ANALYSIS OF ASSOCIATED DISEASES IN PATIENTS WITH ACUTE CRITICAL LOWER LIMB ISCHEMIA

**Analysis of Associated Diseases in Patients with Acute Critical Lower Limb Ischemia**

Vladimir MANOJLOVIĆ, Vladan POPOVIĆ, Dragan NIKOLIĆ, Đorđe MILOŠEVIĆ, Janko PASTERNAK and Miloš KAČANSKI

**Summary**

**Introduction.** Acute critical lower limb ischemia refers to the state of severely impaired vitality of lower limbs due to acute occlusion of arterial blood vessel by a thrombus or emboli. Surgical revascularization in the first 6-12 hours after the onset of symptoms gives the best results. However, a high mortality rate and probability of limb loss make this problem more debatable, and can be related with associated diseases.

**Material and Methods.** This research included 95 patients who had been operated within the first 12 hours after the onset of symptoms of critical limb ischemia. We collected the following data: age and sex of patients, etiology of limb ischemia, type of operation, associated diseases and outcome of treatment.

**Results and Discussion.** Most of the patients were 70 to 80 years old, both sexes being equally represented. There was significantly more arterial embolism (70%) than thrombosis on the prior arterial lesion. Most of the embolizations were treated with Fogarty balloon catheter embolectomy (98%); however, a great number of arterial thrombosis demanded more complex “inflow” and “outflow” ensuring procedures such as thromboendarterectomy and bypass (33%). The performed surgical procedures showed no statistical differences when final outcome was analyzed. Amputation had to be performed in about 3% of the patients and all of them were diabetics. Mortality rate in this research was 10.5% and 7/10 with this outcome had severe form of chronic myocardiopathy and metabolic decompensation.

**Conclusion.** Acute critical lower limb ischemia should be treated surgically as soon as possible. Negative outcomes are associated with comorbidity and general condition of the patient.

**Key words:** Acute critical ischemia; Thrombosis; embolism; Thrombectomy; Bypass; Chronic cardiomyopathy; Diabetes

**Sažetak**

**Uvod.** Akutna kritična ishemija donjih ekstremiteta označava stanje ugroženog ekstremiteta nastalo usled naglog začepljenja njezinstvenog suda trombom ili embolom. I pored hitne hirurške revaskularizacije, krajnji rezultat je neizvesan na šta u velikoj meri utiče opšte stanje bolesnika. **Materijal i metode.** Ovaj rad je obuhvatio 95 pacijenata oba pola sa akutnom kritičnom ischemijom donjih ekstremiteta koji su tretirani hirurški unutar 12 sati od početka simptoma. Analizirana je starost i pol pacijenata i etiologija ishemije, vrsta tretmana i ishod tretmana. **Rezultati i Diskusija.** Pоказано je da je najveći broj pacijenata bio starosti između 70 i 80 godina i da su oba pola bila podjednako zastupljena. Bilo je sigurno sažetno više arterijskih embolija (70%) u odnosu na trombozne arterije na hroničnoj leziji. Najveći broj embolije (98%) tretiran je embolektomijom Fogartijevim katetorom dok je kod pacijenata sa trombozom, izraženo visokim procentom (33%), bila potrebna složena procedura trombendarterektomije ili bajpsa radi poboljšanja utoka i otoka. Bez obzira na vrstu operacije, krajnji ishod nije pokazivao statistički značajne razlike. Uspešna revaskularizacija postignuta je kod 86% pacijenata, amputacija je učinjena kod 3,2% i svi pacijenti su bili dijabeticari. Smrtni ishod zabeležen je kod 10 pacijenata (10,5%) od kojih je kod 7 zabeležena srčana i metabolijska dekompenzacija. **Zaključak.** Akutna kritična ishemija donjih ekstremiteta mora se tretirati što ranije i hirurški. Neuspjeh se može pripisati udruženim bolestima i lošem opštem stanju pacijenta. **Ključne reči:** Akutna kritična ishemija; Tromboza; Embolija; Trombektomija; Bajpsa; Hronična bolest srčanog mišića; Šećerna bolest

**Introduction**

Acute ischemia of the lower extremities is caused by a sudden interruption of arterial circulation. The most frequent causes are the obstruction of blood circulation by thrombus and embolus, and due to trauma, dissection, or external compression of the vessel.
The typical clinical picture consists of a sudden onset of pain in the affected extremity, pallor, coldness, numbness, loss of arterial pulsation on predilection sites. Further on, ischemic neurological deficit of the sensory and motor neuron can deteriorate and if paresis or paralysis develops, it becomes acute critical ischemia of the lower limb (ACLI) [1]. The term "critical ischemia" refers to the vitally threatened limb when only emergency (surgical) revascularization can prevent amputation. The acronym "six P’s" stands for pain, pressure, paralysis, paresthesia, pallor and pulselessness.

According to Rutherford classification of acute ischemia of the lower extremity, there are three classes: class I and IIa for sub-critical ischemia, class IIb for vitally threatened limb without indications for immediate amputation, and class III for critical ischemia and irreversible changes and necessary surgical ablation at the appropriate level [2].

The first changes in extremities occur 2-3 hours after the occlusion and are visible in the microcirculation: reduced flow in the capillaries, subintimal edema, tearing of the elastic lamina and interaction of fibrin, thrombosis of the vasa vasorum as well as hemorrhage in the media. The metabolism is shifted toward anaerobic, there is a loss of potassium from the cells and hyperkalemia, acid products accumulate and the activity of proteolytic enzymes increases. As a final result, irreversible changes may occur 6 hours after the onset of symptoms especially in case of insufficient collateral blood supply, thus exaggerating the patient’s general condition.

In case of revascularization, a sudden release of acid and decay products and potassium from the extremities to the systemic circulation results in myoglobinuria, acute renal failure and heart failure. At the same time oxygen radicals in the revascularized extremity cause further tissue damage through lipid peroxidation. Intumescence of tissues caused by osmotic pressure inside the fascial compartments exerts further external compression of the blood vessels, thereby worsening ischemia even after revascularisation. In this case the urgent fasciotomy is indicated. These changes make the "reperfusion syndrome" [3].

Thrombosis and embolism, as the leading cause of acute ischemia of the lower extremities, can be differentiated according to the clinical picture. Thrombosis occurs in the blood vessels that are already affected and altered by systemic atherosclerosis, it is often preceded by claudication; the symptoms develop slowly; and the signs of peripheral atherosclerotic disease (PAD) are evident in the contralateral extremity. Acute exacerbation is caused by plaque rupture and thrombosis or hypercoagulable-hypokinetic conditions such as heart failure, dehydration, etc.

Embolism of large vessels is usually cardiogenic and embolus is formed due to atrial fibrillation after myocardial infarction or in the presence of cardiac aneurysm, valvular disease, etc. The bifurcation of the great arteries of the lower limbs is affected, 60% of the femoral and 30% of popliteal bifurcation [4].

Time is a decisive factor in the treatment of ACLI. It is a medical emergency that must be recognized in due time and the patient must be transported promptly and properly to a surgical facility. Only necessary diagnostic procedures should be implemented if it is the case of critical ischemia and threatened limb. Surgical intervention should be done within 6 hours after the onset of symptoms. Prompt surgical treatment is not the only condition of favorable outcome. According to literature, the death rate is up to 20% and 30% of patients may lose an extremity, even if they are operated within the "golden period" [5].

The reason for this lies in the fact that the patients presenting with acute ischemia of lower extremities already have a number of diseases associated with the described ischemic reperfusion damage and form a vicious circle of feedback. Acute ischemia of the lower limbs is considered to be a disease that occurs at the end of life ("life-end disease") [6], but at the same time, it is also a symptom of serious health disorder or some other disease condition. It is important to see the patient as a whole and begin to treat associated disease at the same time and try to prevent systemic and local effects of acute ischemia.

The study was aimed at determining the effect of etiology of acute ischemia, type of surgical treatment and associated diseases on the final outcome in patients with acute critical ischemia of lower limbs by analyzing the early results of urgent surgical revascularization.

Material and Methods

This retrospective study covered the period from 2006 to 2010 at the Department of Vascular and Transplantation Surgery Clinical Center of Vojvodina. The study included 95 patients who came to the emergency surgical service with typical clinical signs of acute lower limb ischemia and who were surgically treated within 6 hours after the onset of symptoms. All patients were classified as class IIb according to Rutherford with a vitally affected limb and the indication for urgent surgical intervention.

This study did not include those patients who had previous reconstructive procedures on blood vessels and where acute ischemia had been induced by trauma or aneurysmal disease of the peripheral blood vessels.

The following parameters were included:
General characteristics: gender, age, duration of hospitalization

Etiology of acute ischemia: embolism or thrombosis, as well as the level of occlusion, which was estimated by the clinical presentation and the final diagnosis was given according to the operative findings.

Type of surgical revascularization: restorative - means a reset to the level before the ischemic incident; reconstructive - changes in vascular bed to improve the in-flow or run-off

Data on co-morbidities were obtained from the medical documentation of patients and on the basis of additional examinations performed on admission and advice of other specialists.

The following diseases and conditions were observed:
1. chronic disease of the heart muscle (CMP) according to the New York Heart Association (NYHA) classification
2. condition after acute myocardial infarction (AMI)
3. atrial fibrillation and absolute arrhythmia
4. diabetes mellitus (DM)
5. peripheral vascular disease (PAD)
6. multiple organ dysfunction with clinical and laboratory signs of acidosis, electrolyte disbalance, dehydration, anemia, uremia
7. other major diseases - chronic renal failure (CRF), malignant disease, condition after stroke, deep venous thrombosis.

The treatment outcome was monitored for 30 days after the first operation and the following outcomes were indicated as possible in that period:
1. the preserved extremity
2. amputation - as the secondary amputation within 30 days
3. fatal outcome

The results are given in percentage and they are presented in graphs. The statistical significance of differences between groups was tested by  $\chi^2$ test. Statistical processing was done in commercial statistical software package MedCalc for W7.

Results

Male and female ratio was 54:41 (56.4% men and 43.6% women) and the difference was not statistically significant. Half of the patients were between the age of 70 and 80, the youngest and the oldest being 41 and 94 years old, respectively.

Significantly more patients were found to have embolism of blood vessel (70 patients, i.e. 73.7%) compared to the number of patients whose etiology of thrombosis was at a chronic lesion (25, i.e. 26.3%) and the $\chi^2$ test, $p <0.05$.

The most frequently performed surgical treatment was Fogarty catheter thrombectomy (89%), whereas fasciotomy was indicated in 6 out of 78 patients (8%) in case of restorative revascularization.

Urgent reconstructive revascularization was indicated in 10 patients (11%) who needed additional procedures because simple restorative procedures were not sufficient:
1) thromboendarterectomy (TEA) of a segment of artery in 7 patients (7.8%) - at the level of bifurcation of the femoral artery in 2 patients and at the popliteal artery bifurcation (below the knee) in 5 patients
2) autologous femoro-popliteal below knee bypass procedure in 3 (3.2%) patients. When the occlusion of blood vessel was caused by emboli, simpler procedures were mostly sufficient, where-

Graph 1. Operative procedures performed in patients with thrombotic and embolic etiology of acute critical ischemia of lower extremities

Graph 2. Statistical significance of differences in treatment outcome in patients with thrombosis and thromboembolism as a cause of acute ischemia of the lower extremities

Graph 3. The most important associated diseases are presented in percents in the attached graphs. The statistical significance of the gaps was tested by $\chi^2$ test.
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is within primary health care. Number of primary amputations could be smaller with the correct initial management of ACLI so it is required continuing education of ordinating doctor who first come into contact with such patients.

This study included patients who had been treated surgically within 6 hours after the onset of symptoms. The decision for surgical treatment was made in relation to the presence of ischemic motor deficit as a criterion for acute critical ischemia. An alternative to the surgical treatment is systemic or catheter induced thrombolysis, but the data in current literature show that such a treatin critical limb ischemia (Class IIb and III) gives significantly worse results. It is indicated in case where sub-critical ischemia is presented, when it provides a quicker recovery, fewer complications, and equally good results as the surgical procedure [7].

In this study, successful revascularization of the lower extremities was achieved in 85% of cases, which is a very good result in comparison with published data, especially if we consider the fact that we included only the patients with critically affected limb [8,9]. Only 3 cases of secondary amputation of limbs were recorded (3.4%) in the follow-up period, which confirms the benefits of early operative treatment in case of critical limb ischemia.

Medical history and clinical picture may be reliable in determining whether a cause of ischemia was thrombosis or embolism and they are often in line with the subsequent intraoperative findings. In the patients with clinical presentation of thrombosis on the chronic lesion, Duplex ultrasonography is a fast and non-invasive method for determining the appropriate level of occlusion, whereas urgent Digital Subtraction Arteriography (DSA) has no advantage over ultrasound at this stage [10].

A significantly higher proportion of patients with thromboembolism in this study was expected since thrombosis in chronic arterial lesions mostly occurred in the patients with more developed collateral circulation, thus it is often manifested by sub-critical ischemia with a gradual and sustained development of symptoms.

Surgical tactics differed in relation to etiology. However, both groups of patients were found to have a similar success rate of revascularization, with no statistically significant differences in relation to the vitality of the limb and overall mortality [11].

The mortality rate of patients with acute critical ischemia of 10.5% is consistent with the data found in the literature [12]. It is the second highest specific mortality rate at our Clinic - after ruptured aortic aneurysm (17%) and the second leading cause of death in the monitored period. Data analysis showed that our patients were mostly 70-80 years old with advanced and poorly controlled form of chronic heart disease and heart failure, polivascular disease, metabolic disorders and other chronic conditions (end-life disease). Thrombosis and embolism of the lower extremities develop in patients who already have a
number of associated diseases and they usually represent their symptoms.

In case when embolism was confirmed as a cause of acute arterial occlusion, chronic myocardial disease and atrial fibrillation with absolute arrhythmia were significantly more frequent than other associated diseases [13]. This finding is not surprising since the heart is the origin of emboli in 70% of cases, the basis being most often atrial fibrillation, myocardial scar, cardiac aneurysm or valvular heart disease. Those patients in whom the diagnosis of embolism had not been made represented a diagnostic problem.

Obliterated PAD is pathognomonic in a similar way for arterial thrombosis and is manifested by a history of claudication and previous clinical findings through the involvement of the contralateral extremity pulse lacking.

Diabetes mellitus is often associated with diseases of blood vessels and contributes to their emergence and development through a number of mechanisms described. It was found in more than a third of patients in our study, being significantly more frequent in the patients with arterial thrombosis in chronic lesions. Diabetes mellitus is a factor that contributes to the reduction of revascularization success since it was present in all three patients who had their affected limb amputated after the initial attempt of revascularization [14].

The worst "ad vitam" prognosis was found in those patients who on admission showed signs of heart failure and disturbed homeostasis, with an imbalance of electrolytes, acid-base disorder status, dehydrated and anemic. The fatal outcome occurred in 2/3 patients with associated chronic heart disease in stages III and IV according to NYHA or Multiple Organ Dysfunctional Syndrome (MODS) [15]. The question is whether the prognosis for these patients would have been better if the intensive treatment measures had been initially combined with the conservative approach to acute ischemia and they had been subjected to delayed surgery. If so, the number of amputations would certainly have been higher.

**Conclusion**

Surgical revascularization in patients with acute critical ischemia of the lower extremities within the first 6 hours after the onset of symptoms provides good results regardless of the cause of ischemia (thrombosis or embolism) and operative treatment.

Early recognition by a local doctor is the first prerequisite for successful treatment. Identification of associated disease may help in diagnosing the etiology of acute ischemia; however, it is also a predicting factor of revascularization success and life prognosis.

In spite of the success of the surgical procedure, the morality rate is very high in patients who have poor general condition, metabolic decompensation and heart failure.

**References**