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DIAGNOSTIC AND TREATMENT APPROACH IN NON-TRAUMATIC ACUTE LIMB ISCHEMIA

321.13 SURGERY

Summary of PhD thesis in medical sciences

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The thesis was developed within the Department of General surgery-semiology nr.3 at „Nicolae Testemițanu" State University of Medicine and Pharmacy

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CONTENT

CONCEPTUAL PROBLEMS IN THE RESEARCH

Actuality and importance of the studied topic. Acute limb ischemia (ALI), defined as an abrupt cessation or a critical decrease in peripheral vascular perfusion that threatens its viability and requires immediate diagnostic and treatment measures, represents one of the most frequent acute pathologies in vascular surgery [1, 2]. The etiology of ALI varies and determines the differences in clinical aspects as well as in patient management. In most cases the acute non-traumatic ischemia is caused by embolic or thrombotic occlusion of the arterial lumen and can affect both native arteries and arteries with previous vascular interventions [3, 4]. There is a noticeable discrepancy in the reporting between embolism and thrombosis in different publications which can be explained by challenges in determining the precise etiology of ALI and the demographic peculiarities of the studied patient cohorts. Thrombotic occlusions are more common in groups with high life expectancy where adequate vascular interventions and atrial fibrillation treatments are carried out while embolic-related ALI is identified in populations with low life expectancy [2, 5, 6].

According to cumulative data from specialized literature the incidence of ALI affecting the lower extremities is estimated to be between 10 and 15 cases per 100,000 residents annually and remains unchanged in the last decade. ALI that affects superior extremities is diagnosed approximately 3-5 times less [7, 8, 9]. It is extremely important to remember that the presence of acute ischemia not only increases the chance of losing an extremity but can also be fatal to a patient even in the context of timely and effective treatment. In terms of significant advancements, especially in vascular surgery, the rate of amputations and ALI mortality remains unacceptably high. Based on current clinical studies, systematic reviews, and meta-analyses, the rate of negative outcomes from immediate revascularization procedures for ALI is approximately 10 to 15% during the first 30 days following surgery and rises to 20–47% within the first year [10, 11, 12, 13, 14, 15]. Given the increased incidence and severity of the disease, the high rate of complications, and urgent need for medical assistance, there are no doubts regarding the actuality of research in ALI diagnosis and treatment.

Despite numerous national and international protocols dedicated to ALI in the last years, many aspects in the management of this extremely severe vascular condition still require attention and specific approaches that are not sufficiently supported by evidence [1, 3, 16]. Scientific data contains numerous controversies and inconsistencies in almost every aspect and stage in caring for individuals who have experienced ALI. More specifically, there have been no objective causes identified for patient hospitalization retention and delay of specialized treatment; there are not enough studies on prescribing anticoagulants and the appropriateness of medicating; as well as the impact of particular factors upon treatment outcomes of the acute arterial occlusion. Accurate preoperative evaluation of ALI patients is essential whilst vascular imaging methods are critical in determining the optimal approach for revascularization procedures. The development of accurate and clear methods for predicting the outcomes of ALI surgical treatments will enable the scientific community to argue whether to prioritize vascular surgical intervention over primary amputation or palliative care. Undoubtedly, one of the challenges facing modern vascular surgery is identifying modifiable risk factors associated with unfavorable outcomes of revascularization intervention in the early and late post-operative period and generating scientifically valid methods to eliminate these factors. Improving techniques for evaluating the effectiveness of treatment that incorporate patients' quality of life in addition to the fact of limb salvage is another essential component. Hence, the advancement of treatment measures featuring an extremely vulnerable category of ALI patients will undoubtedly bring a positive impact in medical, scientific, economical, and social aspects.

The purpose of the study. Determination of the possibilities for improving the diagnosis and treatment of patients with acute limb ischemia, based on the identification of perioperative factors that have a negative impact on the results of urgent revascularization interventions.

The research objectives:

1. Analysis of the contemporary demographic, clinical and paraclinical characteristics of the patient cohort with acute limb ischemia undergoing revascularization procedures.
2. Evaluation of preoperative management and assessment of the value of various techniques for diagnosis of acute limb ischemia.
3. Development of the prognostic methods of prediction of early outcomes of revascularization procedures, based on the criteria available during preoperative period.
4. Analyzing the early and late results after urgent revascularization procedures and determining factors associated with risk of amputation and/or patient death.
5. Determining the particularities of clinical evolution and surgical treatment results in acute upper limb ischemia and acute ischemia associated with SARS-CoV-2 infection.

The methodology of scientific research. The current study had an observational character and included patients with acute non-traumatic ischemia of extremities who underwent urgent revascularization procedures. In addition to validating current criteria and determining the diagnostic effectiveness of various clinic and paraclinical approaches in patients with acute ischemia, this study also elaborated new methods for predicting the risk of amputation or patient's death following surgical intervention. There were identified modifiable and non-modifiable risk factors associated with treatment failure. The primary criteria used to evaluate the efficacy of ALI treatments was the ratio of deceased patients and/or patients who underwent major amputations of the affected limb during the span of 30 days. The secondary criteria used to evaluate treatment results were: the need for an unplanned reintervention, the effectiveness of revascularization based on the anatomic permeability of the arterial segment and the functional characteristics of the vascularized limb, the length of hospital stay, amputation free survival (AFS), and the patient's assessment using specialized questionnaires. The clinical and paraclinical data from the study were statistically analyzed and conclusions were derived from the results. The ethical committee of "Nicolae Testemitanu" State University of Medicine and Pharmacy of the Republic of Moldova approved the research design (decision nr.1 from 14.01.2021).

Novelty and scientific originality of the obtained results. This is the first prospective scientific study on a cohort of ALI patients in the Republic of Moldova where an extensive supervision for a full year was included that allowed to evaluate clinical demographic characteristics as well as the unique aspects of diagnostic-curative management and treatment outcomes in a complex way.

It has been established that the late admission for medical assistance is the main factor contributing to delayed revascularization for ALI patients whilst anticoagulant treatment during the pre-operative stage is ineffective in most cases.

As a debut, infrared non-contact thermometry was proposed as a diagnostic tool for assessing ALI patients both pre- and post-surgery, and it was demonstrated to be an essential diagnostic method for evaluating the degree of ischemia and the prognosis for treatment effectiveness.

The degree of ischemia and the patient fragility, as measured quantitatively using the "MoST-Do" score, developed during the study, have been shown to represent the true risk factors associated with unfavorable results of the revascularization intervention as well as these factors may also be used for prognostic purposes prior to surgery.

For the first time, the external validation of the duplex sign Baligh (the difference in diameters between the occluded and the contralateral one) was made in ALI patients and demonstrated a successful diagnostic achievement in identifying the causes of arterial occlusion.

The prospective analysis of the revascularization effectiveness using open, endovascular, and hybrid techniques was performed, and it was established that there was no correlation between the surgical technique used and the main treatment's outcomes.

Using the multivariable statistical methods, it was shown that postoperative levels of creatinine, myoglobin, and CFK-MB were associated with a risk of death in the early and late periods following revascularization, and that hypoalbuminemia had a negative impact on the survival rate of ALI patients.

For the first time, the effectiveness of the ALI treatment was evaluated in terms of patient quality of life – using the "VascuQoL-6" and "Quick DASH" questionnaires, which demonstrated good functional outcomes in revascularization intervention.

Originally, a comparative analysis of the development and therapy outcomes for ALI associated with SARS-CoV-2 infection revealed high rates of re-intervention and mortality in early postoperative stages and allowed identification of death risk factors.

Scientific-applicative issue. The relevant research in this thesis focuses on determining the current clinical-paraclinical aspects unique to ALI patients as well as factors influencing the immediate and delayed outcomes of revascularization treatments in order to optimize diagnosis and treatment management.

Theoretical importance. This research represents a prospective multidimensional analysis of the patient population who suffers from ALI that were examined, treated, and supervised at the specialized tertial hospital level and allowed, for the first time in the Republic, to identify particularities in the management of this patient group; these findings were compared with data obtained from studies conducted in other countries. The successful completion of the study contributed with completely new scientific information to the body of knowledge regarding the ALI domain, including: the diagnostic value of infrared thermometry, the patients' fragility impacting treatment options, the correlation between surgical patient survival rates and IRS lab indicators, the quality of life of ALI patients who have had revascularization procedures, and the particular conditions surrounding the development of acute ischemia associated with COVID-19. The study's results identified both modifiable and non-modifiable risk factors associated with vascular intervention failure and highlighted the areas of further research that should be prioritized: possibility for prognosis, prevention of IRS; optimal anticoagulant treatment, improving fragility diagnosis techniques, and hypoalbuminemia analysis over treatment outcomes.

The applicative value of the research. The identification of preoperative risk factors associated with revascularization intervention failure in patients with ALI made it feasible to predict surgical outcomes and choose the optimal course of therapy based on scientific facts. Derived from study results, it demonstrated the importance and usefulness of infrared non-contact thermometry to examine the patient when diagnosing ALI. The study acknowledged a number of opportunities to enhance the outcomes of ALI treatment, including patient education; rational utilization and monitorization of the antithrombotic treatment efficiency; assurance of a continuous access to vascular imaging and open, endovascular and hybrid revascularization techniques; early diagnosis, prognosis and adequate treatment of compartment syndrome and IRS; and ongoing patient management following surgery. Obtained data and scientific evidence demonstrate that an ALI episode can be fatal and supports the necessity for a centralized, specialized medical care to improve

multidisciplinary patient management at the ambulatory level in accordance with its causes and comorbidities.

The implementation of the research results. The study led to the implementation of new and improved techniques for the diagnosis and management of patients with ALI in the surgical units of the Institute of Emergent Medicine in Chisinau, Moldova. Similarly, study results such as: interpretation of clinical assessment data, evaluation of imagistic methods, prognosis of revascularization interventions, development of new concepts related to medical tactics, were incorporated into the educational process at Department of General surgery-semiology nr.3 at "Nicolae Testemitanu" State University of Medicine and Pharmacy.

Approval of scientific results. The obtained results from the study were presented and discussed in the following scientific forums:The 8-th International Medical Congress for Students and Young Doctors „MedEspera" (Chisinau, 2020); Congress dedicated to 75th anniversary of USMF „Nicolae Testemițanu" (Chisinau, Moldova, 2020); Respirology Association Conference „VIAREMO" (Chisinau, Moldova, 2021); Charing Cross Symposium „Vascular & Endovascular Controversies Update" (London, UK, 2021); Hybrid Annual Meeting of European Society for Vascular Surgery (Rotterdam, Netherland, 2021); 21-st PanHellenic Congress of Vascular and Endovascular Surgery-Angiology (Athens, Greece, 2022); Annual Scientific Conference „Exploration in biomedicine and health: quality, excellence, performance" (Chisinau, Moldova, 2021); „Amputation Prevention Symposium" (Chicago, Illinois, 2022) – I-st place Young Investigator Award; „The 8-th Top-to-Toe Transcatheter Solutions Conference – digital edition" (Dubai, United Arab Emirates, 2022); Annual Scientific Conference „Exploration in biomedicine and health: quality, excellence, performance" (Chisinau, Moldova, 2022); Congress „Week of balkanic medicine, the XXXVII-th edition" (Chisinau, Moldova, 2023); the XIV-th Congress of Surgery Association „Nicolae Anestiadi" and the IV-th Congress of Endoscopy, mini-invasive and Ultrasonographic Surgery Society „V.M.Gutu" from Republic of Moldova (Chisinau, Moldova, 2023).

The results of the study reflected in the thesis were discussed and approved at the meeting of Department of General surgery-semiology nr.3 from State University of Medicine and Pharmacy „Nicolae Testemitanu" (protocol nr.6 from 12.01.2024), Scientific Seminar "Surgery (321.13), Pediatric surgery (321.14), Urology and Andrology (321.22)" (protocol nr.2 from 14.02.2024).

Publications on the research topic. Twenty-two scientific papers were published on the researched topic including: articles in international journals indexed in SCOPUS/PubMed – 3, articles in journals from the National Register of specialized journals – 5, materials/thesis at international conferences (abroad) – 6, materials/thesis at national conferences (organized in Republic of Moldova) – 8.

Summary of the thesis. The thesis includes the list of abbreviations, introduction, 5 chapters, general conclusions, and practical recommendations. The paper is followed by the list of bibliographic references with 218 sources, attachments, a statement of accepting responsibility, and author's CV. The thesis's introductory section highlights the significance of the studied issue in terms of actuality, scientific novelty, and aim as well as the paper's theoretical importance and applicability, and endorsement of the research findings.

The key words: acute limb ischemia, risk factors, diagnostic methods, vascular imaging, surgical treatment, amputation free survival.

THESIS CONTENT

1. THE EVOLUTION OF DIAGNOSTIC AND TREATMENT METHODS FOR ACUTE NON-TRAUMATIC LIMB ICHEMIA

This section represents a narrative reference from specialized literature dedicated to different aspects of surgical management of patients with ALI. Fundamental milestones are reflected in the development of scientific vision and practical approach regarding diagnostic and treatment of acute arterial occlusion. The critical analysis from previous research revealed disagreements and gaps in this domain and argues the need for and identification of additional study.

2. MATERIALS AND METHODS OF THE RESEARCH

2.1. The general methodology of the research

The study was conducted in the vascular surgery clinic (the Department of Vascular Surgery of the Institute of Emergent Medicine, Chisinau, Republic of Moldova) and is based upon analysis of clinical and paraclinical data and treatment results of the patients who were hospitalized for 42 consecutive months - from August 2019 till January 2023, and had acute ischemia of superior limbs and/or inferior limbs (ALI). Patients who met specific criteria were included in the research: (1) must be over 18 years old; (2) ALI caused by acute embolic or thrombotic occlusions of native arteries, peripheral arterial aneurysms or vascular prosthesis (bypass and stent); (3) the duration of ischemia ≤ 14 days; (4) ALI consistent with grade I-IIB Rutherford; (5) revascularization by open, endovascular or hybrid surgery. The following conditions were excluded from the study : (1) cases of ALI resulting from trauma to peripheral vessels, arterial spasms, aorta dissections and cases of thrombosis of vascular bypasses and stents that had developed in the early postoperative period; (2) cases of acute intermittent claudication that does not endanger the viability of the limbs; (3) cases of irreversible ALI requiring primary amputation; (4) patients that are solely subjected to conservative or palliative treatments. The research protocol was validated by the Ethical Committee of Research from USMF "Nicolae Testemitanu" (approval nr.1 from 14.01.2021).

A total of **280 cases** of diagnosed ALI over a period of 3,5 years were included in the study where **266 patients** of them underwent positive revascularization (14 patients had two limbs affected simultaneously: both inferior limbs in 12 cases, and one superior and inferior limb in 2 cases). Following the revascularization intervention, patients underwent a prospective monitorization that lasted up to a year and included four follow-up appointments: at 1, 3, 6 and 12 months post-operatively. The assessment of the saved and surviving limb, compliance with antithrombotic treatment, and hemorrhagic sequelae were all part of each follow-up appointment while the ankle-brachial pressure index (ABI) was recorded at one and six months, and the outcomes of questionnaires reflecting the functional interventions were recorded at the same time. The primary criteria in evaluating ALI treatments was the patient index of revascularization failure defined as patient death (indifferent cause) and/or major amputation of the limb that was documented for the period of monitorization.

2.2. Methods used for diagnosis and surgical treatment of acute ischemia

Acute limb ischemia diagnosis was clinically confirmed in all patients included in the study. A portable Doppler device (CW-Doppler) was used for assessing blood flow during clinical examination in 195 (69,9%) patients. The Rutherford classification was utilized to evaluate the severity of ALI. The following vascular imaging methods were used: duplex ultrasound (DUS) in

114 (42.8%) patients, Computed Tomography Angiography (CTA) - in 112 (42,1%) patients and Digital Subtraction Angiography (DSA) - in 19 (7.1%) patients. A combination of multiple imagistic vascular techniques was used in 51 (19,1%) cases whereas 82 (30,8%) patients underwent surgery based only on a clinical evaluation. Laboratory analysis included: complete blood count and urine tests, coagulation tests (prothrombin, INR, fibrinogen, aPTT), biochemical blood tests (creatinine, urea, protein and albumin, lactate levels, hepatic enzymes and ionogram), immunologic tests (CFK-MB fraction, myoglobin, reactive C protein, procalcitonin, troponin T) as well as blood type and Rh factor.

Three different approaches were used for urgent revascularization treatments: open, endovascular and „hybrid". Open interventions involved thromboembolectomy (TEE), thromboendarterectomy, bypass or prosthesis. Endovascular interventions were performed in a designated operating room equipped with a stationary angiographic device.

2.3. Methods of scientific research and statistical analysis

The Edmonton Frailty Scale (EFS) questionnaire was validated and translated into Romanian in order to assess and diagnose patients' frailty. In accordance with the EFS scale authors' recommendations, the results were interpreted as follows: 0–7 points indicate no „frailty", 8–9 points indicate mild form, 10–11 points indicate moderate form, and 12–17 points indicate severe type of „frailty".

A non-contact thermometric assessment was performed to objectively determine the degree of the affected poikilothermy limb (authors' right certificate series OPI nr. 6917, from 02.06.2021). The standard infrared medical thermometer CK-T1501 (Cooligg, China) was used for temperature measurements with ranges between 0-60°C and an error of ±0,2°C. The temperature was checked in three locations: the dorsal and plantar part of the foot (or dorsal and palmar part of the hand), the metatarsal area (metacarpal) and forehead. The maximum gradient of temperature, or $\triangle T_{max}$ F-M, was determined by calculating the difference in temperature at the limb level compared to the forehead value. The $\triangle T_{max}$ F-M was determined pre-operatively in 207 patients (77,8%) whereas post-operatively in 211 patients (one-hour post-op) and in 203 patients (6–12 hours post-op) respectively.

Prior to revascularization, the lumen diameter of the occluded artery and the diameter of the symmetrical artery of the contralateral limb (Baligh sign) were measured using DUS. The absolute and relative differences were calculated using the formula $\triangle$Da (mm) = diameter of occluded artery (mm) - diameter of lively artery (mm) and correspondingly: $\triangle$Dr (%) - ((diameter of occluded artery – diameter of lively artery) / diameter of lively artery) x 100%. The CTA images were examined both in multiplanar reconstruction and in axial mode. The arteries were divided into 10 anatomical segments: from the infrarenal aorta to ankle arteries.

General data obtained from the complete blood count were utilized to calculate: the ratio between neutrophils and lymphocytes (NLR); ratio between platelets and lymphocytes (PLR); and systemic immune – inflammation index (SII). Two devices were used to measure the pressure in the ankle's muscular compartment: Stryker Pressure Monitor (Stryker™, Kalamazoo, SUA) and an improvised system developed by T.E Whitesides. Two questionnaires were utilized to examine the patient's responses to the ALI treatment – VascuQoL-6 (Vascular Quality of Life 6 items questionnaire) in patients with surgical interventions to inferior limbs and Quick DASH (Disabilities of the Arm, Shoulder and Hand questionnaire) in patients with superior limb ischemia.

Statistical analysis of the collected data was completed using specialized programming: SPSS 22.0 (SPSS Inc., Chicago, IL, SUA), „GraphPad Prism" (version 8.0.1, GraphPad Software, San

Diego, SUA) and online statistic software: „GraphPad QuickCalcs" (www.graphpad.com/quickcalcs, San Diego, SUA), „MedCalc Statistical Software" (www.medcalc.org/calc/index.php, Ostende, Belgium). Significance threshold for all statistical analysis was established at the p value of <0,05.

3. CLINICAL AND PARACLINICAL EVALUATION AND MANAGMENT OF PATIENTS WITH ACUTE ISCHEMIA IN PRE-OPERATIVE PERIOD

3.1. Clinical and demographical characteristics of patients with acute ischemia

The patient population in the study ranged in age from 44 to 97 years, with a median age of 71,5±9,3 years; more than a half of ALI procedures were performed on patients of 70 years and above. There was a predominance of male patients as they took over 150 out of 266 (56,3%) of total patients. Additional comorbidities were identified in 261 (98,1%) of patients: diabetes mellitus – in 61 (22,9%) patients, atrial fibrillation – in 186 (69,9%) patients, ischemic cardiomyopathy – in 212 (79,6%) patients, hypertension – in 236 (88.7%) patients, pleuro-pulmonary pathology – in 72 (27%) patients, anemia – in 56 (21%) patients, and renal insufficiency – in 94 (35,3%) patients. The number of comorbidities varied from one to seven with a median of three (IQR 3-4) chronic diseases per patient. The planned surgical interventions were categorized as ASA II – in 31 (11,6%) patients, ASA III – in 181 (68%) and ASA IV – in 54 (20,3%) patients according to ASA classification.

The scores of the EFS „frailty" questionnaires varied from 1 to 17 points whilst the median score for all patients was 7 (IQR 5-10) points. Nearly half of the individuals with ALI were classified as „frail" - 93 (47,4%) patients of which 32 (34.4%) had severe cases. Ultimately, female patients had a higher median EFS score - 8 (IQR 6-11) compared to male patients' - 6 (IQR 4-9) points (p <0,0001), similarly to the rate of patients who exhibited both „frailty" and „severe frailty": 47/82 (57,3%) vs 43/114 (37,7%), p<0,01 and 19/82 (23,1%) vs 13/114 (11,4%), p<0,05 respectively.

The majority of patients, 246 (92,4%), were included in this study after experiencing their first ALI episode. The remaining 20 cases had 1 to 2 previous ALI episodes where 18 (90%) cases implied the same limb. The most frequent cause of ALI recurrency, occurring in 17 out of 20 cases, was recurrent thromboembolism caused by atrial fibrillation. Of the 186 patients with atrial fibrillation, only 122 patients (65,5%) were on β-blocker medications on a regular basis, 65 (34,9%) - on anticoagulation therapy (warfarin – 54, rivaroxaban – 11) and 52 (27,9%) were receiving antiplatelet medications. Hence, over 40 percent of patients with atrial fibrillation did not receive any antithrombotic treatment. Moreover, of all the patients treated with warfarin, only 8 (14,8%) had INR levels ≥2 at the time of admission. The CHA2DS2VASc score was zero for just three patients (1,6%); one point for three additional patients (1,6%); and ≥2 points for 180 patients (96,7%). Thus, among 183 patients with atrial fibrillation, only 19 (10,3%) followed the current recommendation for anticoagulant medication. Twenty-six (32,5%) out of 80 patients with no history of atrial fibrillation received antithrombotic medication for other purposes. Consequently, slightly over half of the patients in the study group - 145 (54.5%) received ongoing antithrombotic treatment.

ALI cases were dominated by lower limb ischemia, accounting for 218 (77,8%) of the 280 patients. Respectively, superior limb ischemia was encountered in 62 (22,1%) of the cases. Out of 266 patients, 14 (5,2%) had a simultaneous impact on both inferior limbs, while 2 cases had an impact on one superior and one inferior limb. The proximal level of arterial occlusion in lower limb ischemia was localized at: above inguinal ligament level (aorto-iliac occlusion) in 47 (21,5%) cases, common femoral artery in 24 (11%) cases, femoro-popliteal segment – in 96 (44%) cases and in tibial-popliteal segment in 51 (23.3%) cases. The proximal level of arterial occlusion in superior limbs was localized at brachial artery in 11 (17,7%) patients.

There have been identified the following ALI causes: thromboembolism – 210 (75%) cases, atherothrombosis (based on a significant atherosclerotic lesion) - 46 (16,4%) cases, thrombosis of an arterial aneurysm – 12 (4,2%) cases, thrombosis of a previous arterial reconstruction – 12 (4,2%) cases. The rate of thromboembolic occlusions was significantly higher in superior limbs compared to inferior ones – 61/62 (98,3%) vs 149/218 (68,3%) cases (p<0,0001). Limb ischemia was described with the following degrees of severity: grade I (viable limb) - 11 (3,9%) cases, grade IIA (minor threat of limb viability) - 100 (35,7%) cases and grade IIB (immediate threat of limb viability) - 169 (60,3%) cases. Grade IIB ischemia was highly prevalent in both patient groups with superior limb ischemia – 32/62 (51,6%) and acute inferior limb ischemia – 137/218 (62,8%).

3.2. Significance of clinical and paraclinical assessment in the management of patients with acute limb ischemia

The majority of patients – 272 in all, or 97.1% – have primarily reported limb ischemia-related pain. The absence of the pulse in the distal arteries was proved in all cases. Other ALI symptoms were diagnosed with the following prevalence: sensory deficit in 254 (90,7%), motor deficit in 169 (60,3%), skin discoloration in 203 (72,5%) and cool sensation of the limb in 276 (98,5%) cases. The CW-Doppler analysis of blood flow showed that a venous signal was detected in every case, but an arterial signal was only found in 15 (8,2%) of the 181 performed examinations. The ABI value for the same patients ranged from 0,29 to 0,68 with a median of 0,43±0,11.

The value of the temperature gradient between the patient's forehead and the dorsal and plantar surfaces of the foot was of 10 (IQR 7-12) ℃ and 9,5 (IQR 7-12) ℃ respectively, whilst the maximum gradient value $\triangle T_{max}$ F-M was 10 (IQR 7,5-12,5) ℃. There was no certain correlation between $\triangle T_{max}$F-M values and the duration of ALI episode (rs = -0,13 [95%Cl –0,28-0,01], p>0,05), and did not vary for emboli and ALI based on PAD – 10 (IQR 7,6-12,7) ℃ vs 10,1 (IQR 7-12,3) ℃ (p>0.05); additionally, there was no significant difference between the level of suprainguinal and infrainguinal occlusions – 10,5 (IQR 8-12,9) ℃ vs 10 (IQR – 7,2-12,5) ℃ (p>0,05). Nevertheless, as the data in table 1 show, the findings of the foot thermometry were heavily dependent on the degree of ischemia in accordance with the Rutherford classification.

Table 1. **The results of thermometry in patients with different grades of ALI severity conform to Rutherford classification**

Variable	Grade I ALI (n = 4)	Grade IIA ALI (n = 55)	Grade IIB ALI (n = 111)	P value
T forehead (℃)	36,5 (IQR 35,9-36,7)	36,5 (IQR 35,9-36,7)	36,5 (IQR 35,9-36,7)	NS
T dorsal surface of the foot (℃)	29,9 (IQR 27,4-30,7)	29,7 (IQR 27,8-30,5)	25 (IQR 23,8-27,3)	<0,05*
T plantar surface of the foot (℃)	30,1 (IQR 27,4-31,6)	29,6 (IQR 28,2-30,8)	25,3 (IQR 23,7-27,8)	<0,05*
ΔT_{max} F-M (℃)	7 (IQR 5,8-8,6)	7,6 (IQR 6,1-9)	11,8 (IQR 9,9-12,9)	<0,05*
T – temperature *- Kruskal-Wallis test (ANOVA) for grade I and IIA vs IIB ALI				

The findings indicate a substantial difference in the plantar surface temperature between patients with ALI grade IIB Rutherford and those with grades I and IIA. The diagnostic relevance of the thermometry was validated by the ROC curve analysis. For each of the three parameters – plantar, dorsal temperature, and △Tmax F-M gradient, the AUC value was greater than 0,8 suggesting that a reliable diagnosis of ALI grade IIB could be made in more than 80% of cases (figure 1).

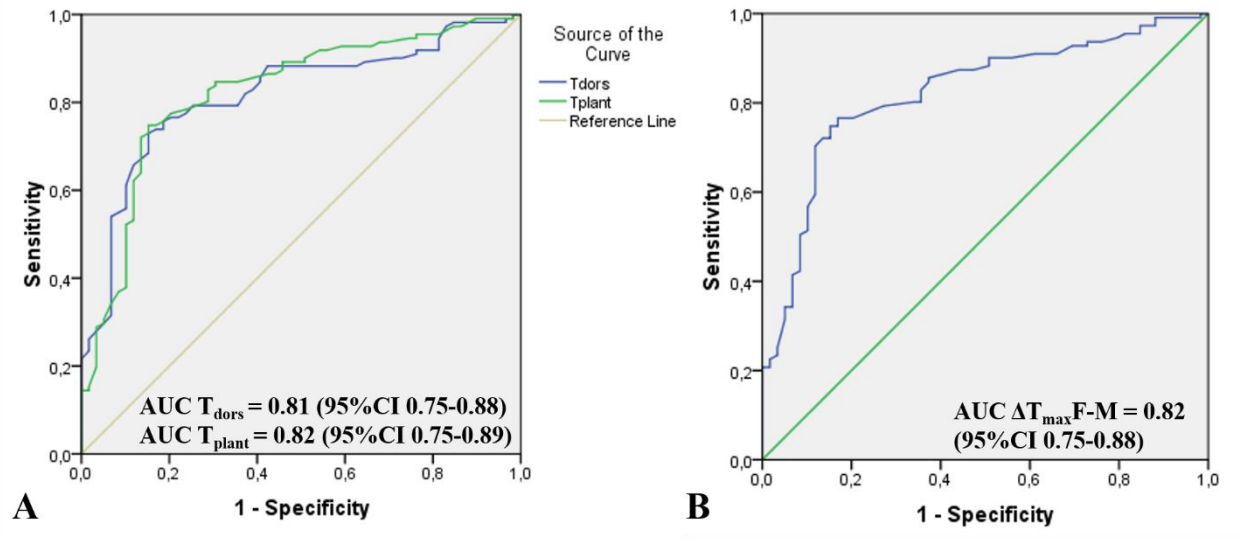

Figure 1. **ROC curves that demonstrates the efficiency of plantar thermometry in diagnosis of ALI grade IIB Rutherford**

According to Youden index the following optimal thresholds were established: ≤26,7 ℃ for the temperature of the dorsal foot surface (sensitivity – 73%, specificity – 84,7%); ≤27,6 ℃ – for the temperature of the plantar foot surface (sensitivity – 74,8%, specificity – 84,7%); and ≥9,4 ℃ for $\triangle T_{max}$ F-M criteria (sensitivity – 76,6%, specificity – 83,1%). A positive diagnosis of ALI grade IIB indicates that revascularization interventions are required immediately; therefore, it is reasonable to assume that, in practical terms, a gradient of ≥7 ℃ is the ideal value, providing a high level of sensitivity (above 90%) and an acceptable precision (above 70%).

Preoperatively, it is important to predict the etiology of ALI as well as the risk of TEE failure and the necessity of reconstructive surgery. For this reason, the diagnostic importance of the duplex Baligh sign was evaluated. The absolute diameter (△Da) and the relative diameter (△Dr) of the affected and healthy arteries differed by 0,8 (IQR 0,4-1,5) mm and 18,9% (IQR 6,7-30), respectively. The comparative analysis showed a significant difference of △Da and △Dr values in embolism vs atherothrombosis (figure 2). The median value of △Da in the group with embolism was equal to 1,0 (IQR 0,6-1,5) mm vs 0,2 (IQR 0,1-0,4) mm in patients with atherothrombosis, while △Dr value was equal to 21,4% (IQR 13,6-32,1) vs 2.8% (IQR 1,4-9,9), ($p<0,0001$ in both groups). Hence, in cases of pure embolic occlusion the artery diameter enlarged by one millimeter (or ≈ 25%) whereas it was extremely mild in cases of atherothrombosis (<0,4mm). Positive results were revealed evaluation of Baligh sign displaying the value of AUC ROC of 0,83±0,05 (95%CI 0,72-0,94) for △Da and value of 0,87±0,04 (95%CI 0,79-0,95) for △Dr. The optimal threshold values of △Da and △Dr were >0,4mm (sensibility 85,4% and specificity 76%) and ≥7,5% (sensibility 87,6% and specificity 76%) respectively. The proportion of additional endovascular interventions or conversions to reconstructive interventions was 43,7% in the patient group with a △Da value of less than 0,4mm, compared to just 4,8% ($p<0,0001$) in the study group with a △Da value greater than 0,4mm.

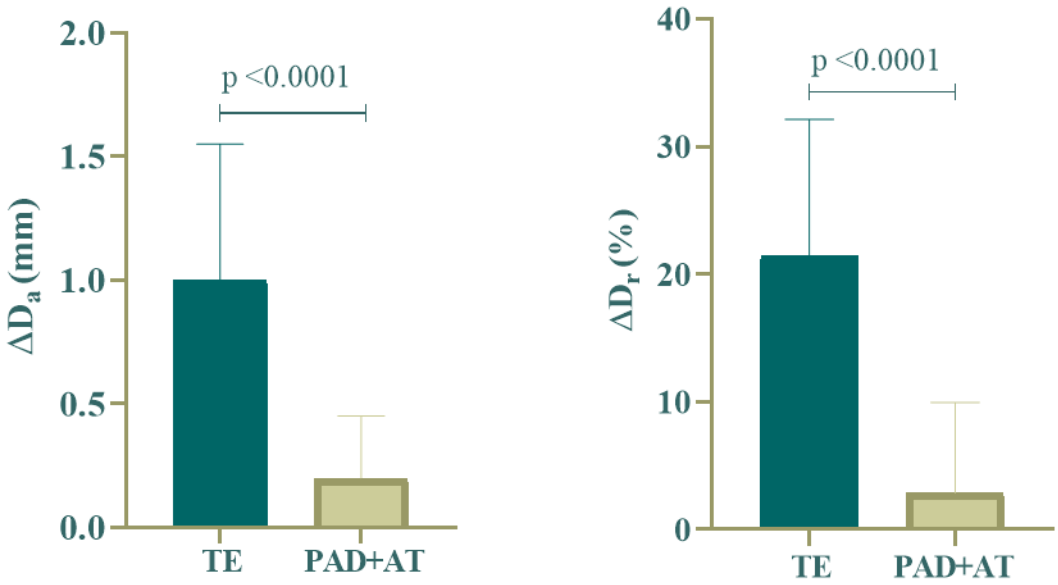

Figure 2. **Comparison of absolute and relative differences in diameter of occluded and contralateral artery at the symmetrical level in thrombembolism (TE, n = 89) and PAD with atherothrombosis (PAD+AT, n = 25)**

CTA examinations were conducted on 112 (42,1%) patients in the current study (115 cases of acute ischemia of inferior limbs). The proximal level of the arterial occlusion was located at: the infrarenal level of abdominal aorta in 7 (6%) cases, common iliac artery – in 17 (14,7%), external iliac artery – in 6 (5,2%), common femoral artery – in 19 (16,5%), superficial femoral artery – in 39 (33,9%) and popliteal artery – in 27 (23,4%) cases. Insufficient contrast of the tibial arteries made it challenging to evaluate their permeability in 20 (17,3%) out of the 115 cases. An inconsistency was observed when comparing CTA and DUS data – the k coefficient value (kappa Cohen) for posterior tibial artery was 0,26±0,1 (95%CI 0,05-0,48), whereas for the anterior tibial artery values were solely 0,03±0,08 (95%CI –0,13-0,21). The obtained data should be interpreted with the minimum consistency between those two approaches with a 10% chance of accuracy. Similarly, it should be highlighted that CTA and DUS data coincided and confirmed the diagnosis of tibial artery occlusion in 57,7% cases whereas only in 22,9% cases in the diagnosis of arterial permeability. It can be concluded that: (1) the absence of tibial arteries contrasting during CTA should not be considered as a complete lack of „out-flow" and impossibility of revascularization; (2) CTA and DUS methods in ALI are complementary procedures rather than concurrent.

Despite the dominance of thromboembolism in ALI, according to CTA data, 87 (75,6%) cases out of 115 lower limb assessments presented signs of PAD. Chronic occlusive-stenotic lesions of the aortoiliac segment were diagnosed in 65 (56,5%), femoro-popliteal - in 78 (67,8%) and infrapopliteal - in 62 (53,9%) cases. As predicted, patients' age with PAD was significantly higher compared to patients without atherosclerosis: 71,8±8,1 (95%CI 70-73,5) years vs 67,3±10,4 (95%CI 63,3-71,4) years ($p<0.05$). Moreover, during CTA examinations, 63 patients (54.7%) were diagnosed with concomitant lesions of visceral arteries or arteries of contralateral inferior limbs. Thus, it must be concluded that despite embolism being the most common cause of ALI, acute occlusion of the lower limb arteries had developed due to chronic atherosclerotic lesion („acute on chronic ischemia") in the majority of cases.

3.3. Predicting outcomes of lower limb acute ischemia treatment during the preoperative stage

Analysis of demographic criteria and current comorbidities demonstrated that none of the studied risk factors (age, gender, number of concomitant diseases, ASA grade, EFS score) differ between the patient subgroups with saved limbs and those with amputations. However, the „frailty" score has shown the greatest difference for both the compound and mortality values. When patient age was included as an additional variable, a significant association was found between the EFS score and the risk of amputation and/or death – ORadj 1,35 (95%CI 1,16-1,57), p<0,0001. The presence of „frailty" was associated with a higher risk of death – RR 12,0 (95%CI 2,9-48,7), p<0,001; and with a risk of negative outcomes – RR 4,0 (95%CI 1,8-8,5), p<0,001; but not with an increased risk of amputations – RR 1,6 (95%CI 0,5-4,6), P =0,38.

The second group of studied risk factors included: the probable cause of occlusion; the occlusion's position relative to the inguinal ligament; the degree of ischemia and foot thermometry results. It was demonstrated that there were no differences in anatomical locations and the causes of arterial occlusions. On the contrary, there were significant differences found in the ΔTmax F-M values and the patient rate with grade IIB ischemia with successful and unsuccessful revascularizations. The logistic regression revealed a strong association between the two indices and the likelihood of a negative composite outcome: OR 1,15 (95%CI 1,0-1,3), P=0,01 and OR 2,5 (95%CI 1,1-5,9), P=0,02 respectively. At the same time, AUC ROC values were higher for the thermal gradient – 0,72 (95%CI 0,57-0,87) than for the grade IIB ischemia – 0,55 (95%CI 0,4-0,7).

Considering the limitations and potential deficiencies of the Rutherford classification, the current study developed a new clinical score called „MoST-Do" (Motor, Sensory, gradient of Temperature, Doppler signal) based on the quantitative assessments of the three components of the combined classification using plantar thermometry. Each of the four criteria received a point value between 0 to 2 depending on the severity of ischemia (table 2).

Table 2. **The quantitative score „MoST-Do" developed to predict the results of revascularization procedures**

Clinical-diagnostic criteria	Number of points		
	0	1	2
Sensory deficit	Absent	Minimal (at digit level)	At plantar and digit level
Motor deficit	Absent	Limited digit movement	Minimal or absent digit movement
CW-Doppler exam	Audible arterial signal, ABI ≥0.5	Audile arterial signal, ABI <0.5	Absent arterial signal
$\triangle T_{max}$ F-M value	< 5 °C	5-9,9 °C	≥ 10 °C
ABI – ankle branchial index			

Logistic regression showed a positive correlation between the „MoST-Do" score and the risk of amputation – OR 1,66 (95%CI 1,1-2,48), p<0,05; the risk of death – OR 1,38 (95%CI 1,0-1,8), p<0,05; and the risk of amputation and/or death – OR 1,57 (95%CI 1,2-2,0), p<0,001. In the patients with score values between 1-3 points the rate of amputation and/or mortality was 1/19 (5,2%), with values of 4-6 points – 19/80 (23,7%), with value of 7 points – 10/25 (40%), and with value of 8 points – 11/17 (64%). The probability of negative composite outcome was twice as high when the „MoST-

Do" values were 7-8 points as opposed to 4-6 points (RR 2,1 [95%CI 1,2-3,4], p <0,01) and nine times higher compared to the „MoST-Do" score value of 1-3 points (RR 9,5 [95%CI 1,37-65,5], p <0,05). Regarding the prediction of revascularization failure, the „MoST-Do" score results revealed AUC ROC values of 0,69±0,05 (95%CI 0,59-0,79).

Vascular imaging data did not show a significant difference between patient population groups who responded successfully and those who failed the interventions. Patients who underwent successful revascularization had a statistically higher median ΔDa criteria value than those who did not: 1,2 (IQR 0,7-2,0) vs 0,5 (IQR 0,2-1,1) mm, p<0,05. Upon evaluating the composite results of the interventions (amputation and/or decease), there were significant variations found solely for the NLR value when comparing laboratory tests: 3,2 (2,4-6,6) for success and 4,1 (2,9-7,3) for failure (p <0,05).

In the multivariable model, the Baligh sign and NLR have lost their statistical significance. Nonetheless, EFS and „MoST-Do" scores remain independent risk factors for amputation and/or death: OR 1,3 (95%CI 1,1-1,5), p<0,0001 and OR 1,4 (95%CI 1,1-1,9), p<0,01 respectively. After „dichotomization" (>7 points for EFS and >6 points for „MoST-Do") both risk factors continued to have significant correlation with the risk of poor revascularization results – OR 5,4 (95%CI 2,0-13,9), p<0,001 for the EFS and OR 2,8 (95%CI 1,1-7,1), p<0,05 – for the „MoST-Do" score. Depending on the number of risk factors (0, 1 or 2), the probability of amputation and/or death increased progressively: OR 5,15 (95%CI 1,73-15,3), p<0,001 when one of the two factors was present, and OR 14,4 (95%CI 4,13-50,5), p<0,0001 when both factors were present. Therefore, the following three-stage classification of ALI cases can be applied in the preoperative stage to predict the treatment's outcome: (1) patients with no „frailty" and with the „MoST-Do" values ≤6; (2) patients with only one of the two risk factors present and (3) „frail" patients with the „MoST-Do" values >6. The rate of unfavorable results of interventions in these patient categories is shown in table 3.

Table 3. **Rate of unfavorable results for acute lower limb ischemia treatment in different risk categories**

Risk factors	Revascularization results		P* value
Amputation			
	n (%)	Relative Risk	
EFS <7 and „MoST-Do" ≤6	3/55 (5,4%)	-	-
EFS >7 or „MoST-Do" >6	5/58 (8,6%)	1,58 (95%CI 0,39-6,3)	NS
EFS >7 and „MoST-Do" >6	6/26 (23%)	4,2 (95%CI 1,14-15,6)	<0,05
Death			
	n (%)	Relative Risk	
EFS <7 and „MoST-Do" ≤6	2/55 (3,6%)	-	-
EFS >7 or „MoST-Do" >6	13/58 (22,4%)	6,16 (95%CI 1,45-26)	=0,01
EFS >7 and „MoST-Do" >6	10/26 (38,4%)	10,5 (95%CI 2,49-44,8)	=0,001
Amputation and/or death			
	n (%)	Relative Risk	
EFS <7 and „MoST-Do" ≤6	5/55 (9%)	-	-
EFS >7 or „MoST-Do" >6	17/58 (29,3%)	3,22 (95%CI 1,27-8,14)	=0,01
EFS >7 and „MoST-Do" >6	14/26 (53,8%)	5,92 (95%CI 2,38-14,69)	=0,0001
*- in comparison of absent risk factors			

Presented data suggest that there is a significant influence of „frailty” and clinical „MoST-Do” score upon the negative results of revascularization. The suggested prognostic model with an acceptable level of precision (AUC ROC values 0,743±0,48, 95%CI 0,64-0,83, p<0,0001), allows to estimate the success of vascular interventions with sufficient accuracy and to choose an individual optimal treatment tactic for each patient with acute lower limb ischemia.

4. THE CHARACTERISTICS AND TREATMENT RESULTS ANALYSIS OF ACUTE LOWER LIMB ISCHEMIA

4.1. Preoperative „pathway” of the patients and causes for delay of revascularization

The „onset-referral” time ranged from zero (an ALI episode occurred in the hospital) to 336 hours, with a median value of 18 hours (IQR 4-71). The length of this interval was noticeably shorter when the occlusion was located in the aorto-femoral segment opposed to the infrainguinal occlusion – 7 (IQR 1,8-42,5) vs 28 (IQR 6-95) hours (p<0,001). The time from onset to admission for patients experiencing their first ALI episode was 22 (IQR 4-79,5) hours vs 8 (IQR 2-41) hours in patients with recurrent episodes (p <0,05). Anticoagulant administration prior to revascularization was carried out in 172 patients (95,5%), most of whom – 141 (81,9%) received it within the first 6 hours. The „referral-anticoagulant” interval had a median value of 2,5 hours (IQR 1-5). Upon admission the aPTT values ranged from 18-120 seconds, with a median value of 21 seconds (IQR 28-38,5). At most 10% of patients achieved the therapeutic level of anticoagulation at the time of admission (aPTT >45 sec) and just 28% of patients had readings over the upper normal limit (aPTT >37 sec).

The median „admission-revascularization” time was 3,7 hours (IQR 2-8), and it was considerably shorter in situations of embolic ALI opposed to atherothrombosis ALI and depended on anatomical localization of suprainguinal artery occlusion: 3,0 (IQR 2-7) vs 4,5 (IQR 2-20,2) hours and 3,0 (IQR 1,5-6) vs 4,0 (IQR 2-13,5) hours, respectively. The duration of the study interval expanded, on average, by one hour when CTA and/or DUS testing was performed from 3,0 hours (IQR 1,7-6) when no vascular imaging was done to 4,0 hours (IQR 2-12) in cases when it was (p<0,05). The main contributing factor in the delay of revascularization was the patient's late address for medical assistance (figure 3).

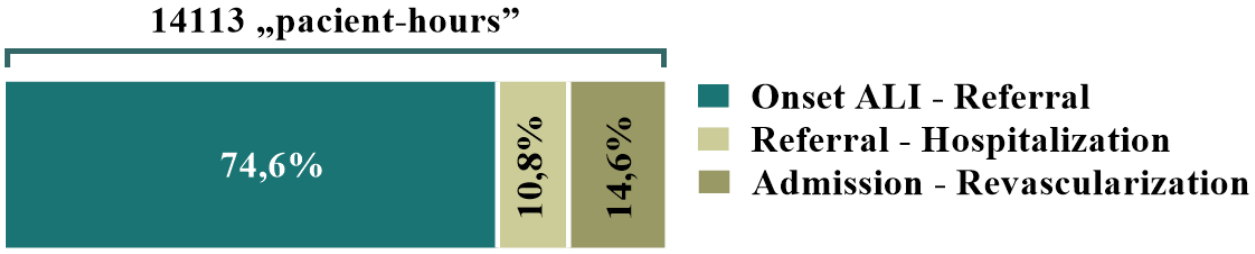

Figure 3. **The relative proportion of different time intervals that constitutes the patient's „pathway” from ALI onset to revascularization initiation**

Seventy-five percent, or 10524 „patient-hours” of the total 14113 „patient-hours” (average 77,1 hours per patient) from the onset of symptoms to surgical interventions occurred prior to the patient's initial contact with a physician. The percentage of „referral-hospitalization” and „hospitalization-revascularization” intervals were substantially lower at 10,8% and 14,6% respectively which corresponds to 10,7 hours per patient and 10,8 hours per patient, respectively.

4.2. The structure, technical features and selection criteria of the different types of interventions for acute ischemia

The absolute majority of the 190 interventions performed for lower limb ischemia – 171 cases (90%) were open approaches. TEE was the most frequently used method accounting for 133/171 (77,7%) cases completed by endarterectomy and angioplasty in 12 (7%) patients. Reconstructive vascular procedures were performed in 26/171 cases (15,2%): (1) ilio-femoral or femoro-femoral crossover bypass – 6 cases (22,2%); (2) distal femoro-popliteal bypass – 12 cases (44,4%); (3) femoral/popliteal-tibial bypasses – 5 cases (18,5%); (4) other types of reconstructions (common femoral artery grafting, reconstruction of distal anastomosis of aorto/iliofemoral or femoro-popliteal bypass – 4 cases (14,8%). The total number of surgeries was 27, since one of the patients underwent both an extraanatomical ilio-femoral bypass and a distal bypass to the anterior tibial artery. The predominant reconstruction material being used during the procedure was the great saphenous vein – 19/27 cases (70,3%).

Out of 11 cases of endovascular interventions 2 (18,1%) were performed via brachial access, 5 (45,4%) – via anterograde femoral access and 4 (36,3%) – via contralateral retrograde femoral access (crossover). In 7 cases (63.6%), thromboaspiration was used utilizing a specialized device called „Penumbra ENGINE®" with negative pressure values of 1.98 atm. Vacuum thromboaspiration solely was applied in one patient. Residual stenotic lesions were visualized after thrombus aspiration in the remaining 6 cases requiring balloon angioplasty ± stenting. In the other 4 cases (36,3%) balloon angioplasty was used as the main method of treatment of acute arterial occlusion. Four cases (36,3%) required bailout stenting at the site of thromboaspiration and/or angioplasty due to severe arterial dissection or residual stenosis of more than 50% of the arterial diameter. Two additional cases involved the use of local thrombolysis via catheter.

Hybrid interventions were performed step by step in all 8 cases during the study due to the absence of a dedicated operating room. Open approach was always performed first: TEE from popliteal artery (n = 3), TEE ± endarterectomy from common femoral artery (n = 2), TEE from occluded femoral-popliteal bypass (n = 1), or femoral-popliteal bypass (n = 2). The second stage was performed in an endovascular operating room and involved balloon angioplasty with proximal stenting in two cases (25%) and/or distal stenting in six cases (75%).

Peak pressures in leg compartments were considerably greater in patients who underwent early fasciotomy than in those who did not have decompression – 40 (IQR 32-44) vs 20 (IQR 14-25,7) mm Hg, ($p<0,0001$). Patients with ΔTmax F-M values of less than 10°C had a higher likelihood of undergoing fasciotomy compared to those who had less severe poikilothermia – 25/73 (34,2%) vs 7/70 (10%) observations, RR 3,42 (95%CI 1,58-7,4), $p<0,01$. Moreover, this criterion maintained a substantial connection with risks of fasciotomy that included Rutherford's grade IIB ischemia as an additional variable in the multivariate analysis – ORadj 1,2 (95%CI 1,0-1,4) per °C, $p<0,05$.

4.3. Early treatment results and perioperative risk factors for revascularization failure

Within one month from surgery, a major amputation was performed in 18 (9,4%) cases while 27 (15%) patients passed away. Of these patients, 5 (2,7%) died following a secondary amputation. Thus, within the first month the AFS rate in this patient group was 76,3%. In patients with revascularization failure the time interval from vascular intervention to amputation ranged from 1 to 27 days, with a median value of 2 days (IQR 1-23,3). Six cases (33,3%) involving limb revascularization attempts were followed by amputations during the first 24 hours. The „revascularization-patient death" interval was equal to 6 days (IQR 2-11).

Aside from surgical stress, the main factor of thanatogenesis in ALI is the development of IRS. Merely fifty-five patients (30,5%) in the studied group did not present a pathological increase in any of these parameters during the postoperative period. In other cases, abnormal results were found for one laboratory test in 44 (24,4%) of the patients, two to three tests in 65 (36,1%) of the patients, and more than three tests in 16 (8,8%) of the patients. The association between the number of positive IRS markers and revascularization failure is illustrated in figure 4.

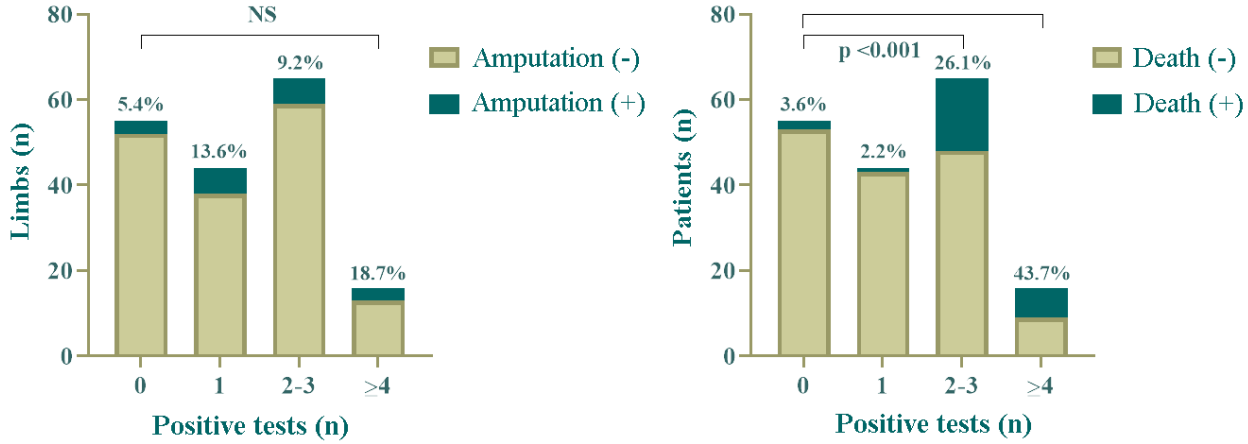

Figure 4. **Major amputation and mortality rates among patient groups with different numbers of positive laboratory tests of IRS**

The mortality rate has progressively increased in tandem with the rise in the number of positive tests and the presence of 2-3 IRS markers exceeded the corresponding index by 7-10 times compared to the subgroup with 0-1 markers, while in the presence of 4 or more IRS markers - by 10-20 times. On the contrary, there was no increase in the rate of amputations concomitant with the increase in the number of laboratory tests with pathological results. To identify intra- and postoperative risk factors for treatment failure, the characteristics of revascularization intervention were compared (table 4).

Tabelul 4. **Characteristics of surgical treatment in patients with successful and unsuccessful lower limb revascularization (30 days postoperatively)**

Variables	**Revascularization results (190 extremities, 180 patients)**		**P Value**
	Amputation (-)	Amputation (+)	
Local anesthetic*, n (%)	50/172 (29%)	3/18 (16,6%)	NS
Open approach**, n (%)	156/172 (90,6%)	15/18 (83,3%)	NS
Fasciotomy, n (%)	28/172 (16,2%)	7/18 (38,8%)	<0,05
Duration of surgery, min	80 (IQR 60-113,8)	122,5 (IQR 65-178)	=0,05
„Out-of-hours”, n (%)	91/172 (52,9%)	5/18 (27,7%)	<0,05
	Decease (-)	Decease (+)	
Local anesthetic*, n (%)	39/153 (25,4%)	10/27 (37%)	NS
Open approach**, n (%)	136/153 (88,2%)	25/27 (92,5%)	NS
Fasciotomy, n (%)	30/153 (19,6%)	5/27 (18,5%)	NS
Duration of surgery, min	80 (IQR 61,2-120)	90 (IQR 65-120)	NS
„Out-of-hours”, n (%)	70/153 (45,7%)	19/27 (70%)	<0,05
*- spinal or general anesthesia; **- endovascular or hybrid surgery			

The next group of analyzed risk factors included instrumental data that reflected the effectiveness of limb revascularization. The results of the comparative statistical analysis are displayed in table 5.

Tabelul 5. **Association between the immediate effect of revascularization of the affected lower limb with the baseline treatment outcomes at the 30 days**

Variables	**Revascularization results (190 extremities, 180 patients)**		**P Value**
	Amputation (-)	Amputation (+)	
SpO_2 within 1 hour, (%)	95 (IQR 92-98)	89 (IQR 0-90)	<0,001
SpO_2 within 24 hours, (%)	95 (IQR 94-98)	0 (IQR 0-0)	<0,0001
Perfusion index within 1 hour	2,1 (IQR 0,9-3,7)	0,05 (IQR 0-0,7)	<0,0001
Perfusion index within 24 hours	2,7 (IQR 1,8-3,9)	0 (IQR 0-0)	<0,0001
△Tmax F-M within 1 hour, (%)	1,2 (IQR 0,3-2,2)	5,7 (IQR 1,6-8)	<0,01
△Tmax F-M within 24 hours, (%)	0,4 (IQR 0,2-1,0)	8,9 (IQR 2,1-15,3)	<0,0001
ABI within 24 hours	0,9 (IQR 0,7-1,0)	0,1 (IQR 0-0,9)	=0,0001
DUS score within 24 hours, (points)	4,0 (IQR 3,0-6,0)	0 (IQR 0-0,7)	<0,0001
	Death (-)	Death (+)	
SpO_2 within 1 hour, (%)	95 (IQR 90-98)	94 (IQR 90-95,5)	NS
SpO_2 within 24 hours, (%)	95 (IQR 94-98)	92 (IQR 0-95)	<0,01
Perfusion index within 1 hour	2,0 (IQR 0,7-3,7)	3,1 (IQR 0,5-3,8)	NS
Perfusion index within 24 hours	2,7 (IQR 1,2-4,0)	2,0 (IQR 0-2,9)	<0,05
△Tmax F-M within 1 hour, (%)	1,1 (IQR 0,3-2,1)	2,2 (IQR 1,2-6,0)	<0,01
△Tmax F-M within 24 hours, (%)	0,4 (IQR 0,2-0,8)	1,6 (IQR 0,45-7,4)	=0,0001
ABI within 24 hours	0,93 (IQR 0,68-1,0)	0,8 (IQR 0-1,0)	<0,05
DUS score within 24 hours, (points)	4,0 (IQR 3,0-6,0)	5,5 (IQR 2,7-6,0)	NS
SpO_2 - determined at plantar digit level with pulse oximetry			

There was a notable increase in the risk of irreversible ischemia and the need for amputation with perfusion index values of <0,9 or $\triangle T_{max}$ F-M gradient >1,5℃ in contrast to the diametrically opposite values of these tests: 33,3% vs 4,7%, RR 7,0 (95%CI 2,0-23,8), P=0,001 and 16,9% vs 3,9%, RR 4,2 (95%CI 1,2-14,5), P=0,01 respectively. Repeated revascularization has not been linked to an increased risk of amputation, RR 1,1 (95%CI 0,1-7,9) P=0,08 or death, RR 0,3 (95%CI 0,02- 4,7) P =0,4, justifying its use in cases of persistent or recurrent ischemia. The data presented in the table suggests that there is a considerable increase in both the risk of death and amputation associated with unsuccessful revascularization.

The third group of examined risk factors were laboratory tests, performed within the first 12 hours after surgery (table 6). Although an association of risk for death has been established with most laboratory tests, only three of these tests were significantly different in patients with and without amputations. D-dimer and fibrinogen levels evaluated in the initial hours following surgery were significantly higher in revascularization failure cases - 4100 (IQR 2065-6185) vs 1000 (IQR 497,5-2518) ng/ml and 4,9 (IQR 4-8.2) vs 4,1 (IQR 3,3-4,9) g/L, respectively (p<0,05 for both parameters). Vice versa, aPTT values were lower in patients with failed revascularization compared to those who underwent successful procedures – 26,5 (IQR 23,7-35) vs 32 (IQR 27,4-41) sec (P =0,01).

Table 6. **Association between laboratory test results* and patient death within 30 days postoperatively**

Variables	Revascularization results (190 extremities, 180 patients)		P Value
	Deces (-)	Deces (+)	
NLR	5,3 (IQR 2,9-9,9)	12,5 (IQR 6,9-21,7)	<0,0001
Fibrinogen, g/L	4,2 (IQR 3,3-5,0)	4,2 (IQR 3,1-4,9)	NS
aPTT, sec	31,4 (IQR 27-38,1)	34,6 (IQR 25,5-43)	NS
D-dimer, ng/ml	950 (IQR 480-2395)	2365 (IQR 525-4015)	NS
Albumin, g/L	36,8 (IQR 32-40,3)	31,0 (IQR 27,2-35,1)	<0,0001
Serum creatinine mmol/L	87 (IQR 72,7-104,5)	144 (IQR 100-275)	<0,0001
Potassium (K+), mmol/L	4,6 (IQR 4,2-4,9)	5,3 (IQR 4,5-5,9)	<0,0001
Reactive C-protein, mg/L	12,0 (0,35-48,0)	33,0 (10,9-131,9)	=0,054
Lactate dehydrogenase, U/L	250 (IQR 191-371)	277 (IQR 197-343)	NS
Serum lactate, mmol/L	1,9 (IQR 1,6-2,1)	1,8 (IQR 1,7-2,0)	NS
Myoglobin, ng/ml	144,7 (IQR 55,3-316)	540 (IQR 153,2-600)	<0,001
Creatinine phosphokinase, ng/ml	4,1 (IQR 2,6-14,2)	20,2 (IQR 3,9-36,8)	=0,001
T-troponin, ng/ml	0,02 (IQR 0-0,5)	0,06 (IQR 0-0,5)	NS
*- performed within the first 12 hours following revascularization			

In a multivariate regression analysis, the performing of fasciotomy, the perfusion index and all laboratory values lost their association with the probability of amputation. Rather an independent association existed between the risk of amputation and the revascularization performed during „out-of-hours" – OR_{adj} 0,11 (95%CI 0,01-0,97), p<0,05, as well as with the ΔT_{max} F-M gradient values one hour after surgery – OR_{adj} 2,13 (95%CI 1,34-3,37), p<0,001.

When creating multivariate models for the „patient death" criterion, only two factors maintained an independent connection: creatinine level - OR_{adj} 1,04 (95%CI 1,01-1,06), p<0,001 and myoglobin level - OR_{adj} 1,003 (95%CI 1,001-1,005), p<0,01. The ROC curve analyses for both creatinine and myoglobin values showed acceptable AUC values of 0,86 (CI95% 0,77-0,94) and 0,71 (95%CI 0,56-0,85). The thresholds with the greatest informative values, as determined by curve coordinate analysis, were creatinine level >160 mmol/L (sensitivity 54,2%; specificity 98,9%) and myoglobin level ≥356,5 ng/ml (sensitivity 71,4%; specificity 80%).

4.4. Evaluation at long-term after revascularization: clinical results and patients' quality of life

At the end of the study, all survived patients had their 6-month evaluation results while only 89,4% of them completed their one-year evaluation, with the mean number of days under observation being 266±139. A major amputation of the operated limb was performed in 24 (12,6%) out of 190 cases during the follow-up and 58 (32,2%) out of 180 patients passed away, indicating a 57,8% AFS rate. Just six (25%) of the twenty-four limb amputations were performed later than 30 days following revascularization implying a revascularization-amputation interval value of 8,5 (IQR 1,2-33,2) days. Conversely, 32 (55,1%) out of 58 fatalities occurred later than 30 days after the intervention, and the median revascularization to death interval value was 155 (IQR 6,7-308) days. The Kaplan-Meier curves for patient survival and limb salvage are displayed in figure 5.

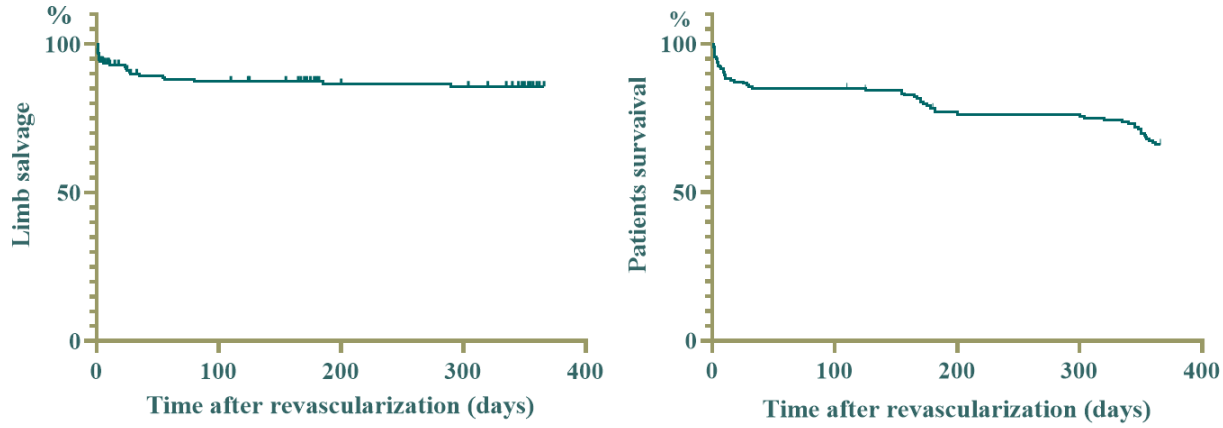

Figure 5. **Kaplan-Meier curves for lower limb salvage and patients' survival at one year following revascularization**

The impact of pre-, intra- and postoperative risk factors on the long-term outcomes of ALI treatment has been reviewed. As illustrated in table 7, the univariate analysis revealed that the following factors were associated with risk of amputation: „frailty" degree, severity of ischemia determined by „MoST-Do" score, „surrogate" markers of blood flow restoration, as well as patient compliance with antithrombotic treatment. Furthermore, neither the patients' age nor the presence of grade IIB ischemia manifested any statistical significance.

Table 7. **Risk factors for major amputation following revascularization of acute lower limb ischemia in the long term**

Risk factors	Univariate Cox regression HR (95%CI)	Multivariate Cox regression HR (95%CI))
Age, years	0,97 (0,93-1,01); p = 0,22	Not included
EFS, points	1,16 (1,0-1,34); p <0,05	NS
Embolic etiology	0,6 (0,27-1,34); p = 0,21	Not included
Grade IIB Rutherford	1,43 (0,61-3,3); p = 0,4	Not included
„MoST-Do", points	1,4 (1,03-1,93); p <0,05	NS
„Out-of-work hours"	0,51 (0,22-1,2); p = 0,12	Not included
CTA/DUS testing	1,17 (0,43-3,14); p = 0,74	Not included
Type of surgery*	1,5 (0,43-5,24); p = 0,52	Not included
Fasciotomy	2,8 (1,24-6,52); p = 0,01	11,1 (0,99-124,8); p = 0,05
PI within 1 hour p/o	0,4 (0,21-0,74); p <0,01	NS
PI within 24 hours p/o	0,33 (0,18-0,58); p <0,0001	NS
$\triangle T_{max}$ F-M within 1 hour p/o	1,25 (1,13-1,39); p <0,0001	NS
$\triangle T_{max}$ F-M within 24 hours p/o	1,37 (1,24-1,52); p <0,0001	1,84 (1,07-3,15), p <0,05
ABI p/o	0,06 (0,02-0,2); p <0,0001	0,005 (0,0001-0,58), p <0,05
Compliance with AT scheme	0,2 (0,06-0,71); p =0,01	0,03 (0,002-0,82), p <0,05
PI – perfusion index (pulse oximetry); p/o – postoperatively; AT – antithrombotic; * – TEE vs bypass / endarterectomy vs endovascular / hybrid		

„Frailty" and the initial degree of ischemia were no longer significant in the multivariate analysis and the association between fasciotomy and risk of amputation was at the limit of statistical

significance. As per the evaluation of preliminary results, the degree of compensation of blood circulation was found to be the independent risk factor for major amputation. The chance of amputation was shown to be directly associated with $\triangle T_{max}$ F-M gradient values one day after surgery, while the ABI value was found to be inversely correlated. Long-term outcomes after revascularization indicated that while patient compliance with antithrombotic medication had a meaningful impact, the operation done during „out-of-hours" became not significant. To study the factors linked with risk of **patients' death** at long term after revascularization, the impact of the same variables was primarily explored. In addition, major comorbidities and IRS biochemical markers were included in the analysis and examined one day following revascularization (table 8).

Table 8. **Risk factors for patient death at long-term after revascularization for acute lower limb ischemia**

Risk factors	**Univariate Cox regression HR (95%CI)**	**Multivariate Cox regression HR (95%CI**
Age, years	1,03 (1,0-1,05); p <0,05	NS
Female gender	0,81 (0,47-1,39); p = 0,46	not included
EFS, points	1,26 (1,13-1,4); p <0,0001	1,56 (1,29-1,88); p <0,0001
Embolic etiology	1,4 (0,79-2,5); p = 0,24	not included
Grade IIB Rutherford	1,8 (1,03-3,28); p <0,05	NS
"MoST-Do", points	1,38 (1,1-1,7); p <0,01	NS
Diabetes mellitus	1,89 (1,09-3,27); p <0,05	3,0 (1,26-7,33), p = 0,01
Atrial fibrillation	1,23 (0,67-2,24); p = 0,49	not included
Chronic renal insufficiency	1,92 (1,14-3,21); p = 0,01	NS
Anemia	1,16 (0,62-2,15); p = 0,63	not included
Cardiac insufficiency	1,3 (0,95-1,78); p = 0,09	not included
Type of surgery*	1,94 (0,6-6,2); p = 0,26	not included
Fasciotomy	0,72 (0,35-1,46); p = 0,36	not included
NLR	1,01 (0,99-1,03); p = 0,28	not included
Myoglobin, ng/ml	1,01 (0,99-1,02); p = 0,09	not included
Creatinine, mmol/L	1,008 (1,005-1,01); p <0,001	2,76 (1,18-6,46), p = 0,01**
CFK MB, ng/ml	1,02 (1,01-1,04); p <0,0001	3,83 (1,41-10,42), p <0,01**
Serum Albumin g/L	0,92 (0,87-0,96); p = 0,001	2,67 (1,07-6,66), p <0,05**
$\triangle T_{max}$ F-M within 24 hours	1,06 (1,0-1,13); p <0,05	NS
Secondary amputation	1,26 (0,57-2,79); p = 0,55	not included
AT compliance scheme	0,46 (0,21-1,01); p = 0,05	not included

CPK MB – creatine phosphokinase (MB fraction); AT – antithrombotic;
* – open approach (TEE, bypass, endarterectomy) vs endovascular / hybrid;
** – test value above a norm's superior limits

The data presented in the table indicates that the patients' initial level of „frailty" has a major influence on the risk of death. Only diabetes mellitus among all comorbidities exhibited a correlation with death risk, which tripled in the presence of corresponding disease. From a practical standpoint, it has been demonstrated that hypoalbuminemia and the patient's mortality risk are related in a way that is modifiable and can be adjusted in the postoperative period.

The mean „VascuQoL-6" score among patients with an AFS greater than six months was 21,0±2,8 (95%CI 20,5-21,5) points where values greater than 18 points (a characteristic score for patients with mild claudication) were observed in 110 cases (83,3%). When evaluating the influence of various risk factors on patients' quality of life, lower values were found for patients who developed ALI on background of PAD – 20,1±2,6 (95%CI 19,3-20,8) vs embolism with 21,4±2,9 (95%CI 20,8-22,0) points, and for aorto-femoral segment occlusion vs infrainguinal segment – 19,8±3,6 (95%CI 18,7-20,9) vs 21,5±2,2 (95%CI 21,0-22,0) points (p <0,01 in both cases).

5. DIAGNOSTIC-CURATIVE APPROACH AND TREATMENT RESULTS IN PARTICULAR FORMS OF ACUTE LIMB ISCHEMIA

5.1. Acute upper limb ischemia

Fifty cases of acute upper limb ischemia have been documented in the current study, accounting for 20,8% of all ALI observations (not including COVID-19 patients). Median EFS score in patients with upper limb ischemia was lower - 5 (IQR 3,5-8,5) opposed to 7 points (IQR 5-10) for lower limb impairment (p<0,05). Thromboembolism was the cause of almost all upper limb ALI cases 49 (98%) compared to 124 cases (65,2%) for lower limbs (p<0,0001). The reduced rate of grade IIB ischemia at the level of the upper limbs showed borderline viridity with 23 (46%) observations in contrast to 116 (61%) in the comparison group (P = 0,07). The ΔT_{max} F-M gradient measured preoperatively in the upper and lower extremities showed a more significant difference: 7,6 (IQR 5,8-10) °C vs. 10 (IQR 7,2-12,5) °C, respectively (p <0,001). Similarly, the rate of cases with gradient values ≥10 °C was significantly lower in superior extremities - 27% (10/37 thermometers performed) vs. 51% (73/143) patients with lower limb ALI (p<0,01). This result suggests a more objective nature of temperature criteria when evaluating the severity of circulatory disorders compared to a more conventional method. The brachial artery was the most often observed site for the proximal level of arterial occlusion, accounting for 40 observations (80%).

The „onset – referral" timeframe for upper limb ALI was found to be considerably shorter at 5 (IQR 2-15) compared to 18 (IQR 4-71) hours for lower limb ischemia (p <0,0001) when the time periods for providing specialized care were compared. Revascularization procedure was completed nearly four times faster in patients with upper limb ischemia than in those with lower limb ischemia with an average of 8 hours (IQR 5,2-33) compared to 32 hours (IQR 10,7-99,5), (p <0,0001). CTA test was performed less frequently in patients with ALI at upper limb level denoting only 4 (8%) patients compared to 98 (54,4%) in lower limb ALI cases (p<0,0001). With one exception, TEE was used for upper limb revascularization in 49 (98%) events. Upper limb fasciotomy was not necessary for any patient.

The immediate results of surgical interventions were distinctly better for the upper limbs. The values of the ΔT_{max} F-M gradient and perfusion index were 0,0 (IQR -0,2-0,2) °C vs 0,5 (IQR 0,3-1,6) °C and 4,8 (IQR 3,6-6) versus 2,5 (1,0-3,7) respectively (p<0,0001). There has been noted of a decreased systemic inflammatory response and IRS severity when superior limbs are involved: potassium level – 4,3 (IQR 3,9-4,8) vs 4,6 (IQR 4,3-5,2) mmol/L; CPK – 2,9 (IQR 0,0-9,3) vs 4,7 (IQR 2,7-19,9) ng/ml; myoglobin level – 79,6 (IQR 30,3-203,5) vs 169,7 (64,5-485,2) ng/ml; C reactive protein - 6,0 (IQR 0,0-24) vs 18,0 (6,0-48) mg/L; and fibrinogen level – 3,8 (IQR 3,0- 4,5) vs 4,2 (IQR 3,3-5,0) g/L (p<0,05 in all cases).

All fifty patients (100%) had their upper limbs saved over the thirty days that followed revascularization; two patients (4%) died on the third- and ninth-day following operation. Therefore, initial treatment results were noticeably better compared to those of the lower limbs. At the same

time, analysis of survival curves revealed no significant differences and the cumulative death rate at the conclusion of the research was 20/50 (40%) for upper limb ischemia and 58/180 (32,2%) for lower limb ischemia (figure 7).

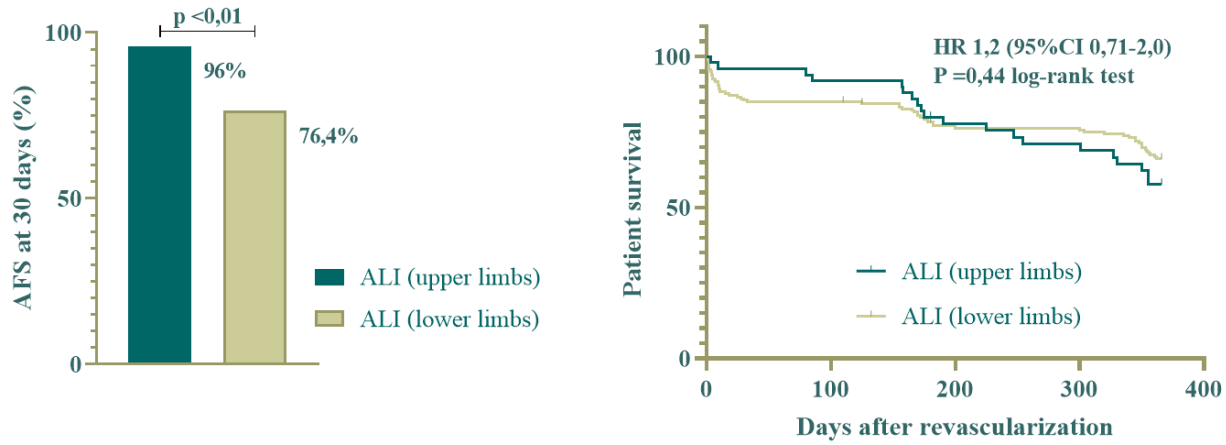

Figure 7. **A comparison of amputation-free survival (AFS) at 30 days postoperatively and Kaplan-Maier survival curves in patients with acute upper and lower limb ischemia**

In univariate analysis, the patient's age, anaemia upon admission, number of concurrent conditions, creatinine and CPK-MB levels, and ΔT_{max} F-M values one day after revascularization were found to be similar to mortality risk factors in upper limb ischemia. Whilst in the multivariate analysis, only the CPK-MB level and the presence of anemia remained statistically significant. The final factor had the strongest independent impact upon mortality risk: RR 3,18 (95%CI 1,6-6,22), NNH 1,9 (95%CI 3,8-1,3), p<0,001. The „Quick DASH" questionnaire was used to assess upper limb function one month following revascularization in 48 (94,1%) patients. The results ranged from 0 to 11,36 points where the median score was 1,13 points (IQR 0-6,25), indicating nearly a full recovery of limb function and a lack of severe complaints in the majority of patients.

5.2. Revascularization interventions for COVID-19-related acute ischemia

Patient cohort studies included cases of ALI associated with SARS-CoV-2 infection. A total of 40 cases of ALI were registered (14,2% of the total number of observations) and 38 patients were diagnosed. In this subgroup, the time interval between the COVID-19 diagnosis and the ALI episode ranged from 1 to 6 weeks, with a median of 1,5 weeks (IQR 1-3,7).

Twelve patients (57,1%) were transferred from other medical facilities where they had received COVID-19 treatment, whereas nine patients (42,8%) came from their homes. An intensive care admission was required for twelve of the cases (57,1%). Pulmonary changes characteristic to SARS-CoV-2 were diagnosed in 15 patients (71,4%) with a mean Brixia score of 7,0 points (IQR 3-11). Laboratory tests analysis showed a significant increase in the level of inflammatory markers in cases of ALI linked to SARS-CoV-2 infection compared to uninfected patients: NLR – 7,2 (IQR 3,6-15,5) vs 3,7 (IQR 2,6-7,1); PLR – 22,7 (IQR 11,2-39,2) vs 12,3 (IQR 9,1-21,9); SII – 1798 (IQR 774-3329) vs 861 (IQR 593-1700) and fibrinogen – 4,8 (IQR 3,6-6,2) g/L vs 4,1 (IQR 3,3-5,2) g/L (p <0,05 in all cases). Patients with COVID-19 underwent CTA and DUS less frequently than those in the group without SARS-CoV-2 infection with 11 (27,5%) and 12 (30%) cases, respectively, compared to 108 (45%) and 106 (44,1%) cases (p <0,05 for CTA). A defining hallmark of the CTA findings in infected patients was the presence of intra-aortic thrombus observed in 4 (36,3%) out of

11 individuals who underwent examination. In the absence of COVID-19, this phenomenon was diagnosed solely in 6 (5,7%) cases, P=0,01.

The operational structure analysis showed that TEE was a more common procedure in the context of COVID-19-related ALI than reconstructive and endovascular procedures which were only used in two and one case, respectively. The postoperative anticoagulation strategy for patients with infection has been characterized by limited use of low molecular weight heparins - only in 45% of cases. The remaining 22 individuals received unfractionated heparin. In the absence of infection, heparins with low molecular weight were used in majority of cases - 174 (72,5%) observations ($p<0,001$). When ALI was associated with COVID-19 infection, anticoagulant therapeutic dosages were prescribed far more frequently – in 4 patients (10%) compared to 6 patients (2,5%) in the group without infection ($p<0,05$).

The initial results of the revascularization procedures were significantly worse in patients infected with SARS-CoV-2. Repeated vascular interventions were needed nearly 4 times more frequently in infected patients than in uninfected individuals - in 6 (15%) vs 9 (3,7%) cases, ($p<0,01$). The AFS rate at 30 days was only 63,1% in COVID-19 patients, compared to 84,6% in patients without infection ($p<0,01$). The primary cause of this discrepancy was the significantly greater mortality rate among infected patients—12 (31,5%) cases compared to 28 (12,2%) cases in the uninfected group ($p<0,01$). At the same time, the rate of limb amputations in the comparison groups showed similar proportion - 4 (10%) observations in ALI with COVID-19 and 18 (7,5%) in the uninfected group ($p>0,05$). Therefore, the development of ALI in conjunction with a novel coronavirus infection considerably increased the risk of mortality – RR 2,57 (95%CI 1,4-4,6), P=0,001, but not of amputation – RR 1,3 (95%CI 0,4-3,7), P =0,58.

Two indicators showed a genuine correlation in a univariate logistic regression with the likelihood of an adverse composite outcome of revascularization in patients with COVID-19: NLR – OR 1,12 (95%CI 1,02-1,23), P = 0,01 and the level of serum albumin – OR 0,8 (95% CI 0,68-0,95), P = 0,01. A limited statistical significance was observed in the relationship between the probability of amputation and/or mortality within 30 days following surgery and EFS score values - OR 1,18 (95% CI 0,99-1,4), P = 0,05. When all three variables were included in a multivariate analysis, the postoperative NLR value became insignificant. Serum albumin levels, on the other hand, demonstrated a true inverse relationship, and EFS scale scores revealed a direct correlation with the probability of an early unfavorable outcome of ALI treatment: OR_{adj} 0,75 (95%CI 0,61-0,93), $p<0,01$ and OR_{adj} 1,27 (95%CI 1,0-1,61), respectively $p<0,05$.

GENERAL CONCLUSIONS

1. Patients with ALI in the study cohort were distinguished by: mean age of more than 70 years, significant number of comorbidities, high rate of „frailty" – 47% (95%CI 38,3-58,1) and severe „frailty" – 34% (95%CI 23,5-48,5), presence of chronic occlusive-stenotic atherosclerotic lesions of the lower limbs in 75% cases (95%CI 64,1-87,6), predominance of Rutherford grade IIB ischemia cases, as well as inadequate antithrombotic treatment prior to hospital admission.

2. The degree of poikilothermia of the affected limb is a reliable indicator of the severity of acute ischemia while the quantitive evaluation of the thermal gradient ΔT_{max} F-M allows to identify with a sufficient degree of accuracy (AUC ROC 0,82) cases that require immediate revascularization, to specify the indications for fasciotomy and to predict the risk of secondary amputation.

3. Among the risk factors, available for assessment during the preoperative period, the significant independent association with likelihood of revascularization failure demonstrate: the

patient's frailty determined by the Edmonton scale and the severity of lower limb ischemia quantitatively assessed with the "MoST-Do" score.

4. The mortality rate after treatment of acute lower limb ischemia is 15% in the first month and 32% one year following surgery, which significantly exceeds the amputation rate of 9,4% (95%CI 6,0-13,6). Factors that are significantly associated wuth the risk of death include: the presence of frailty, diabetes mellitus, hypoalbuminemia, and elevated levels of laboratory markers for ischemia-reperfusion syndrome (creatinine, myoglobin, creatinine phosphokinase).

5. Despite favorable early results of acute upper limb ischemia treatment (amputation rate – 0%, 30-day mortality rate after revascularization – 4%), the mortality rate increase up to 40% (95%CI 32,9-48,1) during the first year of follow-up and did not statistically differ from patients with lower limb ischemia.

6. Distinctive features of ALI associated with SARS-CoV-2 infection are: the presence of an excessive systemic inflammatory response, frequent diagnosis of parietal (mural) aortic thrombosis (36%; 95%CI: 20,1-61,8), decreased efficacy of anticoagulant therapy as well as an increased need for repeated revascularizations (15%; 95%CI: 5,7-34,3), and higher postoperative mortality rate in the early phase (31,5%).

PRACTICAL RECOMMENDATIONS

1. The time interval from ALI onset should not be used as a stand-alone factor in determining treatment tactics and the likelihood of limb salvage. An initial dose of heparin bolus should be administered immediately if ALI is suspected. An optimal level of anticoagulation must be maintained if revascularization is delayed; ideally, this can be done by continuous infusion of unfractionated heparin.

2. In order to objectively confirm the severity of the ALI prior to surgery and to determine correctly the Rutherford category in equivocal cases, it is advised to measure the temperature gradient between the patient's forehead and the foot/hand of the acutely ischemic limb using a standard non-contact infrared medical thermometer. A patient has a 74% the probability of having grade IIB ischemia when their ΔTmax F-M gradient values are ≥7 °C, and an almost 90% risk when their ΔT_{max}F-M gradient values are ≥10 °C.

3. To predict the risk of amputation and death when performing revascularization procedure for ALI it is rational to use the following criteria: the Edmonton Frailty Scale (score >7 points) and the “MoST-Do” quantitative system of lower limb ischemia evaluation (score >6 points). The rate of an negative composite outcome of surgery rises threefold and reaches approximately 30% in the presence of one of the risk factors and is six times higher (surpassing 50%) when both risk factors are present.

4. Vascular ultrasound is recommended to determine the absolute and/or relative difference in the diameters of the affected and contralateral arteries at the symmetric level (Baligh sign) in cases where it is difficult to determine the likely cause of acute arterial occlusion (embolism vs. atherothrombosis) and to assess the chances of TEE technical success. If the difference in artery diameter is more than or equal to 0,4 mm (or 7,5%), a reasonable suspicion of an embolism must be made; if the difference is smaller, a higher risk of TEE failure is considered and reconstructive or hybrid procedures are required.

5. CTA should be attempted in most patients with ALI not only to plan the optimal revascularization strategy but also to identify the source of the embolization (intracardiac, intra-aortic thrombosis), anatomical variations of the magistral vessels, concomitant lesions of the visceral

arteries or contralateral limb arteries, and extravascular pathology. The combined use of CTA and DUS increases the diagnostic value of the examinations in the infrapopliteal segment.

6. In the presence of conditions restricting the use of standard accesses to the popliteal artery (medial or posterior), a suitable alternative is the lateral access which can be performed under local tumescent anesthesia and does not significantly affect the results of thrombectomy.

7. Aside from using conventional revascularization techniques such as thrombectomy and reconstructive procedures in cases of ALI, centres providing specialized vascular surgical care should ensure the availability of endovascular techniques such as thrombaspiration, angioplasty, and thrombolysis, along with the option to perform a hybrid approach.

8. When assessing the indications for fasciotomy in ALI, in addition to the clinical criteria, it is recommended to include limb thermometry results (presence of ΔT_{max} F-M gradient ≥10 °C) and the findings of direct measurements of the leg fascial compartments pressures. In this situation, an improvised system that provides adequate measurement accuracy can be used. It is not contraindicated to perform primary rare sutures of skin in a prophylactic fasciotomy.

9. When revascularization fails to restore peripheral pulse, „surrogate" parameters of arterial perfusion – the pulse oximetry perfusion index and the ΔT_{max} F-M temperature gradient, might be used to assess the degree of blood flow compensation in the early postoperative phase. Perfusion index values less than 0,9 or a thermal gradient more than 1,5°C a few hours following surgery point to an inadequate circulation compensation and the eventual need of reoperation or a significant risk of amputation.

10. On the first postoperative day following revascularization for ALI, it is recommended to test laboratory markers for ischemia-reperfusion syndrome. The mortality risk increases in proportion to the number of abnormal tests results. In this case, the most informative parameters are creatinine, myoglobin, and creatinine phosphokinase (MB fraction) levels. Additionally, it is advised to monitor and correct serum albumin levels since hypoalbuminemia increases the risk of death in the latter stages following revascularization.

11. To improve the outcomes of ALI treatment, the following organizational measures are required: optimizing primary prophylaxis while adhering to guideline recommendations for antithrombotic therapy; educating patients about ischemia signs, the need for immediate medical referral, and the importance of pharmacotherapy compliance; ensuring ALI patients have continuous access to a specialized facility that can offer a wide range of diagnostic and treatment services; and providing ongoing interdisciplinary monitoring of the operated patients.

BIBLIOGRAPHY

1. Aboyans V, Ricco JB, Bartelink MEL, et al. 2017 ESC Guidelines on the diagnosis and treatment of peripheral arterial diseases, in collaboration with the European Society for Vascular Surgery (ESVS). *Eur J Vasc Endovasc Surg.* 2018;55(3):305-368.

2. Natarajan B, Patel P, Mukherjee A. Acute lower limb ischemia-etiology, pathology, and management. *Int J Angiol.* 2020;29(3):168-174.

3. Björck M, Earnshaw JJ, Acosta S et al. European Society for Vascular Surgery (ESVS) 2020 Clinical Practice Guidelines on the management of acute limb ischaemia. *Eur J Vasc Endovasc Surg.* 2020;59(2):173-218.

4. McNally MM, Univers J. Acute limb ischemia. *Surg Clin North Am.* 2018;98(5):1081- 1096.

5. Castraveț A., Tabac D., Ţurcan A., et al. Tratamentul chirurgical al ischemiei acute periferice. *Arta Medica.* 2019;3(72):23-24.

6. Olinic DM, Stanek A, Tătaru DA, Homorodean C, Olinic M. Acute limb ischemia: an update on diagnosis and management. *J Clin Med.* 2019;8(8):1215.
7. Andersen LV, Mortensen LS, Lindholt JS, Faergeman O, Henneberg EW, Frost L. Upper- limb thrombo-embolectomy: national cohort study in Denmark. *Eur J Vasc Endovasc Surg.* 2010;40(5):628-634.
8. Chisari A, Pistritto AM, Bellosta R, Ferraresi R, Danzi GB. Upper limb ischemia from arterial thromboembolism: a comprehensive review of incidence, etiology, clinical aspects, diagnostic tools, treatment options and prognosis. *Minerva Cardioangiol.* 2016;64(6):625-634.
9. Eyers P, Earnshaw JJ. Acute non-traumatic arm ischaemia. *Br J Surg.* 1998;85(10):1340-1346.
10. Davis FM, Albright J, Gallagher KA, Gurm HS, Koenig GC, Schreiber T. et. al. Early outcomes following endovascular, open surgical, and hybrid revascularization for lower extremity acute limb ischemia. *Ann Vasc Surg.* 2018;5:106-112.
11. de Athayde Soares R, Futigami AY, Barbosa AG, Sacilotto R. Acute arterial occlusions in COVID-19 times: a comparison study among patients with acute limb ischemia with or without COVID-19 infection. *Ann Vasc Surg.* 2022;83:80-86.
12. Enezate TH, Omran J, Mahmud E, Patel M, Abu-Fadel MS, White C et. al. Endovascular versus surgical treatment for acute limb ischemia: a systematic review and meta-analysis of clinical trials. *Cardiovasc Diagn Ther.* 2017;7(3):264-271.
13. Grip O, Wanhainen A, Michaëlsson K, Lindhagen L, Björck M. Open or endovascular revascularization in the treatment of acute lower limb ischaemia. *Br J Surg.* 2018;105(12):1598-1606.
14. Teodoro C, Bertanha M, Girard FPCM, Sobreira ML, Yoshida RA, Moura R et. al. Results of treatment of acute occlusions of limb arteries at a university hospital – retrospective study. *J Vasc Bras.* 2020;19.
15. Veenstra EB, van der Laan MJ, Zeebregts CJ, de Heide EJ, Kater M, Bokkers RPH. A systematic review and meta-analysis of endovascular and surgical revascularization techniques in acute limb ischemia. *J Vasc Surg.* 2020;71(2):654-668.
16. Casian D, Guțu E, Culiuc V, Smolnițchi R, **Predenciuc A**. Protocol Clinic Național nr. 388 „Ischemia acută a extremităților la adult". Ministerul Sănătății al Republicii Moldova, 2021. 60 p., disponibil pe https://msmps.gov.md/legislatie/ghiduri-protocoale-standarde/chirurgie-2.

LIST OF SCIENTIFIC PUBLICATIONS

at which the results of the research for the doctoral thesis in Medical Science with the topic "Diagnostic and treatment approach in non-traumatic acute limb ischemia" were presented

Articles in international scientific journals:

- ✓ **articles in international scientific journals: SCOPUS / PUBMED**

1. **Predenciuc A.**, Casian D., Culiuc V. Outcomes of surgical revascularization for acute limb ischemia in COVID-19 patients comparing to non-infected cohort: a single-center observational prospective study. In: *Annals of Vascular Surgery*. 2023, nr. 4(91), pp. 81-89. ISSN 0890-5096. DOI: 10.1016/j.avsg.2022.11.024. (**IF: 1.607**).
2. Casian D., **Predenciuc A.**, Culiuc V., Nordanstig J., Morgan M. Romanian translation and validation of vascular quality of life questionnaire „VascuQoL-6" in patients with lower extremity arterial disease. In: *Surgery,Gastroenterology and Oncology*. 2023, nr. 3(28), pp. 167-173. eISSN 2601-1700. DOI: 10.21614/sgo-592. (**IF: 0.109**).

3. Casian D., **Predenciuc A.**, Culiuc V. Clinical value of foot thermometry in patients with acute limb ischemia. In: *Vascular*. 2024, Mar 1:17085381241237494. DOI: 10.1177/17085381241237494 (Epub ahead of print). ISSN 1708-5381. **(IF: 1.1)**

Articles in acredited national scientific journals:

✓ **articles in category B journals**

4. **Predenciuc A.**, Casian D. Actualități în diagnosticul ischemiei acute non-traumatice a extremităților: revista literaturii. În: *Arta Medica*, 2021, nr. 3(80), pp. 18-24. ISSN 1810-1852.

5. **Predenciuc A.** Tendințe actuale în tratamentul ischemiei acute ale extremităților: revista literaturii de specialitate. În: S*ănătate publică, economie şi management în medicină.* 2022, nr. 2(93), pp. 107-114. ISSN 1729-9697.

6. **Predenciuc A.**, Casian D., Culiuc V. Early results of endovascular treatment using percutaneous vacuum-assisted thromboaspiration in acute lower limb ischemia. În: *Moldovan Journal of Health Science.* 2023, nr. 3(10), pp. 35-42. ISSN 2345-1467.

7. **Predenciuc A.**, Casian D., Culiuc V. Caracteristicile clinice și comorbiditățile pacienților cu ischmie acută a extremităților revascularizați în mod urgent: studiu prospectiv. În: *Buletinul Academiei de Științe a Moldovei.* 2023, nr. 3(77); pp. 157-162. ISSN 1857-0011.

8. Culiuc V., **Predenciuc A.**, Casian D. Ischemia acută periferică asociata infecției SARS-CoV-2: experiența de diagnostic și tratament. În: *Buletinul Academiei de Științe a Moldovei.* 2023, nr. 3(77); pp. 162-168. ISSN 1857-0011.

Abstracts / thesis submitted at scientific conferences:

✓ **international conferences from abroad**

9. **Predenciuc A.**, Casian D., Culiuc V. Diagnostic and predictive value of infrared foot thermometry in patients with acute lower limb ischemia: the pilot study. *Charing Cross Symposium „Vascular & Endovascular Controversies Update" 2021 (virtual)*; https://www.cxsymposium.com/cx2021/cx-2021/?set=3.0000.

10. **Predenciuc A.**, Culiuc V., Casian D. Effect of weekend and out of hours admission in management of patients with acute limb ischemia. In: *EJVES Vascular Forum.* 2022, Volume 54, p. e15. ISSN 2666-688X.

11. **Predenciuc A.**, Culiuc V., Casian D. Impact of frailty upon outcomes of revascularization in patients with acute limb ischemia. In: A*bstracts of the 21-st Panhellenic Congress of Vascular and Endovascular Surgery – Angiology.* Athens, Greece, 2022, p. 26.

12. **Predenciuc A**., Culiuc V., Casian D. Outcomes of Surgical Revascularization for Acute Limb Ischemia in COVID-19 Patients Comparing to Noninfected Cohort: A Single-Center Observational Prospective Study. In: *Abstracts from the Amputation Prevention Symposium (AMP), August 17-20, 2022, Chicago, Illinois. In: Vascular Disease Management,* 2022, nr. 4(91), p. 81. ISSN 2152-4343.

13. **Пределчук А.**, Загадайлов Д., Смольницкий Р., Кулюк В., Касьян Д. Факторы, влияющие на решение о выполнении предоперационной ангиографии у пациентов с острой ишемией конечностей. *В: Материалы XVI Всероссийского конгресса лучевых диагностов и терапевтов «Радиология – 2022»*. Красногорск, Россия, 2022, с. 55-56. ISBN 978-5-906484-67-3.

14. **Predenciuc A.**, Culiuc V., Smolnitchi R., Istrati V., Casian D. Initial experience of percutaneous mechanical thromboaspiration in acute limb ischemia. *The 37-th Balkan Medical Week „Perspectives of the Balkan Medicine in the Post COVID-19 Era". In: Abstract book.* 2023, p. 305.

✓ **national conferences organized in Republic of Moldova**

15. **Predenciuc A.** Rare complication of surgical intervention for acute limb ischemia: case report. In: *MedEspera: the 8th International Medical Congress for Students and Young Doctors. Abstract book.* Chisinau, Republic of Moldova; 2020, p. 27-28.

16. **Predenciuc A**., Culiuc V., Bzovii Fl., Smolnitchi R., Casian D. Caracteristicele clinice și demografice ale pacienților cu ischemie acută a extremităților. In: *Congresul consacrat aniversării a 75-a de la fondarea Universității de Stat de Medicină şi Farmacie „Nicolae Testemiţanu”. Abstract book.* 21-23 octombrie 2020, Chișinău, p. 439

17. **Predenciuc A.**, Culiuc V., Smolnitchi R., Casian D. Initial experience of hybrid procedures performed for acute limb ischemia. In: *Abstract book: Conferința științifică anuală "Cercetarea în biomedicină și sănătate: calitate, excelență și performanță",* 20-22 octombrie 2021, p. 251.

18. **Predenciuc A.**, Culiuc V., Casian D. The role of fasciotomy for compartment syndrome in patients with acute limb ischemia. *Culegere de rezumate ale conferinței științifice anuale „Cercetarea în biomedicină și sănătate: calitate, excelență și performanță. În: Moldovan Journal of Health Science. Revista de Științe ale Sănătății din Moldova*. 2022, nr. 3(29), p. 307. ISSN 2345-1467.

19. **Predenciuc A.,** Casian D. The predictive role of neutrophil-lymphocyte ratio in acute limb ischemia. *Culegere de rezumate ale conferinței științifice anuale „Cercetarea în biomedicină și sănătate: calitate, excelență și performanță. În: Moldovan Journal of Health Science. Revista de Științe ale Sănătății din Moldova.* 2022, nr. 3(29), p. 342. ISSN 2345-1467.

20. Culiuc V., Casian D., **Predenciuc A.,** Spinei Ig., Vescu L. Rezultatele clinice ale revascularizării extremităților inferioare prin bypass-uri extra-anatomice. *Rezumatele celui de-al XIV-lea Congres al Asociației Chirurgilor „Nicolae Anestiadi” și al IV-lea Congres al Societății de Endoscopie, Chirurgie miniminvazivă și Ultrasonografie „V.M.Guțu” din Republica Moldova. În: Arta Medica.* 2023, nr. 3(88), p. 77-78. ISSN 1810-1852.

21. **Predenciuc A.,** Spinei Ig., Bzovîi Fl., Culiuc V., Casian D. Tratamentul ischemiei acute a extremităților (IAE) la pacienții cu infecție COVID-19: evaluarea rezultatelor. *Rezumatele celui de-al XIV-lea Congres al Asociației Chirurgilor „Nicolae Anestiadi” și al IV-lea Congres al Societății de Endoscopie, Chirurgie miniminvazivă și Ultrasonografie „V.M.Guțu” din Republica Moldova. În: Arta Medica*. 2023, nr. 3(88), p. 84-85. ISSN 1810-1852.

22. **Predenciuc A.** Validarea prospectivă a semnului ecografic „Baligh” pentru diferențierea etiologiei ischemiei acute a extremităților. *In: MJHS Abstract Book, Conferința științifică anuală "Cercetarea în biomedicină și sănătate: calitate, excelență și performanță"*, Chișinău, Republica Moldova, 2023. p. 463. ISSN: 2345-1467

ADNOTARE

Predenciuc Alexandru **„Conduita de diagnostic și tratament în ischemia acută non-traumatică a extremităților”**. Teză de doctor în științe medicale, Chișinău, 2024.

Structura tezei. Teza este expusă pe 167 pagini de text de bază: introducere, 5 capitole, concluzii generale și recomandări practice, 25 figuri și 21 tabele. Bibliografia include 218 surse. Rezultatele principale ale studiului au fost publicate în 22 lucrări științifice.

Cuvinte-cheie: ischemia acuta a extremităților, diagnostic clinic, diagnostic imagistic, tratament chirurgical.

Scopul lucrării. Determinarea posibilităților de perfecționare a conduitei de diagnostic și tratament în ischemia acută a extremităților, în baza identificării factorilor peri-operatori cu impact negativ asupra rezultatelor intervențiilor urgente de revascularizare.

Obiectivele cercetării. Studierea caracteristicelor demografice, clinice și paraclinice ale cohortei contemporane de pacienți cu ischemia acută a extremităților, supuși intervențiilor de revascularizare. Evaluarea conduitei preoperatorii și aprecierea valorii diferitor metode de diagnostic ale ischemiei acute a extremităților. Elaborarea metodei de prognozare a rezultatului precoce a intervențiilor de revascularizare, bazate pe criterii disponibile pentru analiză la etapa preoperatorie. Analiza rezultatelor precoce și la distanță după intervenții de revascularizare urgente și identificarea factorilor asociați cu risc de amputație și / sau decesul bolnavului. Determinarea particularităților clinico-evolutive și a rezultatelor tratamentului chirurgical ale formelor particulare de ischemie acută – cu afectarea membrului superior și asociate infecției SARS-CoV-2.

Noutatea și originalitatea științifică. Pentru prima dată în Republica Moldova a fost realizat un studiu științific prospectiv de cohortă la pacienții cu ischemie acută a extremităților și a permis evaluarea complexă a caracteristicelor clinico-demografice, particularităților conduitei diagnostico-curative și a rezultatelor tratamentului. În premieră, a fost propusă utilizarea termometriei infraroșii non-contact pentru examinarea pre- și postoperatorie a pacienților cu ischemie acuta a extremităților. S-a demonstrat că gradul de fragilitate a pacientului și severitatea ischemiei, evaluată cu ajutorul scorului „MoST-Do” elaborat în cadrul studiului, reprezintă factorii veridici de risc asociați cu rezultatul nefavorabil al intervențiilor de revascularizare. S-a efectuat validarea externă prospectivă a valorii semnului ecografic Baligh care a demonstrat performanța diagnostică acceptabilă a acestuia în stabilirea cauzei ocluziei arteriale.

Semnificația teoretică și valoarea aplicativă a lucrării. Identificarea factorilor de risc preoperatori, asociați cu eșecul intervenției de revascularizare la bolnavii cu ischemie acuta a extremităților, a permis prognozarea rezultatului operației și selectarea științific argumentată a tacticii curative. În baza rezultatelor cercetării a fost demonstrată necesitatea și utilitatea includerii examenului prin termometrie infraroșie non-contact în conduita diagnostică, aplicată pacienților cu ischemie acută a extremităților. Datele studiului au identificat o serie de posibilități pentru ameliorarea rezultatelor tratamentului ischemiei acute a extremităților: educația pacienților din grupe de risc; utilizarea rațională și monitorizarea eficacității tratamentului antitrombotic; prognozarea, diagnosticarea precoce și tratamentul adecvat al sindromului de compartiment și sindromului ischemie – reperfuzie.

Implementarea rezultatelor științifice. Rezultatele obținute au fost implementate în activitatea secțiilor de chirurgie a Institutului de Medicină Urgentă, Chișinău. S-au obținut 7 acte de implementare a inovațiilor.

SUMMARY

Predenciuc Alexandru, „**Diagnostic and curative approach in non-traumatic acute limb ischemia**”. The thesis for the degree of Doctor of Medical Science, Chisinau, 2024.

Structure of the thesis. The thesis includes 167 pages of the main text: introduction, five chapters, general conclusions and practical recommendations, 25 figures and 21 tables. The bibliography includes 218 references. The principal results of the study were published in 22 scientific papers.

Key words: acute limb ischemia, clinical diagnosis, imaging, surgical treatment.

The aim of study. Determination of the possibilities for improving the diagnosis and treatment of patients with acute limb ischemia, based on the identification of perioperative factors that have a negative impact on the results of urgent revascularization interventions.

Objectives of the study. Study of the demographic, clinical and paraclinical characteristics of the contemporary cohort of patients with acute limb ischemia undergoing revascularization interventions. Evaluation of preoperative management and assessment of the value of different diagnostic methods of acute limb ischemia. Development of the method for predicting the early outcome of revascularization interventions, based on available criteria for analysis at the preoperative stage. Analysis of early and long-term results after urgent revascularization interventions and identification of factors associated with amputation risk and/or patient death. Determining the clinical-evolutionary particularities and the results of surgical treatment of special forms of acute ischemia - with upper limb ischemia and associated with SARS-CoV-2 infection.

Scientific originality and novelty. For the first time in the Republic of Moldova, a prospective scientific cohort study was carried out in patients with acute limb ischemia and allowed the complex evaluation of the clinical and demographic characteristics, the peculiarities of the diagnostic-curative approach and the results of the treatment. For the first time, the use of non-contact infrared thermometry was proposed for the pre- and postoperative examination of patients with acute limb ischemia. It has been shown that the degree of patient frailty and the severity of ischemia, evaluated with the help of the "MoST-Do" score developed in the study, represent the true risk factors associated with the unfavorable outcome of revascularization interventions. Prospective external validation of the value of the Baligh ultrasound sign was performed and demonstrated its acceptable diagnostic performance in determining the cause of arterial occlusion.

Theoretical significance and applicative value. The identification of preoperative risk factors, associated with the failure of the revascularization intervention in patients with acute limb ischemia, allowed the prediction of the outcome of the operation and the scientifically reasoned selection of the curative tactics. Based on the research results, was demonstrated the necessity and usefulness of including non-contact infrared thermometry examination in the diagnostic procedure, applied to patients with acute limb ischemia. The study data identified a number of possibilities for improving the outcomes of treatment of acute limb ischemia: education of patients in risk group; rational use and monitoring the effectiveness of antithrombotic treatment; prognosis, early diagnosis and appropriate treatment of compartment syndrome and ischemia-reperfusion syndrome.

Implementation of scientific results. The results of study were implemented in the clinical activity of the departments of surgery at Institute of Emergency Medicine from Republic of Moldova. Seven acts of implementation of the results were registered.

РЕЗЮМЕ

Преденчук Александр **„Диагностические и лечебные подходы при острой нетравматической ишемии конечностей”**. Диссертация на соискание учёной степени кандидата медицинских наук, Кишинэу, 2024.

Структура диссертации. Работа изложена на 167 листах и включает: введение, 5 глав, выводы и практические рекомендации, 25 иллюстраций и 21 таблицу. Библиография насчитывает 218 источников. По теме диссертации опубликовано 22 научные работы.

Ключевые слова: острая ишемия конечностей, клинический диагноз, инструментальная диагностика, хирургическое лечение.

Цель работы. Определение возможностей усовершенствования подхода к диагностике и лечению острой ишемии конечностей на основании выявления пери-операционных факторов, оказывающих негативное влияние на исход срочных реваскуляризирующих вмешательств.

Задачи исследования. Изучение демографических, клинических и параклинических характеристик современной группы больных, реваскуляризированных по поводу острой ишемии конечностей. Оценка предоперационного ведения больных и определение роли различных методов диагностики при острой ишемии. Разработка метода прогнозирования исхода реваскуляризации, основанного на данных предоперационного обследования. Анализ ранних и отдалённых результатов срочных сосудистых вмешательств с идентификацией факторов, влияющих на риск ампутации и/или смертельного исхода. Определение особенностей клинического течения и результатов хирургического лечения частных форм острой ишемии – с поражением верхней конечности, а также случаев, связанных с инфекцией SARS-CoV-2.

Научная новизна. Впервые в Республике Молдова было проведено проспективное научное исследование по проблеме острой ишемии конечностей, позволившее комплексно оценить клинико-демографические характеристики пациентов, особенности применяемых лечебно-диагностических подходов и их результаты. Предложен новый подход с использованием инфракрасной термометрии для пред- и послеоперационного обследования больных с острой ишемией. Доказано, что степень «хрупкости» пациентов и тяжесть ишемии, оцененная при помощи разработанного в исследовании счёта „MoST-Do”, являются достоверными факторами риска неблагоприятного исхода реваскуляризации. Проведена проспективная валидация диагностической роли ультразвукового признака Балиг и доказана возможность его использования для установления причины острой артериальной окклюзии.

Теоретическая и практическая значимость. Выявление факторов риска неудачи реваскуляризации при острой ишемии конечностей позволяет прогнозировать исход вмешательства на предоперационном этапе и научно аргументировать выбор лечебной тактики. Результаты исследования доказали необходимость и рациональность включения инфракрасной термометрии конечности в диагностический подход при острой ишемии. Полученные данные определили ряд возможностей для улучшения результатов лечения острой ишемии конечностей: информирование больных группы риска; рациональное применение и мониторинг эффективности антитромботической терапии; прогнозирование, ранняя диагностика и своевременное лечение компартмент-синдрома и синдрома «ишемия-реперфузия».

Внедрение результатов исследования. Зарегистрировано 7 актов о внедрении полученных научных результатов в практическую деятельность отделений хирургии Института Срочной Медицины Республики Молдова.

ABBREVIATIONS

ABI – ankle brachial index
AFS – amputation free survival
ALI – acute limb ischemia
aPTT – activated partial thromboplastin time
AUC – area under curve
PAD – peripheral artery disease
CFK-MB – creatine phosphokinase, myocardial band
CTA – computed tomography angiography
CW-Doppler – continuous wave Doppler
DSA – digital subtraction angiography
DUS –duplex ultrasound
EFS – Edmonton frailty scale
INR – international normalized ratio
IRS – ischemic reperfusion syndrome
IQR – interquartile range
SII – system immune-inflamation
NLR – neutrophil to lymphocytes ratio
NNH – number needed to harm
NS – not-significant statisticaly
OR – odds ratio
Or_{adj} –adjusted odds ratio
PLR – platelet to lymphocytes ratio
ROC – receiver operating characteristic
RR – relative risk
SD – standard deviation
TEE –trombembolectomy
ΔT_{max} F-M – maximum gradient of temperature between forehead and affected limb

PREDENCIUC ALEXANDRU

DIAGNOSTIC AND TREATMENT APPROACH IN NON-TRAUMATIC ACUTE LIMB ISCHEMIA

321.13 SURGERY

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