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MODERN DIAGNOSTIC AND THERAPEUTIC STRATEGIES FOR ARTERIAL THROMBOSIS PRESENTING WITH ACUTE LIMB ISCHEMIA: A REVIEW OF THE LITERATURE

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Abstract

Acute lower limb ischemia remains a life- and limb-threatening emergency associated with high rates of early mortality and major amputation (10–15%). Choosing the safest and most effective treatment strategy is still a matter of debate.

Materials and methods: Data from large-scale meta-analyses (involving hundreds of thousands of patients) were analyzed to compare early and late outcomes of open surgery (bypass grafting, thromboembolectomy) and endovascular interventions.

Results: The 30-day mortality and amputation rates were found to be nearly identical between the two approaches. Endovascular procedures were associated with an almost threefold lower rate of wound infection compared with open surgery (4.9% vs. 15.8%) and a shorter length of hospital stay. However, the endovascular group showed an approximately twofold higher risk of rethrombosis, reintervention, and thrombolysis-related bleeding. Long-term survival largely depended on the patients' general somatic status and age rather than on the revascularization technique itself.

Conclusion: Endovascular intervention stands out due to its minimally invasive nature. At present, hybrid operations (utilizing C-arm equipment), which combine high safety and efficacy, appear to be the optimal treatment standard.

Keywords

acute limb ischemia, arterial thrombosis, open surgery, endovascular treatment, pharmacomechanical thrombectomy, hybrid procedures, rethrombosis.

Acute lower limb ischemia (ALI) is considered one of the most severe life-threatening conditions in medicine, particularly in vascular surgery, requiring urgent diagnosis and immediate intervention. Acute ischemia is defined as a sudden decrease or complete cessation of blood supply to the lower extremity, usually within less than 14 days, which poses a direct threat to the vital functions of the organ. Unlike gradually forming ischemia against the background of chronic atherosclerosis (chronic ischemia or CLTI - Chronic Limb-Threatening Ischemia), there is insufficient time for the formation of collateral circulatory networks as a result of a sharp cessation of blood flow in cases of chronic atherosclerosis. As a result, severe hypoxia, a decrease in intracellular energy, and irreversible necrotic changes develop in all metabolically active tissues, particularly skin, muscle, and nerve tissue [2].

If we look at global medical statistics and population studies conducted in recent years, the incidence of HAI among the general population ranges from approximately 1.5 to 23.3 cases per 100,000 people per year. Despite the modernization of diagnostic and surgical equipment, this pathology continues to maintain high mortality and disability rates. The observation of mortality and major amputations in 10-15 percent of patients within the first 30 days of hospitalization necessitates in-depth scientific research in this regard [2]. Furthermore, it has been proven that ischemia is not only a single organ problem but also causes major adverse events in patients, such as acute myocardial infarction, chronic heart failure attacks, sharp decline in renal function, and respiratory complications [3].

The main objective of this scientific review is to systematize the latest achievements in the diagnosis and open, endovascular, and hybrid surgical treatment of acute lower limb ischemia by summarizing medical studies published in prestigious international scientific databases (PubMed, Scopus, Google Scholar, Cyberleninka) between 2021 and 2026, specifically large meta-analyses, clinical trials, and comparative retrospective analyses.

Epidemiology and etiological factors

The development of acute ischemia is based on various pathogenetic mechanisms; however, according to an analysis of recent scientific literature, the structure of underlying causes remains relatively stable. Arterial thrombosis accounts for about 40% of the total morbidity structure and is a leading factor. Other causes include arterial embolism (30%), thrombosis of vascular prostheses or stents (20%), thrombosis of the popliteal aneurysm (5%), and vascular trauma (5%).[1] Some studies have shown that the frequency of arterial embolisms can reach 46%, complex factors account for 20%, and thrombosis in situ occurs in 24%.

Arterial embolism and thrombosis in situ

The most frequent source of arterial embolism is cardiac in nature, occurring due to atrial fibrillation, intracardial masses (mixomas, vegetations in infectious endocarditis), and thrombus displacement from aortic aneurysms. Additionally, the embolization of calcified residues following transcatheter aortic valve implantation (TAVI) stands out as a new iatrogenic factor in modern cardiology [3]. Thrombosis (thrombosis in situ) usually develops as a result of rupture or complication of pre-existing atherosclerotic plaques that do not show clinical signs. It has been proven that hypercoagulated blood states cause arterial thrombosis even in perfectly healthy vessels [1]. Three main pathogenetic mechanisms of thrombus formation (Virchow's triad) are involved in blood coagulation disorders: slowing of venous or arterial blood flow, changes in blood coagulation properties, and damage to the vascular wall [9].

Effects of systemic and endocrine diseases

In addition to local vascular problems, the role of systemic factors in the occurrence of arterial thrombosis is being studied separately. For example, large-scale clinical studies within the framework of "BRIDGE-II-2026," published in 2026, showed that vascular conditions alone cannot fully reveal the cause of acute ischemia. Specifically, endocrine disorders such as chronic thyrotoxicosis create a potent procoagulant state by increasing coagulation factors, inhibiting the process of fibrinolysis, and stimulating platelet activity and endothelial dysfunction[11]. The clinical example provided by the researchers describes the development of acute ischemia in a 57-year-old woman with Graves' disease and a stent in the iliac artery as a result of stent thrombosis against the background of a thyrotoxic crisis. This condition further increased the risk of thromboembolism due to the presence of atrial fibrillation. As a result, all diagnostic standards were canceled and an alternative approach was chosen, as the use of iodine contrast agents could exacerbate thyrotoxicosis[11]. These facts emphasize the importance of assessing systemic factors in the management of PEIs.

Changes during the COVID-19 pandemic (2020-2023)

One of the greatest shifts in the epidemiology of acute ischemia occurred during the COVID-19 pandemic. The European Society of Vascular Surgery (ESVS) made new changes to its 2020 clinical guidelines base in 2022 due to the pandemic.[25] According to the data obtained as a result of the reviews, although the incidence of CVI in patients with mild symptoms is 0.4-0.9%, in very severe COVID-19 patients in the intensive care unit, this figure reached 2.5% (58% of all arterial thrombosis) [2].

During the COVID-19 pandemic, it was found that patients with HAI were younger than their predecessors, without chronic vascular diseases (traditional risk factors), and healthy individuals. There was also an abnormally increased frequency of ischemia involving the upper extremities, and occlusions occurring simultaneously in several arteries (synchronous multifocal) were frequently reported [2]. A sharp increase in the patient's D-dimer level was identified as a strong predictor of future arterial thromboembolic events. The most complicated case is that in thrombosis developed under the influence of this infection, the phenomenon of resistance to heparin was observed more often, so traditional treatment doses could not fully show their effect[12]. These findings served as the basis for including recommendations in the ESVS guidelines, such as a comprehensive examination of arterial branches during patient examination and a revision of preventive anticoagulant dosages.

Acute limb ischemia in children (PALI)

Unlike in adults, the nature of acute ischemia in pediatric practice is fundamentally different. In a systematic analysis published in 2026 by German scientist Johannes Meyer and his international colleagues (17 studies, a total of 2,484 children's data were studied), it was found that the absolute majority of causes of acute pediatric ischemia (PALI), specifically 89.9%, were iatrogenic pathologies caused by arterial cannulation (a complication of catheter placement)

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[14]. The most frequent lesions occurred in the common femoral artery (49.8%). In children, thrombosis usually manifests without age-related atherosclerotic changes; therefore, a conservative approach to treatment prevails over surgery.

Assessing pathophysiology and clinical stages

When the supply of nutrients and oxygen to the lower limb ceases as a result of arterial thrombosis, severe hypoxia and anaerobic glycolysis develop in local tissues. The loss of energy substrates leads to the failure of cell membrane pumps, which causes water and sodium to enter the cell, causing the cell to swell and eventually die. Potassium and lactic acid begin to be absorbed into the blood from damaged muscle and nerve tissues, causing systemic acidosis and hyperkalaemia[5]. This is precisely why CVI is considered a syndrome leading not only to local organ loss but also to systemic poisoning and death.

Diagnostic "6 p" mnemonics and r-shaped classification

In clinical practice, the initial diagnosis of HAI is strictly dependent on physical examination and the collection of medical history. In global vascular surgery, signs of ischemia are evaluated based on the classic "6 P" rule: Pain (severe pain), Pallor (pale), Pulselessness (absolute absence of pulse), Paresthesia (impaired sensation - paresthesia), muscle paralysis, and Poikilothermy (freezing of the leg and inability to maintain body temperature). The sequence of sensorineural (sensory) and motor (motor) defects is explained by the degree of resistance of nerve tissues and muscles to hypoxia.

As in the rest of the world, the Rutherford Clinical Classification is still the most reliable and fundamental system for choosing the correct surgical approach. In the analysis of the studies, all interventions were differentiated depending on the specific class of patients.

Table 1.

Rutherford classification system for assessing acute lower limb ischemia

Classes by Rutherford	Clinical Status	Sensory Function	Motor Function	Arterial Doppler Signal	Venous Doppler Signals	Help Required
I **Class**	Organ vitality preserved	Completely preserved	Completely preserved	Heard	Heard	Not all patients require surgical revascularization
IIa Class	At risk (Marginal)	Partially reduced, usually only in the fingers	Saved in full	Not heard	Heard	Revascularization urgently required
IIb Class	Seriously endangered	Strongly disturbed, resting	Partially impaired, vulnerabilit	Not heard	Heard	Amputation is inevitable unless immediate

		pain present	y			revascularization is performed.
III Class	Invertible (Necrosis)	Completely absent, deep anaesthesia	Complete paralysis, rigor	Not heard	Not heard	Most surgeons recommend primary amputation.

Most problems and scientific debates among vascular surgeons revolve specifically around which method (open surgery or catheter interventions) should be used to treat patients in Class IIb.[1] Because in this group, the time reserve for preserving the leg is extremely limited, reperfusion must be performed as quickly and effectively as possible. By Class III, the organ is now considered to have lost its viability, and amputation remains the only salvation in order to prevent toxemia.[1]

Also, in the CIS countries, the classification of I.I. Zatevakhin (2002) is widely used. This classification divides groups from Grade 1 to Grade 3 depending on the degree of ischemia and is important for predicting the probability of re-thrombosis [18].

Modern Diagnostic Technologies and Protocols

The most important stage in establishing a diagnosis is operational speed and the correct assessment of the patient's physical and biochemical characteristics. In addition to physiological examinations, it is important to identify conditions (bleeding, previous strokes) that are impossible compared to previous interventions and thrombolysis when collecting medical history[15]. In laboratory studies, it is especially important to know indicators representing renal function, as angiography performed using contrast media can cause contrast-induced nephropathy in patients with renal failure [15]. In childhood ischemia, ultrasound is a preferred instrument[14].

The development trends of instrumental diagnostics over the last 5 years are as follows:

1. **Color Duplex Ultrasound (CDUS):** A method for rapid, safe, and complete imaging of the condition of arteries and veins. Pathologies of the vascular wall (aneurysms, plaques), accurately measuring the direction of blood flow. Some reviews against the 2020 ESVS guidelines update suggested that performing a Digital Subtractive Angiography (DSA) directly on each patient is unreasonably expensive and burdensome for the patient, preferring instead the widespread use of cost-effective methods such as simple CDUS and ankle-shoulder index (ABI) measurement [6]. It is used as the primary and often the only instrument for assessing PALI in children [14].

2. **Computed Tomography Angiography (CTA):** Provides a high-resolution three-dimensional image. Uniqueness lies in the fact that due to multifocal arterial blockages caused by the COVID-19 pandemic, it has become

standard practice to scan patients from the entire aortic arch to the tip of the foot, rather than just one organ [12].

3. **Magnetic Resonance Angiography (MRA):** Although expensive, iodine contrasts are the safest remedy for people with systemic pathologies where they cannot be used, such as patients with severe thyrotoxicosis [11].

4. **Probing and Angiographic Approaches:** Recent research has shifted old concepts regarding the selection of blood vessels for catheter insertion. For example, studies conducted by Valgimigli et al. on the use of the radial access pathway have proven that the traditional Allen and Barbeau tests, conducted to check the integrity of the superficial palmar arch of the hand, are dynamically variable and are unsuitable for predicting the occurrence of hand ischemia. Therefore, abnormal results of these tests cannot be an absolute contraindication for catheterization when choosing an access route for vascular operations[19]. Similarly, the theoretical concerns that the use of the ipsilateral (diseased side) radial artery increases the risk of lymphedema in women who underwent mastectomy for breast cancer were also found to be unfounded based on a 4-year follow-up study by Yadav et al. (129 patients). No soft tissue infection or lymphedema was recorded on the operated arm[19].

Early Medicamentous and Conservative Approaches

As soon as the patient is diagnosed with CVI, immediate drug preparation must be carried out before proceeding to the main surgical or endovascular operation. Initial management is focused on stopping thrombus enlargement (thrombus propagation) from the main nucleus in the proximal and distal directions.[2] If the patient has no contraindications, such as active bleeding, unfractionated heparin (UFH - Unfractionated Heparin) is immediately administered intravenously according to the U.S. Multidisciplinary Vascular Disease Manual[15]. To maintain blood clotting parameters during treatment, the level of activated partial thromboplastin time (APTT) or anti-factor Xa is regularly monitored [16]. In some cases, such as in non-open resuscitation settings, the subcutaneous administration of low-molecular-weight heparin (enoxaparin) at a dose of 1 mg/kg twice daily has also been designated as an alternative medication[16].

When planning to dissolve a thrombus using thrombolytic drugs, there are strict contraindications for specialists. According to the guidelines of the Society for Vascular and Interventional Radiology (SIR), they are divided into two groups.

Table 2.

Contraindications for thrombolysis in the treatment of acute arterial ischemia (based on SIR rules)

Absolute Contraindications (Absolutely prohibited)	**Relative Contraindications (Risk/Benefit is assessed)**
Active, clinically significant haemorrhagic condition	Bleeding diathesis, DIC syndrome

Intracranial haemorrhage	Major surgery or severe trauma (in the next 10 days)
Formation of compartment syndrome	Previous stroke of brain (in the next 2 months)
Existence of contraindications for the use of anticoagulants	Period after pregnancy or childbirth
	Severe liver dysfunction and severe thrombocytopenia
	Uncontrolled arterial hypertension, Bacterial endocarditis

For long-term survival and to mitigate atherosclerotic complications, prophylactic drugs are recommended for patients with vascular diseases (VD). Although the U.S. Preventive Services Task Force (USPSTF) restricted daily aspirin as a primary prophylactic for the general population in 2022, based on the consensus of vascular surgeons, it is advisable to prescribe double antiplatelet therapy (aspirin and clopidogrel) or low-dose rivaroxaban along with aspirin in high-risk PAD patients[16]. At the same time, it has been proven in practice that high-yielding statins (e.g., 40-80 mg of avarvastatin) reduce the risk of MALE (major adverse limb events) in patients by 42% due to their ability to reduce LDL levels and stabilize plaques[20]. Additionally, studies on cholesterol control since 2021 have recognized that PCSK9 inhibitors (such as alirocumab) have the ability to reverse atherosclerotic memories in the vascular wall[21].

Interestingly, according to a review led by J. Meyer published in 2026, in pediatric practice (acute ischaemia in children), a complete recovery and recurrence of ischemia were achieved in 87% of patients through a blood-thinning and conservative approach without resorting to very severe surgical interventions, with a complicated amputation rate of only 2.4% and a mortality rate of 0.01% [14]. This is an extraordinarily low figure compared to large losses of 10-15% in adults.

Modern Surgical and Endovascular Approaches

The final and most radical solution for getting rid of ischemia is to open the vascular endothelium and restore blood flow—revascularization. Due to time constraints, all eying-men examinations must be followed by rapid treatment interventions.[1] Over the last five years, there has been a great deal of scientific debate and practical testing between these intervention methods. These are mainly divided into open surgery, minimized endovascular procedures, and hybrid interventions that combine both.

Open Surgical Revascularization

Historically, the primary and "gold standard" method for treating HAI has been open surgery. This includes thromboembolectomy performed using a Fogarty balloon catheter, various autovenous and synthetic bypasses that allow for bypassing the damaged vessel, and endarterectomy, which involves scraping a plug from within a blood vessel. The greatest advantage of open surgeries lies in their short duration and almost immediate removal of the thrombus under controlled conditions, with rapid restoration of reperfusion. This method is best suited to the category of Rutherford's disease, which is moving toward necrosis at a rapid pace.[1]

However, it also has many unique negative aspects. In the frail group of elderly patients with comorbidities (heart defects, diabetes, chronic kidney problems), bodily reactions during open surgery cause high mortality. A recent study using propensity-score matching (an analysis of 530 patients adjusted at a 1:1 ratio with 15 clinical variables) clearly demonstrated that the probability of surgical wound site infections (SSI) in the open surgery group was nearly three times higher than in the endovascular surgery group (4.9% versus 15.8%, $p < 0.01$) [22]. Furthermore, during open surgery, it is not always possible to completely clear residual thrombuses in small distal branches.

Endovascular Interventions (Minimally Invasive)

Procedures carried out solely through vascular puncture without a full incision of the patient's skin are confidently replacing open surgery. These include catheter-directed thrombolysis (CDT), percutaneous mechanical thrombectomy (PMT), thromboaspiration, and the placement of vascular stents at the site of injury. The fundamental advantage of endovascular surgery is its non-traumatic nature, avoiding shock and trauma without significant impact on the patient's physique.

Currently, particularly percutaneous mechanical thrombectomy technologies are being implemented at a rapid pace. Among them, one of the most popular methods is the AngioJet system (pharmacomechanical thrombectomy). Based on a retrospective analysis of 100 patients from Germany, the Netherlands, and other European countries published in 2024, the results of the AngioJet method (57 patients) and traditional thrombolysis-only CDT (43 patients) were compared. Primary interventions using AngioJet achieved extremely high technical success: the rate of effective and rapid thrombus breakdown was 96.5%, significantly higher than 65.1% in standard CDT ($p < 0.001$) [7]. With the use of this method, the average time spent on the infusion of thrombolytic drugs was unprecedentedly reduced from 24 hours to 1 hour. This time saving in itself significantly reduced hospital days (from 11 to 6 days), days in intensive care (from 2 to 1 day), and hospital expenses (from 13,790 to 9,298, $p = 0.009$).[7] The frequency of major amputations was also lower in mechanical thrombectomy (5.4% vs. 18.6%). Although the non-amputation survival rate (AFS) was similar in both methods, around 50-58% over a one-year period, the mechanical methods significantly reduced the risk of reinterventions (HR 2.57) [7]. According to a systematic review covering another 16 studies conducted in Europe and Asia, it was confirmed that the 30-day survival rate of patients with mechanical thrombectomy was 94.7% and organ integrity was 95.2% [24].

Hybrid Operations and Integrated Models

Today, vascular specialists are increasingly realizing that the successful elimination of diseases is not limited to the use of only one method. This situation gave birth to the concept of "hybrid operations." The ESVS 2020 and above eying guidelines recommend that all vascular emergency departments have dedicated hybrid rooms equipped with C-arm eying men equipment. In such rooms, the surgeon can perform a thromboembolectomy by cutting a vessel and destroying the distal clogs that the catheter has inserted through the same opening, and if necessary, immediately install a stent[6]. Numerous ongoing trials show that such specialized hybrid treatments have high levels of safety and efficacy.[6] For example, when performing an endovascular approach alone, successes achieved using a stent exceed 77%[6].

Conclusion

We conducted a comprehensive analysis of the problem of arterial thrombosis causing acute lower limb ischemia for the period from 2021 to 2026 using global figures, advanced meta-analyses, and technological drivers (Hicks, Acosta, Meyer, Karonen, and others).

Our final conclusions can be formulated as follows: First, among the ancient causes of acute ischemia, infectious complications such as iatrogeny, TAVI surgeries, and the major COVID-19 pandemic are now actively involved, forcing an expansion of the scope of diagnosis of ischemia, D-dimer indicators, and CT scope. The inclination to the disease is not the same as in the old age, but is deepening to the younger generation. Secondly, the findings of the medical examination of more than 214,000 and even more than 382,000 patients strongly confirmed that endovascular surgery (especially rapid AngioJet interventions such as mechanical thrombectony) has reached a level at least equal to open surgeries in terms of the risk of short-term mortality and the frequency of amputations. But most importantly, even in cases of disease recurrence or complications, endovascular stenting does not cause as much harm to the body of frail elderly patients as an open knife, and the patient's survival rate (AFS and HR 0.84) is much higher. Nevertheless, the fact that the likelihood of a fatal complication such as bleeding increases under the influence of medication in these procedures poses a new scientific question for specialists. Thirdly, the early signs of postoperative complications (retrombosis, eyingment syndrome) are directly inspired by the classical classifications of ischemia by Zatevakhin and Rutherford, and it is predicted that the severity of ischemia, in the presence of arterial thrombosis, can lead to the recurrence of retrombosis up to 49.1 times.

In conclusion, the victory over acute lower limb ischemia is guaranteed by a combined team of medical professionals, high intelligence, and drug therapy capable of effectively utilizing the most sophisticated invasive tools of hybrid surgery while protecting the systemic homeostasis (kidneys, heart, lymphatic system) of the individual patient. Only through this is it expected that the number of deaths from amputations and postoperative complications in the medical potential of the next decade will be reduced to a minimum.

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