, according to previous classification, squamous hyperplasia and mild dysplasia), has low malignant potential, the spectrum of morphological changes ranging from squamous hyperplasia to an augmentation of basal/parabasal cells, occupying up to the middle of the epithelial thickness, upper part being unchanged; (2) high-grade dysplasia/SIL (includes, according to previous classification, moderate and severe dysplasia, and carcinoma in situ), has high malignant potential, the spectrum of atypical epithelial cells, occupying at least lower epithelial half up to the whole epithelial thickness; (3) carcinoma in situ, distinguished from high-grade dysplasia if three-tier system is used—showing features of conventional carcinoma, e.g., structural and cellular abnormalities but without invasion. The last WHO 2017 classification of SIL, that defines lesions with low malignant potential and lesions with high malignant potential, seems to be more practical and relevant than previous ones, with better inter-observer agreement, this being confirmed by Gale et al. [7], offering laryngologists a more clear guidance for the choice of rational management strategy.

Evolution of HLL

Gallo et al. [3] suppose that transformation of laryngeal keratosis to carcinoma happens through a chain of consecutive progressive changes of the normal epithelium, initially into keratosis without dysplasia, then into increasing grades of dysplasia, then into carcinoma in situ and, finally, into invasive carcinoma. Isenberg et al. in a review article state that about half of the patients (53.6%) with laryngeal leukoplakia do not have dysplasia at the time of diagnosis, mention malignant transformation rate of leukoplakia of 8.2%, underlining that even in the absence of dysplasia in initial biopsy specimen, the chance of transformation of leukoplakia into invasive carcinoma in the future is about 3.8% [22]. Weller et al. mention that the average period of malignant transformation for a dysplastic laryngeal lesion is about 5.8 years with an overall malignant transformation rate of 14%. Malignant transformation rate was bigger for severe dysplasia (30.4%), than for low/moderate grade dysplasia (10.6%) [23]. Lee et al., indicating a statistically significant correlation, suggest that the extent of the lesion (more than half of the vocal fold) and the degree of dysplasia are predictive factors for the malignant transformation of leukoplakia [24].

Diagnosis of HLL

The most frequent symptom of HLL is dysphonia that imposes the need for a focused examination. Usually the diagnostic process begins with indirect mirror laryngoscopy, then it is followed by 70° rigid laryngoscopy or flexible laryngoscopy and, finally, by direct transoral microlaryngoscopy. Stroboscopic findings cannot reliably predict the presence of malignancy [25]. New imaging techniques, such as narrow band imaging (NBI), contact endoscopy, seem to have a potential in targeting areas of biopsy [25], but cannot replace a biopsy for the diagnosis. Direct transoral microlaryngoscopy, performed under general anesthesia, is considered too invasive to be used just for laryngeal biopsy [26]. Some authors state that office biopsy often understages the severity of lesions, demonstrating a false-negative rate of 33% and mentioning as reasons poor depth of biopsy and small tissue specimens [25]. Other authors demonstrated that awake laryngeal biopsy and tumour staging is as effective as staging in the operating room [27]. We consider flexible laryngoscopy with biopsy, performed under topical anesthesia, as the method of choice for the diagnosis of SIL that can be successfully practiced in an outpatient basis. For the biopsy of flat lesions (leukoplakia) and some elevated lesions (pachydermia) we use large/jumbo biopsy forceps and often perform staged in depth biopsies, the forceps being withdrawn together with the endoscope so

that not to lose tissue fragments in the working channel. For some elevated lesions and, especially, for verrucous lesions we perform the biopsy by diathermy snare excision that allows obtaining large enough tissue samples for a conclusive histologic response. Direct rigid laryngoscopy under general anesthesia is reserved for rare cases when the patient cannot tolerate unsedated flexible laryngoscopy and in a compromised airway.

Management

There is no consensus among specialists related to the management of SIL. There is a variety of proposed treatment approaches: only observation and conservative therapy, radiotherapy, vocal fold stripping, phonosurgical cold excision, laser excision, laser ablation. The choice of treatment modality for HLL is highly dependent on physician preference, experience and available equipment. Some specialists consider that, due to scarring effect, vocal fold stripping has no role in modern laryngology [28, 29]. Gale et al. report that radiotherapy is never used in Slovenia as the treatment for high-grade SIL and is reserved only for carcinoma management [30]. Taking into account potential complications and side effects, and the fact that typically only a single course of radiotherapy can be applied to a patient, it makes little sense to exhaust its potential for treating a premalignant lesion instead of reserving it for a carcinoma [25]. On the one hand, laryngologists are concerned that insufficient measures could result in progression towards invasive carcinoma, on the other hand, a too aggressive approach to SIL that will not progress could lead to vocal fold scarring and voice impairment. However, the oncological approach, considering the malignant potential of SIL to matter more than voice quality, seems to be more reasonable [30]. The following recommendations were included in a consensus statement by otorhinolaryngologists and pathologists at a meeting on the diagnosis and treatment of laryngeal dysplasia in 2010: in most cases resection of the lesion provides both histological diagnosis and initial management of the disease; the overall appearance of the lesion is considered to be the most important factor in determining management; single and multiple foci should be completely excised; in the presence of widespread, confluent leukoplakia, multiple biopsies should be initially performed, followed by staged resection; transoral microsurgery with cold steel or CO₂ laser resection is recommended [31]. Li et al. select a therapeutic modality for leukoplakia based on the endoscopic appearance of the lesion. "Smooth flat" and "smooth hypertrophy" lesions are initially treated conservatively. Cure rates of, respectively, 77.8% and 67.7%, are reported. Surgical treatment is applied in cases of unsuccessful conservative therapy and as initial treatment for "rough" lesions [9].

Traditional transoral microsurgery is not always possible due to contraindications for general anesthesia or anatomic difficulties (inadequate glottis exposure, temporomandibular joint ankylosis, etc.). Office-based unsedated laryngeal surgery (OBULS) has become one of the emerging trends in modern laryngology, mainly, due to the development of flexible endoscopy and flexible fiber-based laser technology. This approach is successfully used nowadays for the treatment of premalignant laryngeal diseases, because of its indubitable advantages: avoiding of general anesthesia risks, economic efficiency, and time economy [32, 33]. Surgery in an office-based setting seems to be preferred also by patients. Rees et al. mention that 87% of patients that underwent both, traditional operating room surgery and OBULS, gave preference to the last one [34]. Sung, using angiolytic lasers (PDL and KTP laser) in office-based setting, underlines that patients with suspicion for dysplasia are primarily treated in the operating room by traditional surgery to exclude carcinoma [33]. Transitioning patients with recurrent disease to the office for photoangiolytic treatment after initial operating room surgery is mentioned as a trend by Karatayli-Ozgursoy et al. [28]. Zeitels et al., analyzing treatment results with KTP laser through flexible endoscope for 29 patients with glottic dysplasia, report 75–100% lesion regression rate in 62% of cases [35]. Koufman et al. report that 20 of 25 patients (80%) with laryngeal leukoplakia who underwent office-based laser surgery with PDL did not require further treatment [36]. Hu et al. report that 9 of 11 patients (82%) with leukoplakia who received their entire treatment in the office with fiber delivery CO₂ laser showed complete resolution [37]. Wellenstein et al. report the results of SIL treatment with flexible guide-based CO₂ laser in office-based setting, mentioning that in 10 from 16 patients (63%) with leukoplakia and hyperkeratosis there was no residual or recurrent lesion after the treatment [38].

We applied flexible endoscopic laryngeal surgery (FELS) for 37 patients with the following types of HLL: CHLK 5, leukoplakia 18, pachydermia 12, verrucous neoplasia 2. In the majority of cases (35/37), the glottic portion of the larynx was affected, in 2 cases the pachydermia of the interarytenoid space was detected. Histologically, according to WHO Classification (2017), high-grade dysplasia was detected in 1 case and low-grade dysplasia was revealed in the rest of the cases. Actually, altogether we performed FELS in 26 patients with verrucous neoplasia, from which in 24 cases (92%) verrucous carcinoma was revealed. These carcinoma cases are not included in the group of HLL and are not discussed within this publication, dedicated to premalignant lesions, but are discussed in another article. The expected result (total eradication of the visible lesion) was obtained in all the

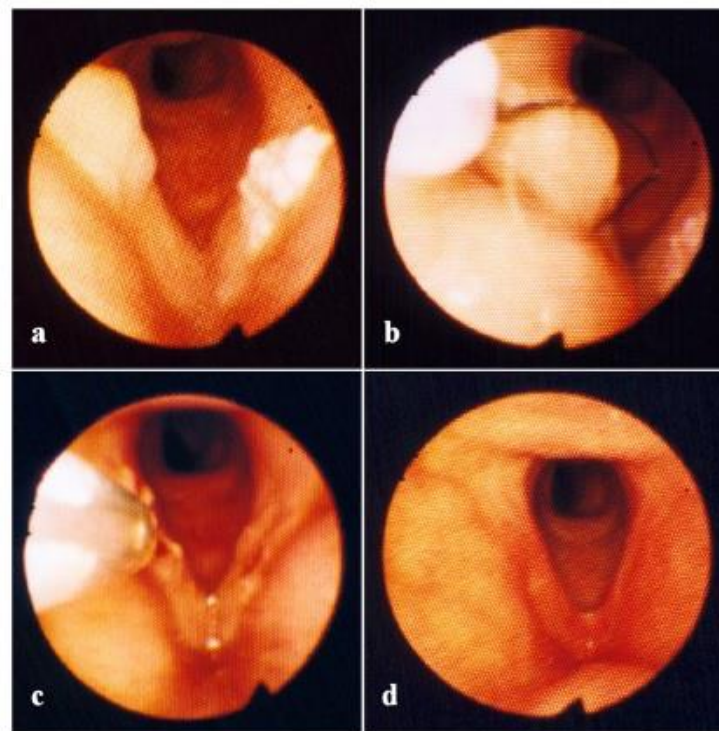


Fig. 5 **a** Pachydermia of vocal folds: elevated lesions with well-defined white plaque appearance affect the posterior third of the right vocal fold and the middle third of the left vocal fold. **b** The moment of diathermy snare excision of the lesion of the right vocal fold. **c** The moment of Nd:YAG laser ablation of the residual lesion of the right vocal fold. **d** Twelve months after laser ablation of glottic pachydermia: no visible lesions

cases (Fig. 5). In one case of leukoplakia, a recurrent lesion was detected in 93 months after surgery that was repeatedly ablated by laser. Invasive carcinoma developed in 2 patients that continued to smoke after surgery (one patient with CHLK—in 22 months and one patient with pachydermia—in 103 months after endoscopic surgery). The follow-up period after surgery varied from 1 to 206 months (average 76 months). Three patients could not be monitored over time. All the patients that could be followed-up stated an improvement of their voice after surgery (21 patients assessed their voice as satisfactory, 9 patients had mild dysphonia and 2 patients had severe dysphonia). The voice quality largely depended on lesion size and location. Anterior commissure involvement and diffuse bilateral process worsen voice quality prognosis.

In selection of treatment methods for HLL both oncological efficacy and preserving of voice function are important. It is always a trade-off, and priorities should be set after determining the malignant potential of the lesion. In low-risk lesions it seems reasonable to

focus on preserving the voice function, and in high-risk lesions the oncological approach seems to be a priority. Authors of some publications, dedicated to comparison of CO₂ laser resection and laser ablation by angiolytic lasers (mainly, KTP laser) for glottic neoplasms, mention superior voice outcome after laser ablation [39, 40], but it is still unclear, which factor is responsible for better voice quality, laser type, or surgical technique [39]. There is no consensus regarding types of lasers that should be used for HLL management and the advantage of one type of laser over another. Rosen et al., in a review article, comparing different types of lasers in office-based treatment (PDL, KTP laser, CO₂ laser, thulium laser, Nd:YAG laser), state that the choice of laser is largely theoretical. Claims of superiority of one type of laser over others are not supported by thorough comparative studies on laryngeal tissues due to, particularly, a big number of variables, beside the wavelength, involved in laser-tissue interactions [27]. Wellenstein et al., in another review on office-based

laryngoscopic procedures, state a lack of comparative studies concerning effectiveness of different laser types for specific lesions [41]. Parker, also in a review publication on vocal fold leukoplakia, concludes that different lasers are simply different tools for achieving the same goal of disease eradication [29]. Yan et al. state that treatment efficacy with all lasers is highly dependent on surgical technique and surgeon's skills [42].

Taking into account that even leukoplakia without dysplasia can progress to malignancy, a close follow-up on patients with HLL is recommended, regardless of the initial histologic response [10, 25]. We recommend follow-up visits after surgery at least once every 3 months over a period of 2 years and, at least, once a year later on.

Conclusion

According to the data from the literature and our own observations, using the proposed classification of HLL (chronic hyperplastic laryngitis, chronic hyperplastic laryngitis with keratosis, leukoplakia, pachydermia, and verrucous neoplasia), the following criteria are suggested for preoperative detection of HLL with high malignant potential: verrucous neoplasia, pachydermia, a lesion affecting more than a half of the vocal fold, mucosal hyperemia, high-grade dysplasia in biopsy samples.

Flexible endoscopic surgery, preceded by large flexible forceps biopsy, is a good alternative for HLL management, taking into account: possibility to avoid general anesthesia related risks, applicability to patients with risks or contraindications to general anesthesia and transoral microsurgery, beneficial cost-efficiency ratio and time economy. This approach is attractive for recurrent lesions management, allowing to avoid repeated general anesthesia. Diathermy snare is a useful tool for diagnosis and first-line treatment in selected patients.

Abbreviations

CHL	Chronic hyperplastic laryngitis
CHLK	Chronic hyperplastic laryngitis with keratosis
CIS	Carcinoma in situ
FELS	Flexible endoscopic laryngeal surgery
FES	Flexible endoscopic surgery
FLS	Flexible laryngoscopy
GERD	Gastroesophageal reflux disease
HLL	Hyperplastic laryngeal lesions
HPV	Human papillomavirus
LJN	Laryngeal intraepithelial neoplasia
NBI	Narrow band imaging
CBULS	Office-based unsedated laryngeal surgery
SHFJV	Superimposed high frequency jet ventilation
SIL	Squamous intraepithelial lesions
SIN	Squamous intraepithelial neoplasia
WHO	World Health Organization

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Author's contributions

The author (PG) contributed to the study conception and design, material preparation, data collection and analysis, the first draft of the manuscript, and approval of the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study has been granted an exemption from requiring ethics approval by Institutional Ethics Committee of "Timofei Moşneaga" Republican Clinical Hospital in view of the retrospective nature of the study and all the procedures being performed were part of routine care. The research was conducted ethically, with all study procedures performed in accordance with the requirements of the World Medical Association's Declaration of Helsinki. This study has been granted an exemption from requiring written informed consent from participants in the study by Institutional Ethics Committee of "Timofei Moşneaga" Republican Clinical Hospital.

Consent for publication

Written informed consent for publication was obtained from the participants whose images are included in the manuscript.

Competing interests

The author declares no competing interests.

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Laryngeal Papillomatosis: A Non-traditional Flexible Endoscopic Approach

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Summary: Objective. To evaluate the efficacy of flexible endoscopic laryngeal surgery (FELS) using un-conventional tools in the treatment of laryngeal papillomatosis (LP).

Methods. We applied FELS using forceps, diathermy snare, and Nd:YAG laser for 47 patients with LP. In 38 cases (81%), surgeries were performed under topical anesthesia with spontaneous respiration and in seven cases we used general anesthesia with superimposed high-frequency jet ventilation. In two cases, both types of anesthesia were used in different sessions. In 22 cases (46.8%), the interventions were performed as outpatient procedures. The Nd:YAG laser was used in the majority (89.4%) of cases.

Results. The expected result (complete eradication of the visible lesion) was obtained in all treated patients without procedure complications. Disease recurrence was established in 16 cases (34%) that led to repeated surgeries.

Conclusions. FELS, using Nd:YAG laser as a main tool, is a safe and effective approach that can be a feasible alternative to the conventional approach in the treatment of LP due to possibility to avoid repeated general anesthesia with its associated risks; applicability for the patients, who have contraindications for general anesthesia and transoral microsurgery; possibility to perform the intervention in an outpatient setting that leads to essential reduction of medical costs; economy of time. Nd:YAG laser ablation, preceded by diathermy snare resection, allows reducing the time of the intervention and thermal injury of the adjacent tissues, compared to using laser alone, and can be used in bulky and obstructive lesions that present a limitation for nonablative techniques.

Key Words: Laryngeal papillomatosis–Flexible endoscopy–Nd:YAG laser.

INTRODUCTION

Laryngeal papillomatosis (LP), as the main manifestation of recurrent respiratory papillomatosis (RRP), is a chronic disease of viral origin with unpredictable evolution and reserved prognosis, that manifests itself by exophytic tumor proliferations on the larynx mucosa, that can impair vocal function and obstruct respiration. Laryngeal papillomatosis in adults is considered as a premalignant disease, malignization rate being 1–7%.^{1–3} The incidence of LP is 1–4 per 100,000.⁴

RRP is categorized into juvenile onset (if the disease is diagnosed before 12 years of age) and adult onset (if the disease is diagnosed after 12 years of age).⁴ The disease can appear at any age. The youngest reported patient was 1 day old and the oldest was 84 years old.⁵

Laryngeal papillomatosis has a viral origin. Two types of human papilloma virus (HPV, HPV6 and HPV11, are responsible for the development of the disease in over 90% of the cases.³ The exact mechanism of getting infected is not completely clear. The virus being present in the larynx mucosa, the conditions that cause clinical manifestation of the disease in some patients and absence

of the disease manifestation in other patients are not completely clear.⁶

The evolution of LP is variable and unpredictable. The disease can evolve in spontaneous remission, can persist in a relatively stable state, demanding only occasionally surgical treatment, or can have an aggressive evolution with the need of surgery every few days or weeks and considering an adjuvant therapy (AT).³

Recurrent respiratory papillomatosis places a huge financial burden on the patients and the entire society, due to the multiple costly surgical interventions over the lifetime of the patients. The average lifetime treatment cost for one patient with RRP in the USA was estimated at \$60,000–470,000.⁴

Currently, there is no definitive treatment for LP. The disease usually has a recurrent nature. Spontaneous remission can happen, but cannot be predicted. At present, surgical treatment is a priority in the management of LP. The goal of surgical interventions is to assure an adequate phonation and respiration by eradication of tumor proliferations until the disease spontaneously resolves.^{2,4}

In approximately 20% of the cases, when surgery alone cannot control the disease, the patients need an AT. The indications for AT are not well established, but usually the surgeon recommends AT for patients who need more than four surgeries per year.^{2,3,5} Multiple methods of AT have been proposed: interferon for systemic administration, cidofovir for intralesional injection, bevacizumab for intralesional injection, HPV vaccine, etc.^{2–5} The efficacy of AT is limited to increasing the time interval between surgical interventions.²

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Currently, there is no definitive treatment for LP, which has a recurrent nature and imposes significant medical costs for the patients. At present, transoral microsurgery (TOMS) has the main role in the management of the disease. Flexible endoscopic laryngeal surgery (FELS) can be an alternative to the traditional approach. The objective of this study was to evaluate the efficacy of FELS using unconventional tools in the treatment of LP.

MATERIALS AND METHODS

This manuscript was approved by Institutional Ethics Committee of "Timofei Moşneaga" Republican Clinical Hospital (Ref. N° 18/2020).

This is a retrospective study. We applied FELS for 47 patients with LP in the time period from 1993 to 2022. Some of the treated patients came from the hospital's catchment area, some patients were referred from other hospitals when certain difficulties in diagnosis or treatment occurred. All the interventions were performed by a single surgeon who applied some interventional bronchology skills for the surgical interventions on the larynx. Patients' age varied from 17 to 77 years, men: 28, women: 19. The surgeries were performed mainly for patients who were not considered good candidates for transoral microsurgery due to general anesthesia risks or difficult anatomy and also in cases when patients preferred to be operated on in an outpatient setting.

Diagnosis of LP was histologically confirmed by biopsy performed under topical anesthesia. Endoscopic interventions were performed with a flexible therapeutic bronchoscope (working channel: 2.8 mm). In 38 cases (81%), surgeries were performed on awake patients under topical anesthesia and in seven cases we used general anesthesia with superimposed high-frequency jet ventilation (SHFJV). In two cases, both types of anesthesia were used in different sessions. In 22 cases (46.8%), the interventions were performed in an outpatient setting. The number of sessions necessary for the eradication of tumor proliferations varied from one to seven (average: 1.5). In 39 cases (83%), the treatment was completed in one session (Table 1).

Written informed consent was obtained from all the patients included in the study. The surgical technique was explained to every patient. The intervention under local

anesthesia was usually recommended to compliant patients with small lesions after diagnostic flexible laryngoscopy with biopsy of the lesion. The option to be operated on under general anesthesia was also explained to the patients. The awake procedure was accepted by 38 patients and usually was chosen by patients with recurrent disease. Nowadays, in cases of an extensive disease, we recommend general anesthesia (if there are no contraindications for general anesthesia and transoral surgery) and, as a rule, perform the ablation in one session. For a period of time, we did not have a jet ventilator, CO₂ laser, and surgical microscope, but we had a flexible bronchoscope and Nd:YAG laser, so we have gained some experience using these tools. The cases with many treatment sessions are connected to that period of lack of equipment. In cases of extensive obstructing lesions, during the first session, we usually performed a debulking by diathermy snare resection or Nd:YAG laser vaporization so that to avoid a tracheostomy, and afterward we performed the ablation of remaining lesions in repeated sessions.

We applied the following techniques to treat papillomatous lesions (Table 2): cold surgery by flexible forceps, excision by diathermy snare, Nd:YAG laser ablation, and combination of the above-mentioned techniques. The Nd:YAG laser (wavelength: 1064 nm) was used in the majority (89.4%) of cases.

If the procedure is performed under topical anesthesia, patients are treated in the upright sitting position. After topical anesthesia of the nasal cavity and the pharynx with 10% Lidocaine spray, the flexible bronchoscope is introduced transnasally close to the larynx. After that, 2% Lidocaine solution (10–15 mL) is instilled onto the larynx during phonation, producing laryngeal gargle, by a catheter placed through the working channel of the bronchoscope. Small papillomas (1–4 mm) are eradicated by flexible jumbo forceps. Bulky, pedunculated, racemose, obstructive lesions are preferably excised by diathermy snare in cutting mode, the Nd:YAG laser (1064 nm) being used as a second-line tool for the ablation of the residual lesions (Figures 1 and 2). Flat papillomas, that are bigger than 4 mm, are primarily treated by laser. Continuous non-contact mode is selected for laser ablation, the power being

TABLE 1.
The Number of Treatment Sessions Necessary for Lesion Eradication

No. of Treatment Sessions per Patient	No. of Patients
1	39
2	5
6	1
7	2
Mean = 1.5	47 (100%)

TABLE 2.
Techniques Used for Laryngeal Papilloma Eradication

Ablative Techniques	No. of Patients
Cold surgery (by forceps)	5
Laser ablation	27
Cold surgery + Laser ablation	1
Diathermy excision + Laser ablation	13
Cold surgery + Diathermy excision + Laser ablation	1
Totally	47

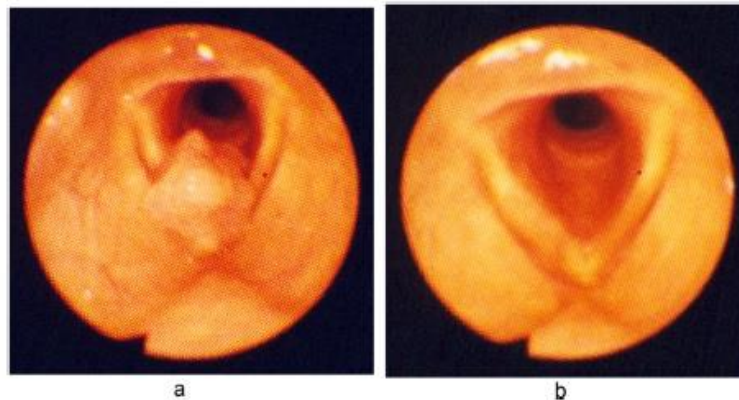


FIGURE 1. a. Papillomatous proliferations affect anterior half of the right vocal fold and anterior commissure. b. Endoscopic view in 3 months after FELS under local anesthesia (Nd:YAG laser ablation preceded by diathermy snare excision). No visible papillomatous proliferations. FELS, flexible endoscopic laryngeal surgery.

set up to 40 W. All the instruments (flexible forceps, diathermy snare, flexible laser guide) are brought to the lesion, being introduced through the working channel of the flexible bronchoscope. When necessary, multiple treatment sessions are performed at 2–7 day intervals. Good cooperation with the patient is essential during the procedure. The grade of patient's compliance is estimated during diagnostic flexible laryngoscopy with lesion biopsy that is done in a separate session, prior to surgery itself. Talking to the patient during the procedure is helpful for the enhancement of patient compliance. Immediately after snare resection of the lesion, the patient is called to cough it out for subsequent histologic examination. In case of

accidental aspiration of resected specimen into the tracheobronchial tree, it could be easily extracted using flexible bronchoscope, but it happened to none of our patients. When thorough anesthesia of the vocal cords is performed, the unsedated procedures are usually well tolerated by the patients. In rare cases, when patients cannot control the gag reflex even with an additional intravenous sedation, we recommend general anesthesia with SHFJV. When performing surgery under general anesthesia with SHFJV, the flexible bronchoscope together with suitable accessories (laser guide, forceps, or diathermy snare) is introduced through the rigid suspended jet laryngoscope. Voice rest during 7 days is recommended after surgery.

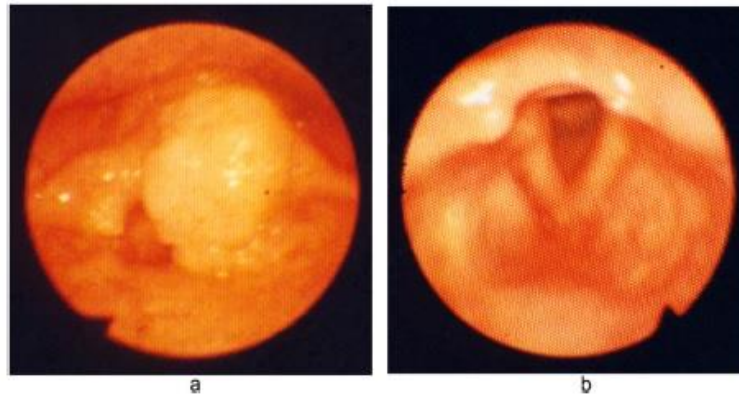


FIGURE 2. a. Massive, obstructive papillomatous proliferations affect supraglottic and glottic portions of the larynx. b. Endoscopic view in 12 months after FELS under local anesthesia (two sessions of Nd:YAG laser ablation preceded by diathermy snare excision). Laryngeal lumen is free. No visible papillomatous proliferations. FELS, flexible endoscopic laryngeal surgery.

The first follow-up exam is usually scheduled 2 months after the intervention. After that, the next follow-up exam is planned at 6 and 12 months after the intervention in the absence of symptoms of disease recurrence (progression of dysphonia or dyspnea), or immediately after the appearance of disease recurrence symptoms. If the patient follows the recommendations and comes to the follow-up exam with a small (up to 10 mm) recurrent lesion, we usually perform tumor eradication under topical anesthesia, in an outpatient setting. In case of massive, obstructing recurrent lesions, we recommend hospitalization and endoscopic surgery under general anesthesia with SHFJV.

RESULTS

The expected result (complete eradication of the visible lesion) was obtained in all treated patients without procedure complications. Disease recurrence was established in 16 cases (34%), which led to repeated surgeries with a time interval from 30 days to 12 years. Three patients could not be followed-up. In the group of patients without established recurrence, the period of observation varied from 3 to 203 months (average: 83 months). In the group of patients with recurrent disease, the recurrence free period after the last surgery varied from 3 to 268 months (average: 53 months). The number of repeated courses of surgical treatment per patient varied from 1 to 7 (average: 2.7) (Table 3).

The limitation of this study is the lack of thorough voice outcome assessment that would be useful for a follow-up study. Concerning voice quality, from 44 patients that could be followed-up after the intervention, 28 patients (63.6%) evaluated their voice after the treatment as satisfactory, 13 (29.6%) had mild dysphonia, 3 (6.8%) had severe dysphonia. All the patients with postoperative dysphonia had the anterior commissure affected by the tumor. All three patients with severe dysphonia had a history of juvenile onset RRP with multiple laryngeal surgeries.

DISCUSSION

At present, transoral microsurgery (TOMS) has the main role in the management of LP. Different modalities of this

type of treatment are practiced, described, and analyzed: cold surgery,⁷ CO₂ laser,⁸ microdebrider,⁹ pulsed-dye laser (PDL),¹⁰ potassium tetanyl phosphate (KTP) laser,¹¹ Nd:YAG laser,¹² diode laser.¹³ Different lasers that are used in laryngology have different absorption characteristics due to different target chromophores that determine the depth of their penetration. CO₂ laser targets water and, therefore, has a minimal penetration depth and good cutting properties. Angiolytic lasers primarily target oxyhemoglobin and, therefore, affect microvessels and induce lesion regression. Nd:YAG laser targets chromophores, such as melanin and carbon, and is only partially absorbed in water and oxyhemoglobin, resulting in bigger depth of penetration of laser radiation (up to 10 mm). Currently, the most used technique is TOMS with CO₂ laser. A drawback of CO₂ laser TOMS is related to safety: active viral DNA has been found in the laser smoke, which could be a potential source of infection.⁵ Janda et al report Nd:YAG laser application during TOMS using a rigid fiber guidance instrument with bendable distal tip for treating LP in continuous non-contact mode.¹² The authors mention the reduction of the recurrence rate of the disease that is thought to be attributed to the fact that Nd:YAG laser, due to its deep coagulation capabilities, causes destruction of the HPV-infected basal cell layer of the mucosa, which is responsible for the regeneration of papilloma tissue. No surgical technique, proposed so far, can prevent the recurrence of the disease, due to the presence of viral particles in visually intact mucoasa of the larynx, adjacent to visible papillomatous proliferations. Avoiding excessive radicalism and protection of anatomical structures, that are important for phonation and respiration, especially anterior and posterior commissure, in order to reduce the risk of postoperative complications, such as synechia and cicatricial glottic stenosis, is recommended.^{2,3,5} It was demonstrated that eradication of papillomatous proliferations in laryngeal areas, which do not produce symptoms, do not reduce the frequency of repeated interventions. Contrarily, it is specified, that excessive injury of laryngeal mucosa can aggravate the evolution of the disease.² The tracheostomy should be avoided, if it is possible, because it favors papillomatous growth in the region of the tracheostoma and spread of the tumor process in distal airways.^{5,14,15} Transoral surgery by suspension microlaryngoscopy, being the traditional method of treatment of LP, is sometimes difficult or impossible because of anatomic particularities, such as short mandible, insufficient neck extension, temporomandibular joint ankylosis, etc.

With evolution of flexible endoscopy and flexible guide-based laser technology, the possibility of endoscopic surgery under topical anesthesia became tempting, considering that general anesthesia increases morbidity rate if administered multiple times. This approach makes possible performing surgical interventions on patients with contraindications or a major risk for general anesthesia and transoral direct microlaryngoscopy, reducing, at the same time, medical costs. In some publications, authors demonstrate using the laser

TABLE 3.
The Number of Repeated Courses of Surgical Treatment Applied for Patients With Recurrent Disease

Nr. of Repeated Courses of Surgical Treatment per Patient	No. of Patients (16)
1	7
2	1
3	4
4	1
5	1
6	1
7	1
Mean = 2.7	

via flexible endoscope under local anesthesia in an outpatient setting, mentioning the advantages of this approach: avoiding the risk of general anesthesia, economic efficacy and time economy.^{16,17}

The flexible endoscope can be coupled with different types of lasers: PDL: 585 nm,¹⁶ KTP laser: 532 nm,¹⁷ thulium:YAG laser: 2013 nm, CO₂ laser: 10,600 nm,¹⁰ diode laser: 810, 980, 445 nm,^{13,18} Nd:YAG laser: 1064 nm.

Zeitels and Burns mention two types of angiolytic lasers used in office-based laryngeal surgery: 585 nm PDL and pulsed-KTP laser (532 nm), favoring KTP laser in the treatment of epithelial lesions.¹⁹ Sung, using the same angiolytic lasers for office-based laryngeal surgery, underlines that patients with suspicion for papillomatosis or dysplasia are primarily treated by traditional surgery with biopsy in the operating room for histologic diagnosis and for excluding carcinoma.¹⁷ Rees et al report about performing PDL office-based unsedated laryngeal surgery (OBULS) for 54 patients that previously underwent interventions for the same pathology in the operating room under general anesthesia, and 87% of them preferred OBULS over the surgery in the hospital operating room, and 83% of the patients felt less discomfort with OBULS than with operating room surgery.²⁰ Rees et al estimated that the average cost-savings per case when performing OBULS with PDL for LP was more than \$5000.²¹

The angiolytic lasers are used rather to induce lesion regression than to obtain complete ablation of the lesion during surgical maneuver. Because of delayed treatment effect, these nonablative techniques are not suitable for bulky lesions, due to the risk of airway obstruction in the postoperative period.²²

There is a lack of publications about using other types of lasers for the treatment of LP. Although Nd:YAG laser (1064 nm) is a widely used tool in interventional bronchology, in accessible English literature we have not found publications concerning the use of Nd:YAG laser via flexible endoscope for LP treatment. To our knowledge, the presented material (42 patients in whom Nd:YAG laser was used alone or in combination with other techniques) is the largest series presented in the literature to date. The caution of the laryngologists concerning Nd:YAG laser can be explained by the fact that its penetration capacity into biological tissue is higher than for other types of used lasers, resulting in a concern about the potential excessive thermal damage to adjacent tissues, superficial lamina propria scarring and anterior commissure web formation. We consider that the collateral thermal injury produced by Nd:YAG laser can be minimized by using the laser after cold surgery or diathermy snare excision, as a second-line tool, ablating only the residual lesion. We find Nd:YAG laser ablation, preceded by diathermy snare excision, safe and effective, especially for bulky, obstructive papillomatous lesions. The point of this study was to demonstrate that if a surgeon does not have a surgical microscope and a

CO₂ laser or an angiolytic laser available, but has a Nd:YAG laser, a flexible bronchoscope, and a jet ventilator, it is still possible to obtain decent results in the treatment of the disease.

CONCLUSIONS

FELS, using Nd:YAG laser as a main tool, is a safe and effective approach that can be a relevant and feasible alternative to the conventional approach in the treatment of LP, taking into consideration the recurrent nature of the disease, due to possibility to avoid repeated general anesthesia with its associated risks; applicability for the patients, who have contraindications for general anesthesia and transoral microsurgery; possibility to perform the intervention in an outpatient setting that leads to essential reduction of medical costs; economy of time. Nd:YAG laser ablation, preceded by diathermy snare resection, allows reducing the time of the intervention and thermal injury of the adjacent tissues, compared to using laser alone, and can be used in bulky and obstructive lesions that present a limitation for nonablative techniques.

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Declaration of Competing Interest

I have no competing interests in relation to the work.

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Flexible Endoscopic Laser Surgery for Glottic Carcinoma After Radiotherapy Failure: A First Experience

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Abstract

Background: Surgery is the only salvage treatment for radiotherapy (RT) failures in glottic carcinoma management, and total laryngectomy is performed in the majority of cases, resulting in a substantial decline in the quality of life for patients. Transoral CO₂ laser microsurgery (TOLMS), as a salvage treatment for RT failures, demonstrated its efficiency, albeit more inferior compared to treatment results obtained in primary glottic carcinoma, but has some limitations, predominantly associated with difficult anatomy and inadequate glottis exposure and also because of mandatory larynx suspension and general anesthesia with myorelaxation that present risks or contraindications for some categories of patients. Flexible endoscopic laser surgery (FELS) can overcome some of the limitations of TOLMS, being a minimally invasive therapeutic option for this category of patients. The study's purpose was to evaluate the long-term (five-year) effectiveness of FELS in treating recurrent/persistent glottic carcinoma after RT failure.

Methods: FELS was performed in nine patients with recurrent (four) and persistent (five) early-stage (T1a: two; T1b: one; T2: six) glottic carcinoma after RT failure (males: eight; females: one), aged 47-66 (mean: 55.4±7.8). FELS under local anesthesia with spontaneous ventilation was performed in five patients (55.6%), and the rest of the patients were operated on under general anesthesia with superimposed high-frequency jet ventilation (SHFJV). Tumor ablation by neodymium-doped yttrium aluminum garnet (Nd:YAG) laser was performed in all the cases, and adjuvant RT (20-22 Gy) was performed in two cases of persistent T2 tumors.

Results: Five-year overall survival and ultimate disease control, including salvage treatment, were obtained in six patients (66.7%), cure with larynx preservation was obtained in five patients (55.6%), disease-free survival was obtained in five cases (55.6%), and ultimate local control with FELS alone was obtained in five cases (55.6%). All three patients with the T1 stage of disease were alive, free of disease, with the preserved larynx due to FELS alone.

Conclusion: FELS can be considered an efficient method of treating recurrent and persistent T1-T2 glottic carcinoma after RT failure, offering a minimally invasive surgical alternative for cure with larynx preservation, especially for patients with risks/contraindications to general anesthesia and transoral microsurgery.

Categories: Oncology, Otolaryngology

Keywords: endoscopic laser surgery, flexible endoscopy, nd:yag laser, radiotherapy failure, recurrent glottic carcinoma

Introduction

Larynx carcinoma represents about 30-50% of all head and neck malignancies, with 75% of the tumors being located in the glottic portion of the larynx [1-3]. At present, external beam radiotherapy (RT) is still largely used in many institutions as the first-line treatment for early glottic carcinoma, demonstrating good oncological results. The tumor recurrence rate after RT varies between 5% and 20% for T1 lesions and between 25% and 50% for T2 lesions [4,5]. The impossibility of repeating RT for a recurrent tumor is a major disadvantage of this treatment method. Consequently, surgery is the only salvage treatment for RT failures, and total laryngectomy is performed in the majority (75%) of cases [6], resulting in a substantial decline in the quality of life of the patients.

Transoral CO₂ laser microsurgery (TOLMS), being applied in recent decades as a salvage treatment for RT failures in early glottic carcinoma, has demonstrated its efficiency, albeit more inferior compared to treatment results obtained in primary glottic carcinoma [7], but has some limitations, predominantly associated with difficult anatomy and inadequate exposure of the glottis and also because of mandatory larynx suspension and general anesthesia with myorelaxation that present risks or contraindications for

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some categories of patients (e.g., ischemic cardiovascular disease, dental mobility or prosthetic work in the anterior maxillary region) [7-13].

Flexible endoscopic laser surgery (FELS) can overcome some of the abovementioned limitations of TOLMS, being a minimally invasive therapeutic option for this category of patients. The objective of this study was to assess the long-term (five-year) effectiveness of FELS in treating glottic carcinoma after RT failure.

Materials And Methods

The retrospective study was conducted at Timofei Moşneaga Republican Clinical Hospital in Chişinău, Republic of Moldova, after obtaining approval from the Institutional Ethics Committee of Nicolae Testemiţanu State University of Medicine and Pharmacy (approval number: 6). FELS was performed in nine patients with recurrent/persistent glottic carcinoma after RT failure. All surgical interventions were performed by a single surgeon. Written informed consent was obtained from the patients. Consecutive patients with recurrent/persistent T1-T2 N0 M0 glottic carcinoma after RT failure who could be followed up for five years after the endoscopic intervention were included in the study.

FELS was performed using a therapeutic bronchoscope (2.6-3 mm working channel) and flexible guide-based neodymium-doped yttrium aluminum garnet (Nd:YAG) laser (model: LTN-102 (Russia); wavelength: 1064 nm) (Figure 1).

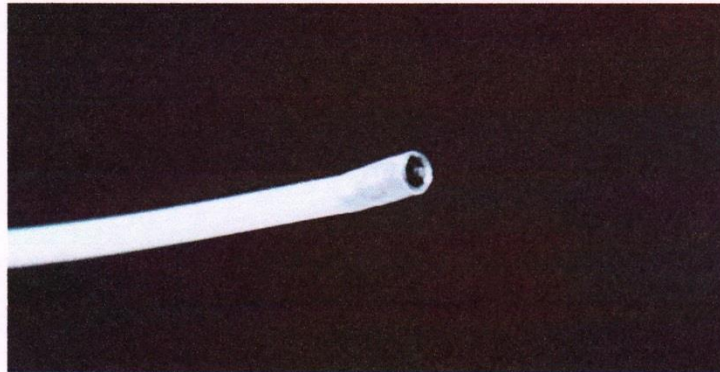


FIGURE 1: Flexible Nd:YAG laser guide

Nd:YAG: neodymium-doped yttrium aluminum garnet

When the intervention was performed with spontaneous ventilation under local anesthesia and moderate intravenous sedation, patients were treated in a sitting position. A flexible bronchoscope was introduced into the larynx transnasally after local anesthesia of the nasal and pharyngeal mucosa with 10% lidocaine spray. Topical anesthesia of the larynx mucosa was performed with lidocaine 2% instilled through a catheter introduced in the working channel of the bronchoscope during phonation, and a flexible laser guide was delivered to the lesion through the working channel of the bronchoscope (Figure 2).

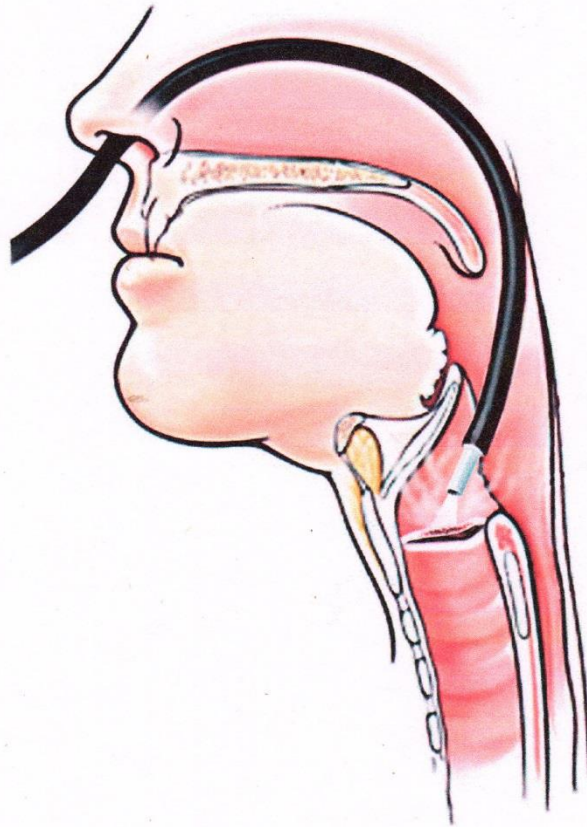


FIGURE 2: Transnasal approach to the glottic lesion

The figure was created using Adobe Photoshop without AI assistance (San Jose, California, United States).

When the intervention was performed under general anesthesia with superimposed high-frequency jet ventilation (SHFJV), a flexible bronchoscope, together with a flexible laser guide, was introduced through the rigid suspensive jet laryngoscope ("Carl Reiner", Austria) (Figure 3).



FIGURE 3: Flexible bronchoscope, together with a flexible laser guide, is introduced through the rigid suspensive jet laryngoscope

Photoablation of tumors was performed in continuous near non-contact mode with power settings of 20-40W (Figure 4). Awake procedures with spontaneous ventilation were chosen in cases of contraindications or major risk for general anesthesia with myorelaxation and/or transoral microsurgery and the patient's desire to undergo an awake endoscopic surgery.

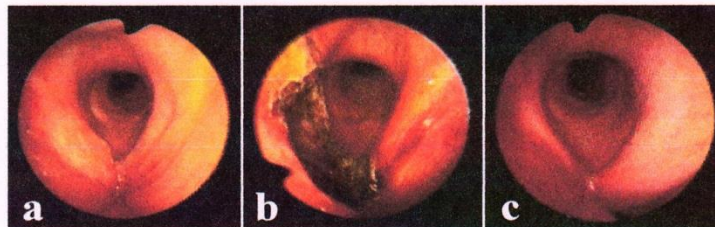


FIGURE 4: Recurrent carcinoma of the right vocal fold

(a) Before the treatment. (b) Immediately after Nd:YAG laser ablation. (c) One year after endoscopic surgery.

Nd:YAG: neodymium-doped yttrium aluminum garnet

The following criteria were analyzed for the evaluation of the long-term (five-year) oncologic efficacy of FELS: ultimate disease control (UDC) (free of primary tumor, regional, and distant metastases), overall survival rate (OS) (alive five years post-surgery), disease-free survival (DFS) (alive five years post-surgery without local or regional recurrence), ultimate disease control with FELS alone (UDC FELS) (free of primary and metastatic tumor after FELS only), cure with larynx preservation (CLP) (free of disease with preserved larynx), death of disease (DD) (death from primary or metastatic tumor), and local recurrence (LRc): LRc included recurrent primary tumors (revealed over six months after the treatment) and persistent primary tumors (revealed within six months after the treatment).

Results

Nine patients with recurrent/persistent T1-T2 glottic carcinoma after RT failure were included in the study: eight males and one female aged 47-66 years (mean: 55.4±7.8 years). The histological structure of the tumors was represented by squamous cell carcinoma in all the cases. According to the tumor extent, two patients had T1a stage, one patient had T1b stage, and six patients had T2 stage of the disease (due to supraglottic and/or subglottic extension of the tumor). The anterior commissure involvement was registered in six cases (66.7%).

In seven cases, only FELS was performed, and in two patients (T2 persistent carcinoma), postoperative RT in a dosage of 20-22 Gy was also offered. The reasons for applying adjuvant RT for those two cases of persistent tumors were completing the preoperative dosage of RT (40 and 46 Gy, respectively) and consolidation of the

therapeutic effect of FELS.

In eight observations, treatment was realized in one session, and for one patient, in two sessions. Awake interventions with spontaneous ventilation were performed in five patients (55.6%), and general anesthesia with SHFJV was used in four cases.

No complications during or after endoscopic interventions were registered. Five-year overall survival and ultimate disease control, including salvage treatment, were obtained in six patients (66.7%). Disease-free survival was achieved in five cases (55.6%). Primary tumor recurrence was registered in three cases (33.3%). Successful salvage treatment (total laryngectomy) for tumor recurrence was registered in one patient. Death of primary tumor progression was registered in two cases (22.2%) after 48 and 53 months from endoscopic intervention. In one case, after seven months from FELS, the patient died of a brain tumor that was considered metastatic, though there was no firm certainty about the association between laryngeal and brain tumors. Cure with larynx preservation was obtained in five cases (55.6%). Ultimate disease control with FELS alone was achieved in five patients (55.6%). All three patients with T1 disease were alive, cured of the disease with preserved larynx due to FELS alone (Table 1).

Results	Overall (n=9)	T1a (n=2)	T1b (n=1)	T2 (n=6)
UDC/OS	6/9 (66.7%)	2/2 (100%)	1/1 (100%)	3/6 (50%)
DFS	5/9 (55.6%)	2/2 (100%)	1/1 (100%)	2/6 (33.3%)
UDC FELS	5/9 (55.6%)	2/2 (100%)	1/1 (100%)	2/6 (33.3%)
CLP	5/9 (55.6%)	2/2 (100%)	1/1 (100%)	2/6 (33.3%)
DD	3/9 (33.3%)	0/2 (0%)	0/1 (0%)	3/6 (50%)
LRc	3/9 (33.3%)	0/2 (0%)	0/1 (0%)	3/6 (50%)

TABLE 1: Five-year results of FELS for recurrent/persistent glottic carcinoma after RT failure related to tumor stage

n: number of patients; UDC: ultimate disease control; OS: overall survival rate; DFS: disease-free survival; UDC FELS: ultimate disease control with FELS alone; CLP: cure with larynx preservation; DD: death of disease; LRc: local recurrence; FELS: flexible endoscopic laser surgery; RT: radiotherapy

Discussion

RT is still the preferred method of treating early glottic carcinoma in many institutions. The tumor recurrence rate after RT varies between 5% and 20% for T1 lesions and between 25% and 50% for T2 lesions [4,5]. The disadvantages of RT include radioresistance of some tumors, reduced efficiency in bulky lesions, verrucous carcinoma, anterior commissure affection, and the impossibility of reusing RT for a recurrent tumor [7,14,15].

Therefore, surgery is the only treatment for RT failures. Though open partial laryngectomy (OPL) can be used for treating RT failures, the method has disadvantages that include major surgical trauma caused by the cutting of normal anatomical structures (muscles, nerves, cartilage, vessels), resulting in pain and postoperative edema, temporary tracheostomy (5-18 days), temporary nasogastric tube placement because of deglutition impairment and aspiration episodes, long hospitalization period (22-35 days), and high rate (up to 51%) of postoperative complications [12,16-18]. The incision of thyroid cartilage that was previously irradiated favors the apparition of severe postoperative complications, such as chondritis, chondronecrosis, and fistula [19]. Consequently, in case of RT failure, total laryngectomy is performed in the majority (75%) of cases [6], resulting in a substantial decline in the quality of life of the patients. TOLMS with CO₂ laser is considered the gold standard in the surgical management of early glottic carcinoma that replaced OPL as a primary treatment modality, having such advantages as minor surgical trauma, preserving the integrity of cartilaginous skeleton of the larynx and avoiding tracheostomy, short treatment duration, the possibility to be repeated, and preserving of all salvage treatment options in case of tumor recurrence [7,9,10,18,20].

TOLMS is not always applicable because of some limitations that are predominantly associated with difficult anatomy and inadequate tumor exposure and also because of mandatory larynx suspension and general anesthesia with myorelaxation that present risks or contraindications for some categories of patients (e.g., ischemic cardiovascular disease, dental mobility, or prosthetic work in the anterior maxillary region) [7-13].

In contrast to primary glottic carcinoma, the experience of using TOLMS for treating recurrent glottic carcinoma after RT failure is still limited. Inferior results of TOLMS in treating recurrent glottic carcinoma

compared to primary carcinoma, a higher treatment complication rate, and frequent necessity of repeated procedures for disease control have been reported [7,21]. Blakeslee et al., analyzing a series of 15 patients, reported local control of 40% in treating recurrent T1 glottic carcinoma after RT failure [22]. Ramakrishnan et al., in a review and meta-analysis publication based on 11 studies, mentioned 56.9% local control after the first intervention [23]. Weiss et al., in a retrospective study, reported a five-year local control of 57.5% after performing TOLMS in 93 patients with recurrent early glottic carcinoma [24]. Roedel et al., analyzing the oncological outcomes of TOLMS for recurrent early glottic carcinoma after primary RT, reported a 42% cure rate after the first intervention [19]. Russo et al., in a recent review and meta-analysis publication, analyzing the results of salvage TOLMS after primary RT for 235 patients, reported a summarized five-year local control of 39.1% [25].

The limitations of TOLMS can be overcome by FELS. In the available English literature, we have not found any studies about using FELS for treating recurrent glottic carcinoma after primary RT failure. To our knowledge, this is the first series of patients treated by FELS and followed up for five years. The laser ablation technique's disadvantage is the impossibility of assessing the margins of the resected specimen. However, close follow-up and the "wait-and-see" strategy for the early detection of possible tumor recurrence can partially compensate for this. We recommend postoperative follow-up flexible laryngoscopy exams once a month during the first year after surgery, once in two months during the second year, once in three months during the third year, once in six months during the fourth and fifth years, and once a year after five years. There is no substantial evidence behind adjuvant reirradiation after salvage surgery. The rationale for such a decision in two of our cases was the following: the mentioned two patients did not receive a complete dosage of RT before salvage endoscopic treatment, so a persistent tumor was detected after the first half of the RT course. Thus, completing the RT program (up to 60-70 Gy) after substantial surgical cytoreduction was considered rational for increasing the chances of local control. The limitations of the study, which include its retrospective nature, the small number of observations, and the absence of a control group, do not permit categorical affirmations. Nevertheless, obtaining disease-free survival, cure with larynx preservation, and ultimate disease control by FELS alone at 55.6% allows us to state that the oncological efficiency of FELS is comparable to that of TOLMS and the method deserves to be applied as a salvage treatment after RT failure, offering patients a chance to preserve their larynx.

Conclusions

From the oncological perspective, FELS can be considered an efficient method for treating recurrent/persistent T1-T2 glottic carcinoma. The method deserves to be used as a minimally invasive surgical alternative for disease control with larynx preservation, primarily for patients with risks/contraindications to general anesthesia with myorelaxation and TOLMS. Prospective studies involving a larger number of patients are needed to validate the proposed approach and provide categorical statements.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Petru Gurău

Acquisition, analysis, or interpretation of data: Petru Gurău, Oleg Arnaut, Eusebiu Sencu, Dumitru Sofroni

Drafting of the manuscript: Petru Gurău

Critical review of the manuscript for important intellectual content: Petru Gurău, Oleg Arnaut, Eusebiu Sencu, Dumitru Sofroni

Supervision: Dumitru Sofroni

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. Institutional Ethics Committee of Nicolae Testemițanu State University of Medicine and Pharmacy issued approval 6. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the

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ABSTRACT BOOK

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Fibroendoscopic approach in verrucous carcinoma of the larynx

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INTRODUCTION: Verrucous carcinoma of the larynx (VCL) is a rare form of larynx cancer (1-3%), that presents difficulties for diagnosis and choice of treatment strategy. Diagnosis is difficult mostly due to massive layer of keratin on the tumor surface, that results in inadequate traditional biopsy and inconclusive histologic response, that usually leads to wrong interpretation of tumor as benign and delay of adequate treatment.

OBJECTIVE: The aim of this study was to assess effectiveness of fibroendoscopic approach in diagnosis and treatment of verrucous carcinoma of the larynx.

METHODS: We present our experience of endoscopic treatment of 16 cases of VCL (glottic region, T1-T2). Traditional forceps biopsy in all cases was inconclusive. In order to obtain an adequate biopsy specimen for histologic confirmation, fibroendoscopic snare diathermoexcision was used. After histological confirmation of tumor nature, fibroendoscopic LASER ablation (FELA) of tumor was performed with Nd:YAG laser and therapeutic fibrobronchoscope. In 13 cases intervention was performed under local anesthesia and premedication with spontaneous respiration. In 3 cases general anesthesia with high frequency jet ventilation (HFJV) was used.

RESULTS: Local control was obtained in 15 cases (93,8%). Average period of observation without recurrence was 63 months (range: 3-193 months). In 13 cases no recurrence was revealed.

CONCLUSIONS: Close cooperation between clinician and pathologist is vital for correct diagnosis of VCL. Obtaining of large biopsy specimen is critical for conclusive histologic response. Provided close endoscopic monitoring, FELA can be proposed as treatment of choice for majority of patients with VCL.



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direction of 12 o'clock in trachea. The patient received high-frequency electrocautery snare, transbronchial cryobiopsy and argon plasma coagulation (APC) treatment via bronchoscope. The symptoms of the patient disappeared after bronchoscopy.

Results: Pathology revealed that the lesions were composed of spindle cells covered with ciliated columnar epithelium and squamous epithelium. Necrosis, cholesterol crystallization, foam cell aggregation, keratin cyst formation are present. The immunohistochemistry results were: progesterone receptor (+), epithelial membrane antigen (EMA) (+), SSTR2 (+), vimentin (+), Ki67 (+) 1%, CD34 (+), CK (-), CD5/6 (-), Desmin (-), GFAP (-), P63 (-), S-100 (scattered +), SAM (focal+), and SOX-10 (-) (Fig 1). A 2 months follow-up, airway mucosa of the patient recovered fully after treatment by tracheoscopy. No mucosal abnormalities were detected on magnetic resonance imaging (MRI).

Conclusion: Conclusions We report a case of ectopic meningioma of upper airway and the treatment through bronchoscopy for the first time. Ectopic meningioma usually have a good prognosis after the tumor removal, but long-term follow-up was required.

PO-519

Flexible endoscopic combined diathermy–laser resections in malignant tumors of larynx, trachea and bronchi.

Gurau, Petru, Petru Gurau
Republican Clinical Hospital "Timofei Mosneaga"

Objective: Minimally invasive interventions in malignant airway tumors present clinical interest in view of improvement of patients life quality and obtaining radical curative outcome. Effectiveness of combined diathermy-laser resections, using flexible endoscopic approach, in malignant laryngotracheobronchial tumors is presented.

Methods: Combined diathermy-laser resections were performed on 60 patients with malignant tumors of larynx (46) and tracheobronchial tree (14). Larynx pathology was represented by squamous cell carcinoma (23), spindle cell carcinoma (2), verrucous carcinoma (18) carcinosarcoma (2) and metastatic melanoma (1). In 23 cases primary tumor was diagnosed at T1 stage, in 22 cases – at T2 stage. In 35 patients treatment was limited by endoscopic intervention, in 11 cases postoperative radiotherapy was done. In 27 cases endoscopic operations were performed under local anesthesia with premedication, in 19 cases – under general anesthesia with high frequency jet ventilation (HFJV). Tracheobronchial pathology was represented by typical carcinoid tumor (6), atypical carcinoid tumor (1), adenoid cystic carcinoma (3), squamous cell carcinoma (2), metastatic melanoma (1) and metastatic breast cancer (1). In 2 cases (adenoid cystic carcinoma and atypical carcinoid tumor) endoscopic intervention was supplemented by postoperative radiotherapy. In 11 cases HFJV was used, in 3 cases interventions were performed under local anesthesia. After snare diathermy excision of the exophytic component of the tumor, Nd:YAG laser vaporization of the residual tumor was performed, flexible laser guide being introduced through the working channel of "Olympus" therapeutic fiberbronchoscope.

Results: In larynx tumors, positive effect (local control with organ preservation) was obtained in 42 from 46 patients (91 %). Average follow-up period constituted 57 months. Treatment failure (recurrence or tumor progression) was registered in 4 cases in time interval from 1 month up to 7 months after intervention. In tracheobronchial tumors local control without recurrence or tumor progression was registered in 9 from 10 patients (90%), treated with radical curative intention (follow-up period varied from 7 months up to 12 years, average - 39 months). In 5 cases a good palliative effect was obtained (in none of the cases deaths was caused by respiratory insufficiency due to tumor obstruction).

Conclusion: Obtained results permit us to state, that using of combined diathermy-laser resection is an effective minimally invasive approach for the treatment of malignant tumors of the larynx, trachea and large bronchi in the presence of a prominent exophytic component, allowing obtaining a radical curative effect for limited tumors in

selected patients and a good palliative effect for inoperable tumors. Snare diathermy excision permits shortening of intervention time, at the same time laser ablation favours radicalism of the operation.

PO-520

Bronchoscopic Cryotherapy as a Bridging Therapy in the management of Endobronchial Mucoepidermoid Carcinoma

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Manila Doctors Hospital

Objective: One of the complications of a mucoepidermoid carcinoma (MEC) that have obstructed a bronchus is recurrent cough and pneumonia, mimicking symptoms of asthma, COPD or lung infection. Chest radiograph and chest CT scan can reveal a mass or nodule. Routine bronchoscopic biopsy is the preferred procedure for diagnosis; however, its yield is quite low due to only a small amount of tissue gathered. Cryotherapy is a new and evolving tool that could enhance the diagnostic yield of such tumor.

Methods: We report a case of a low-grade mucoepidermoid carcinoma (MEC) at the left main bronchus in a 23-year woman who came in for non-resolving pneumonia presenting as cough. Chest Xray and Chest CT scan revealed atelectasis of the left lung with a soft tissue density at the left main bronchus hence bronchoscopy was done. Initial bronchoalveolar lavage (BAL) and tissue biopsy only showed acute on chronic inflammatory pattern. Hence, patient underwent follow up bronchoscopy with cryotherapy.

Results: The left main bronchus was recanalized by tumor debulking with the use of cryotherapy. Post operatively, patient's symptoms improved. The histopathology of the mass revealed a low grade mucoepidermoid carcinoma. Immunohistochemical studies noted that the mass was positive to mucocarmine and p63 and was negative on TTF1. The patient was later re-admitted after 6 months for surgical intervention Patient underwent explorative thoracotomy with pneumonectomy of the left lung and adhesiolysis. She was able to tolerate the procedure well and was discharged stable. Final histopathology report of the resected left lung showed no residual tumor left. Lymph nodes and superior margin of the tumor were negative for malignancy.

Conclusion: Endobronchial mucoepidermoid carcinoma (MEC) of the lung is a rare pulmonary neoplasm comprising only <1% of all lung tumors. The obstructed airway caused by the neoplasm can be worsened by mucous secretions and development of mucous plugs, hence patients with such carcinoma can have dyspnea and recurrent pneumonia. Routine bronchoscopic forceps biopsy can be used to diagnosed such condition; however, the diagnostic yield is very low. A new evolving diagnostic and therapeutic tool called the bronchoscopic cryotherapy can increase diagnostic yield up to 95%, improved patient symptoms, and can serve as bridging therapy prior to actual surgical intervention.

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Chirurgia prin endoscopie flexibilă în tratamentul edemului Reinke

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¹USMF "Nicolae Testemițanu", Chișinău, Republica Moldova

Introducere: Edemul Reinke (ER) este o leziune exudativă a laminei propria, caracterizată prin depozitare excesivă a substanței gelatinoase în spațiul Reinke. Metoda tradițională de tratament al ER este microchirurgia transorală, efectuată în sala de operație sub anestezie generală, care nu e posibilă în toate cazurile din cauza contraindicațiilor pentru anestezie generală sau particularităților anatomice, care împiedică expunerea adecvată a leziunii. În ultimii ani, în tratamentul ER sunt utilizate lasere angiolitice în condiții de ambulator, care produc fotoangioliza selectivă și involuția/regresia ulterioară a leziunii, care poate dura câteva săptămâni. Prin urmare, leziunile voluminoase limitează aplicarea acestei metode, prezentând risc de obstrucție a căii aeriene. Propunem o abordare de alternativă, care permite depășirea limitelor metodelor menționate.

Material și metode: Chirurgia prin endoscopie flexibilă (CEF) a fost efectuată la 17 pacienți cu ER (bărbați- 12, femei- 5, cu vârsta de 16-78 ani). Dimensiunile leziunilor au oscilat de la 1.0 până la 2.0 cm. La 13 pacienți (76.5%) intervenția s-a efectuat sub anestezie topică, prin abord transnazal, utilizând bronhoscopul flexibil. În 9 cazuri (52.9%) intervențiile s-au efectuat în condiții de ambulator. La 15 pacienți (88.2%) eradicarea leziunii a fost posibilă într-o ședință. Pentru eradicarea leziunilor au fost aplicate următoarele tehnici endoscopice: excizie cu ansa diatermică (DEX) (n=7), ablație laser (AL) Nd:YAG (n=5), și combinarea metodelor: DEX+AL (n=5).

Rezultate: În toate cazurile a fost obținută eradicarea completă a leziunilor vizibile. În urma intervenției, 5 pacienți au apreciat vocea loc ca fiind normală, 4 pacienți au prezentat disfonie minoră, 6- disfonie moderată, și 2- disfonie severă.

Concluzii: CEF poate fi considerată o alternativă metodelor tradiționale de tratament al ER, tehnicile utilizate permițând eradicarea inclusiv a leziunilor voluminoase sub anestezie locală, în special, la pacienți cu riscuri/contraindicații pentru anestezie generală și laringoscopie rigidă.

Cuvinte cheie: chirurgie prin endoscopie flexibilă, edemul Reinke

Conferința Națională de Otorinolaringologie și Chirurgie Cervico-Facială cu Participare Internațională



Chirurgia prin endoscopie flexibilă în tratamentul polipilor corzilor vocale

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Introducere: Polipii corzilor vocale (PCV) sunt leziuni exofitice benigne, care afectează stratul superficial al laminei propria. Intervenția chirurgicală, tradițional, este efectuată prin excizie în timpul microchirurgiei transorale în sala de operație sub anestezie generală (AG) cu miorelaxare, care nu este posibilă în toate cazurile din cauza particularităților anatomice, asociate cu expunerea inadecvată a leziunii, și riscurilor AG. În ultimele 2 decenii, în tratamentul de ambulator al PCV sunt aplicate lasere angiolitice, care produc fotoangioliza selectivă, urmată de involuția leziunii, care poate dura câteva săptămâni. Prin urmare, există riscul de leziune persistentă/restantă, care va necesita tratament adițional. Propunem o abordare, care permite depășirea limitelor metodelor menționate.

Material și metode: Chirurgiei prin endoscopie flexibilă (CEF) au fost supuși 269 pacienți cu PCV (bărbați- 179, femei- 90, cu vârsta de 16-81 ani). Dimensiunile leziunilor au oscilat de la 0.2 până la 3.0 cm. La 267 pacienți (99.3%) intervențiile au fost efectuate sub anestezie topică, utilizând bronhoscopul flexibil prin abord transnazal. În 242 din cazuri (90%) operația a fost efectuată în condiții de ambulator. Au fost aplicate următoarele tehnici endoscopice în diferite combinații: chirurgia rece utilizând forsepsul flexibil – în 130 de cazuri (48.3%), excizia cu ansa diatermică – la 126 (46.8%) pacienți, ablația laser Nd:YAG – în 71 (26.4%) de cazuri.

Rezultate: În toate cazurile a fost obținută eradicarea completă a leziunii vizibile. După operație, 262 pacienți (97.4%) au apreciat glasul lor ca fiind normal. Leziuni recidivante au fost constatate ulterior în 2 cazuri (0.7%), iar leziuni maligne - în 3 cazuri, fiind rezolvate cu succes prin CEF.

Concluzii: CEF, având avantaje comparativ cu metodele terapeutice tradiționale (efect economic pozitiv, traumatism minim, posibilitatea efectuării intervenției la pacienți cu contraindicații pentru AG sau laringoscopie suspendată, economie de timp), poate fi o alternativă relevantă în tratamentul PCV.

Cuvinte cheie: chirurgie prin endoscopie flexibilă, polipi ai corzilor vocale

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TEHNICI BRONHOSCOPICE ÎN MANAGEMENTUL LEZIUNILOR NEEPITELIALE BENIGNE ALE LARINGELUI

Petru Gurău

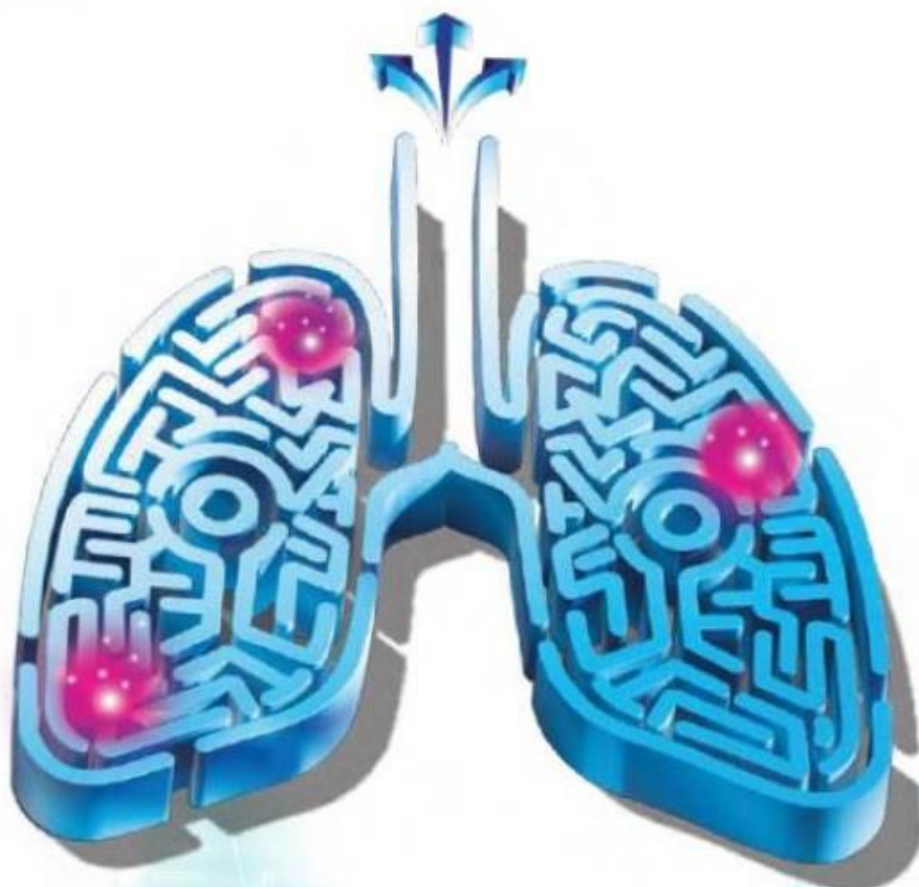
Universitatea de Stat de Medicină și Farmacie „Nicolae Testemițanu”, Chișinău

Metoda predilectă în tratamentul leziunilor neepiteliale benigne laringiene (LNEBL), în prezent, este microchirurgia transorală (MCT), realizată sub anestezie generală (AG) cu miorelaxare, care, pe lângă avantajele indiscutabile are, de asemenea, unele dezavantaje, incluzând traumatismul dentar, cauzat de laringoscopul rigid, și riscuri asociate cu AG. Chirurgia laringiană de ambulator (CLA) cu utilizarea laserelor angiolitice a devenit o tendință aflată în plină dezvoltare în laringologia modernă mai ales în ultimele 2 decenii, posibilitățile metodei fiind limitate în cazul leziunilor voluminoase. Noi am aplicat chirurgia laringiană prin endoscopie flexibilă (CLEF) la 338 de pacienți cu LNEBL. Patologia laringelui a fost reprezentată de următoarele leziuni: polip mixoid, edemul Reinke, polip fibros, polip angiofibros, polip angiomas, granulom nespecific, chist, lipom, neurofibrom, schwanom, tumoră miofibroblastică inflamatorie și amiloidoză. S-au folosit următoarele metode de eradicare a leziunilor laringiene: chirurgia rece prin intermediul forcepsului flexibil, excizia cu ansă diatermică, ablația laser Nd:YAG/laser dioda 980/1470 nm, și tehnici combinate. În 97% din cazuri tratamentul s-a realizat într-o singură ședință. În 327 de cazuri (96,7%) intervenția s-a efectuat sub anestezia locală cu respirație spontană, iar în 11 cazuri (3,3%) am folosit AG cu ventilație cu jet de frecvență înaltă suprapusă (VJFÎS). În 286 de cazuri (84,6%) intervenția s-a efectuat în condiții de ambulator. La toți pacienții tratați a fost obținut rezultatul scontat - eradicarea completă a leziunii vizibile. Leziuni recidivante au fost înregistrate în 9/338 de cazuri (2,7%). La 8 din 9 pacienți (88,9%) tratamentul recidivelor a fost efectuat prin CLEF. La 4 din 338 de pacienți cu LNEBL (1,2%), supuși CLEF, ulterior s-au dezvoltat malignități. În 3 cazuri leziunea malignă a fost eradicată cu succes prin CLEF, iar într-un caz a fost efectuată laringectomia parțială deschisă. Majoritatea pacienților (92%) au apreciat vocea lor după operație ca fiind normală.

Concluzie: CLEF cu utilizarea laserelor non-angiolitice, ansei diatermice și forcepsului de biopsie flexibil, poate fi considerată drept alternativă MCT în tratamentul LNEBL la pacienți selectați, deschizând o direcție nouă în CLA. Tehnicile propuse permit depășirea unor limite ale metodelor chirurgicale utilizate în prezent (MCT și CLA cu utilizarea laserelor angiolitice) și demonstrează aplicabilitate în CLA chiar în cazul leziunilor voluminoase, în special, la pacienți cu riscuri și contraindicații pentru AG și laringoscopia directă suspendată.



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П.П. ГУРЭУ (КИШИНЕВ, МОЛДОВА)

ГИБКАЯ ЭНДОСКОПИЯ В ДИАГНОСТИКЕ И ЛЕЧЕНИИ ВЕРРУКОЗНОЙ КАРЦИНОМЫ ГОРТАНИ

Веррукозная карцинома (ВК) является редкой формой рака гортани (1-3%), представляющей сложности для диагностики и разработки тактики лечения. ВК является особой разновидностью плоскоклеточного рака, характеризующейся медленной локальной инвазией, высокой степенью дифференцировки клеток, преимущественно экзофитным ростом, формированием массивного слоя кератина на поверхности, отсутствием тенденции к региональному и отдаленному метастазированию, а в поздних стадиях – стенозированием просвета, компрессионным некрозом хрящей гортани и летальным исходом.

Сотрудничество клинициста с патологом является критичным для постановки правильного диагноза и разработки адекватной тактики лечения. Диагностические проблемы связаны главным образом с наличием толстого слоя кератина на поверхности опухоли, вследствие чего традиционная биопсия почти всегда является поверхностной и неадекватной, а гистологическое заключение – неинформативным. Гиподиагностика часто приводит к задержке адекватного лечения и прогрессированию опухолевого процесса.

Представляем наш опыт эндоскопического лечения 23 пациентов с ВК гортани. Все

Таким чином, проведені дослідження дозволили зробити висновки, що у нормативних документах України та переважної більшості країн зарубіжжя, які були проаналізовані, переважає морфо-функціональний підхід при визначенні небезпеки для життя при закритій травмі гортані, при якому про загрозу життю свідчать відповідні клінічні симптоми морфологічно визначеного експертом ушкодження. Застосування суто морфологічного підходу, який діє в Російській Федерації, при якому морфологія ЗТГ з переломами її хрящів сама по собі характеризує ушкодження як небезпечне для життя та дозволяє її віднести до тяжких тілесних ушкоджень, незалежно від того, будуть чи ні спостерігатися небезпечні для життя патологічні стани, є недосконалим та необґрунтованим.

пациенты в исследуемой группе были мужчинами в возрасте от 38 до 80 лет. Во всех случаях опухоль поражала средний отдел гортани. В зависимости от степени местного распространения опухоли пациенты распределились следующим образом: T1a – 7 (30,4%), T1b – 4 (17,4%), T2 – 12 (52,2%). Традиционная биопсия во всех случаях была неинформативной («лейкоплакия», «пахидермия», «гиперкератоз», «папиллома»). Для получения адекватного образца ткани с целью гистологического подтверждения характера опухолевого процесса производилась фиброэндоскопическая петлевая диатермоэксцизия опухоли. После гистологического подтверждения опухолевого процесса выполнялась фотоабляция опухоли с помощью YAG:Nd- лазера. Количество сеансов варьировало от 1 до 9 (в среднем – 2,2). В 14 случаях вмешательство производилось под местной анестезией с предварительной премедикацией на спонтанном дыхании. В 9 случаях использовалась подвешная ларингоскопия с высокочастотной струйной вентиляцией легких в комбинации с фиброларингоскопией. В 22 случаях (95,7%) был достигнут локальный контроль. Период безрецидивного наблюдения варьировал от 9 до 193 мес (в среднем – 67 мес). В 19 случаях рецидив не был выявлен. В

1 случае был диагностирован местный рецидив опухоли через 4 мес, который был разрешен с помощью повторной лазерной абляции. В 1 случае после выявленного рецидива опухоли (плоскоклеточный неороговевающий рак (гибридная форма ВК гортани) была проведена лучевая терапия с позитивным эффектом. В 1 случае был выявлен местный рецидив через 4 года, по поводу чего была выполнена ларингофиссура с диатермоэксцизией опухоли и наложением трахеостомы. В 1 случае после 4-го сеанса лазерной абляции контрольная биопсия выявила плоскоклеточный неороговевающий

рак (гибридная форма ВК гортани), произведена тотальная ларингэктомия, через 7 мес после которой наступил летальный исход.

Выводы: Тесное сотрудничество клинициста и патолога является неперемным условием для правильной постановки диагноза. Получение достаточно крупного образца ткани при биопсии является критичным для правильного гистологического ответа. Фиброэндоскопическая лазерная абляция может быть предложена как метод выбора для большинства пациентов с ВК гортани при условии регулярного эндоскопического мониторинга.

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П.П. ГУРЗУ (КИШИНЕВ, МОЛДОВА)

ХИРУРГИЯ НЕСПЕЦИФИЧЕСКОЙ ГРАНУЛЕМЫ ГОРТАНИ С ПОМОЩЬЮ ГИБКОГО ЭНДОСКОПА

Неспецифические гранулемы (НГ) гортани являются доброкачественными новообразованиями, которые обычно локализуются в задней трети голосовой складки, что соответствует голосовому отростку черпаловидного хряща. Этиопатогенез НГ до конца не выяснен. Основными предрасполагающими факторами в возникновении данной патологии считаются желудочно-пищеводный рефлюкс, голосовые нагрузки и ларинго-трахеальная интубация.

Представляем наш опыт лечения 24 пациентов (мужчин – 14, женщин – 10) с НГ гортани с помощью гибкой эндоскопии. Возраст больных варьировал от 17 до 72 лет. В 21 случае новообразования поражали средний отдел гортани, в 1 случае – средний и надскладочный отдел, в 2 случаях – подскладочный отдел гортани. Задняя треть голосовой складки была вовлечена в процесс в 21 из 24 случаев. В 5 случаях процесс был двухсторонним. Размеры новообразований варьировали от 0,4 до 2,0 см в диаметре.

Хирургические вмешательства производились под местной анестезией, в ряде случаев – с предварительной премедикацией, с использованием гибкого бронхоскопа. В 19 случаях вмешательства были выполнены в амбулаторных условиях. Целью хирургического вмешательства во всех случаях было полное удаление патологического образования.

Использовались следующие типы хирургических вмешательств: механическое удаление

– в 3 случаях, диатермоэксцизия – в 9 случаях, лазерная фотоабляция с помощью YAG:Nd-лазера – в 2 случаях, комбинирование методик – в 10 случаях (механическое удаление в комбинации с лазерной фотоабляцией – 3, диатермоэксцизия в комбинации с механическим удалением – 1, диатермоэксцизия в комбинации с лазерной фотоабляцией – 6). В 23 из 24 случаев новообразования были удалены за 1 сеанс, в 1 случае потребовалось 2 сеанса. Во всех случаях была достигнута полная эрадикация видимого патологического образования с хорошим функциональным эффектом. Рецидивы НГ были констатированы в 6 случаях (25%) через 1-6 мес после операции, что потребовало повторных вмешательств.

Полученные результаты позволяют утверждать, что хирургия с помощью гибкого эндоскопа, обладающая некоторыми преимуществами в сравнении с традиционными методиками (экономический эффект, минимальный травматизм, возможность проведения операции у больных с противопоказаниями к общей анестезии), может быть предложена как достойная альтернатива в лечении больных с неспецифическими гранулемами гортани. Представляет интерес изучение влияния послеоперационного консервативного лечения (ингаляции стероидных препаратов, использование ингибиторов протонной помпы, голосовая терапия) на снижение риска послеоперационных рецидивов.

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Российская академия медицинских наук

**Проблемная комиссия РАМН по
эндоскопической хирургии**

**Российское научное общество
"Эндоскопическая хирургия"**

Российский научный центр хирургии РАМН



РОССИЙСКИЙ СИМПОЗИУМ

**ВНУТРИПРОСВЕТНАЯ
ЭНДОСКОПИЧЕСКАЯ
ХИРУРГИЯ**

Москва, 22-23 апреля 1998 г.

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**3-й МОСКОВСКИЙ
МЕЖДУНАРОДНЫЙ КОНГРЕСС ПО
ЭНДСКОПИЧЕСКОЙ ХИРУРГИИ**

Москва, 21-23 апреля 1999 г.

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ANNEX 2

FIGURES

```
```{r}

instalează pachetul pwr dacă nu este deja instalat
install.packages("pwr")

încarcă pachetul
library(pwr)

Parametrii de intrare
effect_size <- 0.3 # Mărimea efectului (0.1 pentru mic, 0.3 pentru mediu, 0.5 pentru mare)
alpha <- 0.05 # Nivelul de semnificație
power <- 0.80 # Puterea testului
df <- 1 # Gradele de libertate (pentru 2 variabile dicotomice, df = (r - 1) * (c - 1) = 1)

Calcularea dimensiunii esantionului
sample_size <- pwr.chisq.test(w = effect_size,
 #N = NULL,
 df = df,
 sig.level = alpha,
 power = power)

Afisează rezultatul
sample_size

```

Chi squared power calculation

      w = 0.3
      N = 87.20954
      df = 1
sig.level = 0.05
power = 0.8

NOTE: N is the number of observations
```

Figure A2.1. Estimation of the minimum sample size required for survival analysis in Study 1

```
```{r}
install.packages('powerSurvEpi')
library(powerSurvEpi)

ssizeCT.default(power = 0.8,
 k = 0.8, |
 pE = 0.4,
 pC = 0.15,
 RR = 0.3,
 alpha = 0.05)
```
```

| nE | nC |
|----|----|
| 53 | 66 |

Figure A2.2. Estimation of the minimum sample size required for the survival analysis in Study 2

Note: power = 0.8 — the test power, indicating the probability (80%) that the test will detect an effect, if one exists; k = 0.8 — the ratio of the number of participants in the T2 group to the number of participants in the T1 group; pE = 0.4 — the probability of the event in the T2 group (e.g., the proportion of people in whom an event, such as death or recurrence, will occur); pC = 0.15 — the probability of the event in the T1 group; RR = 0.3 — the risk ratio, which reflects the ratio of the risk in the T2 patient group to that in the T1 patient group; alpha = 0.05 — the acceptable probability of incorrectly rejecting the null hypothesis.



Figure A2.3. „Olympus” BF-TE2 fiberoptic bronchoscope



Figura A2.4. „Olympus” BF-1TH1100 videobronchoscope



Figure A2.5. Flexible biopsy forceps



Figure A2.6. Diathermy loop/snare



Figure A2.7. ESG-300 electrocautery unit („Olympus”, Japan)



Figure A2.8. Nd:YAG laser unit, model: LTN-102 (Russia)



Figure A2.9. Diode laser device, model: LEONARDO Dual 45 („Biolitec”, Germany)



Figure A2.10. Superimposed high-frequency jet ventilator, model „TwinStream” („Carl Reiner”, Austria)

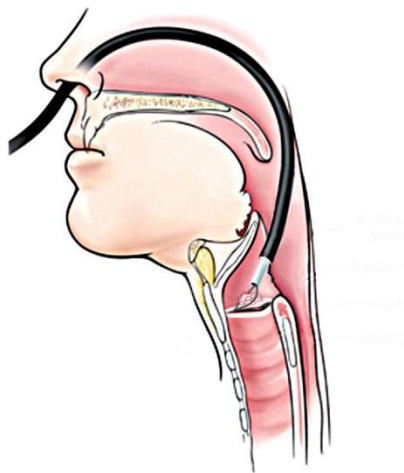


Figure A2.11. The diathermic loop is delivered to the lesion via the working channel of the flexible endoscope

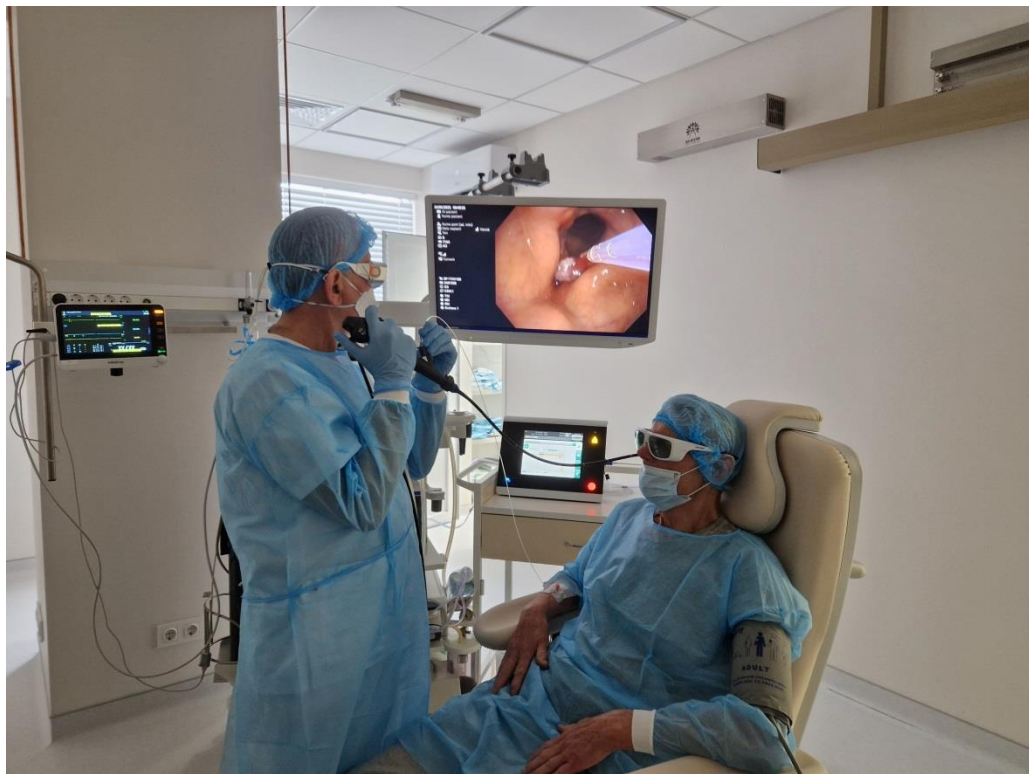


Figure A2.12. Diode laser ablation, performed under local anaesthesia

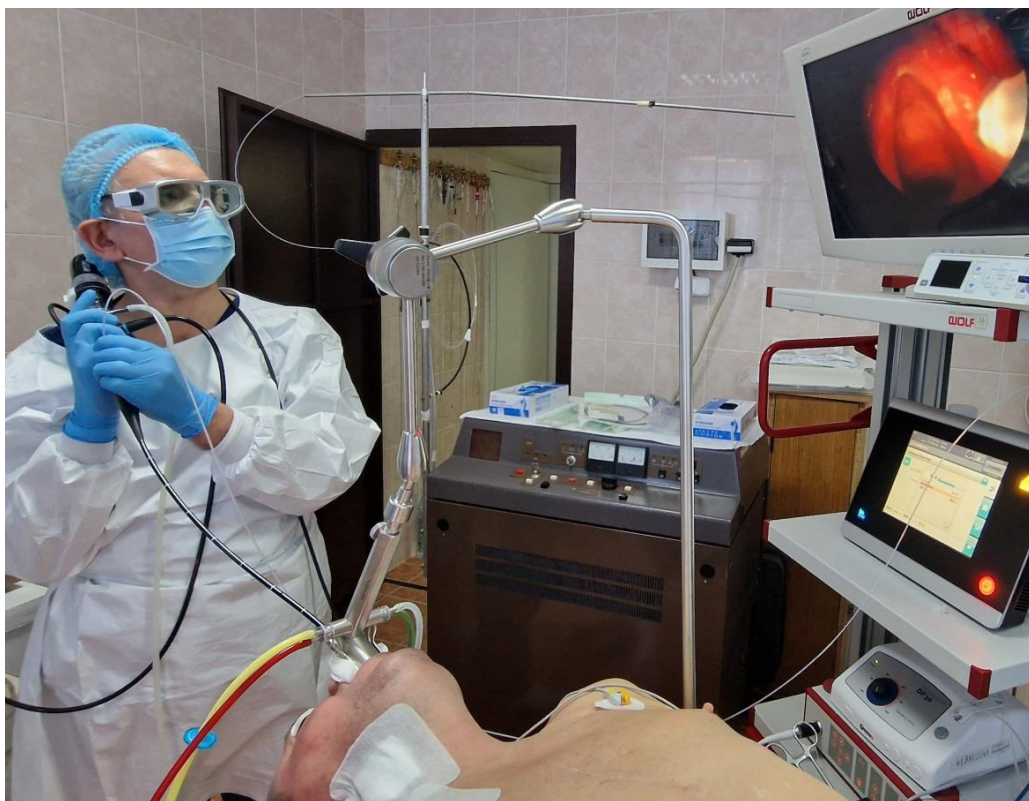


Figure A2.13. Nd:YAG laser ablation, performed under general anaesthesia with SHFJV, via flexible endoscopy, combined with rigid laryngoscopy

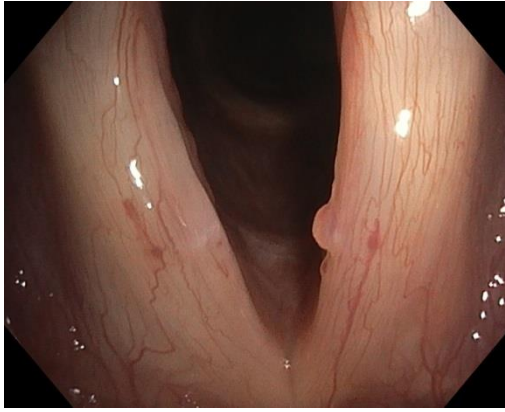


Figure A2.14a: Nodule of the left vocal cord

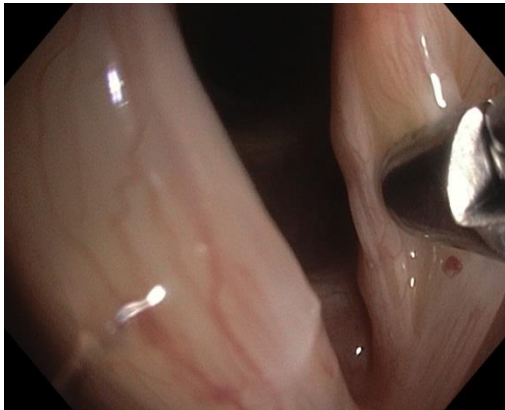


Figure A2.14b: Removal of the lesion using biopsy forceps

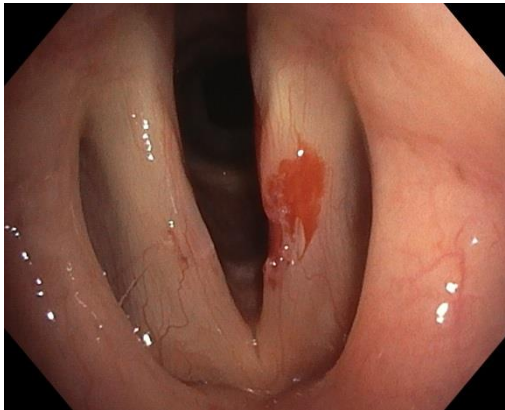


Figure A2.14c: Endoscopic view immediately after removal of the lesion

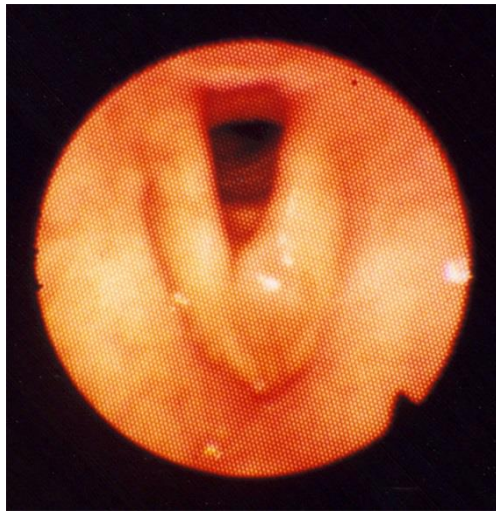


Figure A2.15a. Myxoid polyp of the left vocal cord

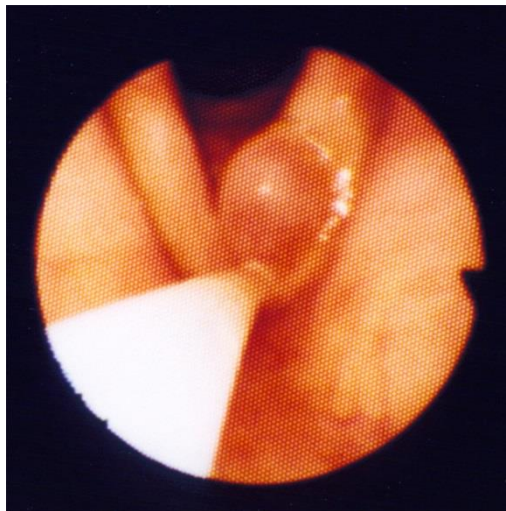


Figure A2.15b. Excision using a diathermic loop

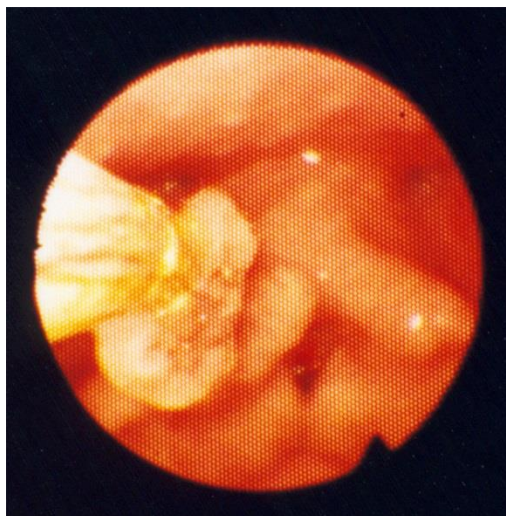


Figure A2.15c. Removal of the resected polyp

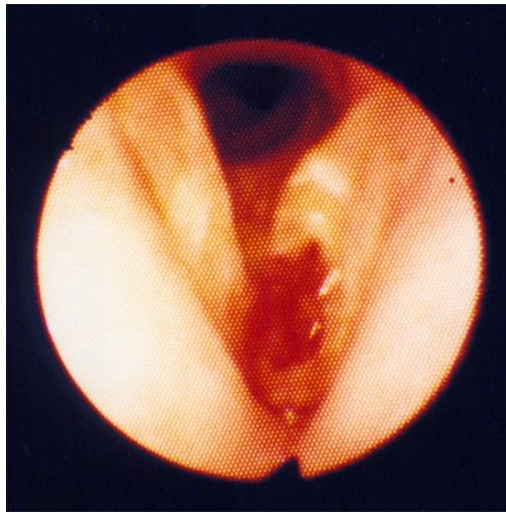


Figure A2.15d. Endoscopic view immediately after resection

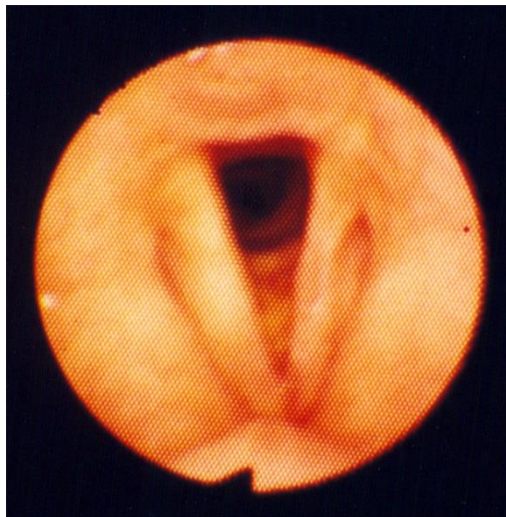


Figure A2.15e. Two months after surgery: no visible lesions

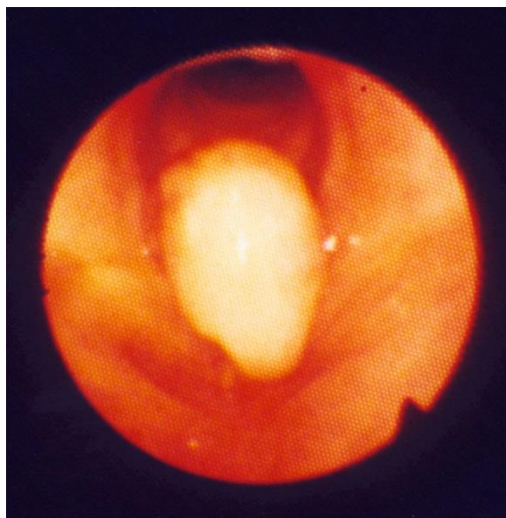


Figure A2.16a. Angiofibrous polyp of the right vocal cord

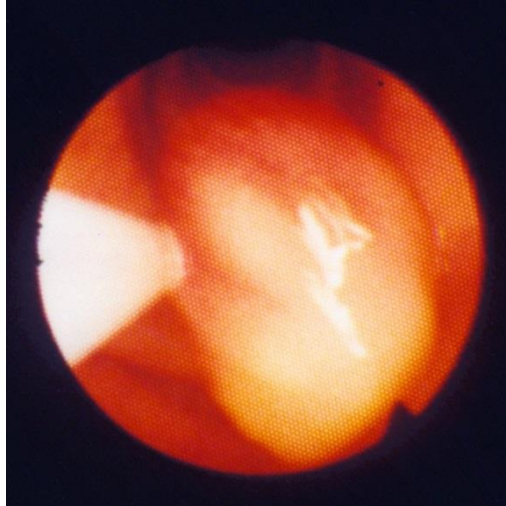


Figure A2.16b. Excision with a diathermy loop



Figure A2.16c. The excised lesion

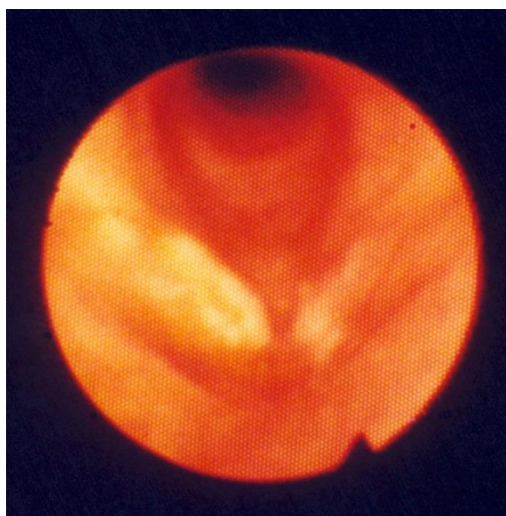


Figure A2.16d. Endoscopic view immediately after resection

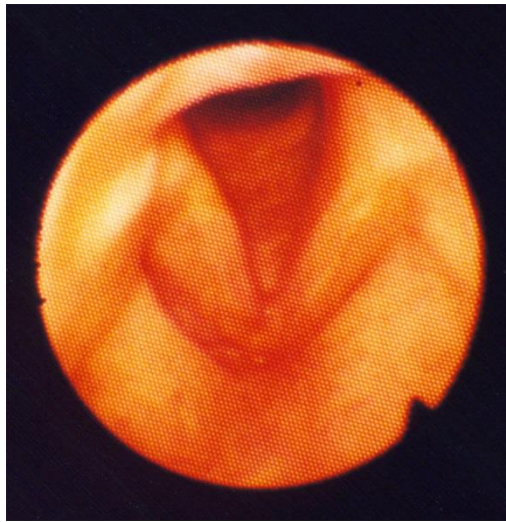


Figure A2.16e. Three months after surgery: no visible lesions



Figure A2.17a. Neurofibroma of the right vocal cord

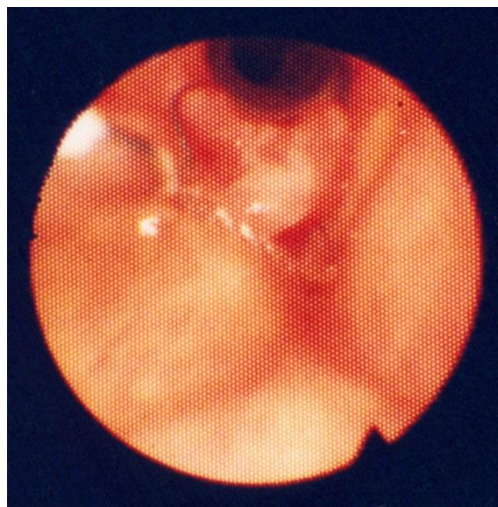


Figure A2.17b. Placement of the diathermic loop at the base of the tumour

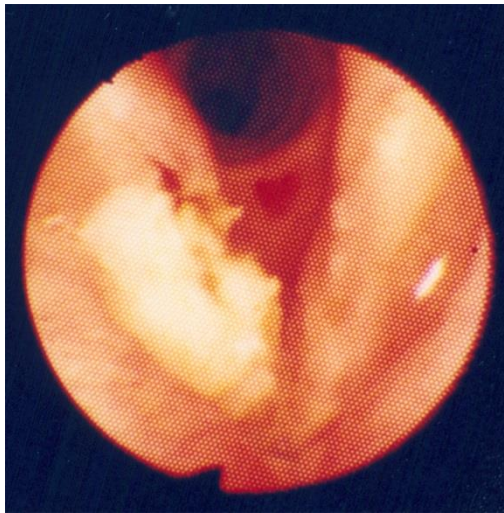


Figure A2.17c. Residual tumour immediately after diathermic excision

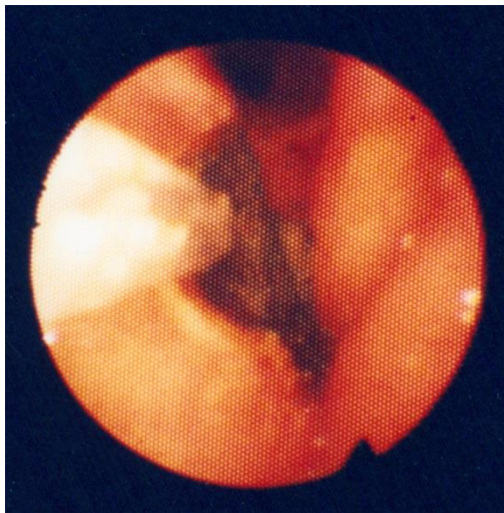


Figure A2.17d. Ablation of the residual tumour with an Nd:YAG laser

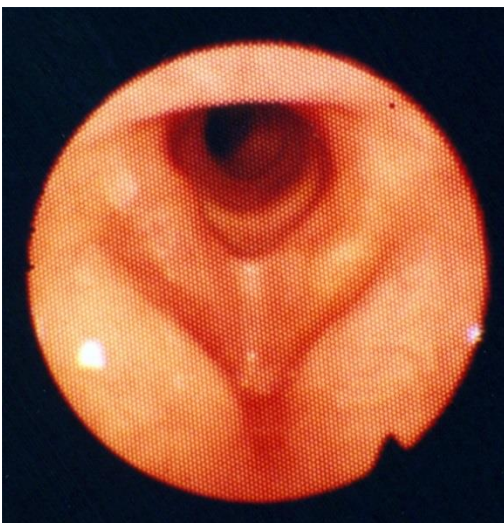


Figure A2.17e. Endoscopic view 3 months after surgery: no residual tumour is visible

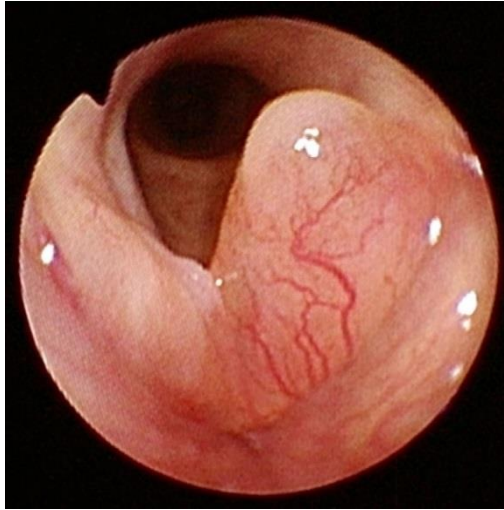


Figure A2.18a. Reinke's oedema affecting both vocal cords



Figure A2.18b. Placement of the diathermy loop at the base of the lesion

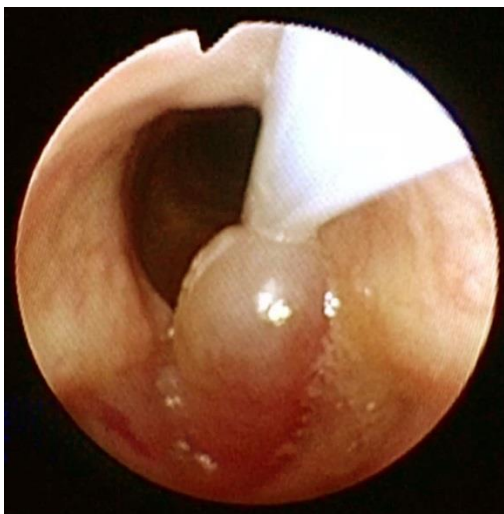


Figure A2.18c. The moment of diathermic excision

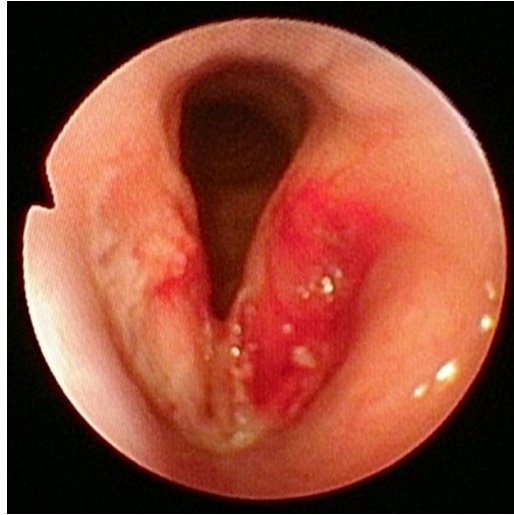


Figure A2.18d. Endoscopic view immediately after resection

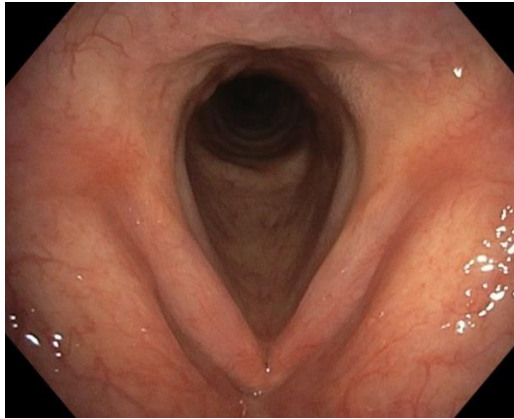


Figure A2.18e. Endoscopic view 3 months after surgery: no visible lesions

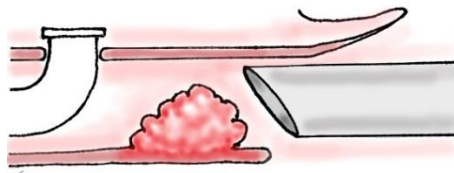


Figure A2.19a. Obstructive exophytic tumour on the posterior wall of the larynx



Figure A2.19b. Anterograde and retrograde laser resection of the tumour using a flexible bronchoscope

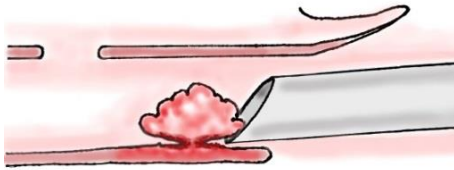


Figure A2.19c. Cold resection of the tumour with the bevel of the rigid bronchoscope

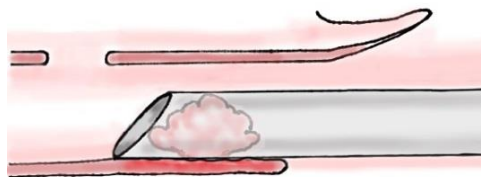


Figure A2.19d. The resected tumour is located in the lumen of the rigid bronchoscope

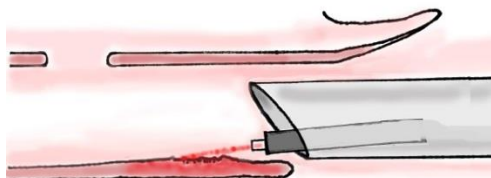


Figure A2.19e. Laser ablation of the residual tumour

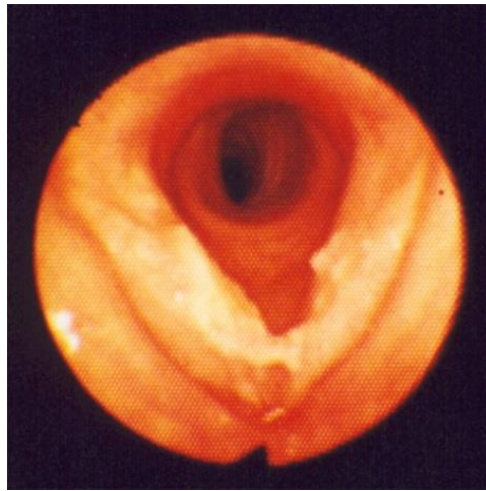


Figure A2.20a. Leukoplakia of the glottic portion of the larynx involving both vocal cords and the anterior commissure



Figure A2.20b. Immediately after photoablation of the lesion with an Nd:YAG laser

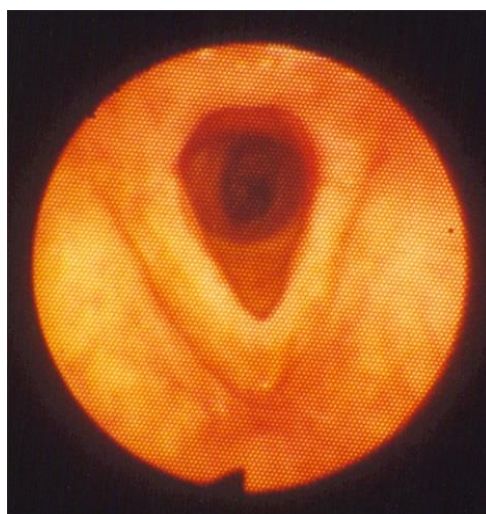


Figure A2.20c. Endoscopic view 6 months after the procedure: no visible lesions



Figure A2.21a. Laryngeal leukoplakia

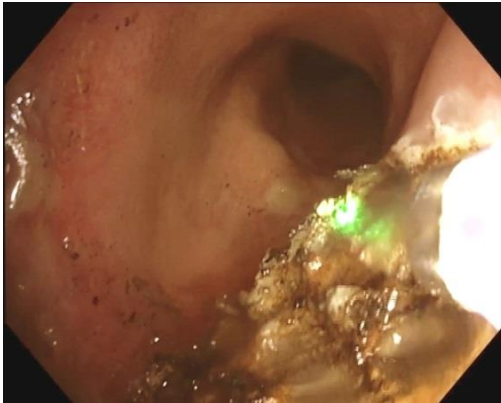


Figure A2.21b. At the time of laser ablation

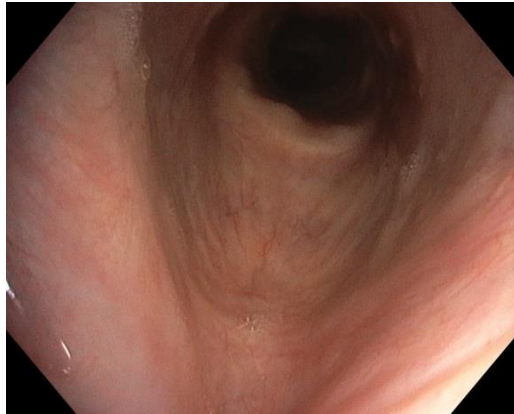


Figure A2.21c. 7 months after surgery: no visible lesions

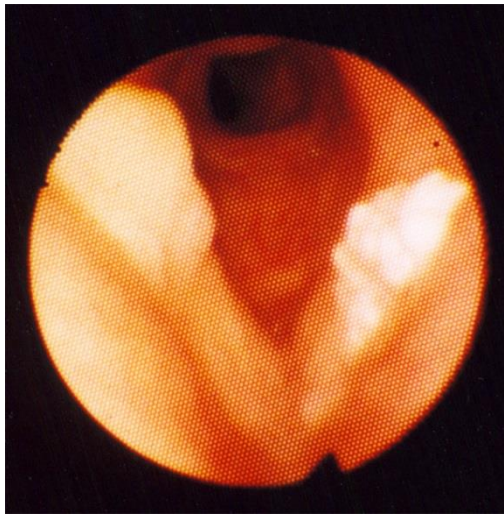


Figure A2.22a. Pachydermia of the glottic portion of the larynx

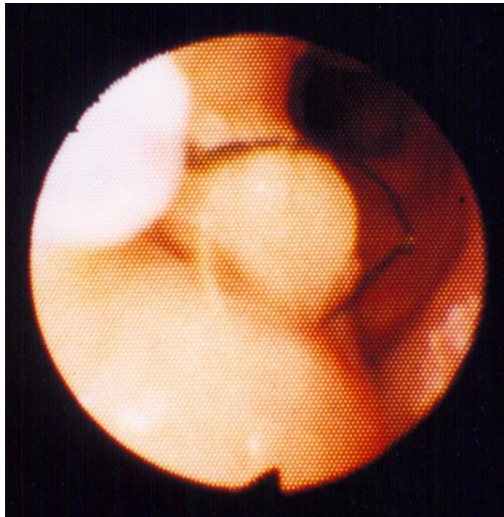


Figure A2.22b. At the time of diathermy loop excision of the exophytic component of the right vocal cord lesion

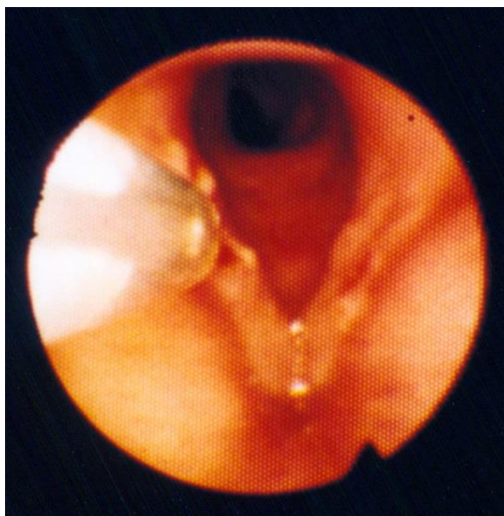


Figure A2.22c. At the time of Nd:YAG laser ablation of the residual lesion

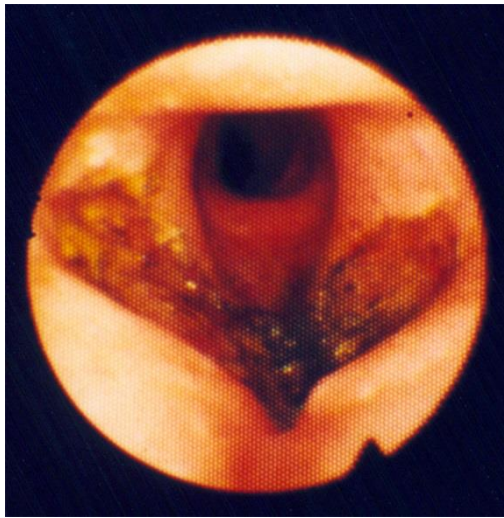


Figure A2.22d. Endoscopic view immediately after photoablation

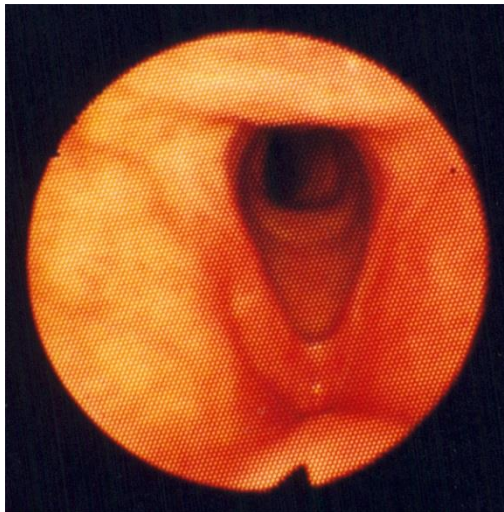


Figure A2.22e. Endoscopic appearance 1 year after surgery: no visible lesions



Figure A2.23a. Papillomatosis of the glottic portion of the larynx

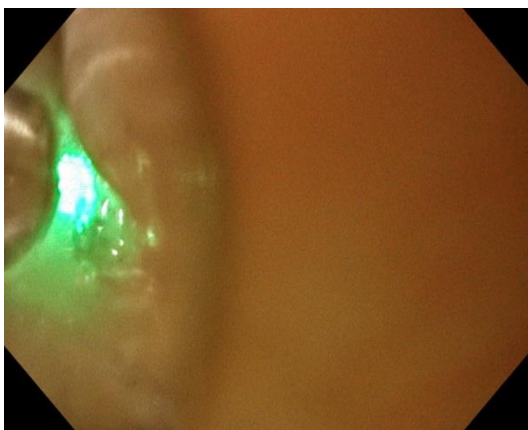


Figure A2.23b. Photoablation of the lesion using a 980/1470 nm diode laser

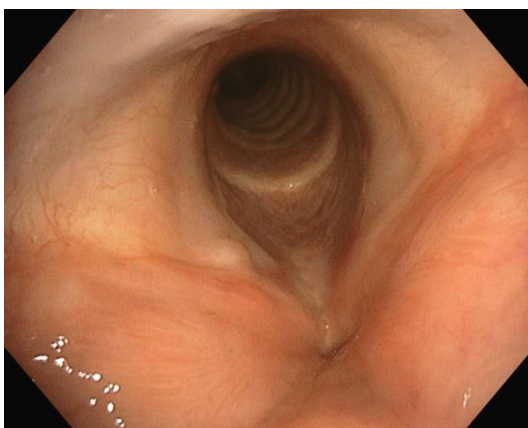


Figure A2.23c. Six months after surgery: no visible lesions

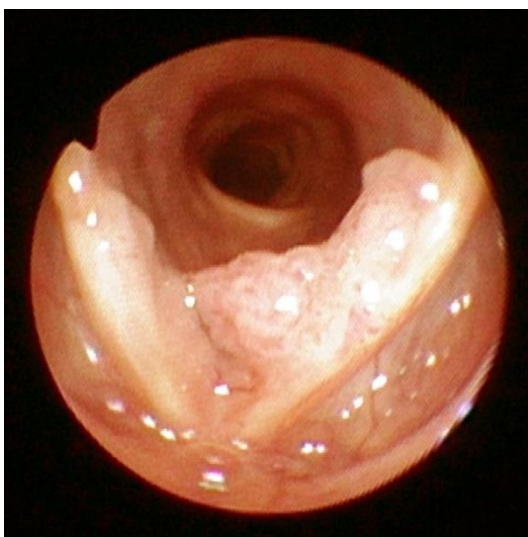


Figure A2.24a. Glottic papillomatosis

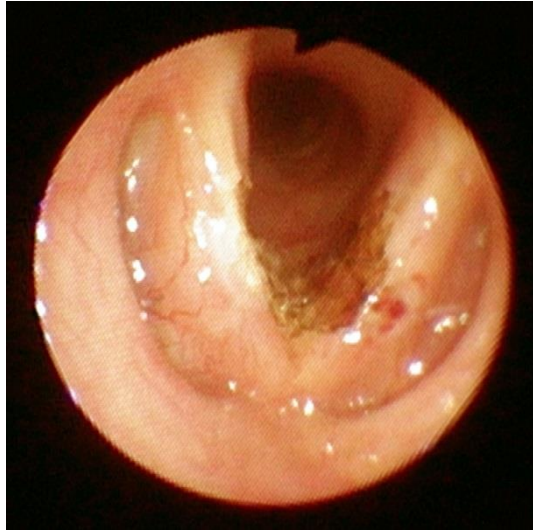


Figure A2.24b. Endoscopic view immediately after ablation with a 980/1470 nm diode laser, preceded by excision with a diathermic loop

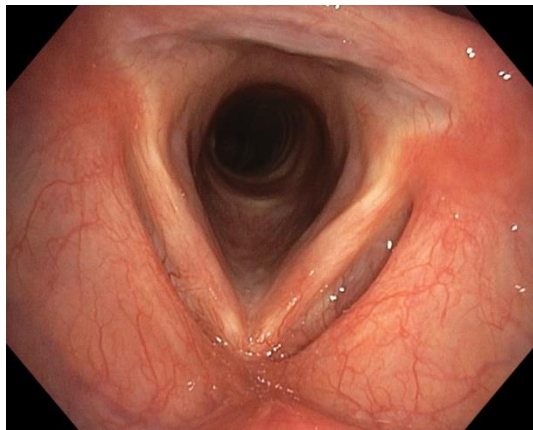


Figure A2.24c. Four months after surgery: no visible lesions

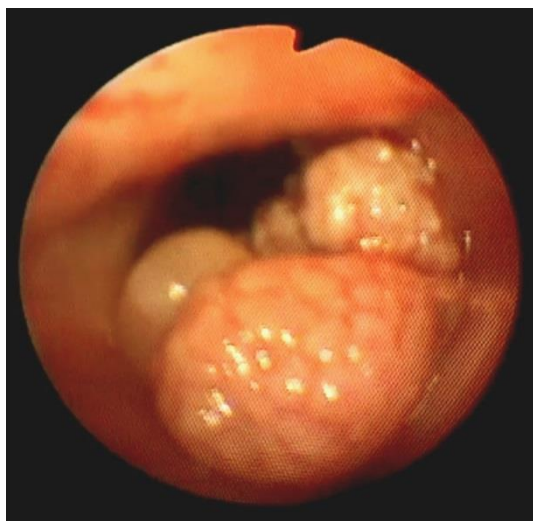


Figure A2.25a. Massive racemose papillomatous proliferations, which considerably obstruct the laryngeal lumen



Figure A2.25b. The moment of excision of the prominent exophytic component of the lesion using a diathermy loop



Figure A2.25c. Photoablation of the remaining lesion using an Nd:YAG laser



Figure A2.25d. Endoscopic view 3 months after the procedure: the laryngeal lumen is clear, with no evidence of tumour proliferation

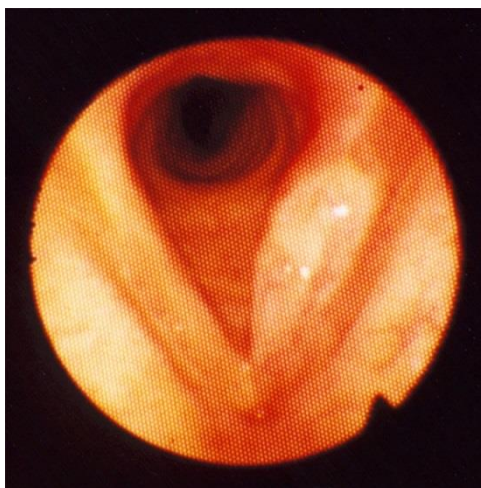


Figure A2.26a. T1a cancer of the left vocal cord: the endophytic (infiltrative-ulcerative) tumour affects the anterior three-quarters of the left vocal cord

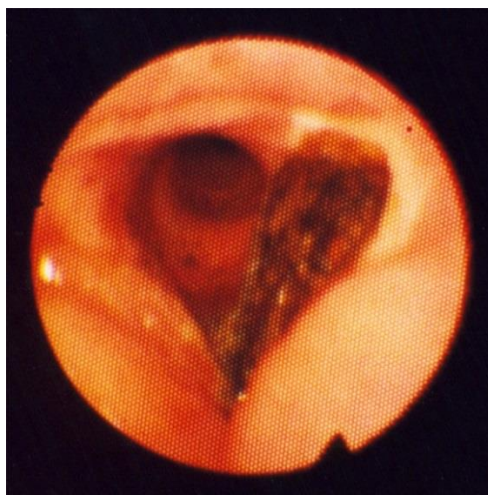


Figure A2.26b. Endoscopic view immediately after laser ablation of the glottic tumour: the postoperative wound is covered with a carbonised coagulation scab



Figure A2.26c. Endoscopic view 1 week after laser ablation of the glottic tumour: the postoperative wound is covered with a dense, whitish-grey fibrinous-necrotic scab



Figure A2.26d. Endoscopic view 2 months after laser ablation of the glottic tumour: flattened granulomatous proliferations (0.2–0.3 cm in diameter) in the area of photoablation

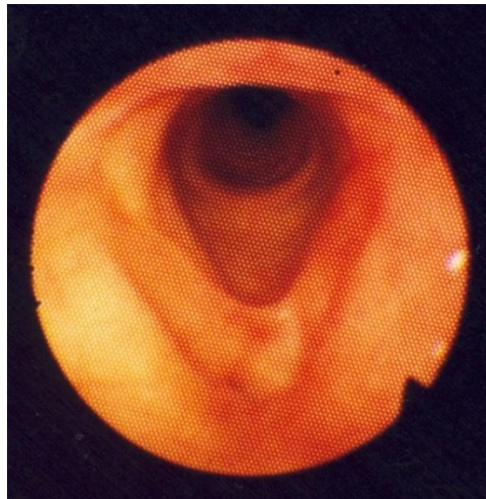


Figure A2.26e. Endoscopic view 3 months after laser ablation of the glottic tumour: the postoperative wound is epithelialised, with scarring of the glottic portion of the larynx involving the anterior commissure

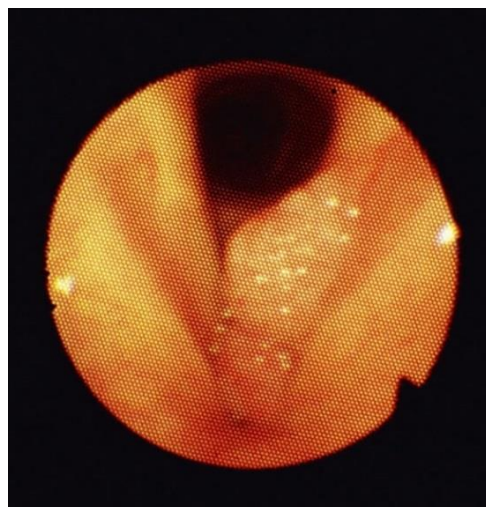


Figure A2.27a. T1b glottic cancer: the tuberos exophytic tumour affects the anterior two-thirds of the left vocal cord and the anterior commissure

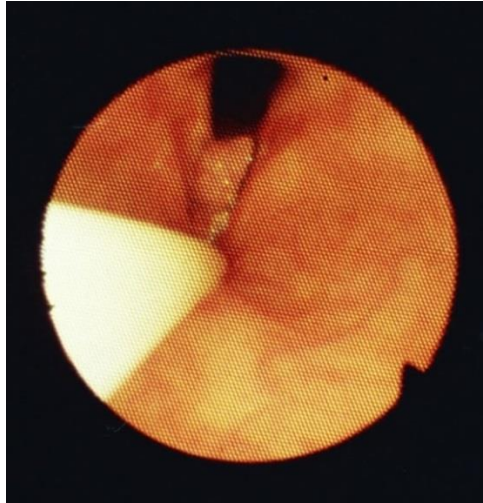


Figure A2.27b. Excision of the exophytic component of the tumour using a diathermic loop

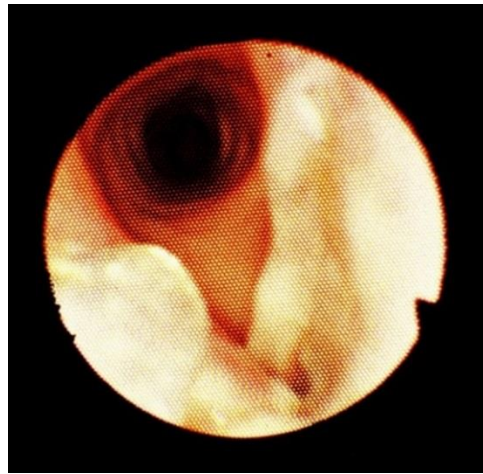


Figure A2.27c. The moment of Nd:YAG laser ablation of the remaining tumour



Figure A2.27d. Endoscopic view 5 years after tumour ablation

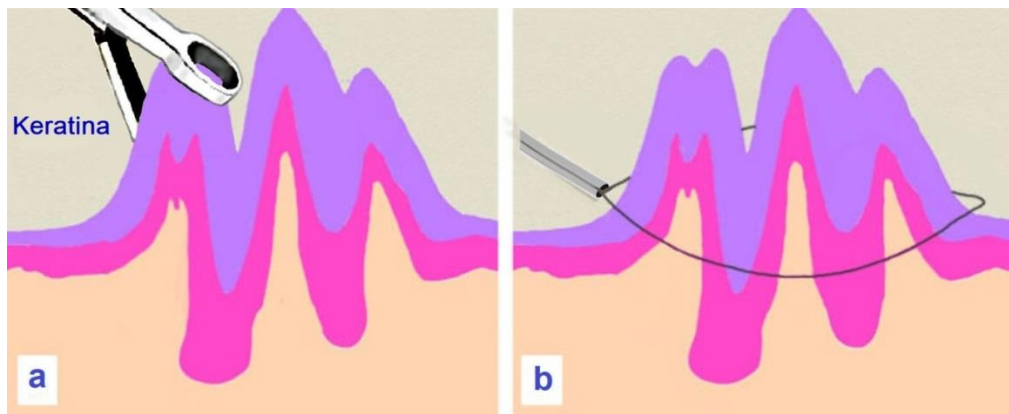


Figure A2.28. Biopsy of VCL: a. inadequate biopsy using forceps; b. adequate biopsy by excision with a diathermic loop



Figure A2.29. The moment of the biopsy of VCL by excision with a diathermic loop



Figure A2.30. Tumour fragments obtained following biopsy using a diathermic loop

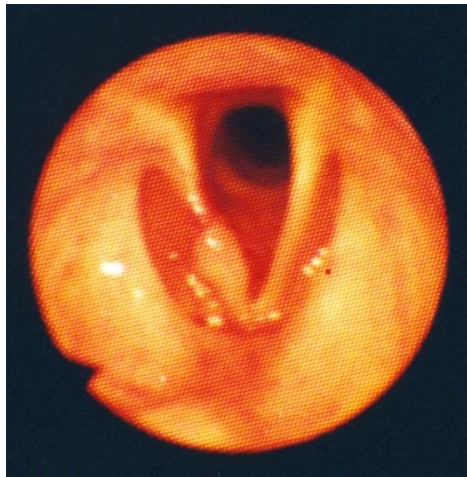


Figure A2.31a. T1a glottic cancer

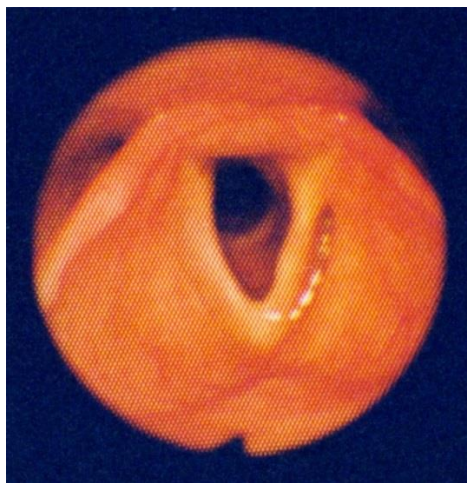


Figure A2.31b. Endoscopic view 4 years after photoablation of the tumour: minor scarring of the glottic portion of the larynx

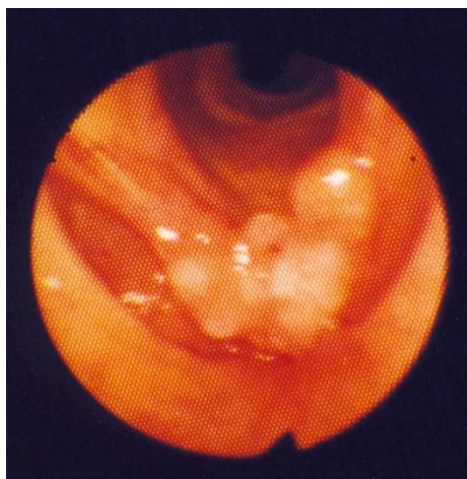


Figure A2.32a. T1b glottic cancer: the tuberos exophytic tumour affects the anterior two-thirds of the left vocal cord, the anterior commissure, and the anterior half of the right vocal cord

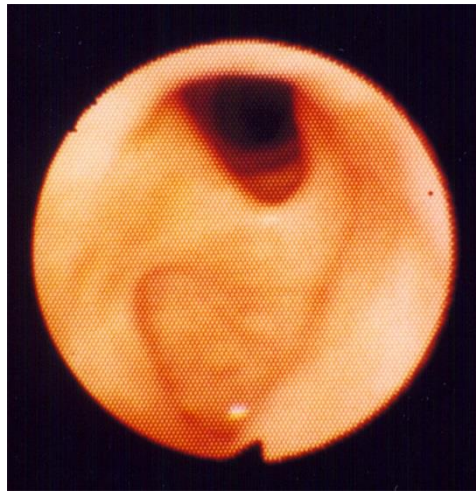


Figure A2.32b. Endoscopic view 1 year after laser ablation of the glottic tumour: deformation and scar-induced stenosis of the glottic portion of the larynx due to the formation of a membranous synechia in the region of the anterior commissure

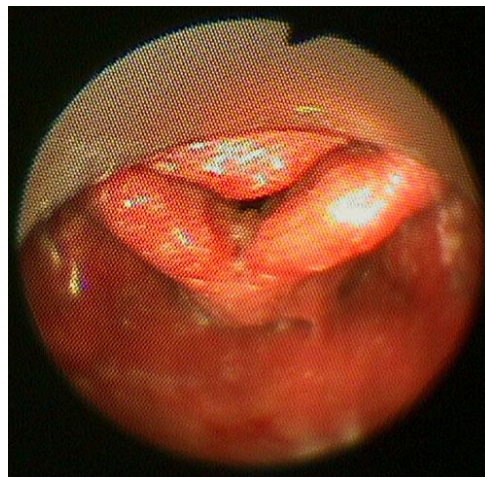


Figure A2.33a. The rigid laryngoscope is inserted into the pharynx until exposing the arytenoid cartilages



Figure A2.33b. Adequate exposure/visibility of the glottic portion of the larynx, achieved by advancing the flexible bronchoscope through the rigid laryngoscope in suspension

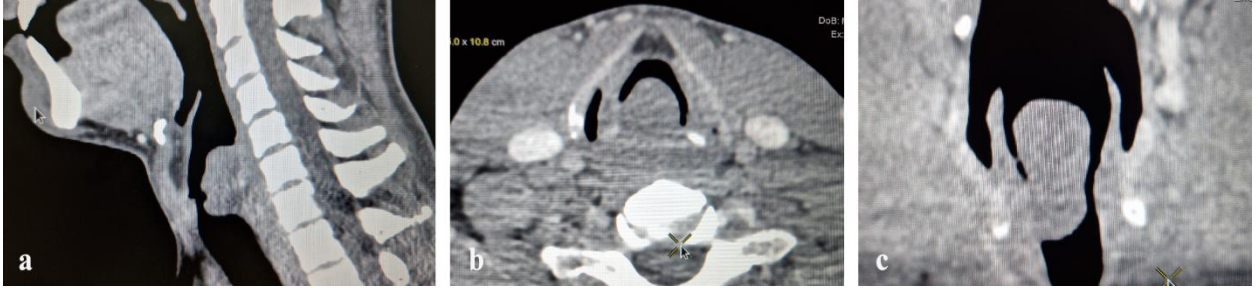


Figure A2.34. Computed tomography view of a laryngeal schwannoma. (a): sagittal section; (b): axial section; (c): coronal section

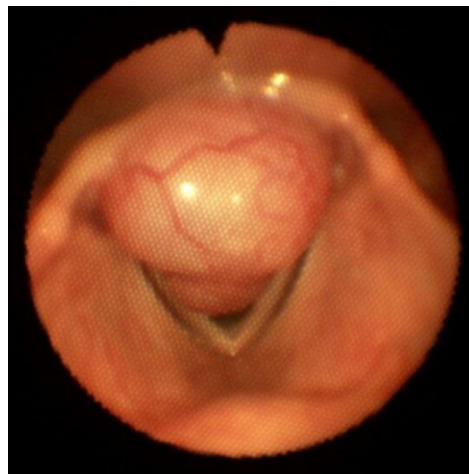


Figure A2.35a. Endoscopic appearance of an obstructive laryngeal schwannoma prior to surgery

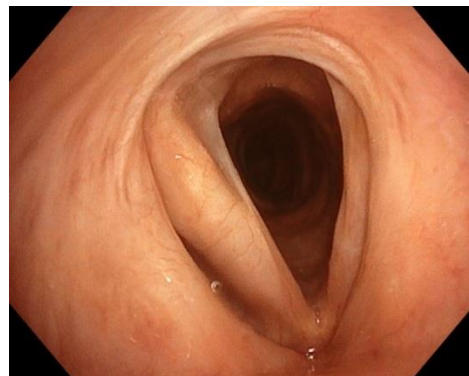


Figure A2.35b. Endoscopic view 18 months after surgery: absence of visible laryngeal tumour

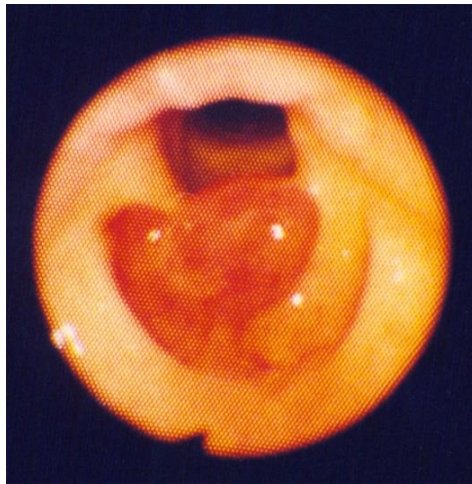


Figure A2.36a. Angiofibrous polyp of the right vocal cord

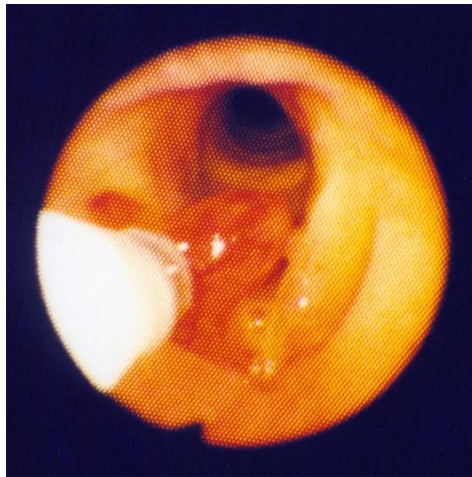


Figure A2.36b. Resection of the polyp with a diathermy loop under local anaesthesia whilst the patient is awake

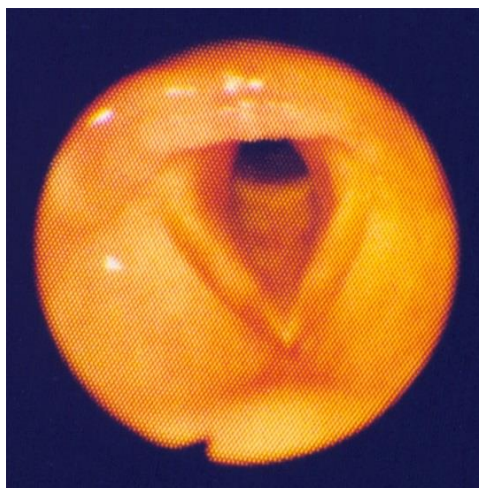


Figure A2.36c. Endoscopic view 2 months after surgery: no visible lesions

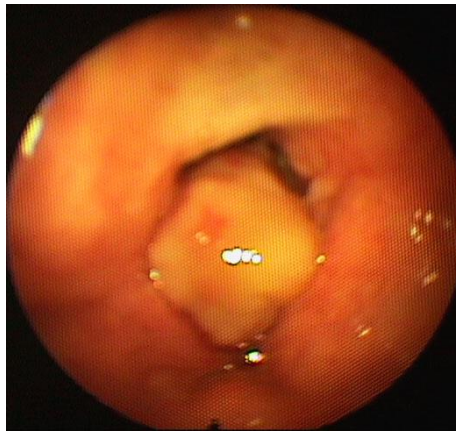


Figure A2.37a. Inflammatory myofibroblastic tumour: a pinkish-white, tuberous, exophytic tumour with a broad base of attachment and a firm consistency, affecting the anterior commissure, the anterior two-thirds of the right vocal cord, the anterior half of the left vocal cord, extending into the subcommissural space and the supracommissural region, with subtotal obstruction of the lumen of the glottic portion of the larynx

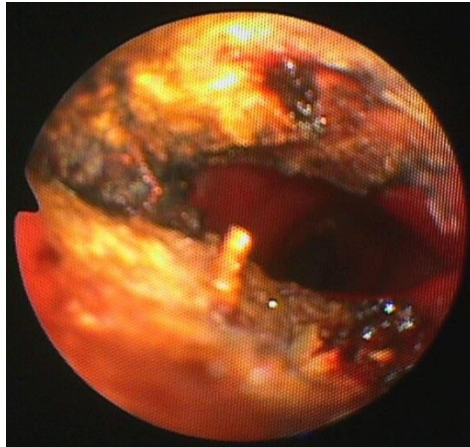


Figure A2.37b. Endoscopic view immediately following tumour ablation with recanalisation of the laryngeal lumen



Figure A2.38a. Massive non-specific granuloma of the right vocal process

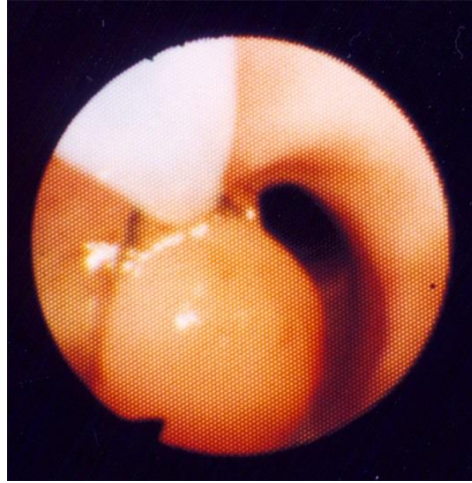


Figure A2.38b. The moment of granuloma resection using a diathermy loop under local anaesthesia



Figure A2.38c. Endoscopic view immediately after resection of the lesion with a diathermic loop



Figure A2.39a. Massive lipoma of the left arytenoid region, with obstruction of the laryngeal lumen

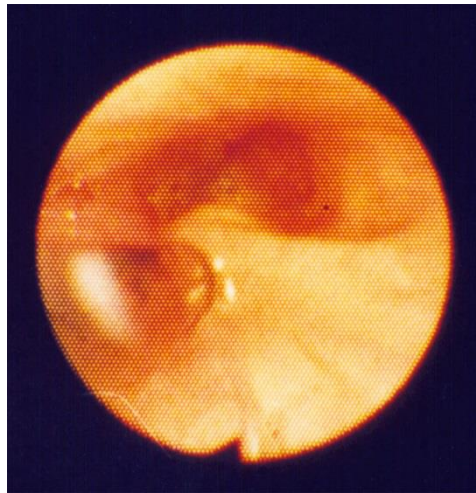


Figure A2.39b. The moment of lipoma excision with a diathermic loop under local anaesthesia whilst the patient is awake

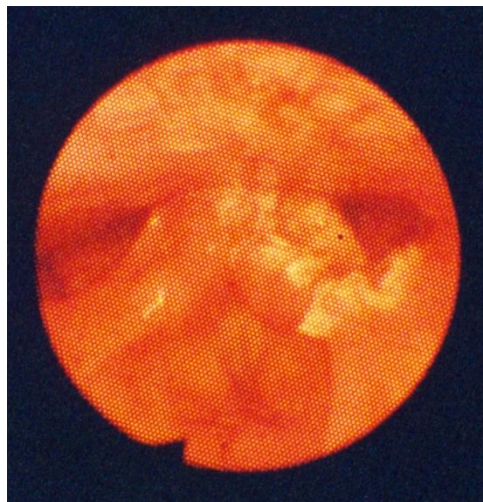


Figure A2.39c. Endoscopic view immediately after diathermic resection of the tumour

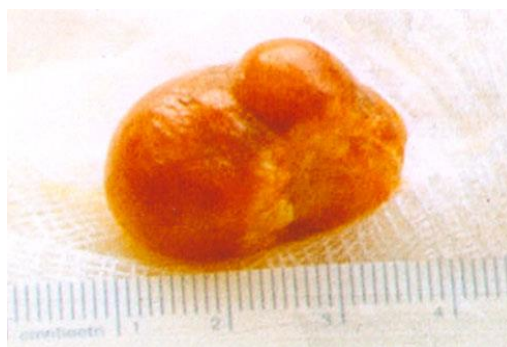


Figure A2.39d. The resected lesion

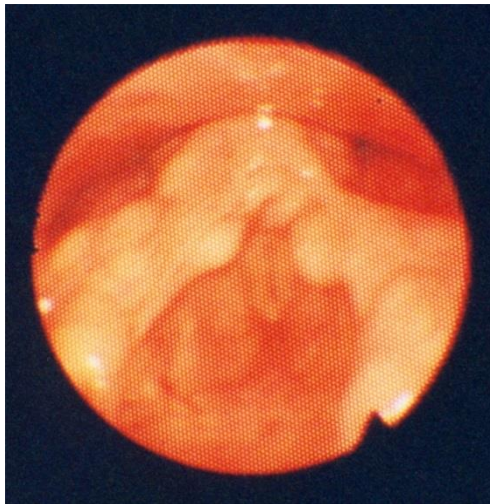


Figure A2.39e. Endoscopic view one month after surgery: the laryngeal lumen is clear

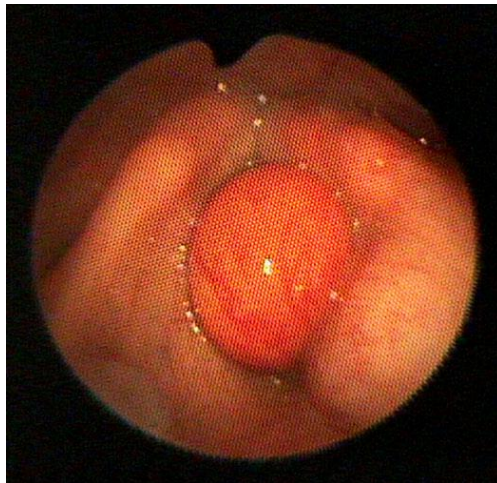


Figure A2.40a. Obstructive sacular cyst of the left laryngeal ventricle



Figure A2.40b. The moment of cyst resection with a diathermic loop under local anaesthesia

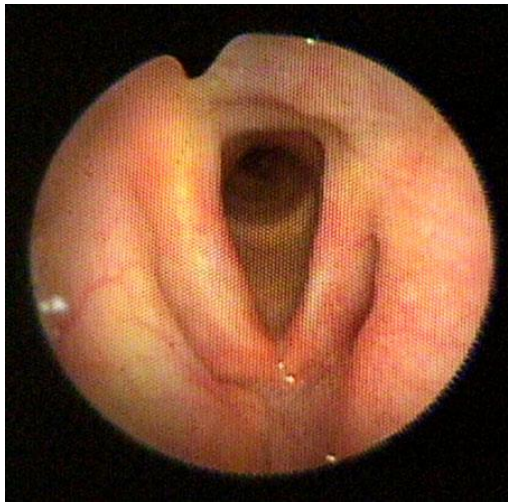


Figure A2.40c. Endoscopic view two months after surgery: the laryngeal lumen is clear



Figure A2.41a. Laryngeal amyloidosis: a tumour-like mass with mixed growth patterns, featuring a submucosal component; the surface is irregular, with a central depression, pink in colour, glossy, and firm in consistency; it affects the left vocal cord and the anterior commissure, extending into the laryngeal ventricle and the left vestibular band

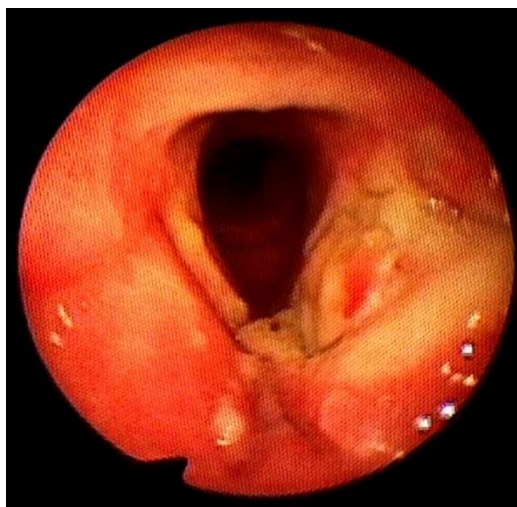


Figure A2.41b. Endoscopic view 2 days after Nd:YAG laser photoablation of the lesion: the wound in the photoablation area is covered with whitish fibrinous-necrotic overlays

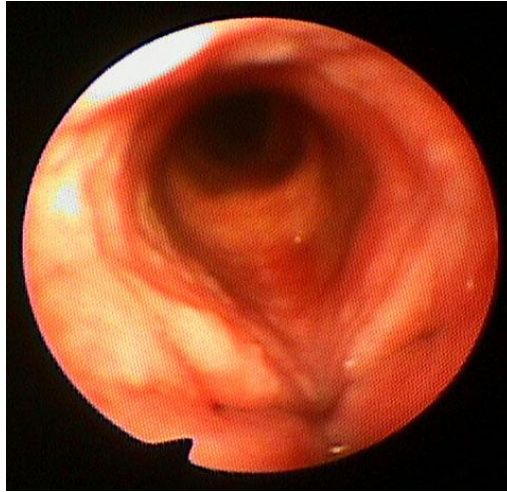


Figure A2.42. Chronic hyperplastic laryngitis

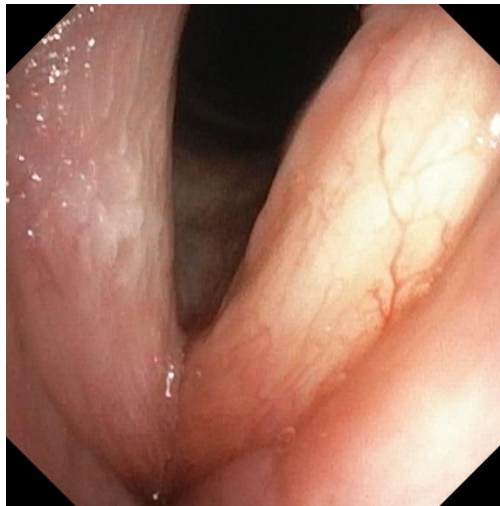


Figure A2.43. Chronic hyperplastic laryngitis with keratosis



Figure A2.44. Leukoplakia of the left vocal cord



Figure A2.45. Pachydermia of the left vocal cord

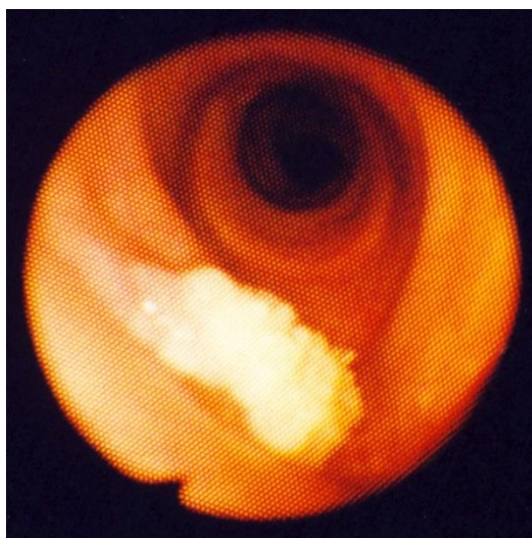


Figure A2.46. Verrucous neoplasia of the right vocal cord

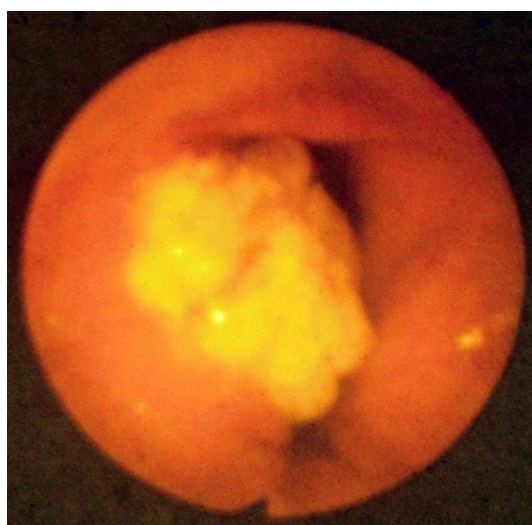


Figure A2.47a. Verrucous neoplasia of the right hemilarynx

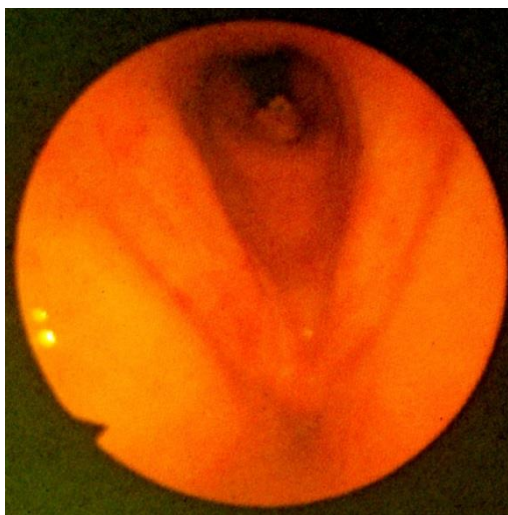


Figure A2.47b. Endoscopic view following photoablation of the tumour with an Nd:YAG laser, performed under local anaesthesia in repeated sessions



Figure A2.48a. Pachydermia of the left vocal cord



Figure A2.48b. Endoscopic appearance 12 months after surgery: no visible lesions

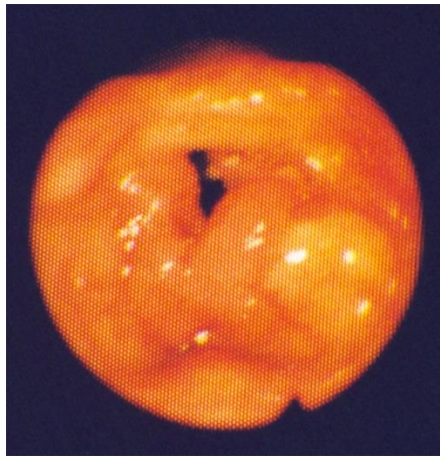


Figure A2.49a. Extensive obstructive laryngeal papillomatosis, involving the glottic and supraglottic regions of the larynx

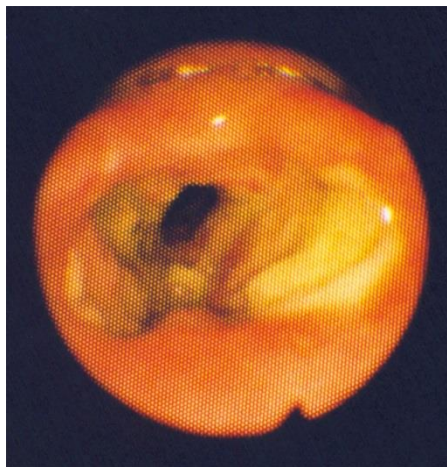


Figure A2.49b. Endoscopic view 1 week after Nd:YAG laser ablation

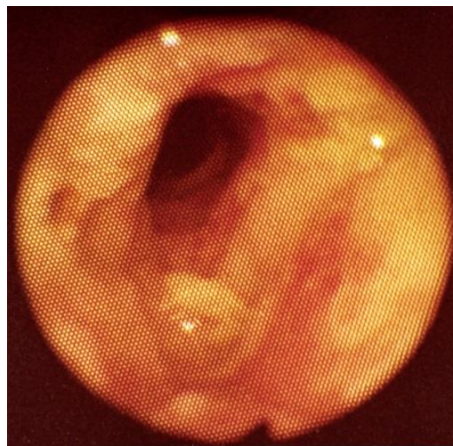


Figure A2.49c. Endoscopic appearance 1 month after Nd:YAG laser ablation: the laryngeal lumen is clear and patent

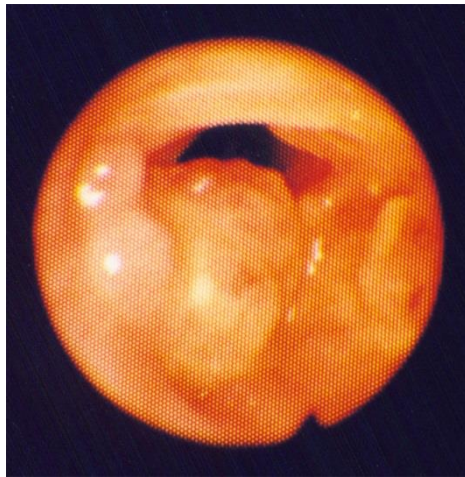


Figure A2.49d. Recurrent papillomatous growths, with significant obstruction of the laryngeal lumen, 1 year after surgery

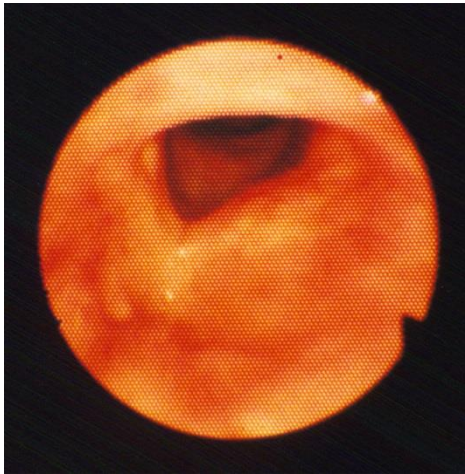


Figure A2.49e. Endoscopic appearance 3 months after Nd:YAG laser ablation of the recurrent papillomatous lesion: no visible lesions

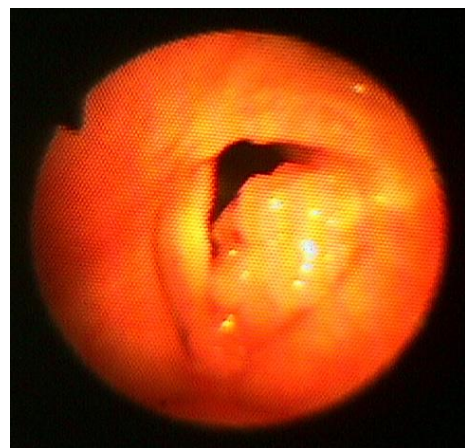


Figure A2.50a. Papillomatosis of the glottic portion of the larynx

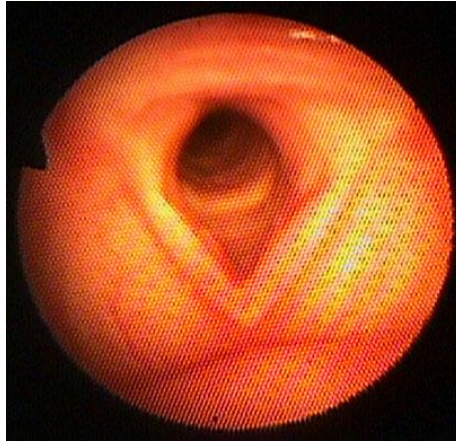


Figure A2.50b. Endoscopic appearance 3 months after FELS: no visible lesions

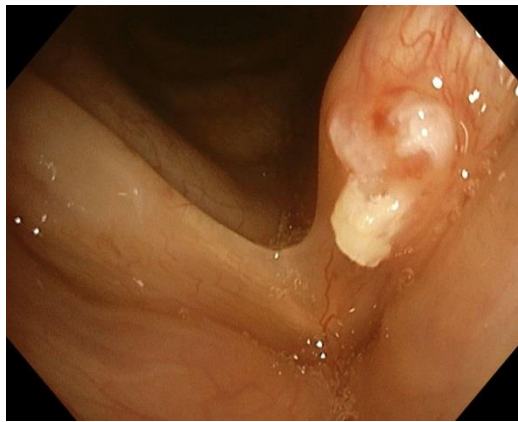


Figure A2.51a. Carcinoma of the left vocal cord (T1a)

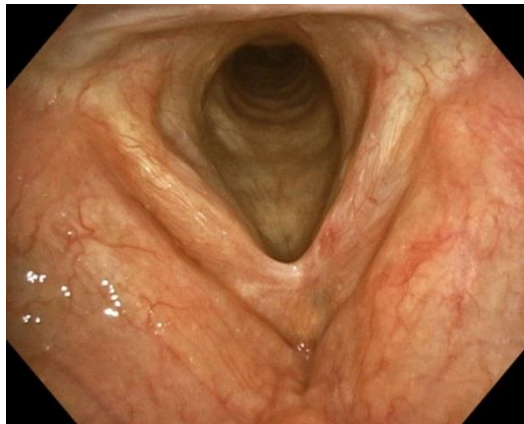


Figure A2.51b. Endoscopic appearance 6 months after laser ablation of the tumour: no visible lesions

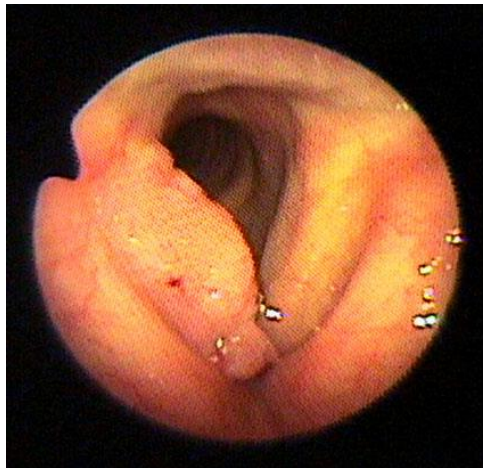


Figure A2.52a. Glottic papillomatosis involving the right vocal cord

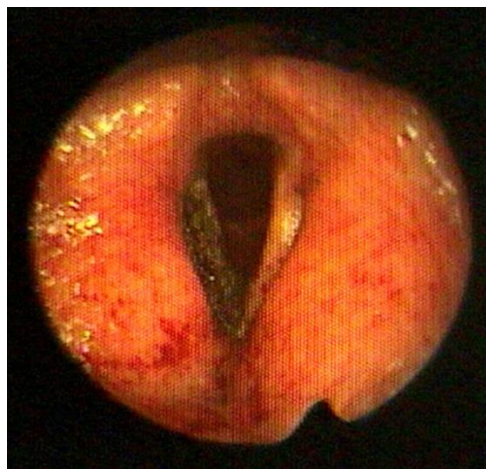


Figure A2.52b. Endoscopic appearance immediately after laser ablation

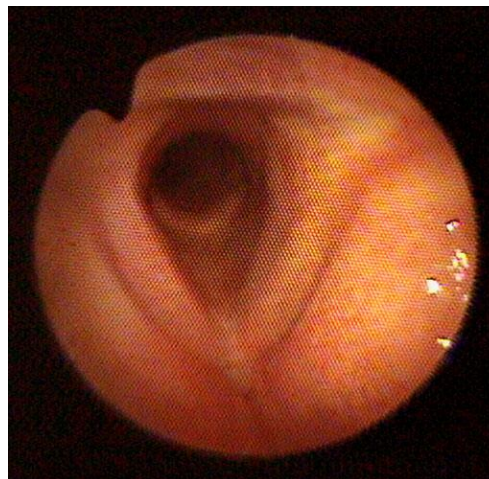


Figure A2.52c. Endoscopic view 3 months after surgery: no visible lesions

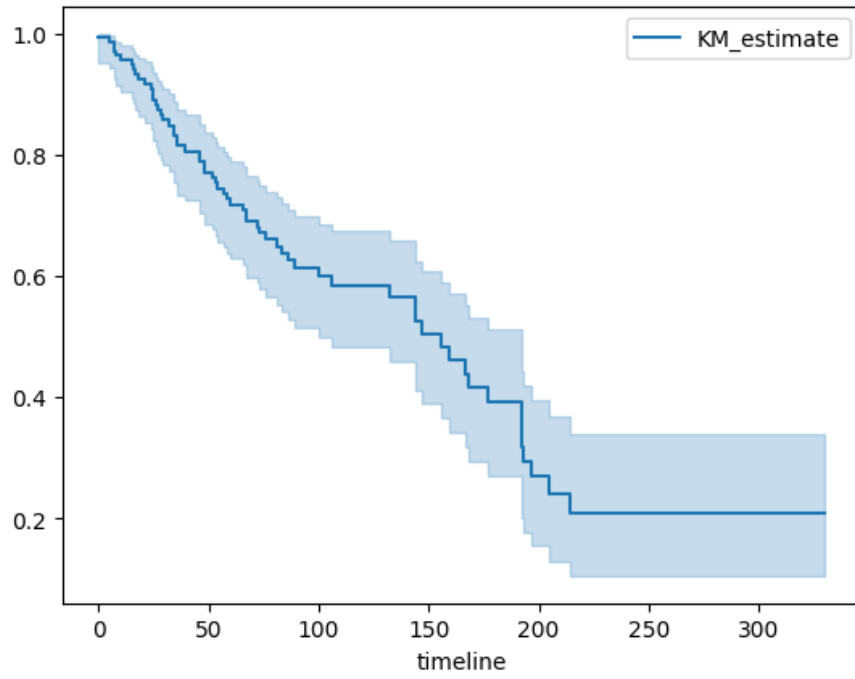


Figure A2.53. Kaplan–Meier curve for overall survival

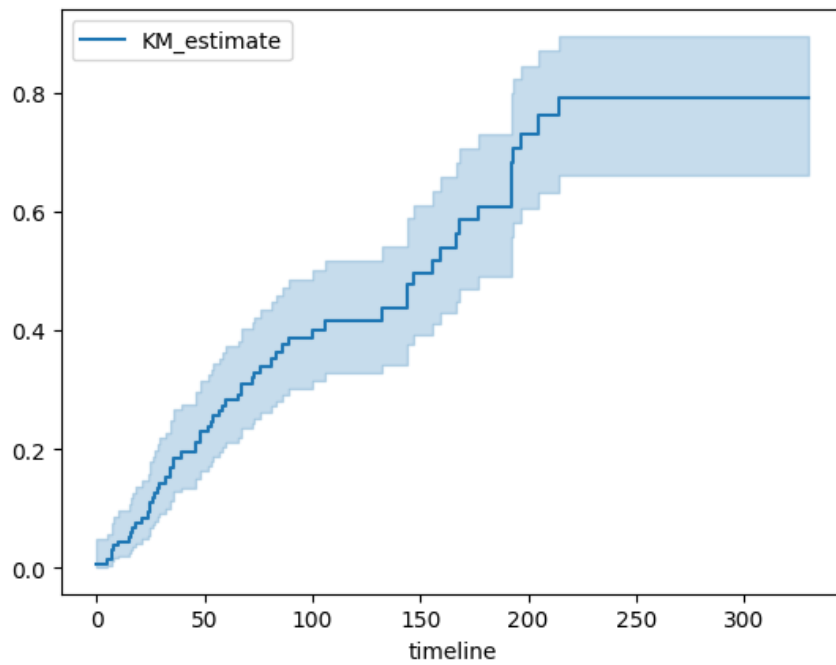


Figure A2.54. Kaplan–Meier curve for the cumulative rate of events/deaths (cumulative incidence)

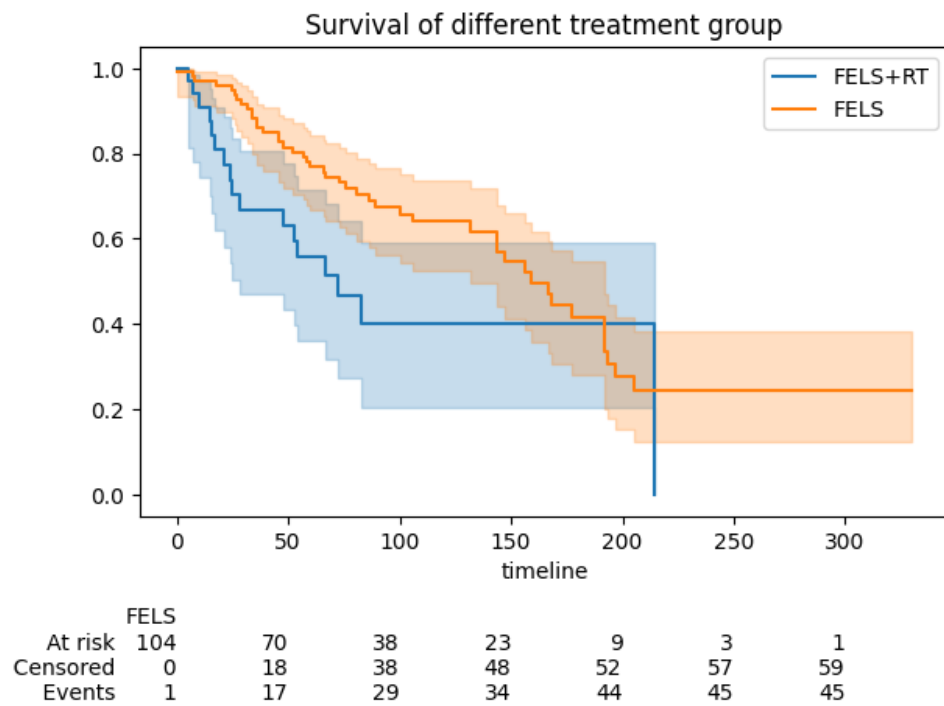


Figure A2.55. Kaplan–Meier analysis of patient survival in different treatment groups
Note: FELS = flexible endoscopic laryngeal surgery; RT = radiotherapy

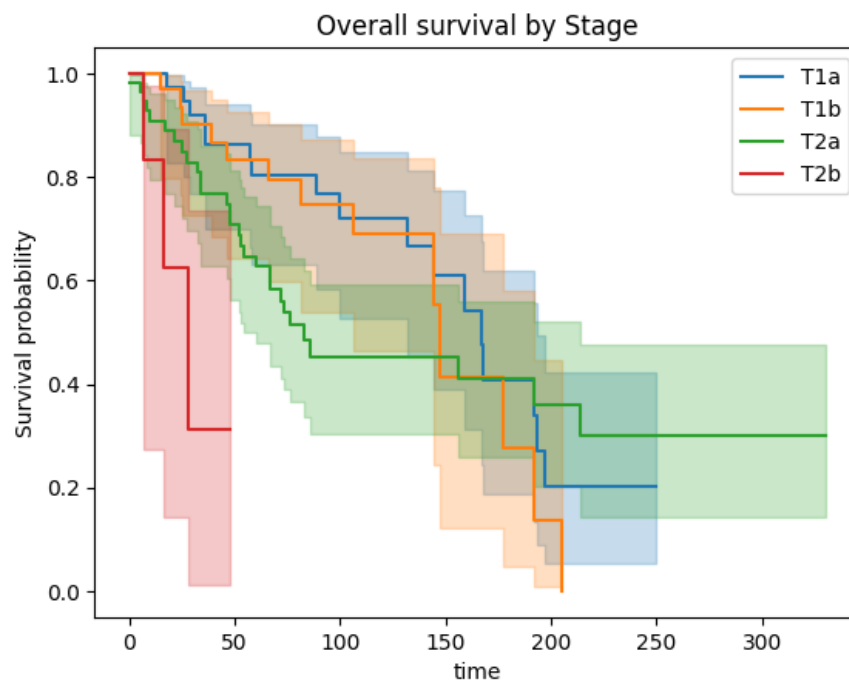


Figure A2.56. Kaplan–Meier analysis of survival by tumour stage

| | |
|----------------------------------|-------------------------|
| model | lifelines.CoxPHFitter |
| duration col | 'time' |
| event col | 'status' |
| baseline estimation | breslow |
| number of observations | 140 |
| number of events observed | 62 |
| partial log-likelihood | -237.25 |
| time fit was run | 2025-10-26 13:40:55 UTC |

| | coef | exp(coef) | se(coef) | coef lower 95% | coef upper 95% | exp(coef) lower 95% | exp(coef) upper 95% | cmp to | z | p | -log2(p) |
|--|-------|-----------|----------|----------------|----------------|---------------------|---------------------|--------|-------|--------|----------|
| Sex | 0.57 | 1.76 | 0.64 | -0.69 | 1.83 | 0.50 | 6.21 | 0.00 | 0.88 | 0.38 | 1.40 |
| Age | 0.05 | 1.05 | 0.01 | 0.02 | 0.07 | 1.02 | 1.08 | 0.00 | 3.13 | <0.005 | 9.14 |
| Endoscopic Techniques | -0.23 | 0.80 | 0.40 | -1.02 | 0.57 | 0.36 | 1.76 | 0.00 | -0.56 | 0.58 | 0.79 |
| Treatment methods | -0.21 | 0.81 | 0.42 | -1.03 | 0.62 | 0.36 | 1.85 | 0.00 | -0.49 | 0.62 | 0.69 |
| Stage_T1b | 0.32 | 1.38 | 0.39 | -0.45 | 1.09 | 0.64 | 2.96 | 0.00 | 0.81 | 0.42 | 1.26 |
| Stage_T2a | 0.33 | 1.39 | 0.37 | -0.40 | 1.06 | 0.67 | 2.87 | 0.00 | 0.87 | 0.38 | 1.39 |
| Stage_T2b | 1.88 | 6.53 | 0.75 | 0.40 | 3.35 | 1.50 | 28.55 | 0.00 | 2.50 | 0.01 | 6.31 |
| Histology_squamous cell carcinoma | -1.55 | 0.21 | 0.68 | -2.88 | -0.21 | 0.06 | 0.81 | 0.00 | -2.27 | 0.02 | 5.45 |
| Histology_spindle cell carcinoma | -0.85 | 0.43 | 0.84 | -2.50 | 0.80 | 0.08 | 2.22 | 0.00 | -1.01 | 0.31 | 1.68 |
| Histology_verrucous carcinoma | -1.26 | 0.28 | 0.69 | -2.62 | 0.10 | 0.07 | 1.10 | 0.00 | -1.82 | 0.07 | 3.86 |

| | |
|----------------------------------|----------------|
| Concordance | 0.68 |
| Partial AIC | 494.49 |
| log-likelihood ratio test | 31.43 on 10 df |
| -log2(p) of ll-ratio test | 10.97 |

Figure A2.57. Multivariate survival analysis (Cox proportional hazards model (CoxPH))



Figure A2.58. VCL: a whitish exophytic tumour with a broad base of attachment and a „fuzzy” appearance, affecting the right vocal cord and the anterior commissure, extending into the subglottic and supraglottic regions, causing subtotal obstruction of the laryngeal lumen

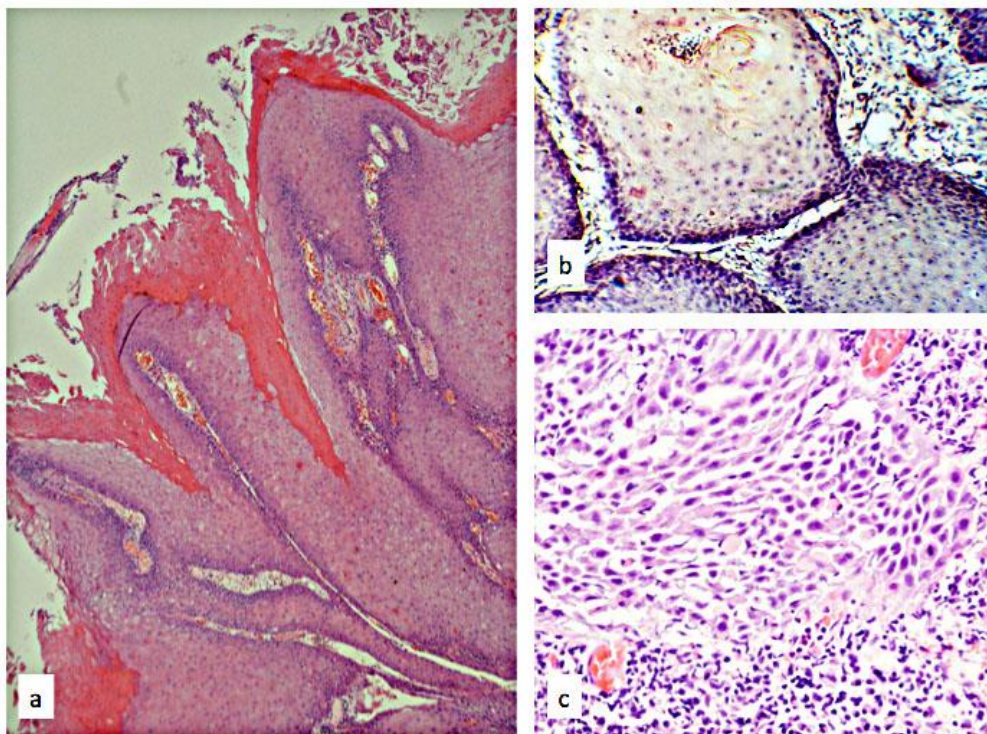


Figure A2.59. Histological appearance of VCL: a – verrucous epithelial papillae, covered by a massive layer of keratin; b – large epithelial invaginations with a keratin pearl and microabscess; c – compressive pushing margin at the interface with the underlying connective tissue, minimal cellular atypia and marked inflammatory reaction

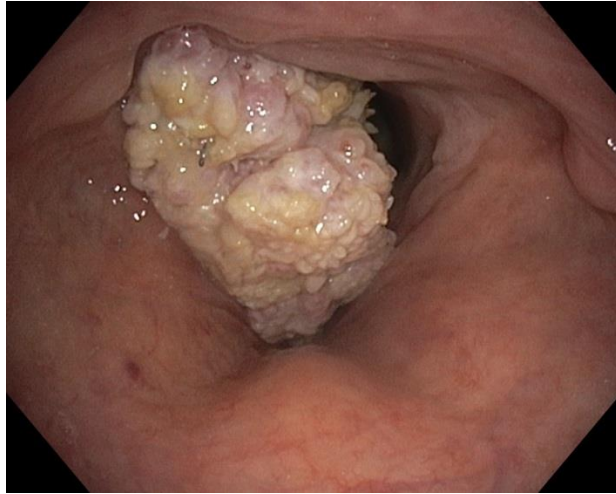


Figure A2.60a. Verrucous carcinoma of the right hemilarynx: a massive, whitish, tubercular tumour with villous projections and a hard consistency, affecting the entire right vocal cord and the anterior commissure, extending into the subglottic space and protruding into the laryngeal vestibule, with approximately 80% obstruction of the laryngeal lumen

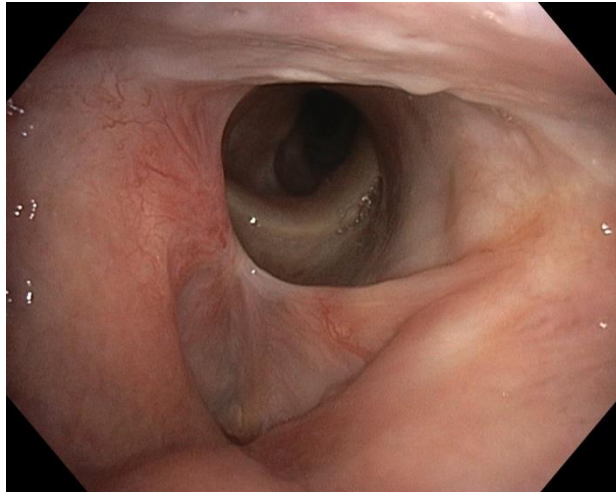


Figure A2.60b. Endoscopic appearance 18 months after endoscopic surgery: no visible tumour lesions

ANNEX 3

TABLES

Table A3.1. Localisation of benign non-epithelial lesions

| Affected part of the larynx | No. of patients (%) |
|-------------------------------------|---------------------|
| Glottic | 326 (96.4%) |
| Supraglottic | 7 (2.1%) |
| Subglottic | 3 (0.9%) |
| Glottic + supraglottic | 1 (0.3%) |
| Supraglottic + Glottic + Subglottic | 1 (0.3%) |
| Total | 338 (100%) |

Table A3.2. Methods for the eradication of benign non-epithelial laryngeal lesions

| Techniques for removing the lesion | No. of patients (%) |
|--------------------------------------|---------------------|
| Cold surgery (with forceps) | 97 (28.7%) |
| Diathermic excision (with loop) | 131 (38.7%) |
| Laser ablation | 31 (9.2%) |
| Cold surgery + Laser ablation | 40 (11.8%) |
| Diathermic excision + Cold surgery | 7 (2.1%) |
| Diathermic excision + Laser ablation | 32 (9.5%) |
| Total | 338 (100%) |

Table A3.3. Number of treatment sessions required to eradicate the lesion

| No. of treatment sessions | No. of patients |
|---------------------------|-----------------|
| 1 | 328 |
| 2 | 8 |
| 3 | 1 |
| 4 | 1 |
| On average – 1.0±0.2 | |

Table A3.4. Recurrent lesions developing after FELS of BNELL

| No. | Pathology (lesion size, cm) | Treatment | Anaesthesia/ventilation | Time interval from surgery to detection of recurrent lesion (months) | Treatment for recurrent lesion (number of repeat procedures) |
|-----|---|-----------|-------------------------|--|--|
| 1 | Nonspecific granuloma (0.8) | CS+LA | l/a | 1 | Repeated FELS (2) |
| 2 | Nonspecific granuloma (0.5) | CS | l/a | 1 | Repeated FELS (1) |
| 3 | Nonspecific granuloma (0.5) | DEX+CS | l/a | 2 | Repeated FELS (1) |
| 4 | Nonspecific granuloma (1.5) | DEX+LA | l/a | 1 | Repeated FELS (1) |
| 5 | Nonspecific granuloma (1.5) | DEX+LA | l/a | 6 | Repeated FELS (1) |
| 6 | Nonspecific granuloma (0.8) | DEX+LA | l/a | 3 | Repeated FELS (1) |
| 7 | Inflammatory myofibroblastic tumour (2.5) | DEX+LA | GA+SHFJV | 9 | Transoral microsurgery (13) |
| 8 | Myxoid polyp (0.5) | CS | l/a | 153 | Repeated FELS (1) |
| 9 | Angiofibrous polyp (0.6) | DEX | l/a | 39 | Repeated FELS (1) |

Note: CS – cold surgery (using forceps); LA – laser ablation; DEX – diathermy loop excision; l/a – local anaesthesia; GA+SHFJV – general anaesthesia with superimposed high-frequency jet ventilation

Table A3.5. Malignant lesions developing after FELS of BNELL

| No. | Pathology (lesion size, cm) | Treatment for BNELL | Type of malignancy developed | Time interval from surgery to detection of malignancy (months) | Treatment of the developed malignancy |
|-----|-----------------------------|---------------------|------------------------------|--|---------------------------------------|
| 1 | Angiofibrous polyp (0.5) | CS+LA | SCC (T1a) | 252 | Successful FELS (LA) |
| 2 | Angiomatous polyp (0.6) | CS | SCC (T1a) | 28 | Successful FELS (LA) |
| 3 | Angiomatous polyp (1.5) | DEX | SCC (T2) | 68 | Successful FELS (LA) |
| 4 | Neurofibroma (1.5) | DEX+LA | SCC (T2) | 48 | Open partial laryngectomy |

Note: CS – cold surgery (using forceps); LA – laser ablation; DEX – diathermy loop excision; SCC – squamous cell carcinoma; FELS – flexible endoscopic laryngeal surgery

Table A3.6. Functional/vocal outcome following FELS of BNELL

| Vocal outcome | Total
n=338 ¹ | 95%
CI ² | Outpatie
nts
n=286 ¹ | 95%
CI ² | Inpatients
n=52 ¹ | 95%
CI ² | Statisti
cal
test ³ | p-value ³ |
|-----------------------|-----------------------------|------------------------|---------------------------------------|------------------------|---------------------------------|------------------------|--------------------------------------|----------------------|
| Normal voice | 311
(92.0%) | 89%,
95% | 271
(94.8%) | 92%,
97% | 40
(76.9%) | 65%,
88% | 35 | <0.001 |
| Minor
dysphonia | 12 (3.6%) | 1.6%,
5.5% | 5 (1.7%) | 0.23%,
3.3% | 7 (13.5%) | 4.2%,
23% | | |
| Moderate
dysphonia | 10 (3.0%) | 1.2%,
4.8% | 9 (3.1%) | 1.1%,
5.2% | 1 (1.9%) | 0.00%,
5.7% | | |
| Severe
dysphonia | 5 (1.5%) | 0.19%,
2.8% | 1 (0.3%) | 0.00%,
1.0% | 4 (7.7%) | 0.45%,
15% | | |

Note: ¹n = number of patients, ²CI = Confidence Interval, ³Pearson's Chi-squared test

Table A3.7. Results of BNELL treatment using FELS

| <i>Participant characteristics</i> | | | | | | | | |
|------------------------------------|---|---------------------|---|---------------------|---|---------------------|----------------------------------|----------------------|
| Group | Overall
n = 338 ¹ | 95% CI ² | Outpatients
n = 286 ¹ | 95% CI ² | Inpatients
n = 52 ¹ | 95% CI ² | Statistical
Test ³ | p-value ³ |
| Age | 44.9 (12.2)
44.0 (18.0)
16.0 81.0 | 44, 46 | 44.0 (11.4)
44.0 (17.0)
16.0 73.0 | 43, 45 | 49.7 (14.8)
51.0 (21.5)
16.0 81.0 | 46, 54 | 5,517 | 0.003 |
| Gender | | | | | | | 0.34 | 0.6 |
| m | 220 (65.1%) | 60%, 70% | 188 (65.7%) | 60%, 71% | 32 (61.5%) | 48%, 75% | | |
| f | 118 (34.9%) | 30%, 40% | 98 (34.3%) | 29%, 40% | 20 (38.5%) | 25%, 52% | | |
| Nosological unit | | | | | | | 43 | <0.001 |
| Angiofibrous polyp | 76 (22.5%) | 18%, 27% | 70 (24.5%) | 19%, 29% | 6 (11.5%) | 2.9%, 20% | | |
| Myxoid polyp | 67 (19.8%) | 16%, 24% | 61 (21.3%) | 17%, 26% | 6 (11.5%) | 2.9%, 20% | | |
| Vocal nodule | 45 (13.3%) | 9.7%, 17% | 39 (13.6%) | 9.7%, 18% | 6 (11.5%) | 2.9%, 20% | | |
| Angiomatous polyp | 43 (12.7%) | 9.2%, 16% | 39 (13.6%) | 9.7%, 18% | 4 (7.7%) | 0.45%, 15% | | |
| Fibrous polyp | 39 (11.5%) | 8.1%, 15% | 34 (11.9%) | 8.1%, 16% | 5 (9.6%) | 1.6%, 18% | | |
| Nonspecific granuloma | 28 (8.3%) | 5.3%, 11% | 19 (6.6%) | 3.8%, 9.5% | 9 (17.3%) | 7.0%, 28% | | |
| Cyst | 18 (5.3%) | 2.9%, 7.7% | 14 (4.9%) | 2.4%, 7.4% | 4 (7.7%) | 0.45%, 15% | | |
| Reinke's disease | 17 (5.0%) | 2.7%, 7.4% | 9 (3.1%) | 1.1%, 5.2% | 8 (15.4%) | 5.6%, 25% | | |
| Others | 5 (1.5%) | 0.19%, 2.8% | 1 (0.3%) | 0.00%, 1.0% | 4 (7.7%) | 0.45%, 15% | | |

| Group | Overall
n = 338 ¹ | 95% CI ² | Outpatients
n = 286 ¹ | 95% CI ² | Inpatients
n = 52 ¹ | 95% CI ² | Statistical
Test ³ | p-value ³ |
|---------------------------------|-----------------------------------|---------------------|-------------------------------------|---------------------|-----------------------------------|---------------------|----------------------------------|----------------------|
| Location | | | | | | | 32 | <0.001 |
| glottic | 326 (96.4%) | 94%, 98% | 282 (98.6%) | 97%, 100% | 44 (84.6%) | 75%, 94% | | |
| supraglottic | 7 (2.1%) | 0.55%, 3.6% | 4 (1.4%) | 0.04%, 2.8% | 3 (5.8%) | 0.00%, 12% | | |
| subglottic | 3 (0.9%) | 0.00%, 1.9% | 0 (0.0%) | 0.00%, 0.00% | 3 (5.8%) | 0.00%, 12% | | |
| glottic+supraglottic | 1 (0.3%) | 0.00%, 0.87% | 0 (0.0%) | 0.00%, 0.00% | 1 (1.9%) | 0.00%, 5.7% | | |
| supraglottic+glottic+subglottic | 1 (0.3%) | 0.00%, 0.87% | 0 (0.0%) | 0.00%, 0.00% | 1 (1.9%) | 0.00%, 5.7% | | |
| Foci dimensions, cm | 0.8 (0.6)
0.6 (0.5)
0.2 4.5 | 0.77, 0.89 | 0.8 (0.5)
0.6 (0.6)
0.2 2.5 | 0.71, 0.83 | 1.2 (0.9)
0.8 (1.0)
0.2 4.5 | 0.92, 1.4 | 5,379 | 0.001 |
| Sessions | 1.0 (0.2)
1.0 (0.0)
1.0 4.0 | 1.0, 1.1 | 1.0 (0.2)
1.0 (0.0)
1.0 3.0 | 1.0, 1.0 | 1.2 (0.5)
1.0 (0.0)
1.0 4.0 | 1.0, 1.3 | 6,683 | <0.001 |
| Endoscopic treatment | | | | | | | 39 | <0.001 |
| DEX | 131 (38.8%) | 34%, 44% | 117 (40.9%) | 35%, 47% | 14 (26.9%) | 15%, 39% | | |
| CS | 97 (28.7%) | 24%, 34% | 93 (32.5%) | 27%, 38% | 4 (7.7%) | 0.45%, 15% | | |
| CS+LA | 39 (11.5%) | 8.1%, 15% | 30 (10.5%) | 6.9%, 14% | 9 (17.3%) | 7.0%, 28% | | |
| LA | 32 (9.5%) | 6.3%, 13% | 22 (7.7%) | 4.6%, 11% | 10 (19.2%) | 8.5%, 30% | | |
| DEX+LA | 32 (9.5%) | 6.3%, 13% | 18 (6.3%) | 3.5%, 9.1% | 14 (26.9%) | 15%, 39% | | |
| DEX+CS | 7 (2.1%) | 0.55%, 3.6% | 6 (2.1%) | 0.44%, 3.8% | 1 (1.9%) | 0.00%, 5.7% | | |

| Group | Overall
n = 338 ¹ | 95% CI ² | Outpatients
n = 286 ¹ | 95% CI ² | Inpatients
n = 52 ¹ | 95% CI ² | Statistical
Test ³ | p-value ³ |
|--------------------------------------|---------------------------------------|---------------------|--------------------------------------|---------------------|---------------------------------------|---------------------|----------------------------------|----------------------|
| Anaesthesia/ventilation | | | | | | | 50 | <0.001 |
| Local | 327 (96.7%) | 95%, 99% | 285 (99.7%) | 99%, 100% | 42 (80.8%) | 70%, 91% | | |
| GA+SHFJV | 11 (3.3%) | 1.4%, 5.1% | 1 (0.3%) | 0.00%, 1.0% | 10 (19.2%) | 8.5%, 30% | | |
| Recurrence | | | | | | | 0.13 | >0.9 |
| No | 329 (97.3%) | 96%, 99% | 278 (97.2%) | 95%, 99% | 51 (98.1%) | 94%, 100% | | |
| Yes | 9 (2.7%) | 0.95%, 4.4% | 8 (2.8%) | 0.89%, 4.7% | 1 (1.9%) | 0.00%, 5.7% | | |
| Malignancy | | | | | | | 0.74 | 0.6 |
| No | 334 (98.8%) | 98%, 100% | 282 (98.6%) | 97%, 100% | 52 (100.0%) | 100%, 100% | | |
| Yes | 4 (1.2%) | 0.03%, 2.3% | 4 (1.4%) | 0.04%, 2.8% | 0 (0.0%) | 0.00%, 0.00% | | |
| Time without LRc
(months) | 10.8 (27.0)
3.0 (3.8)
1.0 189.0 | 7.9, 14 | 9.9 (27.5)
2.5 (2.0)
1.0 189.0 | 6.7, 13 | 15.3 (23.6)
3.0 (23.3)
1.0 95.0 | 8.8, 22 | 7,317 | 0.9 |
| Time without LRc
(years) | | | | | | | 19 | 0.005 |
| up to 1 year | 288 (85.2%) | 81%, 89% | 252 (88.1%) | 84%, 92% | 36 (69.2%) | 57%, 82% | | |
| 1–3 years | 22 (6.5%) | 3.9%, 9.1% | 15 (5.2%) | 2.7%, 7.8% | 7 (13.5%) | 4.2%, 23% | | |
| 5–10 years | 14 (4.1%) | 2.0%, 6.3% | 9 (3.1%) | 1.1%, 5.2% | 5 (9.6%) | 1.6%, 18% | | |
| 3–5 years | 8 (2.4%) | 0.75%, 4.0% | 4 (1.4%) | 0.04%, 2.8% | 4 (7.7%) | 0.45%, 15% | | |
| 10–15 years | 4 (1.2%) | 0.03%, 2.3% | 4 (1.4%) | 0.04%, 2.8% | 0 (0.0%) | 0.00%, 0.00% | | |

| Group | Overall
n = 338 ¹ | 95% CI ² | Outpatients
n = 286 ¹ | 95% CI ² | Inpatients
n = 52 ¹ | 95% CI ² | Statistical
Test ³ | p-value ³ |
|----------------------------|---------------------------------|---------------------|-------------------------------------|---------------------|-----------------------------------|---------------------|----------------------------------|----------------------|
| 15–20 years | 2 (0.6%) | 0.00%, 1.4% | 2 (0.7%) | 0.00%, 1.7% | 0 (0.0%) | 0.00%, 0.00% | | |
| Postoperative voice | | | | | | | 35 | <0.001 |
| normal | 311 (92.0%) | 89%, 95% | 271 (94.8%) | 92%, 97% | 40 (76.9%) | 65%, 88% | | |
| minor dysphonia | 12 (3.6%) | 1.6%, 5.5% | 5 (1.7%) | 0.23%, 3.3% | 7 (13.5%) | 4.2%, 23% | | |
| moderate dysphonia | 10 (3.0%) | 1.2%, 4.8% | 9 (3.1%) | 1.1%, 5.2% | 1 (1.9%) | 0.00%, 5.7% | | |
| severe dysphonia | 5 (1.5%) | 0.19%, 2.8% | 1 (0.3%) | 0.00%, 1.0% | 4 (7.7%) | 0.45%, 15% | | |

Note: ¹ Mean (SD)
Median (IQR)
Min Max ; n (%)

² CI = Confidence Interval

³ Wilcoxon rank sum test; Pearson's chi-squared test with simulated p-value
(based on 1e+05 replicates)

Table A3.8. Location of hyperplastic laryngeal lesions

| Affected part of the larynx | No. of patients (%) |
|---------------------------------|---------------------|
| Glottic | 41 (89.1%) |
| Supraglottic | 2 (4.3%) |
| Glottic + supraglottic | 1 (2.2%) |
| Glottic + subglottic | 1 (2.2%) |
| Glottic+Supraglottic+Subglottic | 1 (2.2%) |
| Total | 46 (100%) |

Table A3.9. Methods for the removal of hyperplastic laryngeal lesions

| Lesion eradication techniques | No. of patients (%) |
|--------------------------------------|---------------------|
| Cold surgery (with forceps) | 1 (2.2%) |
| Laser ablation | 40 (87.0%) |
| Cold surgery + Laser ablation | 2 (4.3%) |
| Diathermic excision + Laser ablation | 3 (6.5%) |
| Total | 46 (100%) |

Table A3.10. Functional/vocal outcome following FELS of HLL

| Vocal outcome | No. of patients (%) |
|--------------------|---------------------|
| Normal voice | 25 (54.3%) |
| Minor dysphonia | 3 (6.5%) |
| Moderate dysphonia | 12 (26.1%) |
| Severe dysphonia | 6 (13.0%) |
| Total | 46 (100%) |

Table A3.11. Results of HLL treatment using FELS

| <i>Participant characteristics</i> | | | | | | | | |
|------------------------------------|--------------------------------|---------------------|------------------------------------|---------------------|-----------------------------------|---------------------|--------------------------------------|--------------------------|
| Group | Overall
N = 46 ¹ | 95% CI ² | Outpatients
N = 31 ¹ | 95% CI ² | Inpatients
N = 15 ¹ | 95% CI ² | Statistica
1
Test ³ | p-
value ³ |
| Age | 53.4 (12.0) | 50, 57 | 51.5 (13.2) | 47, 56 | 57.1 (8.1) | 53, 62 | 163 | 0.10 |
| | 55.5 (16.5) | | 53.0 (18.0) | | 58.0 (10.5) | | | |
| | 20.0 77.0 | | 20.0 77.0 | | 42.0 70.0 | | | |
| Gender | | | | | | | 1.6 | 0.5 |
| b | 43 (93.5%) | 86%, 100% | 28 (90.3%) | 80%, 100% | 15 (100.0%) | 100%, 100% | | |
| f | 3 (6.5%) | 0.00%, 14% | 3 (9.7%) | 0.00%, 20% | 0 (0.0%) | 0.00%, 0.00% | | |
| Pathology | | | | | | | 3.2 | 0.4 |
| Leukoplakia | 23 (50.0%) | 36%, 64% | 14 (45.2%) | 28%, 63% | 9 (60.0%) | 35%, 85% | | |
| Pachydermia | 14 (30.4%) | 17%, 44% | 12 (38.7%) | 22%, 56% | 2 (13.3%) | 0.00%, 31% | | |
| CHL with keratosis | 7 (15.2%) | 4.8%, 26% | 4 (12.9%) | 1.1%, 25% | 3 (20.0%) | 0.00%, 40% | | |
| Verrucous neoplasia | 2 (4.3%) | 0.00%, 10% | 1 (3.2%) | 0.00%, 9.4% | 1 (6.7%) | 0.00%, 19% | | |
| Dysplasia | | | | | | | 2.6 | 0.3 |
| No | 38 (82.6%) | 72%, 94% | 27 (87.1%) | 75%, 99% | 11 (73.3%) | 51%, 96% | | |
| Low-grade | 7 (15.2%) | 4.8%, 26% | 3 (9.7%) | 0.00%, 20% | 4 (26.7%) | 4.3%, 49% | | |
| High-grade | 1 (2.2%) | 0.00%, 6.4% | 1 (3.2%) | 0.00%, 9.4% | 0 (0.0%) | 0.00%, 0.00% | | |

| Group | Overall
N = 46 ¹ | 95% CI ² | Outpatients
N = 31 ¹ | 95% CI ² | Inpatients
N = 15 ¹ | 95% CI ² | Statistica
1
Test ³ | P-
value ³ |
|---------------------------------|-----------------------------------|---------------------|------------------------------------|---------------------|-----------------------------------|---------------------|--------------------------------------|--------------------------|
| Location | | | | | | | 5.6 | 0.2 |
| glottic | 41 (89.1%) | 80%, 98% | 28 (90.3%) | 80%, 100% | 13 (86.7%) | 69%, 100% | | |
| supraglottic | 2 (4.3%) | 0.00%, 10% | 2 (6.5%) | 0.00%, 15% | 0 (0.0%) | 0.00%, 0.00% | | |
| glottic+subglottic | 1 (2.2%) | 0.00%, 6.4% | 0 (0.0%) | 0.00%, 0.00% | 1 (6.7%) | 0.00%, 19% | | |
| glottic + supraglottic | 1 (2.2%) | 0.00%, 6.4% | 1 (3.2%) | 0.00%, 9.4% | 0 (0.0%) | 0.00%, 0.00% | | |
| glottic+supraglottic+subglottic | 1 (2.2%) | 0.00%, 6.4% | 0 (0.0%) | 0.00%, 0.00% | 1 (6.7%) | 0.00%, 19% | | |
| Foci dimensions, cm | 1.1 (0.6)
0.9 (0.9)
0.3 2.5 | 0.94, 1.3 | 1.1 (0.7)
1.0 (1.2)
0.3 2.5 | 0.89, 1.4 | 1.1 (0.6)
0.8 (0.8)
0.5 2.5 | 0.79, 1.5 | 224 | 0.9 |
| Endoscopic treatment | | | | | | | 1.6 | 0.9 |
| LA | 40 (87.0%) | 77%, 97% | 26 (83.9%) | 71%, 97% | 14 (93.3%) | 81%, 100% | | |
| DEX+LA | 3 (6.5%) | 0.00%, 14% | 2 (6.5%) | 0.00%, 15% | 1 (6.7%) | 0.00%, 19% | | |
| CS+LA | 2 (4.3%) | 0.00%, 10% | 2 (6.5%) | 0.00%, 15% | 0 (0.0%) | 0.00%, 0.00% | | |
| CS | 1 (2.2%) | 0.00%, 6.4% | 1 (3.2%) | 0.00%, 9.4% | 0 (0.0%) | 0.00%, 0.00% | | |
| Anaesthesia, ventilation | | | | | | | 9.1 | 0.008 |
| Local | 42 (91.3%) | 83%, 99% | 31 (100.0%) | 100%, 100% | 11 (73.3%) | 51%, 96% | | |

| Group | Overall
N = 46 ¹ | 95% CI ² | Outpatients
N = 31 ¹ | 95% CI ² | Inpatients
N = 15 ¹ | 95% CI ² | Statistica
1
Test ³ | p-
value ³ |
|--------------------------------------|---|---------------------|--|---------------------|---|---------------------|--------------------------------------|--------------------------|
| GA+SHFJV | 4 (8.7%) | 0.55%, 17% | 0 (0.0%) | 0.00%, 0.00% | 4 (26.7%) | 4.3%, 49% | | |
| Recurrence | | | | | | | 0.00 | >0.9 |
| No | 43 (93.5%) | 86%, 100% | 29 (93.5%) | 85%, 100% | 14 (93.3%) | 81%, 100% | | |
| Yes | 3 (6.5%) | 0.00%, 14% | 2 (6.5%) | 0.00%, 15% | 1 (6.7%) | 0.00%, 19% | | |
| Malignancy | | | | | | | 0.29 | >0.9 |
| No | 44 (95.7%) | 90%, 100% | 30 (96.8%) | 91%, 100% | 14 (93.3%) | 81%, 100% | | |
| Yes | 2 (4.3%) | 0.00%, 10% | 1 (3.2%) | 0.00%, 9.4% | 1 (6.7%) | 0.00%, 19% | | |
| Time without LRc
(months) | 62.4 (72.0)
24.0 (99.5)
1.0 266.0 | 41, 84 | 66.2 (79.1)
24.0 (128.0)
1.0 266.0 | 37, 95 | 54.4 (56.1)
22.0 (59.0)
2.0 192.0 | 23, 85 | 238 | >0.9 |
| Time without LRc
(years) | | | | | | | 5.6 | 0.5 |
| 1–3 years | 15 (32.6%) | 19%, 46% | 9 (29.0%) | 13%, 45% | 6 (40.0%) | 15%, 65% | | |
| up to 1 year | 14 (30.4%) | 17%, 44% | 11 (35.5%) | 19%, 52% | 3 (20.0%) | 0.00%, 40% | | |
| 10–15 years | 7 (15.2%) | 4.8%, 26% | 5 (16.1%) | 3.2%, 29% | 2 (13.3%) | 0.00%, 31% | | |
| 5–10 years | 4 (8.7%) | 0.55%, 17% | 1 (3.2%) | 0.00%, 9.4% | 3 (20.0%) | 0.00%, 40% | | |
| 15–20 years | 4 (8.7%) | 0.55%, 17% | 3 (9.7%) | 0.00%, 20% | 1 (6.7%) | 0.00%, 19% | | |

| Group | Overall
N = 46 ¹ | 95% CI ² | Outpatients
N = 31 ¹ | 95% CI ² | Inpatients
N = 15 ¹ | 95% CI ² | Statistica
l
Test ³ | p-
value ³ |
|----------------------------|--------------------------------|---------------------|------------------------------------|---------------------|-----------------------------------|---------------------|--------------------------------------|--------------------------|
| 3–5 years | 1 (2.2%) | 0.00%, 6.4% | 1 (3.2%) | 0.00%, 9.4% | 0 (0.0%) | 0.00%, 0.00% | | |
| 20–25 years | 1 (2.2%) | 0.00%, 6.4% | 1 (3.2%) | 0.00%, 9.4% | 0 (0.0%) | 0.00%, 0.00% | | |
| Postoperative voice | | | | | | | 3.3 | 0.3 |
| normal | 25 (54.3%) | 40%, 69% | 18 (58.1%) | 41%, 75% | 7 (46.7%) | 21%, 72% | | |
| moderate dysphonia | 12 (26.1%) | 13%, 39% | 6 (19.4%) | 5.4%, 33% | 6 (40.0%) | 15%, 65% | | |
| severe dysphonia | 6 (13.0%) | 3.3%, 23% | 4 (12.9%) | 1.1%, 25% | 2 (13.3%) | 0.00%, 31% | | |
| minor dysphonia | 3 (6.5%) | 0.00%, 14% | 3 (9.7%) | 0.00%, 20% | 0 (0.0%) | 0.00%, 0.00% | | |

Note: ¹ Mean (SD)
Median (IQR)
Min Max ; n (%)

² CI = Confidence Interval

³ Wilcoxon rank sum test; Pearson's Chi-squared test with simulated p-value
(based on 1e+05 replicates)

Table A3.12. Location of papillomatous lesions

| Affected part of the larynx | No. of patients (%) |
|---------------------------------|---------------------|
| Glottic | 27 (52.9%) |
| Supraglottic | 4 (7.8%) |
| Glottic + Supraglottic | 7 (13.7%) |
| Glottic + Subglottic | 6 (11.8%) |
| Glottic+Supraglottic+Subglottic | 5 (9.8%) |
| Glottic+Subglottic+Trachea | 1 (2.0%) |
| Subglottic + Trachea | 1 (2.0%) |
| Total | 51 (100%) |

Table A3.13. Methods of papillomatous lesion removal

| Lesion eradication techniques | No. of patients (%) |
|---|---------------------|
| Cold surgery (with forceps) | 5 (9.8%) |
| Laser ablation | 28 (54.9%) |
| Cold surgery + Laser ablation | 1 (2.0%) |
| Diathermic excision + Laser ablation | 16 (31.4%) |
| Cold surgery/Diathermic excision + Laser ablation | 1 (2.0%) |
| Total | 51 (100%) |

Table A3.14. Number of treatment sessions required to eradicate the lesion

| No. of treatment sessions | No. of patients |
|---------------------------|-----------------|
| 1 | 43 (84.3%) |
| 2 | 5 |
| 6 | 1 |
| 7 | 2 |
| On average | 1.4±1.4 |

Table A3.15. Number of repeat surgical treatment courses performed in patients with recurrent disease (n=18)

| No. of repeat surgical treatment courses per patient | No. of patients |
|--|-----------------|
| 1 | 7 |
| 2 | 3 |
| 3 | 3 |
| 4 | 1 |
| 5 | 2 |
| 6 | 2 |
| On average – 2.7 | |

Table A3.16. Functional/vocal outcome following FELS of LP

| Vocal outcome | No. of patients (%) |
|--------------------|---------------------|
| Normal voice | 30 (58.8%) |
| Minor dysphonia | 6 (11.8%) |
| Moderate dysphonia | 13 (25.5%) |
| Severe dysphonia | 2 (3.9%) |
| Total | 51 (100%) |

Table A3.17. Results of LP treatment using FELS

Participant characteristics

| Group | Overall
N = 51 ¹ | 95% CI ² | Outpatients
N = 24 ¹ | 95% CI ² | Inpatients
N = 27 ¹ | 95% CI ² | Statistical
Test ³ | p-value ³ |
|---------------------------------|---|---------------------|---|---------------------|---|---------------------|----------------------------------|----------------------|
| Age | 44.1 (15.7)
44.0 (22.0)
19.0 77.0 | 40, 49 | 42.2 (16.5)
40.0 (27.0)
19.0 77.0 | 35, 49 | 45.9 (15.1)
45.0 (20.5)
19.0 75.0 | 40, 52 | 277 | 0.4 |
| Gender | | | | | | | 1.8 | 0.3 |
| m | 29 (56.9%) | 43%, 70% | 16 (66.7%) | 48%, 86% | 13 (48.1%) | 29%, 67% | | |
| f | 22 (43.1%) | 30%, 57% | 8 (33.3%) | 14%, 52% | 14 (51.9%) | 33%, 71% | | |
| Location | | | | | | | 8.4 | 0.2 |
| glottic | 27 (52.9%) | 39%, 67% | 16 (66.7%) | 48%, 86% | 11 (40.7%) | 22%, 59% | | |
| glottic+supraglottic | 7 (13.7%) | 4.3%, 23% | 3 (12.5%) | 0.00%, 26% | 4 (14.8%) | 1.4%, 28% | | |
| glottic+subglottic | 6 (11.8%) | 2.9%, 21% | 1 (4.2%) | 0.00%, 12% | 5 (18.5%) | 3.9%, 33% | | |
| glottic+supraglottic+subglottic | 5 (9.8%) | 1.6%, 18% | 1 (4.2%) | 0.00%, 12% | 4 (14.8%) | 1.4%, 28% | | |
| supraglottic | 4 (7.8%) | 0.46%, 15% | 3 (12.5%) | 0.00%, 26% | 1 (3.7%) | 0.00%, 11% | | |
| glottic+subglottic+tracheal | 1 (2.0%) | 0.00%, 5.8% | 0 (0.0%) | 0.00%, 0.00% | 1 (3.7%) | 0.00%, 11% | | |
| subglottic+trachea | 1 (2.0%) | 0.00%, 5.8% | 0 (0.0%) | 0.00%, 0.00% | 1 (3.7%) | 0.00%, 11% | | |
| Foci dimensions, cm | 1.6 (0.8)
1.5 (1.7)
0.2 3.0 | 1.3, 1.8 | 1.3 (0.9)
1.3 (1.5)
0.2 3.0 | 0.97, 1.7 | 1.8 (0.7)
2.0 (1.4)
0.4 3.0 | 1.5, 2.1 | 221 | 0.050 |

| Group | Overall
N = 51 ¹ | 95% CI ² | Outpatients
N = 24 ¹ | 95% CI ² | Inpatients
N = 27 ¹ | 95% CI ² | Statistical
Test ³ | p-value ³ |
|-----------------------------|-----------------------------------|---------------------|------------------------------------|---------------------|-----------------------------------|---------------------|----------------------------------|----------------------|
| Sessions | 1.4 (1.4)
1.0 (0.0)
1.0 7.0 | 1.0, 1.8 | 1.1 (0.3)
1.0 (0.0)
1.0 2.0 | 0.96, 1.2 | 1.7 (1.8)
1.0 (0.0)
1.0 7.0 | 1.0, 2.5 | 276 | 0.2 |
| Endoscopic treatment | | | | | | | 13 | 0.003 |
| LA | 28 (54.9%) | 41%, 69% | 14 (58.3%) | 39%, 78% | 14 (51.9%) | 33%, 71% | | |
| DEX+LA | 16 (31.4%) | 19%, 44% | 3 (12.5%) | 0.00%, 26% | 13 (48.1%) | 29%, 67% | | |
| CS | 5 (9.8%) | 1.6%, 18% | 5 (20.8%) | 4.6%, 37% | 0 (0.0%) | 0.00%,
0.00% | | |
| CS/DEX+LA | 1 (2.0%) | 0.00%, 5.8% | 1 (4.2%) | 0.00%, 12% | 0 (0.0%) | 0.00%,
0.00% | | |
| CS+LA | 1 (2.0%) | 0.00%, 5.8% | 1 (4.2%) | 0.00%, 12% | 0 (0.0%) | 0.00%,
0.00% | | |
| Anaesthesia | | | | | | | 12 | <0.001 |
| Local | 40 (78.4%) | 67%, 90% | 24 (100.0%) | 100%, 100% | 16 (59.3%) | 41%, 78% | | |
| GA+SHFJV | 9 (17.6%) | 7.2%, 28% | 0 (0.0%) | 0.00%, 0.00% | 9 (33.3%) | 16%, 51% | | |
| Local / GA+SHFJV | 2 (3.9%) | 0.00%, 9.2% | 0 (0.0%) | 0.00%, 0.00% | 2 (7.4%) | 0.00%, 17% | | |

| Group | Overall
N = 51 ¹ | 95% CI ² | Outpatients
N = 24 ¹ | 95% CI ² | Inpatients
N = 27 ¹ | 95% CI ² | Statistical
Test ³ | p-value ³ |
|----------------------------------|---|---------------------|--|---------------------|---|---------------------|----------------------------------|----------------------|
| Recurrence | | | | | | | 0.08 | >0.9 |
| No | 33 (64.7%) | 52%, 78% | 16 (66.7%) | 48%, 86% | 17 (63.0%) | 45%, 81% | | |
| Yes | 18 (35.3%) | 22%, 48% | 8 (33.3%) | 14%, 52% | 10 (37.0%) | 19%, 55% | | |
| Malignancy | | | | | | | 1.1 | 0.5 |
| No | 50 (98.0%) | 94%, 100% | 23 (95.8%) | 88%, 100% | 27 (100.0%) | 100%, 100% | | |
| Yes | 1 (2.0%) | 0.00%, 5.8% | 1 (4.2%) | 0.00%, 12% | 0 (0.0%) | 0.00%,
0.00% | | |
| Time without LRc (months) | 72.0 (67.1)
56.0 (88.5)
2.0 268.0 | 53, 91 | 79.1 (72.9)
58.5 (126.5)
2.0 203.0 | 48, 110 | 65.7 (62.3)
40.0 (83.0)
3.0 268.0 | 41, 90 | 336 | 0.8 |
| Time without LRc (years) | | | | | | | 6.0 | 0.5 |
| 1–3 years | 16 (31.4%) | 19%, 44% | 7 (29.2%) | 11%, 47% | 9 (33.3%) | 16%, 51% | | |
| 5–10 years | 13 (25.5%) | 14%, 37% | 5 (20.8%) | 4.6%, 37% | 8 (29.6%) | 12%, 47% | | |
| up to 1 year | 6 (11.8%) | 2.9%, 21% | 3 (12.5%) | 0.00%, 26% | 3 (11.1%) | 0.00%, 23% | | |
| 10–15 years | 6 (11.8%) | 2.9%, 21% | 3 (12.5%) | 0.00%, 26% | 3 (11.1%) | 0.00%, 23% | | |
| 3–5 years | 5 (9.8%) | 1.6%, 18% | 2 (8.3%) | 0.00%, 19% | 3 (11.1%) | 0.00%, 23% | | |

| Group | Overall
N = 51 ¹ | 95% CI ² | Outpatients
N = 24 ¹ | 95% CI ² | Inpatients
N = 27 ¹ | 95% CI ² | Statistical
Test ³ | p-value ³ |
|----------------------------|--------------------------------|---------------------|------------------------------------|---------------------|-----------------------------------|---------------------|----------------------------------|----------------------|
| 15–20 years | 4 (7.8%) | 0.46%, 15% | 4 (16.7%) | 1.8%, 32% | 0 (0.0%) | 0.00%,
0.00% | | |
| 20–25 years | 1 (2.0%) | 0.00%, 5.8% | 0 (0.0%) | 0.00%, 0.00% | 1 (3.7%) | 0.00%, 11% | | |
| Postoperative voice | | | | | | | 5.1 | 0.2 |
| normal | 30 (58.8%) | 45%, 72% | 17 (70.8%) | 53%, 89% | 13 (48.1%) | 29%, 67% | | |
| moderate dysphonia | 13 (25.5%) | 14%, 37% | 6 (25.0%) | 7.7%, 42% | 7 (25.9%) | 9.4%, 42% | | |
| minor dysphonia | 6 (11.8%) | 2.9%, 21% | 1 (4.2%) | 0.00%, 12% | 5 (18.5%) | 3.9%, 33% | | |
| severe dysphonia | 2 (3.9%) | 0.00%, 9.2% | 0 (0.0%) | 0.00%, 0.00% | 2 (7.4%) | 0.00%, 17% | | |

Note: ¹ Mean (SD)
Median (IQR)
Min Max ; n (%)

² CI = Confidence Interval

³ Wilcoxon rank sum test; Pearson's Chi-squared test with simulated p-value
(based on 1e+05 replicates)

Table A3.18. Distribution of patients with glottic cancer according to macroscopic appearance

| Tumour growth pattern | No. of patients (%) |
|----------------------------|---------------------|
| Endophytic | 8 (8.3%) |
| Endophytic with ulceration | 8 (8.3%) |
| Exophytic | 46 (47.9%) |
| Exophytic with ulceration | 2 (2.1%) |
| Mixed | 27 (28.1%) |
| Mixed with ulceration | 5 (5.2%) |
| Total | 96 (100%) |

Table A3.19. Five-year outcomes of treatment for glottic cancer according to tumour stage

| Results | Total, N=
=96 ¹ | 95 %
CI ² | T1a, N=
=27 ¹ | 95 %
CI ² | T1b, N=
=26 ¹ | 95 %
CI ² | T2a, N=
=40 ¹ | 95 %
CI ² | T2b, N=
=3 ¹ | 95 %
CI ² | Statistical test | p-value ³ |
|------------|-------------------------------|-------------------------|-----------------------------|-------------------------|-----------------------------|-------------------------|-----------------------------|-------------------------|----------------------------|-------------------------|------------------|----------------------|
| UDC/OS/DSS | 82 (85.4 %) | 78 %, 92 % | 27 (100 %) | 100 % | 23 (88.5 %) | 76 %, 100 % | 32 (80.0 %) | 68 %, 92 % | 0 (0.0 %) | 0.0 % | 23 | <0.001 |
| DFS | 75 (78.1 %) | 70 %, 86 % | 25 (92.6 %) | 83 % | 21 (80.8 %) | 66 %, 96 % | 29 (72.5 %) | 59 %, 86 % | 0 (0.0 %) | 0.0 % | 15 | 0.002 |
| LC | 76 (79.2 %) | 71 %, 87 % | 25 (92.6 %) | 83 % | 21 (80.8 %) | 66 %, 96 % | 29 (72.5 %) | 59 %, 86 % | 1 (33.3 %) | 0.0 % | 7.9 | 0.048 |
| UDC FELS | 78 (81.3 %) | 73 %, 89 % | 26 (96.3 %) | 89 % | 22 (84.6 %) | 71 %, 98 % | 30 (75.0 %) | 62 %, 88 % | 0 (0.0 %) | 0.0 % | 18 | <0.001 |
| CLP | 80 (83.3 %) | 76 %, 91 % | 27 (100 %) | 100 % | 22 (84.6 %) | 71 %, 98 % | 31 (77.5 %) | 65 %, 90 % | 0 (0.0 %) | 0.0 % | 21 | <0.001 |
| DD | 14 (14.6 %) | 7.5 %, 22 % | 0 (0.0 %) | 0.0 % | 3 (11.5 %) | 0.0 %, 24 % | 8 (20.0 %) | 7.6 %, 32 % | 3 (100 %) | 100 % | 23 | <0.001 |
| LRc | 17 (17.7 %) | 10 %, 25 % | 2 (7.4 %) | 0.0 % | 5 (19.2 %) | 4.1 %, 34 % | 8 (20.0 %) | 7.6 %, 32 % | 2 (66.7 %) | 13 %, 100 % | 7.1 | 0.069 |

Note: ¹ n (%) = number of patients; ² CI = Confidence Interval; ³ Pearson's Chi-squared test

Table A3.20. Five-year outcomes of glottic cancer treatment according to anterior commissure (AC) involvement

| Results | Total, N = 96 ¹ | 95% CI ² | No AC involvement, N=30 ¹ | 95% CI ² | CA involvement, N=66 ¹ | 95% CI ² | Statistical test | p-value ³ |
|------------|----------------------------|---------------------|--------------------------------------|---------------------|-----------------------------------|---------------------|------------------|----------------------|
| UDC/OS/DSS | 82 (85.4%) | 78%, 92% | 29 (96.7%) | 90%, 100% | 53 (80.3%) | 71%, 90% | 3.2 | 0.073 |
| DFS | 75 (78.1%) | 70%, 86% | 27 (90.0%) | 79%, 100% | 48 (72.7%) | 62%, 83% | 2.7 | 0.10 |
| LC | 76 (79.2%) | 71%, 87% | 27 (90.0%) | 79%, 100% | 49 (74.2%) | 64%, 85% | 2.2 | 0.14 |
| UDC FELS | 78 (81.3%) | 73%, 89% | 28 (93.3%) | 84%, 100% | 50 (75.8%) | 65%, 86% | 3.1 | 0.078 |
| CLP | 80 (83.3%) | 76%, 91% | 29 (96.7%) | 90%, 100% | 51 (77.3%) | 67%, 87% | 4.3 | 0.039 |
| DD | 14 (14.6%) | 7.5%, 22% | 1 (3.3%) | 0.00%, 9.8% | 13 (19.7%) | 10%, 29% | 3.2 | 0.073 |
| LRc | 17 (17.7%) | 10%, 25% | 2 (6.7%) | 0.00%, 16% | 15 (22.7%) | 13%, 33% | 2.6 | 0.10 |

Note: ¹ n (%) = number of patients; ² CI = Confidence Interval; ³ Pearson's Chi-squared test

Table A3.21. Five-year outcomes of glottic cancer treatment according to anaesthesia/ventilation method

| Results | Total, N = 96 ¹ | 95% CI ² | General anaesthesia/SHFJV, N = 39 ¹ | 95% CI ² | Local anaesthesia/Spontaneous ventilation, N = 57 ¹ | 95% CI ² | Statistical test | p-value ³ |
|------------|----------------------------|---------------------|--|---------------------|--|---------------------|------------------|----------------------|
| UDC/OS/DSS | 82 (85.4%) | 78%, 92% | 29 (74.4%) | 61%, 88% | 53 (93.0%) | 86%, 100% | 5.0 | 0.025 |
| DFS | 75 (78.1%) | 70%, 86% | 28 (71.8%) | 58%, 86% | 47 (82.5%) | 73%, 92% | 0.98 | 0.3 |
| LC | 76 (79.2%) | 71%, 87% | 29 (74.4%) | 61%, 88% | 47 (82.5%) | 73%, 92% | 0.50 | 0.5 |
| UDC FELS | 78 (81.3%) | 73%, 89% | 28 (71.8%) | 58%, 86% | 50 (87.7%) | 79%, 96% | 2.9 | 0.090 |
| CLP | 80 (83.3%) | 76%, 91% | 28 (71.8%) | 58%, 86% | 52 (91.2%) | 84%, 99% | 5.0 | 0.026 |
| DD | 14 (14.6%) | 7.5%, 22% | 10 (25.6%) | 12%, 39% | 4 (7.0%) | 0.39%, 14% | 5.0 | 0.025 |
| LRc | 17 (17.7%) | 10%, 25% | 9 (23.1%) | 9.9%, 36% | 8 (14.0%) | 5.0%, 23% | 0.75 | 0.4 |

Note: ¹ n (%) = number of patients; ² CI = Confidence Interval; ³ Pearson's Chi-squared test

Table A3.22. Five-year outcomes of glottic cancer treatment according to treatment method

| Results | Total,
N = 96 ¹ | 95%
CI ² | FELS,
N = 71 ¹ | 95%
CI ² | FELS+RT,
N = 25 ¹ | 95%
CI ² | Stati
stical
test | p-value ³ |
|------------|-------------------------------|------------------------|------------------------------|------------------------|---------------------------------|------------------------|-------------------------|----------------------|
| UDC/OS/DSS | 82
(85.4%) | 78%,
92% | 67
(94.4%) | 89%,
100% | 15
(60.0%) | 41%,
79% | 15 | <0.001 |
| DFS | 75
(78.1%) | 70%,
86% | 61
(85.9%) | 78%,
94% | 14
(56.0%) | 37%,
75% | 8.0 | 0.005 |
| LC | 76
(79.2%) | 71%,
87% | 61
(85.9%) | 78%,
94% | 15
(60.0%) | 41%,
79% | 6.0 | 0.014 |
| UDC FELS | 78
(81.3%) | 73%,
89% | 63
(88.7%) | 81%,
96% | 15
(60.0%) | 41%,
79% | 8.2 | 0.004 |
| CLP | 80
(83.3%) | 76%,
91% | 65
(91.5%) | 85%,
98% | 15
(60.0%) | 41%,
79% | 11 | <0.001 |
| DD | 14
(14.6%) | 7.5%,
22% | 4
(5.6%) | 0.27%,
11% | 10
(40.0%) | 21%,
59% | 15 | <0.001 |
| LRc | 17
(17.7%) | 10%,
25% | 9
(12.7%) | 4.9%,
20% | 8
(32.0%) | 14%,
50% | 3.5 | 0.061 |

Note: ¹ n (%) = number of patients; ² CI = Confidence Interval; ³ Pearson's Chi-squared test

Table A3.23. Five-year outcomes of treatment for T2 glottic cancer according to treatment method

| Results | Total,
N = 43 ¹ | 95%
CI ² | FELS,
N = 20 ¹ | 95%
CI ² | FELS+RT,
N = 23 ¹ | 95%
CI ² | Stati
stical
test | p-value ³ |
|------------|-------------------------------|------------------------|------------------------------|------------------------|---------------------------------|------------------------|-------------------------|----------------------|
| UDC/OS/DSS | 32
(74.4%) | 61%,
87% | 17
(85.0%) | 69%,
100% | 15
(65.2%) | 46%,
85% | 1.3 | 0.3 |
| DFS | 29
(67.4%) | 53%,
81% | 15
(75.0%) | 56%,
94% | 14
(60.9%) | 41%,
81% | 0.44 | 0.5 |
| LC | 30
(69.8%) | 56%,
83% | 15
(75.0%) | 56%,
94% | 15
(65.2%) | 46%,
85% | 0.13 | 0.7 |
| UDC FELS | 30
(69.8%) | 56%,
83% | 15
(75.0%) | 56%,
94% | 15
(65.2%) | 46%,
85% | 0.13 | 0.7 |
| CLP | 31
(72.1%) | 59%,
85% | 16
(80.0%) | 62%,
98% | 15
(65.2%) | 46%,
85% | 0.54 | 0.5 |
| DD | 11
(25.6%) | 13%,
39% | 3
(15.0%) | 0.00%,
31% | 8
(34.8%) | 15%,
54% | 1.3 | 0.3 |
| LRc | 10
(23.3%) | 11%,
36% | 4
(20.0%) | 2.5%,
38% | 6
(26.1%) | 8.1%,
44% | 0.01 | >0.9 |

Note: ¹ n (%) = number of patients; ² CI = Confidence Interval; ³ Pearson's Chi-squared test

Table A3.24. Five-year functional outcomes (voice quality) in the group of cured glottic cancer patients with preserved larynx (n=80)

| Stage
Quality of voice | Total (T1-T2), n=80 ¹ | 95% CI ² | T1a, n=27 ¹ | 95% CI ² | T1b, n=22 ¹ | 95% CI ² | T2, n=31 ¹ | 95% CI ² | Statistical test | p-value ³ |
|------------------------------|----------------------------------|---------------------|------------------------|---------------------|------------------------|---------------------|-----------------------|---------------------|------------------|----------------------|
| Satisfactory/Minor dysphonia | 32 (40.0%) | 29%, 51% | 19 (70.4%) | 53%, 88% | 5 (22.7%) | 5.2%, 40% | 8 (25.8%) | 10%, 41% | 22 | <0.001 |
| Moderate dysphonia | 21 (26.3%) | 17%, 36% | 3 (11.1%) | 0.00%, 23% | 11 (50.0%) | 29%, 71% | 7 (22.6%) | 7.9%, 37% | | |
| Severe dysphonia | 27 (33.8%) | 23%, 44% | 5 (18.5%) | 3.9%, 33% | 6 (27.3%) | 8.7%, 46% | 16 (51.6%) | 34%, 69% | | |

Note: ¹ n (%) = number of patients; ² CI = Confidence Interval; ³ Pearson's Chi-squared test

Table A3.25. Number of treatment sessions administered for tumour eradication

| Number of sessions | No. of patients |
|----------------------|-----------------|
| 1 | 17 |
| 2 | 5 |
| 3 | 2 |
| 4 | 2 |
| 6 | 1 |
| 9 | 1 |
| On average = 2.0±1.8 | |

Table A3.26. Results of VCL treatment using FELS

| | | |
|--|-----------------|---|
| Recurrence-free survival | n=22
(78.6%) | |
| Locoregional recurrence or residual tumour | n=6
(21.4%) | <p>Successful salvage treatment (n=2):</p> <p>1) T1a → Residual tumour after 4 months → Repeated FELS → 48 months (4 years) without recurrence.
 2) T2 → Recurrence after 4 years → Open surgery (laryngofissure + tumour resection + tracheostomy) → 96 months (8 years) without recurrence.</p> <p>Treatment failure (n=4):</p> <p>3) T2 (hybrid form of VCL) → Residual tumour after 4 months (keratinised SCC = hybrid form of VCL) → RT (60Gy) → Rc after 5 months → total laryngectomy → death 7 months after laryngectomy.
 4) T1b (hybrid form of VCL) → Residual tumour (keratinised SCC = hybrid form of VCL) after 2 months → FELS + RT (50 Gy) → progression → FELS + Chemotherapy → progression → death (2 years after the first operation).
 5) T2 (hybrid form of VCL) → Residual tumour on follow-up biopsy after the 4th session of FELS (non-keratinised squamous cell carcinoma = hybrid form of VCL) → total laryngectomy → death 7 months after laryngectomy.
 6) T2 (hybrid form of VCL) → Metastases in cervical lymph nodes after 2 years → cervical lymph node dissection → death 54 months (4 years 6 months) after the first operation due to tumour progression (distant metastases involving the lungs and spine).</p> |

Table A3.27. Follow-up period without recurrence after endoscopic treatment

| | |
|--|------------|
| Follow-up period without recurrence after endoscopic treatment | (n= 22) |
| 1–3 years | 6 (27.3%) |
| 3–5 years | 2 (9.1%) |
| Over 5 years | 14 (63.6%) |
| On average – 85 months (7 years 1 month) | |

Table A3.28. Five-year outcomes of treatment for recurrent/residual glottic cancer following RT, according to tumour stage

| Results | Total, N = 9 | T1a, N = 2 | T1b, N = 1 | T2, N = 6 |
|------------------------|--------------|--------------|--------------|-------------|
| UDC/OS | 6/9 (66.7%) | 2/2 (100.0%) | 1/1 (100.0%) | 3/6 (50.0%) |
| LC/DFS | 5/9 (55.6%) | 2/2 (100.0%) | 1/1 (100.0%) | 2/6 (33.3%) |
| UDC FELS | 5/9 (55.6%) | 2/2 (100.0%) | 1/1 (100.0%) | 2/6 (33.3%) |
| CLP | 5/9 (55.6%) | 2/2 (100.0%) | 1/1 (100.0%) | 2/6 (33.3%) |
| DD (primary tumour) | 2/9 (22.2%) | 0/2 (0.0%) | 0/1 (0.0%) | 2/6 (33.3%) |
| DD (metastatic tumour) | 1/9 (11.1%) | 0/2 (0.0%) | 0/1 (0.0%) | 1/6 (16.7%) |
| LRc | 3/9 (33.3%) | 0/2 (0.0%) | 0/1 (0.0%) | 3/6 (50.0%) |

Table A3.29. Recurrence-free follow-up period for patients with glottic carcinoma since their last FELS procedure on an outpatient basis

| Recurrence-free follow-up period since the last organ-preserving procedure | No. of patients |
|--|-----------------|
| Up to 1 year | 5 |
| 1–3 years | 10 |
| 3–5 years | 1 |
| 5–10 years | 1 |
| 10–15 years | 2 |
| 15–20 years | 2 |
| 20–25 years | 3 |
| Total | 24 |

ANNEX 4

COPIES OF THE AUTHOR'S COPYRIGHT CERTIFICATES AND PATENTS RELATING TO THE TOPIC OF THE SYNTHESIS PAPER

REPUBLICA MOLDOVA
Agenția de Stat pentru
Proprietatea Intelectuală

ADEVERINȚĂ
privind înscrierea obiectelor
dreptului de autor și ale drepturilor conexe

SERIA OȘ NR. 8246
DIN 14.07.2025

eliberată în temeiul Legii nr. 230/2022 privind dreptul de autor
și drepturile conexe, prin care se confirmă înscrierea obiectului de pe verso
în Registrul de Stat al obiectelor protejate de dreptul de autor și drepturile conexe

Director general

CHIȘINĂU



Seria: OȘ (operă științifică)

Numărul de înscriere: 8246

Data înscrierii: 25.06.2025

Numărul cererii: 3052

Denumirea obiectului: „ABORDARE ENDOSCOPICĂ NETRADIȚIONALĂ
A SCHWANOMULUI LARINGIAN OBSTRUCTIV”

Autori:

Gurău Petru

Sencu Eusebiu

Vetrician Sergiu

Titularul drepturilor patrimoniale:

Instituția Publică Universitatea de Stat de Medicină și Farmacie

"Nicolae Testemițanu" din Republica Moldova

IDNO: 1007600000794

L.S.



Sefă Direcție Drept de Autor





REPUBLICA MOLDOVA

Agencia de Stat pentru
Proprietatea Intelectuala

ADIVERINTA

privind inscrierea obiectelor
dreptului de autor si ale drepturilor conexe

SERIA OS NR. 8247
DIN 14.07.2025

eliberata in temeiul Legii nr. 230/2022 privind dreptul de autor
si drepturile conexe, prin care se confirma inscrierea obiectul de pe verso
in Registrul de Stat al obiectelor protejate de dreptul de autor si drepturile conexe



Director general

CHISINAU

Seria: OȘ (operă științifică)

Numărul de înscriere: 8247

Data înscrierii: 25.06.2025

Numărul cererii: 3053

Denumirea obiectului: „ABORDARE ENDOSCOPICĂ DE TRATAMENT
MINIINVAZIV AL EDEMULUI REINKE”

Autori:

Gurău Petru

Sencu Eusebiu

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Instituția Publică Universitatea de Stat de Medicină și Farmacie

"Nicolae Testemițanu" din Republica Moldova

IDNO: 1007600000794

L.S.



Sefă Directie Drept de Autor





REPUBLICA MOLDOVA

Agenția de Stat pentru
Proprietatea Intelectuală

**BREVET
DE INVENȚIE
DE SCURTĂ DÛRATĂ**

Nr. 1464

Eliberat în temeiul Legii nr. 50/2008 privind protecția invențiilor

**Titlul: Metodă de tratament chirurgical al cancerului
exofitic T1-T2 al plămânului**

**Titular: UNIVERSITATEA DE STAT DE MEDICINĂ ȘI
FARMACIE "NICOLAE TESTEMIȚANU" DIN
REPUBLICA MOLDOVA, MD**

Data depozit: 2020.07.21

Durata brevetului : 6 ani

Descrierea invenției, revendicările și desenele constituie parte
integrantă a prezentului brevet de invenție de scurtă durată

Director General



COPIE

CHIȘINĂU



MD 1464 Z 2021.06.30

REPUBLICA MOLDOVA



(19) Agenția de Stat
pentru Proprietatea Intelectuală

(11) 1464 (13) Z
(51) Int.Cl: A61B 17/24 (2006.01)

(12) BREVET DE INVENȚIE
DE SCURTĂ DURATĂ

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|---|---|
| (21) Nr. depozit: s 2020 0081
(22) Data depozit: 2020.07.21 | (45) Data publicării hotărârii de
acordare a brevetului:
2020.11.30, BOPI nr. 11/2020 |
| (71) Solicitant: UNIVERSITATEA DE STAT DE MEDICINĂ ȘI FARMACIE "NICOLAE
TESTEMIȚANU" DIN REPUBLICA MOLDOVA, MD | |
| (72) Inventatori: GURĂU Petru, MD; SENCU Eusebiu, MD; VETRICEAN Sergiu, MD | |
| (73) Titular: UNIVERSITATEA DE STAT DE MEDICINĂ ȘI FARMACIE "NICOLAE
TESTEMIȚANU" DIN REPUBLICA MOLDOVA, MD | |
| (74) Mandatar autorizat: COȘNEANU Elena | |

(54) Metodă de tratament chirurgical al cancerului exofitic T1-T2 al plicii vocale

(57) Rezumat:

1
Invenția se referă la medicină, și anume la chirurgia otorinolaringologică, și poate fi utilizată pentru tratamentul chirurgical al cancerului exofitic T1-T2 al plicii vocale.

Esența invenției constă în aceea că se efectuează sedarea și analgezia intravenoasă, anestezia locală de contact a mucoasei nazale cu o soluție de lidocaină de 2% și o soluție de adrenalină de 0,1% în timpul respirației spontane a pacientului. În același timp, se realizează anestezia de contact a faringelui prin aplicarea unui spray cu o soluție de lidocaină de 10%. După care, transnazal se introduce endoscopul flexibil și se vizualizează

2
structurile anatomice în timpul respirației și fonației și totodată, se efectuează anestezia de contact prin insuflare a laringelui cu o soluție de lidocaină de 2% și o soluție de adrenalină de 0,1%. Apoi prin canalul de lucru al fibroscopului se direcționează o ansă diatermică, care se plasează la baza componentului exofitic al tumorii, efectuându-se excizia tumorii în regim diatermic. Ulterior se realizează ablația tumorii restante prin vaporizare cu ajutorul laserului Nd:YAG cu lungimea de undă de 1064 nm.

Revendicări: 1

Figuri: 2

COPIE



REPUBLICA MOLDOVA

Agenția de Stat pentru
Proprietatea Intelectuală

BREVET
DE INVENȚIE
DE SCURTĂ DURATĂ

Nr. 1473

Eliberat în temeiul Legii nr. 50/2008 privind protecția invențiilor

Titlul: Metodă de biopsie în carcinomul verucos de laringe

**Titular: UNIVERSITATEA DE STAT DE MEDICINĂ ȘI
FARMACIE "NICOLAE TESTEMIȚANU" DIN
REPUBLICA MOLDOVA, MD**

Data depozit: 2020.07.21

Durata brevetului : 6 ani

Descrierea invenției, revendicările și desenele constituie parte
integrantă a prezentului brevet de invenție de scurtă durată



Director General

COPIE

CHIȘINĂU



MD 1473 Z 2021.07.31

REPUBLICA MOLDOVA

(19) Agenția de Stat
pentru Proprietatea Intelectuală(11) 1473 (13) Z
(51) Int.Cl: A61B 10/02 (2006.01)
A61B 10/04 (2006.01)(12) BREVET DE INVENȚIE
DE SCURTĂ DURATĂ

| | |
|---|---|
| (21) Nr. depozit: s 2020 0080
(22) Data depozit: 2020.07.21 | (45) Data publicării hotărârii de
acordare a brevetului:
2020.12.31, BOPI nr. 12/2020 |
| (71) Solicitant: UNIVERSITATEA DE STAT DE MEDICINĂ ȘI FARMACIE "NICOLAE
TESTEMIȚANU" DIN REPUBLICA MOLDOVA, MD | |
| (72) Inventatori: GURĂU Petru, MD; SENCU Eusebiu, MD; VETRICEAN Sergiu, MD | |
| (73) Titular: UNIVERSITATEA DE STAT DE MEDICINĂ ȘI FARMACIE "NICOLAE
TESTEMIȚANU" DIN REPUBLICA MOLDOVA, MD | |
| (74) Mandatar autorizat: COȘNEANU Elena | |

(54) Metodă de biopsie în carcinomul verucos de laringe

(57) Rezumat:

1
Invenția se referă la medicină, în special la otorinolaringologie, și poate fi utilizată pentru biopsia diagnostică în carcinomul verucos de laringe.

Esența invenției constă în aceea că se aplică în fosa nazală o meșă nazală, îmbibată cu o soluție de lidocaină de 2% și o soluție de adrenalină de 0,1%, pentru anestezie topică, timp de câteva minute. Concomitent se realizează anestezia locală de contact a faringelui prin aplicarea a 2...3 pufuri de spray cu o soluție de lidocaină de 10%. După care, transnazal se introduce endoscopul flexibil și cu atenție se vizualizează structurile anatomice

2
în timpul respirației și fonației. Prin canalul de lucru al fibroscopului, cu ajutorul unei seringi, care conține o soluție de lidocaină de 2% și o soluție de adrenalină de 0,1% se pulverizează mucoasa laringelui pentru o anestezie locală de contact, apoi prin canalul de lucru al fibroscopului se direcționează o ansă diatermică, care se plasează la baza componentului exofitic al tumorii, și se efectuează excizia porțiunii de țesut necesar prin tăiere în regim diatermic.

Revendicări: 1

Figuri: 1

MD 1473 Z 2021.07.31

COPIE



REPUBLICA MOLDOVA

Agencia de Stat pentru
Proprietatea Intelectuala

BREVET DE INVENTIE DE SCURTĂ DURATĂ

Nr. 1491

Eliberat în temeiul Legii nr. 50/2008 privind protecția invențiilor

Titlul: Metodă de tratament endoscopic al tumorilor de laringe

Titular: UNIVERSITATEA DE STAT DE MEDICINĂ ȘI FARMACIE "NICOLAE TESTEMIȚANU" DIN REPUBLICA MOLDOVA, MD

Data depozit: 2020.07.28

Durata brevetului : 6 ani

Descrierea invenției, revendicările și desenele constituie parte integrantă a prezentului brevet de invenție de scurtă durată

Director General



COPIE

CHIȘINĂU



MD 1491 Z 2021.08.31

REPUBLICA MOLDOVA



(19) Agenția de Stat
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(12) BREVET DE INVENȚIE
DE SCURTĂ DURATĂ

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| (21) Nr. depozit: s 2020 0086
(22) Data depozit: 2020.07.28 | (45) Data publicării hotărârii de
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| (71) Solicitant: UNIVERSITATEA DE STAT DE MEDICINĂ ȘI FARMACIE "NICOLAE
TESTEMIȚANU" DIN REPUBLICA MOLDOVA, MD
(72) Inventatori: GURĂU Petru, MD; SENCU Eusebiu, MD; VETRICEAN Sergiu, MD
(73) Titular: UNIVERSITATEA DE STAT DE MEDICINĂ ȘI FARMACIE "NICOLAE
TESTEMIȚANU" DIN REPUBLICA MOLDOVA, MD
(74) Mandatar autorizat: COȘNEANU Elena | |

(54) Metodă de tratament endoscopic al tumorilor de laringe

(57) Rezumat:

1
Invenția se referă la medicină, și anume la chirurgia otorinolaringologică și poate fi utilizată pentru tratamentul chirurgical endoscopic transoral al tumorilor de laringe.

Esența invenției constă în aceea că sub anestezie generală bolnavul se poziționează cu gâtul în hiperextensie, se introduce tubul de laringoscopie directă suspendată până la observarea cartilajelor aritenoide ale laringelui,

2
apoi prin laringoscopul suspendat se introduce fibroendoscopul cu efectuarea examinării adecvate a porțiunii glotice laringiene și determinarea dimensiunilor formațiunii tumorale, după care se efectuează intervenția chirurgicală cu ajutorul instrumentelor (ansa diatermică, forcepsul, fibra laser), direcționate prin canalul de lucru al endoscopului flexibil.

Revendicări: 2

MD 1491 Z 2021.08.31

COPIE



REPUBLICA MOLDOVA

**Agenția de Stat pentru
Proprietatea Intelectuală**

**BREVET
DE INVENȚIE
DE SCURTĂ DURATĂ**

Nr. 1492

Eliberat în temeiul Legii nr. 50/2008 privind protecția invențiilor

Titlul: Metodă de tratament chirurgical al papilomului de laringe

Titular: UNIVERSITATEA DE STAT DE MEDICINĂ ȘI FARMACIE "NICOLAE TESTEMIȚANU" DIN REPUBLICA MOLDOVA, MD

Data depozit: 2020.07.28

Durata brevetului : 6 ani

Descrierea invenției, revendicările și desenele constituie parte integrantă a prezentului brevet de invenție de scurtă durată

Director General



COPIE

CHIȘINĂU



MD 1492 Z 2021.08.31

REPUBLICA MOLDOVA



(19) Agenția de Stat
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(51) Int.Cl: A61B 17/24 (2006.01)

(12) BREVET DE INVENȚIE
DE SCURTĂ DURATĂ

| | |
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| (21) Nr. depozit: s 2020 0087
(22) Data depozit: 2020.07.28 | (45) Data publicării hotărârii de
acordare a brevetului:
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| (71) Solicitant: UNIVERSITATEA DE STAT DE MEDICINĂ ȘI FARMACIE "NICOLAE
TESTEMIȚANU" DIN REPUBLICA MOLDOVA, MD | |
| (72) Inventatori: GURĂU Petru, MD; SENCU Eusebiu, MD; VETRICEAN Sergiu, MD | |
| (73) Titular: UNIVERSITATEA DE STAT DE MEDICINĂ ȘI FARMACIE "NICOLAE
TESTEMIȚANU" DIN REPUBLICA MOLDOVA, MD | |
| (74) Mandatar autorizat: COȘNEANU Elena | |

(54) Metodă de tratament chirurgical al papilomului de laringe

(57) Rezumat:

1

Invenția se referă la medicină, și anume la chirurgia otorinolaringologică, și poate fi utilizată pentru tratamentul chirurgical endoscopic al papilomului de laringe.

Esența invenției constă în aceea că se efectuează sedarea și analgezia intravenoasă, anestezia locală de contact a mucoasei nazale cu o soluție de lidocaină de 2% și o soluție de adrenalină de 0,1% în timpul respirației spontane a pacientului. În același timp, se realizează anestezia de contact a faringelui prin aplicarea unui spray cu o soluție de lidocaină de 10%. După care, transnazal se introduce fibroendoscopul și se direcționează către

2

rinofaringe, se propulsează vertical în faringe și laringe, totodată se efectuează anestezia de contact prin insuflare a laringelui cu o soluție de lidocaină de 2% și o soluție de adrenalină de 0,1%. Apoi prin canalul de lucru al fibroendoscopului se introduce o ansă diatermică până la baza componentului exofitic al tumorii, și se efectuează excizia tumorii prin tăiere în regim diatermic, iar ablația tumorii restante se efectuează prin vaporizare cu ajutorul laserului Nd:YAG cu lungimea de undă de 1064 nm, cu o margine de siguranță de 1...2 mm de țesut sănătos.

Revendicări: 1

COPIE



REPUBLICA MOLDOVA

Agencia de Stat pentru
Proprietatea Intelectuală

BREVET DE INVENȚIE DE SCURTĂ DURATĂ

Nr. 1895

Prezentul brevet se eliberează în temeiul Legii nr. 50/2008
privind protecția invențiilor.

Titlu: Metodă de tratament endoscopic al schwanomului
laringian obstructiv

Titular: IP UNIVERSITATEA DE STAT DE MEDICINĂ ȘI
FARMACIE "NICOLAE TESTEMIȚANU" DIN
REPUBLICA MOLDOVA, MD

Data de depozit: 2025.02.26

Durata brevetului: 6 ani

Descrierea invenției, revendicările și desenele constituie parte integrantă
a prezentului brevet de invenție.



Director

Mogol



MD 1895 Z 2026.03.31

REPUBLICA MOLDOVA



(19) Agenția de Stat
pentru Proprietatea Intelectuală

(11) **1895** (13) **Z**
(51) Int.Cl: *A61B 17/24* (2006.01)
A61B 18/20 (2006.01)

(12) **BREVET DE INVENȚIE
DE SCURTĂ DURATĂ**

| | |
|---|---|
| (21) Nr. depozit: s 2025 0016
(22) Data depozit: 2025.02.26 | (45) Data publicării hotărârii de
acordare a brevetului:
2025.11.30, BOPI nr. 11/2025 |
| (71) Solicitant: IP UNIVERSITATEA DE STAT DE MEDICINĂ ȘI FARMACIE "NICOLAE
TESTEMIȚANU" DIN REPUBLICA MOLDOVA, MD
(72) Inventatori: GURĂU Petru, MD; SENCU Eusebiu, MD; VETRICEAN Sergiu, MD
(73) Titular: IP UNIVERSITATEA DE STAT DE MEDICINĂ ȘI FARMACIE "NICOLAE
TESTEMIȚANU" DIN REPUBLICA MOLDOVA, MD | |

(54) **Metodă de tratament endoscopic al schwanomului laringian obstructiv**

(57) **Rezumat:**

Invenția se referă la medicină, în special la otorinolaringologie și poate fi utilizată pentru tratamentul pacienților cu schwanom laringian obstructiv.

Esența invenției constă în aceea că preventiv se efectuează traheostomia, apoi sub anestezie generală prin ventilare cu jet de frecvență înaltă suprapusă se efectuează laringoscopia directă rigidă suspendată, totodată se efectuează laringoscopia flexibilă cu ajutorul bronhoscopului flexibil, se examinează tumoarea cu determinarea marginilor ei, apoi prin orificiul traheostomic cu ajutorul unui laser diodă cu lungimile de undă de 980 nm/1470 nm (20W) se efectuează o incizie la marginea superioară și o incizie la marginea inferioară a bazei tumorii, după care prin canalul instrumental al bronhoscopului flexibil se introduce ghidul flexibil al laserului și se efectuează rezecția rece "coring out" a tumorii cu bizoul bronhoscopului rigid, apoi se efectuează fotocoagularea suprafeței hemoragice și vaporizarea cu laserul a țesutului restant tumoral la baza și marginile lojii tumorale.

Revendicări: 1

Figuri: 4

MD 1895 Z 2026.03.31



REPUBLICA MOLDOVA

Agenția de Stat pentru
Proprietatea Intelectuală

BREVET DE INVENȚIE DE SCURTĂ DÜRATĂ

Nr. 1896

Prezentul brevet se eliberează în temeiul Legii nr. 50/2008
privind protecția invențiilor.

**Titlu: Metodă de tratament miniinvaziv al edemului
Reinke**

**Titular: IP UNIVERSITATEA DE STAT DE MEDICINĂ ȘI
FARMACIE "NICOLAE TESTEMIȚANU" DIN
REPUBLICA MOLDOVA, MD**

Data de depozit: 2025.02.26

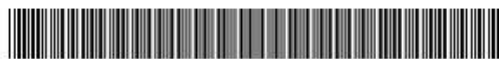
Durata brevetului: 6 ani

Descrierea invenției, revendicările și desenele constituie parte integrantă
a prezentului brevet de invenție.



Director

Mogel



MD 1896 Z 2026.03.31

REPUBLICA MOLDOVA



(19) Agenția de Stat
pentru Proprietatea Intelectuală

(11) **1896** (13) **Z**
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(71) Solicitant: IP UNIVERSITATEA DE STAT DE MEDICINĂ ȘI FARMACIE "NICOLAE
TESTEMIȚANU" DIN REPUBLICA MOLDOVA, MD

(72) Inventatori: GURĂU Petru, MD; SENCU Eusebiu, MD; VETRICEAN Sergiu, MD

(73) Titular: IP UNIVERSITATEA DE STAT DE MEDICINĂ ȘI FARMACIE "NICOLAE
TESTEMIȚANU" DIN REPUBLICA MOLDOVA, MD

(54) **Metodă de tratament miniinvasiv al edemului Reinke**

(57) **Rezumat:**

Invenția se referă la medicină, în special la otorinolaringologie și poate fi utilizată pentru tratamentul miniinvasiv al pacienților cu edemul Reinke.

Esența invenției constă în aceea că se efectuează anestezia locală cu sol. lidocaină de 2% la respirație spontană cu/sau fără sedare analgezică i/v, se introduce transnazal endoscopul flexibil până la formațiunea polipoidă, apoi prin canalul instrumental al endoscopului se introduce ansa diatermică până la baza formațiunii menționate și se efectuează excizia formațiunii în regim diatermic de tăiere.

Revendicări: 1

Figuri: 3

MD 1896 Z 2026.03.31

ANNEX 5

COPIES OF PROGRAMMES CONFIRMING THE PRESENTATION OF RESEARCH RESULTS ON THE TOPIC OF THE SYNTHESIS PAPER AT SCIENTIFIC FORUMS

The image shows the cover of a program for a scientific conference. At the top center is a circular logo of the Romanian Society of Otorhinolaryngology and Cervicofacial Surgery (Societatea Română de ORL și Chirurgie Cervico-Facială). Below the logo, the word "PROGRAM" is written in large, bold, white capital letters. Underneath, the conference title is written in smaller white text: "Conferința Națională de Otorinolaringologie și Chirurgie Cervico-Facială cu Participare Internațională". The background of the cover is a photograph of a beach with large, sand-cast letters spelling "ORL" on the sand. At the bottom, there are three circular icons: a blue one with an ear, a green one with a nose, and a purple one with a face. A blue rounded rectangle at the bottom contains the dates "28-31 Mai 2025" and the location "Eforie Nord, Hotel Europa".

PROGRAM

Conferința Națională de Otorinolaringologie
și Chirurgie Cervico-Facială cu
Participare Internațională

ORL

28-31 Mai 2025
Eforie Nord, Hotel Europa

Conferința Națională de Otorinolaringologie și Chirurgie Cervico-Facială cu Participare Internațională



17:05 - 18:15 SESIUNE FREEPAPERS // FREEPAPERS SESSION

Moderatori/Chairs:

Conf. Univ. Dr. Daniela Vrînceanu,

Asist. Univ. Dr. Cristina Țiple

- 17:05 - 17:15 **Biopsiile optice: o abordare minim invazivă pentru evaluarea leziunilor laringiene // Optical biopsies: a minimally invasive approach to evaluating laryngeal lesions**
Iuliana-Cosmina Paraschivescu^{1,2}, Zainea Viorel^{1,2},
Irina-Gabriela Ioniță^{1,2}, Andreea Rusescu^{1,2}, Raluca Oana Pulpa^{1,2},
Oana-Ruxandra Aliuș^{1,2}, Carmen Davițoiu-Lesu¹, Răzvan
Hainăroșie^{1,2}, Cătălina Voiosu^{1,2}
¹IFACF ORL Prof. Dr. D. Hociotă, București
²UMF "Carol Davila", București
- 17:15 - 17:25 **Chirurgia prin endoscopie flexibilă în tratamentul edemului Reinke // Flexible endoscopic surgery in the treatment of Reinke's edema**
Petru Gurău¹, Oleg Arnăut¹, Eusebiu Sencu¹, Dumitru Sofroni¹
¹USMF "Nicolae Testemițanu", Chișinău, Republica Moldova
- 17:25 - 17:35 **Metastaza ganglionilor limfatici cervicali în melanom: strategii de tratament și prognostic // Cervical lymph node metastasis in melanoma: treatment strategies and prognosis**
Mirela Veronica Păvălean¹, Dr. Cătălina Voiosu^{1,2},
Dr. Oana Ruxandra Aliuș^{1,2}, Dr. Andreea Rusescu^{1,2},
Dr. Irina Gabriela Ioniță^{1,2}, Prof. Răzvan Hainăroșie^{1,2}
¹IFACF ORL "Prof. Dr. Hociota", Bucuresti,
²Universitatea de Medicină și Farmacie "Carol Davila", București

Conferința Națională de Otorinolaringologie și Chirurgie Cervico-Facială cu Participare Internațională



15:20 - 16:30 SESIUNE FREEPAPERS // FREEPAPERS SESSION

Moderatori/Chairs:

Șef Lucrări Dr. Sever Pop, Șef Lucrări Dr. Mihail Tușaliu

- 15:20- 15:30 **Epidemiologia purtătorilor de mutații la nivelul genei GJB2 în NE României // Epidemiology of GJB2 Gene Mutation Carriers in North-Eastern Romania**
Asist. Univ. Dr. Petronela Moraru, Prof. Dr. Luminița Rădulescu
Universitatea de Medicină și Farmacie 'Gr. T. Popa', Iași
- 15:30- 15:40 **Chirurgia prin endoscopie flexibilă în tratamentul polipilor corzilor vocale // Flexible Endoscopic Surgery for the Treatment of Vocal Cord Polyps**
Petru Gurău¹, Oleg Arnău¹, Eusebiu Sencu¹, Dumitru Sofroni¹
¹USMF "Nicolae Testemițanu", Chișinău, Republica Moldova
- 15:40- 15:50 **Microlaringoscopia suspendată în tratamentul polipilor corzilor vocale- Experiența clinicii ORL a Spitalului Republican "Timofei Moșneaga" // Microlaryngoscopy for the Treatment of Vocal Cord Polyps – The Experience of the ENT Clinic at 'Timofei Moșneaga Republican Hospital**
Adrian Vita
Spitalul Clinic Republican, Timofei Moșneaga, Chișinău, Republica Moldova
- 15:50- 16:00 **Evaluarea eficacității diagnostice a NBI-ului în detectarea cancerului laringian // Evaluating the Diagnostic Efficacy of Narrow-Band Imaging for Laryngeal Cancer Detection**
Ileana Alexandra Sanda¹, Prof. Univ. Dr. Răzvan Hainăroșie, Prof. Univ. Dr. Viorel Zainea, Șef. Lucrări.
Dr. Irina Gabriela Ioniță, Asist. Univ. Dr. Ruxandra Oana Aliuș,
Asist. Univ. Dr. Andreea Rusescu,
Asist. Univ. Dr. Marius Răzvan Ristea,
Asist. Univ. Dr. Raluca Pulpă, Șef. Lucrări. Dr. Cătălina Voiosu
¹Universitatea de Medicină și Farmacie „Carol Davila” București

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CONFERINȚELE NAȚIONALE ale SECȚIUNILOR
și GRUPURILOR DE LUCRU
din cadrul
SOCIETĂȚII ROMÂNE de PNEUMOLOGIE



26-29
noiembrie 2025
Crowne Plaza București

A XI-a Conferință de Somnologie și Ventilație Non-Invazivă

A VII-a Conferință de Cancer Pulmonar

A XIII-a Conferință de Bronhologie

A XI-a Conferință de Tabacologie

A VI-a Conferință de Boli Pulmonare Rare

A XI-a Conferință de Pneumologie Pediatrică

A III-a Conferință a Grupului de Lucru pentru Îngrijiri Palliative
în bolile respiratorii

PROGRAM



SRP

Societatea Română de PNEUMOLOGIE



www.conferinte-srp.ro

3. **Utilitatea bronhoscopiei în diagnosticul și managementul complicațiilor căilor aeriene după transplant pulmonar / *The role of bronchoscopy in the diagnosis and management of airway complications after lung transplantation***
Doina Tofolean, Ionuț Stanciu, Ionela Preotesoiu, Constanța
4. **Tehnici bronhoscopice în managementul leziunilor neepiteliale benigne ale laringelui / *Bronchoscopic techniques in the management of benign non-epithelial lesions of the larynx***
Petru Gurău, Republica Moldova
5. **Tratamentul corticosteroid inhalator în stenozele traheale post-procedurale / *Inhaled corticosteroid therapy in post-procedural tracheal stenosis***
Mihai Alexe, București
6. **Discuții / *Discussions***

14:30-16:00

SALA ORHIDEEA / ORHIDEEA HALLSimpozion științific / *Scientific symposium*

Varia II

Moderatori / *Chairpersons*: Oana-Claudia Deleanu, Ștefan Mihăicuță

1. **Tendențele post-pandemice ale pneumoniei comunitare: perspective clinice și epidemiologice / *Post-pandemic trends of community-acquired pneumonia: clinical and epidemiological perspectives***
Doina Rusu, Republica Moldova
2. **Povara hipoxică: un nou marker fiziopatologic al SASO / *Hypoxic burden – a new pathophysiological marker in OSAS***
Oana-Claudia Deleanu, Andreea Roxana Florescu, București
3. **Sindromul de apnee în somn, bolile cardiovasculare și CPAP / *Sleep apnea syndrome, cardiovascular diseases and CPAP therapy***
Ștefan Mihăicuță, Timișoara
4. **Granulomatoza pulmonară cu celule Langerhans: diagnostic și tratament / *Pulmonary Langerhans cell granulomatosis: diagnosis and treatment***
Liliana Grigoriu, București
5. **Discuții / *Discussions***

16:00-16:15 PAUZĂ / *BREAK*

la Ordinul MS nr. 131
din 20 februarie 2023

AGENDA
conferinței naționale interdisciplinare
„Actualități în diagnosticul și tratamentul tumorilor sferei ORL”

24 februarie 2023

Locul desfășurării evenimentului: Sala de conferință, Instituția Medico-Sanitară Publică
Institutul Oncologic, str. Testemițanu, 30, mun. Chișinău

- 13.00-14.00 Înregistrarea participanților la conferință
- 14.00-14.15 Deschiderea oficială
- 14.15-14.40 **Diagnosticul cancerului laringelui și faringelui.**
Andrei Țibîrnă, dr. șt. med., conf. univ., USMF „Nicolae Testemițanu”
- 14.40-15.05 **Tumorile cerebrale cu extindere extacerebrală în ureche – Prezentare de caz.**
Alexandru Didencu, medic ORL, Clinica „Emilian Coțaga”,
Institutul Mamei și Copilului.
- 15.05-15.30 **Limfoamele agresive ale inelului limfatic nazofaringian.**
Vasile Musteață, dr. șt. med., conf. univ., USMF „Nicolae Testemițanu”
- 15.30-15.55 **Particularitățile tumorilor oro-maxilo-faciale la copii.**
Silvia Răileanu dr. hab. șt. Med., conf.univ. USMF „Nicolae Testemițanu.,
- 15.55-16:20 **Endoscopia flexibilă în tratamentul tumorilor laringiene.**
Petru Gurău, d.ș.m., Clinica ORL a SCR Timofei Moșneaga.
- 16:20-16:45 **Rolul Consiliilor Multidisciplinare în aprecierea conduitei terapeutice a cancerului sferei ORL.**
Adrian Clipca, dr. șt. med., IMSP Institutul Oncologic.
- 16:45-17:10 **Principii ale tratamentului citostatic în tumorile sferei ORL.**
Ionela Clipca, dr. șt. med., IMSP Institutul Oncologic.
- 17:10-17:35 **Principii ale tratamentului radiant în tumorile sferei ORL.**
Artiom Mînzătean, medic rezident, IMSP Institutul Oncologic.
- 17:35-18:00 Discuții

CONGRESUL NAȚIONAL DE CHIRURGIE | 21-23 septembrie 2023



AL **XIV**-lea CONGRES AL ASOCIAȚIEI
CHIRURGILOR „NICOLAE ANESTIADI”
DIN REPUBLICA MOLDOVA

AL **IV**-lea CONGRES AL SOCIETĂȚII
DE ENDOSCOPIE, CHIRURGIE
MINIMINVAZIVĂ ȘI ULTRASONOGRAFIE
„V. M. GUȚU” DIN REPUBLICA MOLDOVA

PROGRAM

congres.chirurgie.md



Sâmbătă | 23 septembrie | Sala Endoscopie (etajul II)

Bronhoscopie I

Moderatori: Eleferii Pitel, Petru Gurău, Elena Tudor, Mihai Alexe,
Mihai Olteanu

- | | |
|--------------|---|
| 08:30 | Biopsia pulmonara transbronșică |
| 09:00 | Mihai Alexe |
| 09:00 | Abordarea bronhoscopica a leziunilor pulmonare periferice |
| 09:20 | Marioara Șimon (Video) |
| 09:20 | Rolul EBUS-TBNA in stadializarea medistinală a cancerului bronhopulmonar |
| 09:50 | Mihai Olteanu |
| 09:50 | Administrarea aerosolilor pe cale respiratorie |
| 10:00 | Natalia Zincenco |
| 10:00 | Tumorile carcinoide ale căilor respiratorii centrale: abordare endoscopică |
| 10:30 | Petru Gurău |
| 11:00 | Criobiopsia si Crioterapia în pneumologie |
| 11:30 | Marioara Șimon |
| 11:30 | EBUS-TBNA: aspecte practice |
| 12:00 | Mihai Alexe |
| 12:00 | Managementul leziunilor laringiene neoplazice prin laringoscopia flexibilă |
| 12:30 | Petru Gurău |
| 12:30 | Discuții |





SRP

Societatea Română de PNEUMOLOGIE

AL 27-LEA CONGRES NAȚIONAL al SOCIETĂȚII ROMÂNE DE PNEUMOLOGIE



PROGRAM

**Pneumologia:
de la știință la multidisciplinaritate și inovație**

2 - 6 noiembrie 2022
Hotel Internațional, Sinaia

www.congres-srp.ro



4. **Endoscopia flexibilă intervențională în leziunile neoplazice ale laringelui/**
Interventional flexible endoscopy for neoplastic laryngeal lesions
Petru Gurău (Republica Moldova)

5. **Discuții/ Discussion**

13:00-15:00 SALA OBSERVATOR/ OBSERVATOR HALL

Simpozion major/ Major symposium
Departamentul membrilor afiliați al SRP/
Department of affiliated members of RSP

13:00-14:45
Sesiune 4/ Session 4

**WORKSHOP RESUSCITAREA CARDIO-PULMONARĂ/ CARDIOPULMONARY
RESUSCITATION WORKSHOP**

Daniela Voinea (București)
Viorica Nedelcu

14:45-15:00 Întrebări și răspunsuri/ Q&A

15.00-15.30
Concluzii și închidere/ Conclusions and closure

14:30-14:45 SALA MAGNUM/ MAGNUM HALL

Simpozion satelit / Industry symposium
Partener/ Partner
Dr. Phyto Romania

**Mecanisme de apărare locală în infecțiile de tract respirator/ Local defense mechanisms
in respiratory tract infections**
Roxana Maria Nemeș (București)

14:45-15:00 SALA MAGNUM/ MAGNUM HALL

Simpozion satelit / Industry symposium
Partener/ Partner
Linde Gaz

Progrese tehnologice în diagnosticul SASO - unde suntem și încotro ne îndreptăm/
Technological advances in SASO diagnosis - where are we and where are we going?
Florin Mihăițan, Corina Borcea (București)



WCBIP 2020 SHANGHAI

The 21st World Congress of Bronchology and Interventional Pulmonology
& The 8th National Interventional Pulmonology Congress of Chinese Medical Association
第21届世界支气管和介入呼吸病学大会
暨中华医学会第八届呼吸内镜和介入呼吸病学学术研讨会

New Land New Scope

November 19–22, 2020

Virtual Congress

Sponsored by

The World Association for Bronchology and Interventional Pulmonology (WABIP)
Chinese Medical Association (CMA)
Chinese Thoracic Society (CTS)



| | | | | | |
|---|--------------------|--|--------------------|---|----------------------|
| <p>What after recanalisation of benign airway stenosis?</p> | <p>Zsolt Papai</p> | | | <p>Drug eluting stents</p> | <p>Antoni Rosell</p> |
| <p>Interventional flexible bronchoscopy in neoplasms of the larynx</p> | <p>Petru Gurau</p> | | | | |
| | | | | | |
| <p>Joint session
WABIP/EABIP: cost, quality and value assessments in interventional pulmonology
(Spasoje Popevic)</p> | | | <p>12:00-13:30</p> | <p>Bronchoscopic Technologies on Pathogenic Diagnosis of hardly Diagnostic Pathogens (Guangfa Wang)</p> | |

WCBIP 2020 SHANGHAI

The 21st World Congress of Bronchology and Interventional Pulmonology
 & The 8th National Interventional Pulmonology Congress of Chinese Medical Association
 第21届世界支气管和介入呼吸病学大会
 暨中华医学会第八届呼吸内镜和介入呼吸病学学术研讨会

New Land New Scope
 November 19–22, 2020
Virtual Congress



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[Speaker](#)

Search : Search by Presenter Title [Search](#)

Group : [All](#) The 21st World Congress of Bronchology and Interventional Pulmonology The 8th National International Pulmonology Congress of Chinese Medical Association

Date : [All](#) 2020-11-19[Thur] 2020-11-20[Fri] 2020-11-21[Sat] 2020-11-22[Sun]

Hall : [All](#) Main Venue Room No. 1 Room No. 2 Room No. 3 Room No. 4 Room No. 5 Room No. 6 Room No. 7 Room No. 8 Room No. 9 Workshop

The academic tasks are as follows

| Date | Time | Hall | Session | Name | Role | Theme |
|------------|-------------|------------|--|-------------|-----------|---|
| 2020-11-21 | 11:20-11:45 | Room No. 8 | Challenges in Solving Major Airway Obstruction- Eastern and Central European Experience
Interventional Flexible Bronchoscopy in Neoplasms of the Larynx | Petru Gurau | Symposium | Interventional Flexible Bronchoscopy in Neoplasms of the Larynx |

10:30-12:00 | Challenges in Solving Major Airway Obstruction- Eastern and Central European Experience [▶ Playback](#)

Session Chair : **Marioara Simon** Pulmonology Clinic, Romania | **Zsolt Papai** St. George University Teaching Hospital of Fejér County

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| NO. | Time | Subject | Speaker | Organization |
|-----|-------------|--|----------------|--|
| 1 | 10:30-10:55 | Hot and Cold Combination(s) in Treatment of Central Airway Obstruction | Marioara Simon | Pulmonology Clinic, Romania |
| 2 | 10:55-11:20 | What after Recanalisation of Benign Airway Stenosis? | Zsolt Papai | St. George University Teaching Hospital of Fejér County, Hungary |
| 3 | 11:20-11:45 | Interventional Flexible Bronchoscopy in Neoplasms of the Larynx | Petru Gurau | "Timofei Mosneaga" Republican Clinical Hospital, Moldova |
| 4 | 11:45-12:00 | Discussion | | |

CANAL / CHANNEL 2

Duminica / Sunday // 08.11.2020

2. Rezistența la antibiotice în infecțiile respiratorii - ecuație cu mai multe necunoscute / **Antibiotic resistance in respiratory infections - equation with several unknowns**
Victor Botnaru, Republica Moldova
3. Tratamentul antibacterian al pneumoniilor comunitare în perioada pandemiei COVID-19: provocări și dificultăți / **Antibacterial treatment of community acquired pneumonia during the COVID-19 pandemic: challenges and difficulties**
Doina Rusu, Republica Moldova
4. Rezecție fibroendoscopică combinată diatermo-laser în neoformațiunile benigne ale laringelui, traheii și bronhiilor / **Combined diathermo-laser fibroendoscopic resection in benign tumors of the larynx, trachea and bronchi**
Petru Gurău, Republica Moldova

12:30-14:00

SIMPOZION COMUN / JOINT SYMPOSIUM

1. Societatea Română de Pneumologie – Societatea Română de Cardiologie / **Romanian Society of Pneumology - Romanian Society of Cardiology**
Moderatori / **Chairs:** Ioan Mircea Coman, Miron Bogdan
2. Modificări pulmonare în insuficiența ventriculară stângă / **Pulmonary changes in left ventricular failure**
Miron Bogdan, București
3. ARDS în COVID-19: diavolul e în detalii...microvasculare / **ARDS in COVID-19: the devil is in the details ... microvascular**
Radu Crișan-Dabija, Iași
4. TEP în COVID-19 - anticoagularea deschide calea / **PET in COVID-19 - anticoagulation paves the way**
Antoni Petriș, Iași
5. Disfuncția de ventricol drept secundară patologiei toracice și pulmonare: evaluare și terapie / **Ventricular dysfunction as a secondary to thoracic and pulmonary pathology: evaluation and therapy**
Ioan Mircea Coman, București

14:00-14:50

PAUZĂ / BREAK

Міністерство охорони здоров'я України
Національна Академія медичних наук України
Департамент охорони здоров'я та соціального захисту населення
Одеської обласної державної адміністрації
Одеський національний медичний університет

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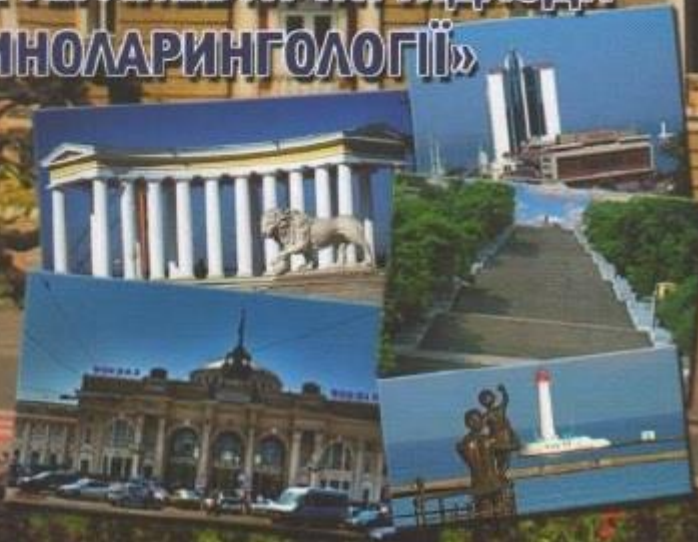
проф. О.С. Коломійченка НАМН України»
«товариство лікарів-оториноларингологів»

ПРОГРАМА

ЩОРІЧНОЇ ТРАДИЦІЙНОЇ ВЕСНЯНОЇ КОНФЕРЕНЦІЇ
УКРАЇНСЬКОГО НАУКОВОГО МЕДИЧНОГО
ТОВАРИСТВА ЛІКАРІВ-ОТОРИНОЛАРИНГОЛОГІВ
З МІЖНАРОДНОЮ УЧАСТЮ

«СУЧАСНІ ДОСЛІДЖЕННЯ,
ХІРУРГІЧНІ ТА ТЕРАПЕВТИЧНІ ПІДХОДИ
В ОТОРИНОЛАРИНГОЛОГІЇ»

20-21 травня 2019 р.
м. Одеса, Україна



11²⁰-13⁰⁰

ТРЕТЄ ПЛЕНАРНЕ ЗАСІДАННЯ ЛОП-ОНКОЛОГІЯ

Співголови:

*Е.В. Лукач, Р.А. Абизов, Ф.Д. Євчев, О.В. Ковтуненко,
В.І. Попович, Ф.О. Тишко, В.І. Троян*

1. Генна інженерія в лікуванні раку – 10 хв.
Діхтярук В.Я. (Київ, Україна)
- ✓ 2. Мікроларингоскопічні операції в ЛОР-онкології
Цьолко Т.Р. (Львів, Україна)
3. Альтернативная антибиотикотерапия при остром бактериальном синусите – респираторные фторхинолоны? Почему?
Деева Ю.В. (Киев, Украина)
- ✓ 4. Гибкая эндоскопия в диагностике и лечении веррукозной карциномы гортани
Гурзу П.П. (Кишинэу, Республика Молдова)
- ✓ 5. Диагностика и тактика лечения больных распространенным раком гортани
Євчев Ф.Д., Гаєвський В.В. Євчева А.Ф. (Одесса, Украина)
6. Пробки в миндалинах, это норма или патология?
Пухлик С.М. (Одесса, Украина)
7. Наш опыт лечения эстезионейробластомы
Заболотный Д.И., Лукач Э.В., Дихтярук В.Я., Исмагилов Э.Р. (Київ, Україна)
8. Променеві ушкодження гортані – основний чинник ускладнень при наступному хірургічному лікуванні онкоотоларингологічних хворих
Абизов Р.А., Лакіза С.О., Самойленко С.С. (Київ, Україна)

14⁰⁰-16⁰⁰

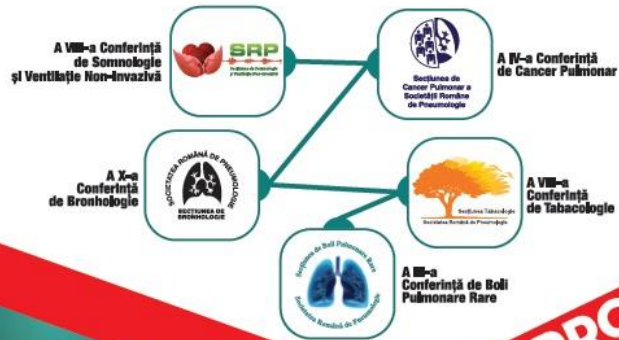
ЧЕТВЕРТЕ ПЛЕНАРНЕ ЗАСІДАННЯ ЗАХВОРЮВАННЯ ВЕРХНІХ ДИХАЛЬНИХ ШЛЯХІВ

Співголови:

**О.Ф. Мельников, В.В. Кіщук, А.Л. Косаковський,
О.О. Мінаєв, О.Г. Плаксивий, А.В. Цимар**

- ✓ 1. Реконструктивно-відновлювальна хірургія глотки, гортані, шийного відділу стравоходу в практиці усунення комбінованих післятравматичних рубцевих стенозів, атрезій та інших набутих і вроджених дефектів
**Тишко Ф.О., Островська О.О., Щукіна Н.Л.,
Затушевський О.В., Стась П.В. (Київ, Україна)**
2. Наш досвід хірургічного лікування СОАС
**Науменко О.М., Денисенко Р.Ю., Діхтярук О.В.,
Деєва Ю.В. (Київ, Україна)**
3. Комплексна терапія алергічного риніту
Пухлік С.М. (Одеса, Україна)
4. Гистологические аспекты синдрома обструктивного апноэ сна
**Енаки В., Сандул А., Антохи А.
(Кишинэу, Республика Молдова)**
5. Реіннервація як метод хірургічного лікування ятрогенного паралічу гортані
**Соломеннікова Н.В., Паламарчук В.О., Деєва Ю.В.
(Київ, Україна)**
- ✓ 6. Хирургия неспецифической гранулемы гортани с помощью гибкого эндоскопа
Гурэу П.П. (Кишинэу, Республика Молдова)
7. Роль місцевої терапії в лікуванні запальних захворювань носа та приноскових пазух
Деєва Ю.В. (Київ, Україна)

CONFERINȚELE NAȚIONALE ALE SECȚIUNILOR Societății Române de Pneumologie



13-15 Noiembrie 2019
Hotel Crowne Plaza,
București

PROGRAM



| JOI, 14
NOIEMBRIE
/
THURSDAY,
14th of
NOVEMBER | SALA CROWN A+B / CROWN
A+B HALL | SALA CROWN C+D /
CROWN C+D HALL |
|---|---|---|
| | <p>1. Factori predictivi ai sindromului obstructiv de apnee în somn: studiu epidemiologic în județul Constanța / Predictive factors of obstructive sleep apnea: epidemiological study in Constanta county
<i>Adelina Anton, Angela Gheorghe, Doina Tofolean</i> (Constanța - Romania)</p> <p>2. Îngrijirea paleativă și ventilația non-invazivă la un pacient vârstnic cu TEP și fibroză pulmonară / Palliative care and non-invasive ventilation in an elderly patient with pulmonary thromboembolism and pulmonary fibrosis
<i>Bianca Domokos</i> (Cluj-Napoca - Romania)</p> <p>3. Apneea în somn și acromegalia - o asociere neglijată / Sleep apnea and acromegaly - a neglected association
<i>Mara Vultur, Alpár Csipor-Fodor, Gabriela Jimborean</i> (Târgu Mureș - Romania)</p> <p>4. Sindromul de apnee în somn și insuficiența cardiacă: lecții din studiile recente / Sleep apnea syndrome and heart failure: lessons from recent studies</p> | <p>1. PET-CT – EBUS/EUS – VAMLA, what should be carried out?
<i>Franz Stanzel</i> (Hemer – Germania / Hemer - Germany)</p> <p>2. Obstrucția de căi aeriene centrale de cauză infecțioasă / Central airway obstruction caused by infections
<i>Petronela Fildan</i> (Constanța - Romania)</p> <p>3. Rezecție fibroendoscopică combinată Diatermo-LASER în tumorile laringo-traheo-bronșice maligne / Diatermo-LASER combined fibroendoscopic resection in malignant laryngeal-tracheo-bronchial tumors
<i>Petru Gurău</i> (Chișinău – Republica Moldova / Chisinau – Republic of Moldova)</p> <p>4. Discuții / Discussions</p> |

15.30 - 17.00

Simpozion Major – PNEUMOPATII INTERSTITIALE DIFUZE – BPOC

Moderatori: Voicu Tudorache, Milena Man

1. Noile ghiduri pentru diagnosticul Fibrozei Pulmonare Idiopatice / The new guidelines for the diagnosis of Idiopathic Pulmonary Fibrosis - *Demosthenes Bouras*
2. Managementul pacientului BPOC "dificil" / Managing the 'difficult' COPD patient - *Peter Calverley*
3. Pneumonia Interstițială cu Trăsături Autoimune – IPAF / Interstitial Pneumonia with Autoimmune Features – IPAF - *Dragana Jovanovic*
4. Impactul sindromului overlap pe cogniție. Focus pe BPOC-PID
Emanuela Tudorache, Daniel Trăilă, Cristian Oancea
5. Discuții

17.00 - 17.15

Pauză de cafea

17.15 - 19.15

Simpozion Major – BRONHOLOGIE I

Moderatori: Mărioara Șimon, Dorin Vancea

- ✓ 1. Asocierea modalităților de tratament diferite în Pneumologia Intervențională - puțin mai bine decât mai mult? / Combining different treatment modalities in IP - less better than more? - *Spasoje Popevic*
- ✓ 2. Când „mai puțin” înseamnă „mai mult” în tratamentul endoscopic al stenozelor traheale - *Mărioara Șimon, Antonia Haranguș*
- ✓ 3. Progrese în bronhologia intervențională: Ce este nou în EBUS? - *Dorin Vancea*
4. Valoarea Bronhoscopiei în Autofluorescență în diagnosticul cancerului bronho-pulmonar - *Amellu Arama, Ciprian Lovin, Gabriel Iosep*
- ✓ 5. Tuberculoza endobronșică – o continuă provocare diagnostică și terapeutică - *Mihai Olteanu, Mimi Nișu, Ileana Bazavan, Ramona Teodorescu, Cristina Călărașu*
6. Endoscopia flexibilă intervențională în patologia neoplazică a laringelui - *Petru Gurău*
7. Capcane de diagnostic sau evoluție imprevizibilă - cazuri clinice - *Camelia Bădescu*

20.00

CINĂ



**AL XXV-lea CONGRES NAȚIONAL
AL SOCIETĂȚII ROMÂNE DE PNEUMOLOGIE**
31 octombrie – 3 noiembrie 2018 Hotel Piatra Mare – Poiana Brașov



Turkish
Respiratory
Society



4th European Congress for Bronchology & Interventional Pulmonology

With the cooperation of Turkish Respiratory Society (TRS) & Respiratory Society of Serbia (RSS)

April 27-30, 2017 - Crowne Plaza Belgrade - Serbia

ECBIP 2017

PROGRAM BOOK

Endorsed by



CHEST[®]
AMERICAN COLLEGE
of CHEST PHYSICIANS

OP-10

• **Brachytherapy as Treatment Option for Lung Atelectasis in Endobronchial Carcinoma**

*Nensi Jovan Lalic, Evica Budisin, Goran Stojanovic, Aleksandar Tepavac, Bojan Zaric
Institution for pulmonary diseases of Vojvodina, Faculty of Medicine, University of
Novi Sad, The Clinic for Pulmonary Oncology, Bronchoscopy Unit*



OP-17

Fibroendoscopic approach in verrucous carcinoma of the larynx

Petru Gurau¹, Vitalie Tirbu²

¹Department of thoracic surgery, Republican Clinical Hospital, Chisinau, Moldova

²Department of pathology, Institute of Oncology, Chisinau, Moldova

16:45-18:15 WABIP REGENTS MEETING

HALL A

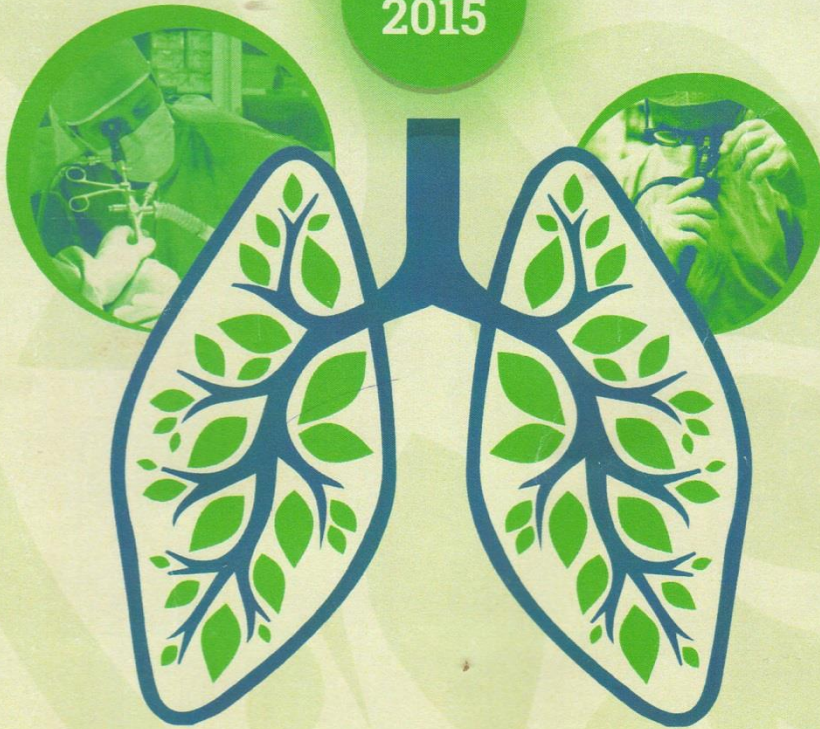
SOCIETATEA ROMÂNĂ DE PNEUMOLOGIE, SECȚIUNEA BRONHOLOGIE

A VIII-A CONFERINȚĂ NAȚIONALĂ DE BRONHOLOGIE

BRONHOLOGIA ROMÂNEASCĂ: SENIORI ȘI JUNIORI ÎMPREUNĂ

Aula UMF "Iuliu Hațieganu" | Cluj-Napoca

20-21
NOIEMBRIE
2015



A VIII-A CONFERINȚĂ NAȚIONALĂ DE BRONHOLOGIE
BRONHOLOGIA ROMÂNEASCĂ: SENIORI ȘI JUNIORI ÎMPREUNĂ

| | |
|---|---|
| 12:20- 13:00 | SIMPOZION ASTRA ZENECA
Mărioara Șimon, Ruxandra Ulmeanu |
| 13:00 - 14:00 | Pauză de prânz |
| BRONHOSCOPIE INTERVENȚIONALĂ DIAGNOSTICĂ ȘI TERAPEUTICĂ
Moderatori: Florin Mihălțan, Tudor Toma, Mărioara Șimon | |
| 14:00 - 14:15 | Criobiopsia și criorecanalizarea-repere practice
Andrada Florian, Mărioara Șimon |
| 14:15 - 14:30 | Posibilitățile laser-chirurgiei fibroendoscopice în tumorile laringo-traheo bronșice
Petru Gurău |
| 14:30 - 14:45 | Challenges in management of N2 NSCLC
Dragana Jovanovic |
| 14:45 - 15:00 | Endosonography for pulmonologists today and tomorrow
Artur Szlubowski |
| 15:00 - 15:15 | Chest ultrasonography: a pluripotent image modality we should all do
Tudor Toma |
| 15:15 - 15:30 | Repere practice în bronhoscopia intervențională
Amuliu Aramă, Iosep Gabriel |
| 15:30 - 15:45 | Provocări în pneumologia intervențională
Mărioara Șimon, Petruț Vremăroiu, Lăcrămioara Toma, Bogdan Pop, Laura Iacoban, Erika Hajdu |
| 15:45 - 16:00 | SIMPOZION BOEHRINGER - INGELHEIM
Dorin Vancea, Mărioara Șimon |
| 16:00 - 16:15 | Pauză de cafea |
| TEHNICI BRONHOSCOPICE DE VIITOR
Moderatori : Ariadna Petronela Fildan, Mihai Olteanu | |
| 16:15 - 16:30 | FICE Nouă tehnologie endoscopică de viitor
Florina Tăriță, Mărioara Șimon, Aletta Vallasek |
| 16:30 - 16:45 | Reducerea endoscopică de volume pulmonare: CÂND? CUM? DE CE?
Aletta Vallasek, Mărioara Șimon |
| 16:45 - 17:00 | Diagnosticul leziunilor periferice pulmonare: tehnici prezente și de viitor
Petruț Vremăroiu, Mărioara Șimon |
| 17:10 - 17:30 | SIMPOZION NOVARTIS - Florin Mihălțan |
| 17:30 - 17:45 | Practică și Training pentru bronhoscopie în România
Mărioara Șimon |
| 17:45 - 18:00 | Adunarea Generală a Secțiunii de Bronhologie |



BULETIN

Buletin informativ al Societății Științifico-Practice a Oncologilor
din Republica Moldova. Apare din 2011. Societatea a fost fondată în 1956.

Nr. 1 (3)

CONGRESUL IV NAȚIONAL DE ONCOLOGIE, 2015

PROGRAM & REZUMATE





17.35 – 17.45

Particularități în tratamentul chirurgical în cancerul glandei tiroide la bărbați.

Rodica Tamaruțcaia, Gheorghe Țibîrnă, Andrei Țibîrnă, Adrian Clipca, Valentina Darii, IMSP Institutul Oncologic, Republica Moldova

09.10.2015

Subsesiunea II

Moderatori:

Gheorghe ȚIBÎRNĂ, Academician AȘM

Ion MEREUȚĂ, profesor universitar

Valentina DARII, doctor în medicină

Nicolae CAPROȘ, profesor universitar

Adrian CLIPCA, doctor în medicină

09.00 – 09.10

Aspecte clinico-morfologice ale carcinomului laringian verucos.

Vitalie Tîrbu, IMSP Institutul Oncologic, Republica Moldova

09.10 – 09.20

Carcinom verucos al laringelui: abordare fibroendoscopică.

Petru Gurău, IMSP SCR

09.20 – 09.30

Ținte moleculare în diagnosticul tumorilor cervico – cefalice.

Mihai Stoicea, SYNEVO

09.30 – 09.40

Tratamentul chirurgical al tumorilor oaselor bazinului.

Ion Dăscăliuc, IMSP Institutul Oncologic, Republica Moldova

09.40 – 09.50

Tehnologii moderne în diagnosticul și tratamentul tumorilor ALM.

Ion Mereuță, Ion Dăscăliuc, Dumitru Butuceș, Sergiu Mura, Diana Eftodii, Nicolae Dolganiuc, IMSP Institutul Oncologic, Republica Moldova

09.50 – 10.10

Actualități în asistența medicală a tumorilor la copii.

Ion Mereuță, Ion Voșian, Laurențiu Bărlădean, IMSP Institutul Oncologic, Republica Moldova

10.10 – 10.20

Tratamentul chirurgical al defectelor osoase provocate de tumori benigne și afecțiuni pseudotumorale.

Nicolae Dolganiuc, Ion Mereuță, IMSP Institutul Oncologic, Republica Moldova

10.20 – 10.30

Aprecierea calității vieții pacienților cu fracturi patologice vertebrale pe focar metastatic tratați prin tehnica combinată minim invazivă (Coblation + vertebroplastie).

Nicolae Caproș, Ion Mereuță, Andrei Olaru, Tatiana Rusu, USMF "N. Testemițanu", IMSP Institutul Oncologic, IMSP INN, Republica Moldova

10.30 – 11.30

Discuții în cadrul sesiunii.



Al IX^{lea} Congres al Asociației
Chirurgilor "N. Anestiadi"
I Congres de Endoscopie
din Republica Moldova



Sub înaltul patronaj al Președintelui Republicii Moldova
Vladimir Voronin



Chișinău, 17-19 septembrie 2003

Program



19.09.2003 (11.³⁰ - 13.³⁰)
Sala C, Sesiunea 5

Tema: Endoscopia Sistemului Bilio - Pancreatic. Endoscopia Diagnostică și Curativă a Sistemului Bronho - Pulmonar.

Moderatori:

Conf. Dr. V. Gutu (Chișinău, Moldova)
Dr.ș.m., Iu. Simionică (Chișinău, Moldova)
Prof. Dr. O. Pascu (Cluj-Napoca, România)

- 1 11.³⁰-11.⁴⁰ POSIBILITĂȚILE ENDOSCOPICE DE REZOLVARE A LITIAZEI BILIARE
V.Hotineanu, R.Bodrug, A.Vitiuc, A.Cotonet, A.Ferdohleb (Chișinău, Moldova)
- 2 11.⁴⁰-11.⁵⁰ DIVERTICULUL JUXTAPAPILAR DUODENAL ÎN PATOLOGIA ZONEI BILIOPANCREATICE
A.Cotonet, V.Guțu (Chișinău, Moldova)
- 3 11.⁵⁰-12.⁰⁰ PANCREATOCOLANGIOGRAFIA RETROGRADĂ ȘI PAPILOSFINCTEROTOMIA ENDOSCOPICĂ: VALOAREA DIAGNOSTICĂ ȘI CURATIVĂ
Larisa Datco, R.Gaidău (Chișinău, Moldova)
- 4 12.⁰⁰-12.¹⁰ РЕЗУЛЬТАТЫ ХИРУРГИЧЕСКОГО И ЭНДОСКОПИЧЕСКОГО ДРЕНИРОВАНИЯ ЖЕЛЧНЫХ ПРОТОКОВ ПРИ ИХ ЗЛОКАЧЕСТВЕННОЙ ОБСТРУКЦИИ
В.И.Малярчук А.Г.Фёдоров, С.В.Давыдова (Москва, Россия)
- 5 12.¹⁰-12.²⁰ CONSECINȚELE RETROSPECTIVE ÎNDEPĂRTATE A PAPILOSFINCTEROTOMIEI LA PACIENȚII CU COLEDOCOLITIAZĂ
E.Pitel, V.Guțu (Chișinău, Moldova)
- 6 12.²⁰-12.³⁰ DUCTUL CISTIC: ANATOMIE NORMALĂ ȘI PROCESE PATOLOGICE
V.Istrate, N.Curmel (Chișinău, Moldova)
- 7 12.³⁰-12.⁴⁰ CONTRIBUȚII IMPORTANTE ALE PCGR ÎN DIAGNOSTICUL ICTERULUI LITIAZIC
Liuba Streltov, I.Băbălău, N.Ciobanu, D.Racu, D.Saghin (Chișinău, Moldova)
- 8 12.⁴⁰-12.⁵⁰ MANAGEMENTUL FIBROENDOSCOPIC AL NEOFORMAȚIUNILOR VASCULARE ALE LARINGELUI ȘI FOTODISTRUCȚIA FIBROENDOSCOPICĂ ÎN TRATAMENTUL DISKERATOZELEI LARINGIENE
P.Gurău (Chișinău, Moldova)
- 9 12.⁵⁰-13.⁰⁰ FIBROBRONHOSCOPIA DE TRATAMENT ȘI EFICIENȚA EI ÎN CAZUL LEZĂRII DISTALE A BRONHIILOR ÎN TUBERCULOZA PULMONARĂ
Iu.Simionică (Chișinău, Moldova)
- 10 13.⁰⁰-13.¹⁰ TAMPONADA TEMPORARĂ A BRONHIILOR ÎN PRACTICA FTIZIOPULMONOLOGICĂ
P.Levcenco, V.Djugostran, Gh.Groza, Elena Tudor (Chișinău, Moldova)
- 11 13.¹⁰-13.²⁰ CORPII STRĂINI AI ARBORELUI BRONHIAL ÎN PRACTICA PEDIATRICĂ
Ina Garbi, Valentina Rașcov (Chișinău, Moldova)
- 12 13.²⁰-13.³⁰ DEPISTAREA TUBERCULOZEI TRAHEOBRONȘICE ÎN CHIȘINĂU ÎN PERIOADA 1993-2002
A.Palade, A.Zbanț, Carmina Palade, Maria Reniță (Chișinău, Moldova)

Repaus – Lunch (13.³⁰-15.⁰⁰)

**Российское научное общество
"Эндоскопическая хирургия"**

**Проблемная комиссия РАМН
"Эндоскопическая хирургия"**



**Российский
научный центр
хирургии
РАМН**

**3-й МОСКОВСКИЙ МЕЖДУНАРОДНЫЙ
КОНГРЕСС ПО
ЭНДОСКОПИЧЕСКОЙ ХИРУРГИИ**

21-23 апреля 1999 г., г. Москва

ПРОГРАММА КОНГРЕССА

Среда, 21 апреля 1999 г.

ОТКРЫТИЕ КОНГРЕССА – 10.00

Академик РАМН **Б. А. Константинов**

Профессор **Ю. И. Галлингер**

10.30-13.00

**ЭНДОХИРУРГИЯ ПРИ ЗАБОЛЕВАНИЯХ
ОРГАНОВ ДЫХАНИЯ**

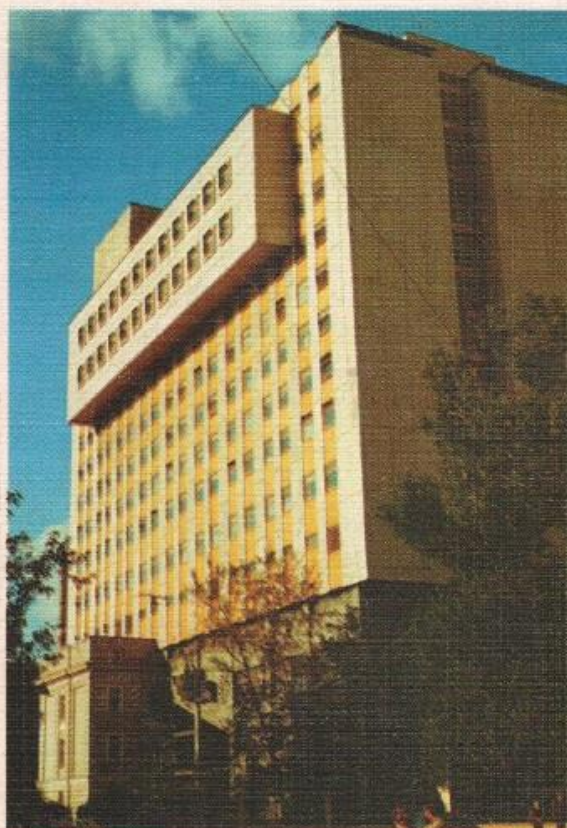
Председатели: акад. РАМН **М. И. Перельман**
проф. **А. А. Овчинников**
проф. **Б. К. Поддубный**

1. **П. П. Гурэу** (г. Кишинев, Молдова)
Фиброэндоскопическая лазерная хирургия рака
среднего отдела гортани (10 минут)
2. **А. А. Овчинников, А. А. Федоров** (г. Москва)
Опыт применения различных типов лазеров и
эндопротезов в лечении стенозирующих процессов
трахеи и крупных бронхов (15 минут)
3. **М. А. Русаков** (г. Москва)
Оперативная бронхоскопия при опухолях и рубцовых
стенозах трахеи и бронхов (15 минут)
4. **К. К. Козлов, В. К. Косенок, И. А. Кузнецов,
В. Г. Шаляпин, С. Г. Ильин, М. С. Коржук** (г. Омск)
Эндоскопия в хирургии стенозов трахеи (10 минут)

РОССИЙСКАЯ АКАДЕМИЯ МЕДИЦИНСКИХ НАУК

**Проблемная комиссия РАМН
"Эндоскопическая хирургия"**

**Российское научное общество
"Эндоскопическая хирургия"**



**Российский
научный центр
хирургии
РАМН**

РОССИЙСКИЙ СИМПОЗИУМ

**"ВНУТРИПРОСВЕТНАЯ
ЭНДОСКОПИЧЕСКАЯ ХИРУРГИЯ"**

22-23 апреля 1998 г., г. Москва

ПРОГРАММА СИМПОЗИУМА

Среда, 22 апреля 1998 г.

11.45-13.00

№5

ЛЕЧЕБНАЯ ТРАХЕОБРОНХОСКОПИЯ

Председатели:

проф. **Ф. А. Астраханцев**, проф. **Ю. В. Бирюков**,
проф. **А. А. Овчинников**

1. **А. А. Овчинников** (г. Москва) *Фотодиагностическая техника + сегменты.*
Основные тенденции и проблемы современной бронхоскопии (20 минут)
2. **М. А. Русаков** (г. Москва) *132 Б.*
Эндоскопическое лечение больных с опухолями трахеи и бронхов (15 минут)
3. **В. В. Грубник, П. П. Шипулин, Ю. Г. Ткач, И. Н. Дмытрив, С. В. Агеев, В. А. Мартынюк** (г. Одесса, Украина) *424 Б.*
Эндоскопическая лазерная хирургия трахеи и бронхов (10 минут) *эндобронхоскопия.*
4. **Б. Б. Шафировский, И. В. Двораковская** (г. Санкт-Петербург)
Возможности бронхоскопической хирургии в радикальном лечении типичных карциноидов трахеи и крупных бронхов (10 минут)
5. **Е. Г. Григорьев, Р. Г. Трухан, С. В. Журавлев, В. Г. Неустроев, В. И. Капорский, М. В. Владимирова** (г. Иркутск)
Методика обтурации долевого и сегментарного свищеобразующих бронхов с помощью фиброскопа - эффективный, качественный и щадящий метод эндоскопического лечения бронхиальных свищей (10 минут)
6. **П. П. Гурзу** (г. Кишинев, Молдова)
Фиброэндоскопическая хирургия доброкачественных и предраковых поражений гортани (10 минут)

Перерыв 13.00-14.00

ANNEX 6

AWARDS RECOGNIZING RESEARCH ACHIEVEMENTS RELATED TO THE TOPIC OF THE SYNTHESIS PAPER (DIPLOMAS AND MEDALS)

AGEPI AGENȚIA DE STAT
PENTRU PROPRIETATEA
INTELECTUALĂ
A REPUBLICII MOLDOVA

Expoziția Internațională Specializată

„INFOINVENT”

Ediția a XVII-a

DIPLOMĂ

MEDALIA DE AUR

se acordă

Petru Gurău, Eusebiu Sencu, Sergiu Vetrician

pentru

Ciclul de invenții „Metode de tratament ale tumorilor de laringe”



Eugeniu RUSU,
Președintele
Comitetului organizatoric



Svetlana COJOCARU,
Președintele Juriului

17-20 noiembrie 2021,
Chișinău, Republica Moldova



Diploma of Honor

GOLD MEDAL

Offered to

GURĂU PETRU, SENCU EUSEBIU, VETRICEAN SERGIU

„Nicolae Testemitanu” State University of Medicine and Pharmacy of the Republic of Moldova

METHOD FOR ENDOSCOPIC TREATMENT OF LARYNGEAL TUMORS

in recognition of high scientific contribution and loyalty to the XXVI-th INTERNATIONAL EXHIBITION OF INVENTICS

INVENTICA 2022

Iasi, Romania

22-24 June 2022

GENERAL MANAGER
NATIONAL INSTITUTE OF INVENTICS
Prof. Neculai-Eugen SEGHEDEAN PhD



Expoziția Internațională Specializată

„INFOINVENT”

Ediția a XIX-a

DIPLOMĂ

MEDALIA DE AUR

se acordă

GURĂU Petru, SENCU Eusebiu, VETRICEAN Sergiu

pentru

Ciclul de invenții: METODĂ DE TRATAMENT MINIINVAZIV AL EDEMULUI REINKE
și METODĂ DE ABORDARE ENDOSCOPICĂ NETRADIȚIONALĂ A SCHWANOMULUI
LARINGIAN OBSTRUCTIV

Eugeniu RUSU,
Președintele
Comitetului organizatoric

Ion TIGHINEANU,
Președintele Juriului

3-5 decembrie 2025,
Chișinău, Republica Moldova

INFORMATION ON THE VARORIZATION OF RESEARCH RESULTS

LIST OF PUBLICATIONS AND PARTICIPATION IN SCIENTIFIC FORUMS

by Mr. **Petru Gurău**, compiled for the synthesis paper submitted to obtain the degree of Doctor Habilitatus in Medical Sciences, on the topic “Surgical Treatment of Neoplastic Laryngeal Lesions via Flexible Endoscopic Approach”

SCIENTIFIC WORKS

- **Monographs:**

1. **Gurău P.** Endoscopia flexibilă în diagnosticul și tratamentul leziunilor neoplazice ale laringelui. Chișinău: Tipografia „Bons Offices SRL”; 2025. 143 p. ISBN 978-5-36241-484-9. <https://library.usmf.md/ro/gurau-p-endoscopia-flexibila-diagnosticul-si-tratamentul-leziunilor-neoplazice-ale-laringelui>

- **Articles in international scientific journals:**

- ✓ **articles in ISI, SCOPUS journals, and other international databases recognized by ANACEC**

2. **Gurău PP.** [Recurrent cancer of the middle part of the larynx after radiotherapy: a fibroendoscopic approach]. Vestn Otorinolaringol. 2005;(6):61-62. Russian. PMID: 16408380. (SCOPUS, PubMed)
3. **Gurau P, Sencu E, Balica I.** Lipoma of the larynx: fibroendoscopic approach (case report). Revue de Laryngologie Otologie Rhinologie. 2016; 137(5): 135-136. ISSN 0035-1334 (SCOPUS)
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• **Poster presentations at scientific forums:**

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STATEMENT OF RESPONSIBILITY

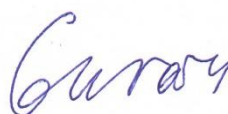
I, the undersigned, Petru Gurău, hereby declare on my own responsibility that the synthesis paper submitted to obtain the degree of Doctor Habilitatus in Medical Sciences, on the topic “Surgical Treatment of Neoplastic Laryngeal Lesions via Flexible Endoscopic Approach” was written by me personally and has not been previously submitted to any institution of higher education in Republic of Moldova or abroad, and the materials presented are the results of my own research and have not been plagiarized from other scientific works.

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Date: 07.04.2026

Postdoctoral researcher: Petru Gurău



Scientific consultant: Dumitru Sofroni



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ANNOTATION

Petru Gurău

SURGICAL TREATMENT OF NEOPLASTIC LARYNGEAL LESIONS VIA FLEXIBLE ENDOSCOPIC APPROACH

The synthesis paper for obtaining the title of Doctor Habilitatus in Medical Sciences
Chişinău, 2026

Topicality of the study. The efficient use of flexible endoscopic laryngeal surgery (FELS) in treating laryngeal neoplasms allows for increased comfort for patients and a considerable economic effect, given the possibility to apply the method on an outpatient basis. FELS can overpass the limits of traditional approaches in treating laryngeal neoplastic lesions, but, so far, the method is positioned at the beginning of its evaluation, the experience being limited, and the consensus and guidelines are missing. Long-term results of treating glottic carcinoma by FELS are not elucidated in the specialty literature.

Purpose of the work. Studying the possibilities of flexible endoscopy in treating benign neoplasms, precancerous lesions, and early malignant tumors of the larynx, the analysis of factors that influence treatment efficacy, and the establishment of the value of the method in improving the management of patients with laryngeal neoplasms.

Research objectives. Studying the efficacy of FELS in treating benign nonepithelial laryngeal lesions (BNELL), hyperplastic laryngeal lesions (HLL), and papilloma/papillomatosis in adults; estimation of results of FELS for early glottic carcinoma (T1-T2), and determining the factors that influence treatment efficacy (tumor stage, anesthesia method, adjuvant radiotherapy, etc.).

Scientific novelty, originality, and theoretical significance. For the first time, based on a large clinical material, a complex study of the possibilities of FELS in treating laryngeal neoplasms has been conducted. The endoscopic techniques applied for the first time in the management of laryngeal neoplasms have been analysed. An original clinical/endoscopic classification of HLL has been proposed. For the first time, the efficacy of FELS for early glottic carcinoma based on long-term results (5 years) has been studied.

Major new results obtained. (1) FELS using non-angiolytic lasers, diathermy snare, and flexible biopsy forceps is an efficient method for treating benign nonepithelial and precancerous lesions of the larynx, offering a relevant alternative to presently used surgical methods and opening a new direction in office-based laryngeal surgery. (2) The endoscopic classification of HLL, elaborated and proposed by the author, contributes to a clear delimitation between HLL with high malignant potential and HLL with low malignant potential, which influences the diagnostic and therapeutic strategy. (3) FELS for early glottic carcinoma demonstrates oncological results that are comparable with those obtained by traditional treatment methods, from the oncologic perspective can be considered as an efficient treatment method for T1-T2 glottic carcinoma, and as an alternative to the traditional approaches, both, for the primary and recurrent carcinoma, and can be recommended for the management of early glottic carcinoma in an outpatient basis, especially, for T1a lesions.

Implementation of scientific results: The research results have been implemented in the daily practice of the „Avangard-Med” clinic, Chişinău, Republic of Moldova.

The synthesis paper structure: Introduction, five chapters, general conclusions and recommendations, bibliography of 212 references, six appendices, 77 pages of basic text, 131 figures, 29 tables, and 55 publications on the thesis topic.

Keywords: flexible endoscopy; endoscopic surgery; Nd:YAG laser; diode laser; benign laryngeal lesions; precancerous laryngeal lesions; hyperplastic laryngeal lesions; laryngeal papillomatosis; glottic carcinoma; office-based laryngeal surgery.