The Egyptian Journal of Hospital Medicine (October 2021) Vol. 85 (1), Page 3179-3184

Bypass Surgery versus Endovascular Therapy for Lower Limb Ischemia Due to Infragenicular Lesions

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ABSTRACT

Background: Endovascular and open surgical revascularization are delivered to patients by a variety of vascular specialists. Critical limb ischemia (CLI) is compounded by the fact that there is limited high quality data guiding vascular specialists on the optimal treatment approach.

Objective: The aim of the present study was to assess the better management of patients with critical lower limb ischemia.

Patients and methods: This study included 24 participants diagnosed with critical lower limb ischemia (CLI) due to Infragenicular lesions. They were allocated into two groups: group (1), which include 12 patients undergoing the endovascular therapy (EVT) and group (2) that include 12 patients undergoing the bypass surgical therapy. All patients were subjected to radiological evaluation including X-ray foot, arterial Duplex U-S on affected limb, CT angiography on lower limb arteries and the saphenous vein. The patients followed an appropriate risk factor modification program.

Results: There was no significant difference between the studied groups regards Rutherford classifications ($p > 0.05$). There was a statistically significant increase in frequency of amputation among EVT group versus bypass group ($p = 0.04$). Furthermore, there was a statistically significant increase in frequency of thrombosis among EVT group versus bypass group ($p = 0.03$). On the other hand, there was no statistically significant difference between the studied groups that underwent different surgical techniques regarding complications. Kaplan Meier curve showed cumulative survival from major amputation following infrapopliteal angioplasty and bypass treatment over the study period.

Conclusion: Endovascular intervention is considered a safe and efficient technique in the treatment of critical limb ischemia. The technique has many advantages over open surgical procedures, being tolerable, easy, safe, and effective with general anesthesia avoidance and has low mortality and morbidity.

Keywords: Endovascular Therapy, Bypass Surgery, Lower Limb Ischemia.

INTRODUCTION

Among known peripheral limb ischemia (PAD) patients, prevalence of critical limb ischemia (CLI) may be as high as 11%. In fact, 5-10% of asymptomatic PAD patients or those with claudication will progress to CLI over a period of 5 years. The rate of limb loss is as high as 40% in this group of patients. According to a German registry involving 40,000 PAD patients, two-thirds of those belonging to CLI had their limb amputated within 4 years after diagnosis. In Bangladesh, most of the PAD patients present in advanced stages of CLI with features of tissue loss [(1)].

The decision to recommend surgical or endovascular revascularization for CLI patients varies substantially among providers. The United Kingdom multicenter bypass versus angioplasty in severe ischemia of the leg (SIL) trial remains the only randomized controlled trial (RCT) to compare a bypass-first with an endovascular-first revascularization strategy for infrainguinal arterial occlusive disease. However, this study did not specifically address the effectiveness of treatment for the infragenicular arteries [(2)]. For the aortoiliac and femoropopliteal arterial areas, the therapeutic results of lower limb enodovascular therapy (EVT) including long-term outcomes have improved and became equivalent to those of bypass surgery [(3)]. Application of EVT for the first treatment has been shown to be appropriate, although there are some exceptions. Regarding EVT for PAD with lesions mainly below the knee, the long-term patency rate is still low, and which of EVT or bypass surgery should be performed for the first treatment is the most controversial issue. CLI frequently extends over many regions, and lesions are present in below-the-knee arteries in many cases [(4)].

The current study aimed to assess the better management of patients with critical lower limb ischemia. To compare the efficacy and durability of a bypass-first vs endovascular-first strategy for revascularization in patients with CLI due to infrageniculate arterial disease.

PATIENTS AND METHODS

The randomized controlled trails study was conducted in Outpatient Clinic in the Vascular Surgery Department at Zagazig University Hospitals during the period from June 2020 to July 2021. The study included 24 participants diagnosed with CLI due to infragenicular lesions with mean age of 69.01 ± 7.11 years (range, 55-75 years). Regarding sex majority were

Received: 29 /5 /2021
Accepted: 25 /7 /2021

males (16) and 8 were females. They were allocated in two groups:

Group 1: Included 12 patients undergoing the endovascular therapy (EVT). They were 7 (58.3%) males and 5 (41.7%) were females with mean age of 67.58 ± 5.93 years.

Group 2: Included 12 patients undergoing bypass surgical therapy. They were 9 (75.0%) males and 3 (25.0%) females with mean age of 70.50 ± 6.06 years.

Inclusion criteria: All patients in the study were suffering from CLI (rest pain, or non-healing ulcer or gangrene), the foot was salvegable and the ulcer of gangrene was not affecting very deep. Their infragenicular arterial tree has multilevel diseased segment tibial or tibioperoneal lesions. The diseased segments at the arteries were occlusion (long > 5 cm or short < 5 cm) or stenosis (significant > 50% or tight > 75%) or both occlusion and stenosis.

Exclusion criteria: Patients suffering from claudication only, patients with combined supragenicular or iliac arterial lesions, patients with renal impairment (S. Cr > 1.8) and patients with missing information about the lower extremity revascularization technique.

All patients were subjected to full history taking including age, sex, diabetes mellitus (non-insulin requiring, or insulin requiring), ongoing tobacco use, chronic obstructive pulmonary disease, congestive heart failure, hypertension requiring medication, disseminated cancer, chronic steroid use, weight loss >10% within 6 months before the index operation, bleeding disorder.

Anthropometric measurements: including weight, height and body mass index. Careful clinical examination including general and vascular examination and Ankle Brachial Index (ABI). Radiological evaluation including X-ray foot (if there is foot ulceration or gangrene). Imaging studies, which can be one of the following: arterial Duplex U-S on affected limb, CT angiography on lower limb arteries and the saphenous vein was evaluated in all patients.

Preoperative laboratory investigations including CBC, PT, PTT and INR, random blood sugar; HbA1c, liver and kidney function tests, HIV, HbSAg and HCV Abs.

Ethical consideration:

The study was approved by the Ethical Committee of Zagazig Faculty of Medicine. An informed consent was obtained from each patient in this research. Every patient received an explanation for the purpose of the study. All given data were used for the current medical research only. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

I- Surgical procedure for endovascular (Group 1):

A double-dose anti-platelet therapy with aspirin (100 mg daily) and 300 mg of clopidogrel as a loading dose and then 75 mg daily. Protective kidney treatment in patients with creatinine level greater than 1.3 mg/dl with an infusion of normal saline solution at a dose of 1 ml/kg per hour (0.5 ml/kg per hour in patients with a history of heart failure) 12 hours before and 24 hours after the procedure and the use of N-acetylcysteine with a dose of 600 mg twice daily before and after the intervention. Antibiotic was given in cases that had foot ulcers post incision and drainage.

The procedure was done under local anesthesia in a vascular surgery room with a mobile C-arm with vascular imaging capabilities. A wire with a diameter of 0.014" was used to cross the lesion. Full stenosis preferably was re-canalized through the arterial lumen with a specific coronary wire with a diameter of 0.014". The selected vessel was punctured under fluoroscopic guidance or sonar guidance with a 21-G micropuncture kit. The micropuncture wire was removed, and the distal aspect of the occlusion was approached with a 0.018-inch angled Glide wire (Boston Scientific/Medi-tech, Natick, MA, USA) under angiographic visualization. Dilatation was done through long tibial balloons 3Fr and 2.5Fr semi compliant (Amphirion, INVATEC) and high pressure (Mustang, Boston Scientific) for highly calcified lesions. In the case of arterial spasm, 0.1to 0.2 mg nitroglycerin was administered as intra-arterial bolus.

II- Bypass Surgery (Group 2):

In operation room under complete aseptic conditions, and spinal anesthesia arterial bypass by use of the popliteal artery for the proximal anastomosis was performed by reversed saphenous vein, no patient received a prosthetic bypass graft. The proximal anastomosis was placed on the popliteal artery, below the knee, on the basis of the appearance of the popliteal artery pulsation and angiography. The distal anastomosis was placed on the posterior tibial artery in 7 bypasses and anterior tibial artery in 5 cases. Operative systemic heparinization was performed routinely. Intra-operative completion angiography was performed in all patients to assess the technical adequacy of the distal anastomosis. Local wounds debridement was done to all the patients in the two groups, closed space soft tissue infections were debrided before revascularization. Areas of dry gangrene, osteomyelitis, and/or open infected areas were debrided and/or amputated several days to a week late time of bypass surgery. Minor amputations were defined as forefoot amputations, up to and including a Chopart's amputation.

Post-operation care and follow up:

The patients puncture site was 24 hours inspected for hematoma or pseudoaneurysm. ABI was measured and compared to pre-procedural level and recorded. After the procedure, all patients were prescribed low molecular weight heparin (LMWH) anticoagulation for 72 hrs. Then aspirin (150 mg/day),

clopidogril (75 mg/day) and statins (20 mg/day) were given during the whole follow up period. The patients followed an appropriate risk factor modification program. Follow up was done by the Rutherford recommended standards for reports dealing with lower extremity ischemia by using the life table and Kaplan-Meier survival curve. All patients were followed up regarding life table and Kaplan-Meier survival curve [5]. Patients' visits were done weekly till first month, then every 3 months.

Statistical analysis

Data were collected and analyzed using Microsoft Excel software then imported into Statistical Package for the Social Sciences (SPSS version 20.0) software for analysis. According to the type of data, qualitative were represented as number and percentage, while quantitative continues group was represented as mean ± SD. The following tests were used to test differences for significance; difference and association of qualitative variable by Chi square test (χ^2). Differences between quantitative independent groups by t test. P value was set at $p \leq 0.05$ for significant results and $p < 0.001$ for highly significant result.

RESULTS

The study conducted in 24 patients with critical lower limb ischemia (CLI) due to Infragenicular lesions. The age was distributed as 67.58 ± 5.93 years and 70.50 ± 6.06 years respectively for the studied groups. Statistically, there was no significant difference between the studied groups among age and sex distribution ($p > 0.05$) (Table 1). There was no significant difference between the studied groups regarding laboratory parameters investigations ($p > 0.05$) (Table 2). There was no significant difference between the studied groups regards Rutherford classifications ($p > 0.05$) (Table 3).

There was a statistically significant increase in frequency of amputation among EVT group versus bypass group ($p = 0.04$). Also there was a statistically significant increase in frequency of thrombosis among EVT group versus bypass group ($p = 0.03$). On the other hand, there was no statistically significant difference between the studied groups that underwent different surgical techniques regarding complications as infections, pulmonary embolism or mortality ($p > 0.05$) (Table 4).

There was no significant difference in thrombosis survival times from major thrombosis following infrapopliteal angioplasty and bypass treatment (Table 5).

Kaplan Meier curve showed cumulative survival from major amputation following infrapopliteal angioplasty and bypass treatment over the study period (Figure 1).

Table (1): Age and sex distribution between studied groups

Variable	EVT Group (n=12)	Bypass Group (n=12)	Significant Test	P value
Age Mean ± SD	67.58 ± 5.93	70.50 ± 6.06	*t*=1.191	0.25 NS
Sex (No. %) Male Female	7 (58.3 %) 5 (41.7%)	9 (75%) 3 (25%)	$\chi^2 = 0.75$	0.38 NS

Sd: Standard deviation, t: Independent *t*-test, χ^2:Chi square test, NS: Non significant (P>0.05)

Table (2): LAB distribution between studied groups

Variable	EVT Group (n=12)	Bypass Group (n=12)	t-test	P value
HB Mean ± SD	11.28±0.61	11.10±0.91	0.578	0.57 NS
HA1c Mean ± SD	8.51±1.88	7.78±1.86	0.958	0.35 NS
LDL Mean ± SD	139.91±42.3	119.33±38.18	1.114	0.29 NS
TG Mean ± SD	146.75±51.36	129.50±34.3	1.851	0.07 NS
PT Mean ± SD	14.68±0.73	14.98±0.51	1.161	0.26 NS
INR Mean ± SD	1.25±0.12	1.18±0.14	1.133	0.27 NS

Sd: Standard deviation, t: Independent t test, NS: Non significant (P>0.05)

Table (3): Rutherford clinical categories of treated patients

Variable	EVT Group (n=12)	Bypass Group (n=12)	χ^2	P value
Rutherford 4	8 (66.6%)	7 (58.3%)	0.27	0.88 NS
Rutherford 5	2 (16.7%)	2 (16.6%)		
Rutherford 6	2 (16.7%)	3(25%)		

χ^2:Chi square test, NS: Non significant (P>0.05)

Table (4): Comparison between the groups of patients regarding complications

Variable	EVT Group (n=12)	Bypass Group (n=12)	χ^2	P value
Prevention of amputation (limb salvage)				
Yes	10 (16.7%)	7 (41.7 %)	4.44	0.04* S
No	2 (83.3%)	5 (58.3 %)		
Complications (Hematoma)				
Yes	1 (91.7%)	1 (91.7%)	0.0	1 NS
No	11 (8.3%)	11 (8.3%)		
Complications (Secondary infection)				
Yes	2 (17.7%)	2 (17.7%)	0.0	1 NS
No	10 (83.3%)	10 (83.3%)		
Complications (Thrombosis)				
Yes	2 (17.7%)	6 (50 %)	5.08	0.03* S
No	10 (83.3%)	6 (50 %)		
Complications (Pulmonary embolism)				
Yes	0 (0.0%)	2 (17.7%)	2.18	0.14 NS
No	12 (100 %)	10 (83.3%)		
Mortality	0 (0.0%)	0 (0.0%)	-	-

χ^2:Chi square test, NS: Non significant (P>0.05), *:Significant (P<0.05)

Table (5): Survival time form major thrombosis following infrapopliteal angioplasty and bypass treatment over the study period

Treatments	Median Survival time	CI 95%	Long Rank	P value
EVT	5.333	4.49-6.177	1.732	0.18 NS
Bypass	4.500	3.429-5.571		

NS: Non significant (P>0.05)

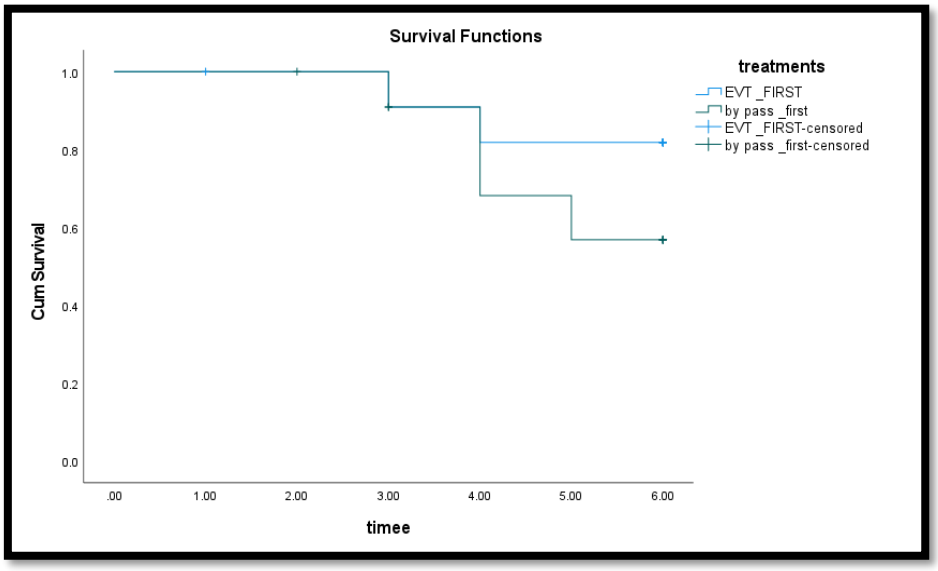

Figure (1): Kaplan Meier curve shows cumulative survival from major amputation following infrapopliteal angioplasty and bypass treatment over the study period

DISCUSSION

Critical limb ischemia (CLI) is associated with peripheral complications such as ulceration, gangrene, infection and a high risk of lower limb amputation estimated in 10%–40% of patients at 6 months, especially in non-treatable patients [6]. The objectives of treatment of CLI are to provide sufficient blood flow to relive rest pain symptoms, to heal skin lesions, and ultimately prevention of the most annoying complication that is major amputation. These objectives can be achieved by either surgical bypass or endovascular procedure. The ideal revascularization procedure is the one that avoid general anesthesia, has a lesser systemic stress, and has fewer serious complications [7]. Therefore, the current study amid to investigate the better management of patients with critical lower limb ischemia. These objectives can be achieved by either surgical bypass or endovascular procedure. Also, to compare the efficacy, durability and the complications of a bypass-first versus endovascular-first strategy for revascularization in patients with CLI due to infrageniculate arterial disease. Additionally, the goal of this study was to assess a short-term survival group identified by stratification with risk factors including all patients treated with revascularization in the analytical set.

The study was conducted on 24 patients with critical lower limb ischemia (CLI) due to infragenicular lesions. The mean age was 69.01 ± 7.11 years (ranged from 55 to 75 years; 16 males and 8 females). All patients can be achieved by either surgical bypass or endovascular procedure. They were allocated into two groups. Group 1 (EVT-first group) included 12 patients that underwent the endovascular therapy. They were 7 (58.3%) males and 5 (41.7%) females with mean age of 67.58 ± 5.93 years. Group 2 (Bypass-first group) include 12 patients that underwent the bypass-first surgical therapy. They were 9 (75.0%) males and 3 (25.0%) females with mean age of 70.50 ± 6.06 years. Regarding patients' characteristics, there was no statistical significant difference between groups regarding age and sex distribution. Patient follow-up ranged from 1 to 6 months. **Antoniou *et al.*** [8] revealed that the average of male gender was 75.2% and the mean age of all patients included in the study was 70 years old. Moreover, the percent of gender in the current study was comparable to other studies on patients with symptomatic chronic occlusive lower limb ischemia.

The current study revealed that, there was no significant difference between the studied groups regarding laboratory parameters investigations which included HB, HA1c, LDL, TG, PT, and INR. These results go with the result of **Tsuchiya *et al.*** [9] and **Hicks *et al.*** [10].

Patients categorized Rutherford category IV might have different characteristics compared to Rutherford category V and VI. The current study revealed that there was no significant difference between the studied groups regarding Rutherford classifications. This finding agrees with the study of **Tsuchiya *et al.*** [9] who demonstrated that Rutherford category IV should be recognized to have quite different backgrounds and better outcomes from Rutherford category V and VI.

For revascularization of Rutherford 5/6 CLI accompanied by necrosis, long-term retention of blood flow to the defective region is necessary, and it is difficult to complete treatment by a single application of EVT in the course of wound healing [11].

The current study revealed that, there was no statistically significant difference between the studied groups that underwent different surgical techniques regarding complications as infections, pulmonary embolism or mortality**.** In contrast, the study of **Yanase *et al.*** [12] reported perioperative complications occurred in six cases in the bypass group (11.5%) and in four cases in the EVT group (7.2%). There was no statistical differences between two groups with regard to perioperative complications (p = 0.671).

Moving to intraprocedural complications in our study, we experienced a couple of cases of arterial perforation and another couple of cases with groin hematoma that were managed conservatively. **Romiti *et al.*** [13] in their meta-analysis study reported that after crural angioplasty in patients with chronic CLI compared to a meta-analysis of popliteal-to-distal vein bypass graft, they found that groin hematoma was 3.1% and vessel perforation was 0.74%.Furthermore, study of **Fekry *et al.*** [14] showed low rate of peri-operative morbidity, only 2 patients suffered from complications; one with access site hematoma and the other with superficial surgical wound infection. Previously, **Siracuse *et al.*** [15] collected a total of 1513 patients undergoing revascularization and showed that the 30-day postoperative mortality rate was 1.5%. Postoperative morbidities included cardiac (1.0%), pulmonary (1.9%), renal (0.4%), urinary tract infection (1.7%), thromboembolic (0.5%), neurologic (0.4%), sepsis (2.7%), superficial (6.3%), and deep surgical site complications (2.0%). At least one complication, either major or minor, was seen in 7.9% of the patients. In addition, study of **Fekry *et al.*** [14] also achieved no major peri-operative complication (death or amputation) and a low rate of local complications (11%), including surgical wound infection, bleeding, and anastomotic false aneurysm.

The current study showed that, there was no significant difference in thrombosis survival times from major thrombosis following infrapopliteal angioplasty and bypass treatment. This finding is in accordance with **Patel *et al.*** [16] who concluded that, there was no difference in limb salvage rates, but patency and amputation-free survival rates were better 1 year after bypass surgery.

Survival time form major amputation following infrapopliteal angioplasty and bypass treatment over the study period; the current study showed that there was no significant difference in amputation survival times from

major amputation following EVT and bypass treatment ($p > 0.05$). This finding is in accordance with the study of **Yanase *et al.*** [12].

Bypass surgery to the foot is the gold standard; its benefit may be lost unless it is applied to appropriate patient. The application of EVT within a range not interfering with bypass surgery to the foot or its decision is difficult for physicians other than vascular surgeons. The introduction of novel devices, such as Drug Coating Balloon, is expected for infrapopliteal arterial EVT [17].

CONCLUSION

Endovascular intervention is considered a safe and efficient technique in the treatment of critical limb ischemia. The technique has many advantages over open surgical procedures, being tolerable, easy, safe, and effective with general anesthesia avoidance and has low mortality and morbidity.

Financial support and sponsorship: Nil.
Conflict of Interest: Nil.

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