Evaluation of Medical and Surgical Management of Critical Extremity Ischemia Caused by Atherothrombosis

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Aim: To assess efficacy of surgical and medical (conservative) treatment of acute exacerbation of chronic extremity ischemia by evaluating their early therapeutic outcomes in terms of mortality, extremity amputation and reamputation rate, limb salvage rate and length of hospitalization period.

Patients and methods: Patients were divided into two groups based on method used for the treatment of critical ischemia. Group A consisted of 40 patients that were subjected to surgical treatment of critical extremity ischemia during period 2004-2009. All patients were subjected to thrombectomy in local anesthesia (2% lidocaine) as initial step of treatment protocol. Urgent Seldinger angiography was performed for all patients that have undergone thrombectomy regardless of successfulness of thrombectomy. Based on angiography findings decision was made about further definitive treatment. It consisted of either using antiaggregating drugs (acetyl salicylic acid; 150 mg/day) if no significant postthrombectomy stenotic lesion was found or subjecting patients to further surgical revascularization in the form of bypass were significant stenosis or occlusion was identified. Group B consisted of 40 patients; all of them received conventional heparin anticoagulation therapy supplemented with vasoactive infusion treatment (Pentoxyohylline 300 mg/day) during period 1998-2004. On the third day of hospitalization oral anticoagulation (Sintrom) was included in the therapy protocol using dosage 2-8mg/day in order to achieve INR 2-4, once therapeutic INR was obtained heparin was withdrawn. Study was clinical, designed as retrospective prospective and was conducted at the Clinic for vascular surgery in Sarajevo.

Results: Mean age in group A was 66,5 years and in group B it was 65,78 years. Lenght of hospital stay in group A was 13,78 days while in group B it was 34,25 days (P value <0,001). Limb salvage rate was 70% in group A and 17,5% in group B (P value < 0,001). In group A, nine amputations were performed (22,5%) while in group B we had to perform 38 amputations (95%), P value <0,001. Only one reamputation was performed in group A (2,5% of patients) while in group B ten reamputations were performed (25% of patients). Mortality rate between groups was not statistically significant (P value <0,077).

Conclusion: Surgical thrombectomy as introduction to definitive treatment of critical limb ischemia caused by atherothrombosis gives statistically superior results in comparison to conservative treatment.

Key words: atherothrombosis, surgical thrombectomy, treatment.
then it is followed by relaxation of arterial wall with consequent deposition of thrombus in arterial segment located distally from the site of occlusion that in turn leads to occlusion of collateral vessels with exacerbation of ischemia (2). Skeletal muscles and nerves tolerate ischemia for about 8 hours without irreversible damage. Skin marmorization due to appearance of reticular cyanosis takes place. Skin can tolerate ischemia for about 24 hours. When period of ischemia tolerance is used up, irreversible phase of ischemia sets in (3). Primary aim of treatment is prevention of mortality and limb loss. Five year mortality in patients with critical limb ischemia reaches up to 70%. Desirable outcome is survival without limb loss (4). Treatment options are aimed at removal of thrombus by surgical or pharmacological means. Then angiographic mapping of affected artery and radiological insight into position, extent and degree of stenotic atherosclerotic lesion is done with subsequent planning of reconstructive procedure. The aim of this study was to assess efficacy of surgical and medical (conservative) treatment of acute exacerbation of chronic extremity ischemia by evaluating their early therapeutic outcomes on basis of following parameters:

- Length of hospitalization period.
- Efficacy of limb salvage between analyzed groups.
- Number of amputation procedures.
- Number of reamputation procedures.
- Mortality rate.

In addition primary, patency of revascularization procedure will be determined.

Current management of this condition is based on urgent thrombolytic treatment followed by additional endovascular or surgical revascularisation of arterial stenotic lesion. In our setting, instead of active thrombolysis we attempted to remove thrombus with Fogarty catheter and then based on angiographic findings we decided about further definitive treatment.

2. PATIENTS AND METHODS

Patients were divided into two groups based on method used for the treatment of critical ischemia. Inclusion criteria were: rest pain, confirmed positive history of previous intermittent claudication, positive risk factors for atherosclerosis. Exclusion criteria were: absolute arrhythmia, extremity rest pain after myocardial infarction, thromboangitis obliterans and thrombosis of arterial aneurysm.

Group A consisted of 40 patients that were subjected to surgical treatment of critical extremity ischemia during period 2004-2009. After confirming diagnosis of atherothrombosis, patients were subjected to urgent thrombectomy of affected artery. Thrombectomy was made in local anesthesia (2% lidocaine). Approach to occluded arterial segment was made via arteriotomy on common femoral artery in case of lower extremity ischemia or through arteriotomy made on brachial or cubital artery in case of ischemia of upper extremity. Fogarty embolectomy catheters Ch 4 or 6 (depending on the size of artery) were used for extraction of thrombus from the artery exploiting technique of anterograde or retrograde Fogarty thrombectomy. Urgent Seldinger angiography was performed for all patients that have undergone thrombectomy regardless of successfulness of thrombectomy. Based on angiography findings that might have revealed the cause of atherothrombosis decision was made about definitive treatment. It consisted of further therapy using anti-aggregating drugs (acetyl salicylic acid 150 mg/day) or subjecting patients to further surgical revascularization in the form of bypass.

Group B consisted of 40 patients; all of them received conventional heparin anticoagulation therapy supplemented with vasoactive infusion treatment (Pentoxyphylline 300 mg/day) during period 1998-2004. Heparin was used as part of a standard protocol for treatment of extremity atherothrombosis at our Clinic until year 2004. On admission, patient received heparin solution intravenously during 6 hour period (20000 IU in 500 ml of Normal Saline) and then every 6 hours bolus intravenous heparin supplementation was administered depending on APTT value according to the following scheme (Table 1).

On the third day of hospitalization oral anticoagulation (Sintrom) was included in the therapy protocol and once value of INR 2-4 was achieved, heparin was withdrawn. In case of favorable response patients continued to receive Sintrom, maintaining INR in therapeutic range (for maximum of 6 months when they would replace Sintrom with Aspirin-100 mg/day indefinitely). Concomitantly with heparin, pentoxyphiline infusion was administered to patients with favorable clinical response for 10 days in total. After that period patients would receive pentoxyphiline per os (400 mg, tid.). Discrepancies in anticoagulation response are based on individual differences in heparin clearance as well as to the value of APTT on administered quantity of heparin (5). Study was clinical, designed as retrospective prospective and was conducted at the Clinic for vascular surgery in Sarajevo.

3. RESULTS

Mean age in group A was 66,5 years and in group B it was 65,78 years. (Table 2). Length of hospital stay in group

![Table 1](image)

<table>
<thead>
<tr>
<th>APTT</th>
<th>HEPARIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-60 sec</td>
<td>10000 IU</td>
</tr>
<tr>
<td>60-80 sec</td>
<td>5000 IU</td>
</tr>
<tr>
<td>80-100 sec</td>
<td>-</td>
</tr>
<tr>
<td>Over 100 sec</td>
<td>Protamine sulphate</td>
</tr>
</tbody>
</table>

**Table 1. Bolus dosage according to APTT**

![Table 2](image)

**Table 2. Age difference between analyzed groups (in years) and statistical significance**

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean</th>
<th>Std. Dev.</th>
<th>t-stat</th>
<th>df</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>66.65</td>
<td>0.388</td>
<td>-0.714</td>
<td>27</td>
<td>0.237</td>
</tr>
<tr>
<td>B</td>
<td>65.78</td>
<td>0.875</td>
<td>2.176</td>
<td></td>
<td>0.034</td>
</tr>
</tbody>
</table>

**Table 3. Length of hospital stay between analyzed groups (in days) and statistical significance**
A was 13.78 days while in group B it was 34.25 days, P value<0.001, (Table 3, Figure 1). Limb salvage rate in group A was 70% and in group B it was 17.5%, P value<0.001 (Table 4, Figure 2). In group A, nine amputations were performed (22.5%) while in group B we had to perform 38 amputations (95%), 33 major amputations and 5 minor amputations; major amputation stands for amputation performed above ankle joint and minor for amputations at the level of foot-below ankle joint (Table 5 and Figure 3). Only one reamputation was performed in group A (2.5% of patients). In group B, 10 reamputations were performed (25% of patients), difference in reamputation rate was statistically significant (Table 6, Figure 4). Mortality rate between groups was not statistically significant, P value<0.077, though in group A we had three cases with death outcome. In group B mortality rate was zero (Table 7).

4. DISCUSSION

Mean age for group A was 66.65 years while for the group B it was 65.78. Difference was not statistically significant to the mean age in other relevant studies (6). Age is important determinant of peripheral arterial disease (PAD) and with advancing age prevalence of PAD increases.

Length of hospital stay is expressed in days and it varies significantly between analyzed groups, (group A= 13.78 days, group B= 34.25; p<0.001). Mean patient hospital stay in surgical group is below mean hospital stay mentioned in Report of National Survey of Great Britain and Ireland (6). 679 patients were included in that study and 70% of them received revascularization treatment; mean hospital stay in that study was 25 days. Length of hospital stay of patients in the group B was longer due to obviously ineffective therapeutical response in terms of failure to improve oxygen delivery to limb periphery and consequently it required higher rate of extremity amputation and reamputation treatments.

Limb salvage rate in group A was successful in 28 out of 40 patients. In group B it was significantly less, it was achieved only in case of 7 out of 40 patients (70 vs. 17.5 %; p<0.001). Although some studies (7,8) report certain therapeutical effect of pentoxifylline in the treatment of chronic critical ischemia in our study its effect was obviously inferior when compared to the results obtained by surgical intervention. Lapestalo et Matzke also noticed significant reduction of limb salvage percentage in the absence of reconstruction for the treatment of chronic critical limb ischemia (9).

In the group that received conservative treatment (group B), 33 amputations were done above ankle joint (major amputations), 5 patients had amputations of digits and 2 patients did not require amputation treatment at all. In summary, conservative therapy was effective in the case of 7 patients (2 patients did not required amputation treatment at all, while 5 patients after minor amputations of digits had successful wound healing and their walking function of foot was undisturbed).

In surgically treated group (group A) thrombectomy was successfully achieved in 29 out of 40 patients. In remaining 11 patients tip of Fogarty catheter came across hard intraluminal resistance that could not be traversed without danger of penetrating arterial wall therefore thrombectomy procedure was abandoned. After urgent Seldinger angiography was performed, thrombectomy per se proved to be sufficient revascularization procedure in case of 20 patients since no haemodynamically significant stenosis was found in affected artery. All these cases coincided with intraoperative finding of soft plaque and thrombus extraction from the artery with remaining denuded arterial wall that was devoid of presence of significant stenosis. Lifelong acetyl salicylic acid therapy - 150 mg/day was administered to all those patients. 3 out of remaining 9 patients after thrombectomy procedure was performed ended up with amputation due to progression of irreversible leg ischemia while other 6 patients were subjected to additional revascularization procedure in the form of bypass with resulting successful limb sal-
complex institutional support. We report need for one reamputation (2.5%) in group A. On the other hand, in the group B due to wound dehiscence of amputation stump and ascending infection, 10 reamputations (25%) were performed. Difference in number of reamputation procedures between analyzed groups is significant; \( p<0.003 \).

There were no statistically significant difference in mortality rate between analyzed groups (\( p<0.077 \)), the first patient died due to postprocedural myocardial infarction, second patient succumbed to massive pulmonary thromboembolism while third patient was lost because of aggravation of general status following stroke for which he was admitted to the stroke unit prior to occurrence and treatment of acute atherothrombotic limb ischemia. Aune and Trippested reported 14% operative mortality after 30 days (12). Wolf and Wyatt reported 26% high mortality rate after one year of follow up period (13).

In National Survey of Great Britain and Ireland total mortality rate for the treatment of critical limb ischemia was 13.5%. Overall score of surgical treatment after 30 days of follow up period was: 28 successful limb salvages (70%), 3 dead cases (7.5%) and 9 patients with major amputations (22.5%). Results of limb salvage rate in our study did not significantly differ from limb salvage rate (75%) reported in National survey of Great Britain and Ireland regarding treatment of critical limb ischemia (1). According to Baily and Saha after analyzing 130 patients in their one year prospective study, limb salvage rate was 61% (14). Primary patency of revascularization treatment in the group A, after 30 days, was 70%. 50% (n=20) of revascularizations were in the form of thrombectomy while 20% (n=8) of them were bypass reconstructions. In British and Irish National survey for the treatment of critical limb ischemia, primary patency of performed revascularization procedures at the time of patient discharge from the hospital was 75% (1).

5. CONCLUSION

Surgical thrombectomy as introduction to definitive treatment of critical limb ischemia caused by atherothrombosis gives far superior results in comparison to conservative treatment in terms of higher limb salvage rate as well as lower rate of amputations and reamputations. Furthermore, patient hospital stay is significantly shorter in the group that received surgical treatment.

Primary patency rate of revascularization procedures performed in this study was 70% and it positively correlates with published results of other European vascular centers.

REFERENCES