Surgical bypass versus hybrid approach for management of multilevel critical limb ischemia: a randomized clinical study

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Objective
Interventions for multilevel critical limb ischemia include endovascular and surgical bypass revascularization. A hybrid approach combining both techniques is progressively used worldwide. The present randomized study proposed to compare the postoperative and clinical outcomes of surgical bypass and hybrid approach in patients with multilevel critical lower limb ischemia.

Patients and methods
This clinical randomized study was conducted in the period from September 2014 through April 2019. The study included 52 patients with multilevel critical limb ischemia. Patients were subjected to open surgical bypass (n=29) or hybrid intervention (n=23). Assessment included clinical examination, ankle-brachial pressure index measurement, arterial duplex (including ankle peak systolic velocity), and computed tomography angiography. Postoperatively, patients were followed at 1, 3, 6, 12 months, and then annually. The primary outcome in the present study was patency (primary, primary assisted, and secondary). Other outcome parameters included technical success (residual stenosis <30%), postoperative complications, ICU admission, hospital stay, major amputation, and mortality.

Results
Technical success was achieved in all the studied patients in both groups. Patients in surgical bypass group had higher rate of ICU admission and significantly longer hospital stay. In addition, they experienced significantly higher rate of postoperative wound infection and seroma formation. However, no significant differences were found between the studied groups regarding primary patency (62.1 vs. 60.9%, P=0.93), primary assisted patency (75.9 vs. 69.6%, P=0.61), secondary patency (86.2 vs. 87.0%, P=0.94), major amputation (13.8 vs. 13.0%, P=0.94), and mortality (10.3 vs. 4.3%, P=0.42).

Conclusion
Hybrid intervention provides patency and limb salvage rates equivalent to Open surgery. Moreover, the hybrid approach is associated with lower need of ICU admission and shorter hospital stay, which can reduce the clinical resource utilization.

Keywords:
critical limb ischemia, hybrid intervention, peripheral arterial disease, surgical bypass

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Introduction

Peripheral arterial disease (PAD) is a serious consequence of advanced atherosclerosis that can non-uniformly affect any segment of the arterial tree starting from infrarenal aorta. The condition gains its devastating nature from the high rate of underdiagnosis together with the possible grave complications [1].

In the lower extremity, PAD is associated with poor quality of life, increased odds of amputation, and significant risk of mortality. Early diagnosis is essential for appropriate care. However, the disease may be frequently asymptomatic as occurs in diabetic patients [2]. As PAD progresses, patients can develop critical limb-threatening ischemia characterized by multivessel and multilevel diseases [3].

In the early stages of PAD, conservative treatment options include lifestyle modification and progression-limiting medications. Surgical intervention is indicated in patients with lifestyle-limiting claudication not responding to conservative measures and in those with acute and limb-threatening ischemia [4].

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Revascularization options include endovascular approach and surgical bypass. In recent times, a third hybrid approach combining both techniques is progressively used by many centers worldwide. This modality has continued to evolve throughout the past decade and gained increasing recognition as a well-established technique for management of critical multilevel limb ischemia [5–8].

However, choice of the appropriate approach remains a debatable issue, and the current evidence has major limitations [9]. Although many studies have compared endovascular and surgical bypass approaches [10–13], only two retrospective studies compared the surgical bypass and hybrid approaches [14,15].

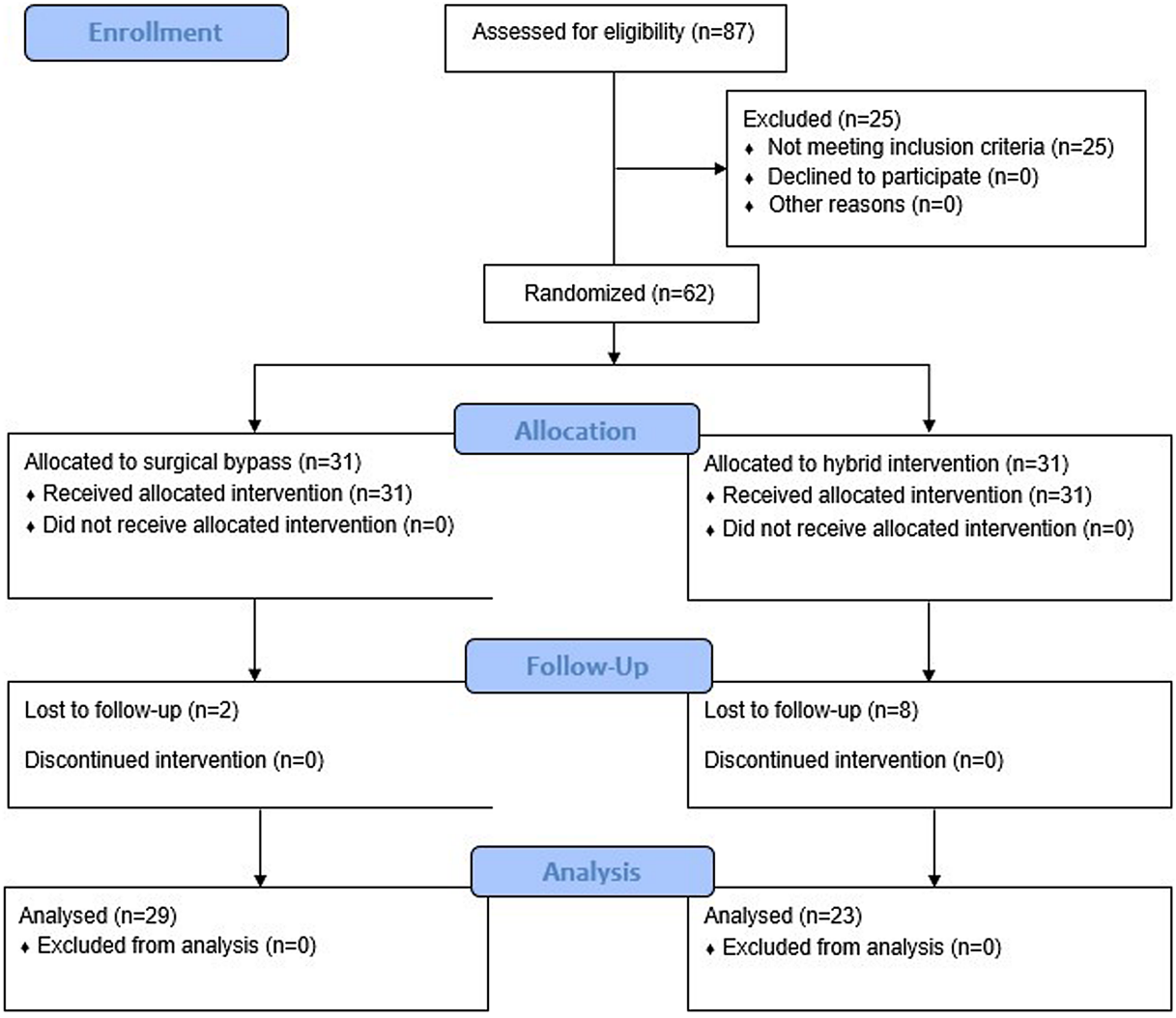
The present randomized study proposed to compare the postoperative clinical outcomes of surgical bypass and hybrid approach in patients with multilevel critical lower limb ischemia.

Patients and methods

Patient recruitment and allocation

This clinical randomized study was conducted in Zagazig University hospitals and Medical Research Institute, Alexandria University, in the period from September 2014 through April 2019. The study protocol was approved by the local ethical committee, and all patients gave informed consent before participation in the study. The study is registered at Clinialtrials.gov (NCT04490408). We screened 87 consecutive patients for eligibility for both surgical bypass and hybrid intervention. Only 62 patients were found fit for both interventions on the basis of recruitment criteria and agreed to participate in the study. The CONSORT chart is shown in Fig. 1. Inclusion criteria were TransAtlantic InterSociety Consensus (TASC II) type D femoral lesions (longer than 20 cm), chronic heavy calcified total occlusion affecting superficial

Figure 1



Consort chart.

femoral artery (SFA) from its origin accompanied with TASC II type A or B infrapopliteal lesions, Fontaine classification stage IV (gangrene or necrosis) or Rutherford grade III and IV category 5 and 6 with salvageable foot, and good distal runoff with at least one patent distal runoff vessel with good pedal arches and suitable great saphenous vein as a conduit. Exclusion criteria were heart failure [New York Heart Association (NYHA) class IV, liver failure (Child-Pugh class C), renal impairment (creatinine level more than 2 mg/dl], life expectancy less than 1 year, vasculitis, ipsilateral complete paralysis, concomitant other vascular pathologies, history of any ipsilateral revascularization procedure, or history of dye sensitivity.

Upon recruitment, patients were allocated into surgical bypass (n=31) or hybrid (n=31) intervention groups using randomly generated allocation table and concealed envelops. Randomization and patients' allocation were conducted by an independent researcher who was not aware of the scope of the study.

Preoperative assessment

Preoperatively, all patients were subjected to thorough physical examination, ankle-brachial pressure index (ABI) measurement, arterial duplex [including ankle peak systolic velocity (PSV)], and computed tomography angiography (CTA).

Operative procedures

All surgical procedures were conducted under spinal or epidural anesthesia under appropriate antibiotic prophylaxis and anticoagulation. The same surgical team performed all the procedures. In the bypass group, ultrathin radio translucent operative table and C-arm machine were used. The inflow was the common femoral artery in all the cases. The conduit was *in-situ* saphenous. The outflow was anterior tibial artery, posterior tibial artery, and peroneal artery (according to the CT findings and angiography pattern of the foot lesion).

In the hybrid group, the performed interventions included femoropopliteal bypass. The inflow was common femoral artery, and the outflow was the popliteal artery with *in-situ* saphenous vein graft with infragenicular angioplasty (transpopliteal). The secondary procedures aiming at limb salvage (in failing and failed procedures) included thrombectomy of occluded grafts, catheter-directed thrombolysis, and inflow and/or outflow revision.

Postoperative assessment and follow-up

Postoperatively, patients were followed at 1, 3, 6, 12 months and then annually. Assessment included clinical examination, ABI measurement, arterial duplex, ankle PSV, and CTA. The need for further interventions was determined on the basis of clinical and radiological findings.

Outcome measures

The primary outcome in the present study was patency (primary, primary assisted, and secondary). Other outcome parameters included technical success (residual stenosis <30%), postoperative complications, ICU admission, hospital stay, major amputation, and mortality.

Statistical analysis

Results obtained from the following study were presented as mean±SD, median and interquartile range, or number and percentage. Numerical data were compared using t-test, whereas categorical data were compared using χ^2-test. Kaplan–Meier survival analysis with long-rank comparison was used to compare patency duration. All statistical calculations were performed using SPSS 26 (IBM, USA) (SPSS Inc. was a software house headquartered in Chicago and incorporated in Delaware), with a significant P value level of less than 0.05.

Results

In the present study, no significant differences were found between the studied groups regarding the preoperative data (Table 1). Technical success was achieved in all the studied patients in both groups. Postoperatively, no statistically significant differences were found between the studied groups regarding ABI and ankle PSV. Patients in surgical bypass group had higher rate of ICU admission when compared with the hybrid group (31.0 vs. 8.7%, P=0.05) and significantly longer hospital stay [median (interquartile range): 5.0 (4.0–6.5) vs. 3.0 (2.0–4.0) days, P<0.001]. In addition, they experienced significantly higher rate of postoperative wound infection and seroma formation (41.4 vs. 8.7%, P=0.008).

However, no significant differences were found between the studied groups regarding the postoperative time to foot wound healing. Moreover, no significant differences were found between the studied groups regarding primary vascular patency (62.1 vs. 60.9%, P=0.93), primary assisted patency (75.9 vs. 69.6%, P=0.61), and secondary patency (86.2 vs. 87.0%, P=0.94). Moreover, the studied groups were comparable regarding rates of major amputation (13.8 vs. 13.0%, P=0.94) and mortality (10.3 vs. 4.3%, P=0.42) (Table 2).

In addition, it was found that both groups were comparable regarding primary patency duration

Table 1 Baseline data in the studied groups

	Surgical bypass group (*N*=29) [*n* (%)]	Hybrid revascularization group (*N*=23) [*n* (%)]	*P* value
Age (years) (mean±SD)	74.2±5.7	72.5±5.2	0.25
Male/female (n)	16/13	12/11	0.83
Comorbidities			
Diabetes mellitus	8 (27.6)	4 (17.4)	0.39
Hypertension	25 (86.2)	19 (82.6)	0.72
Ischemic heart disease	14 (48.3)	10 (43.5)	0.73
Smoking	11 (37.9)	7 (30.4)	0.57
Rutherford classification			
III	12 (41.4)	9 (39.1)	0.87
IV	17 (58.6)	14 (60.9)	
Fontaine classification (IV)	29 (100.0)	23 (100.0)	NA
TASC IID	29 (100.0)	23 (100.0)	NA
ABI (mean±SD)	0.26±0.1	0.24±0.09	0.46
Peak systolic velocity at ankle level (cm/s) (mean±SD)	27±3	25±4	0.32

ABI, ankle-brachial index; TASC, TransAtlantic interSociety consensus.

Table 2 Operative and postoperative outcomes in the studied groups

	Surgical bypass group (*N*=29)	Hybrid revascularization group (*N*=23)	*P* value
Operative duration (h) (mean±SD)	3.0±0.8	2.9±0.8	0.69
ABI (mean±SD)			
Immediate postoperative	0.99±0.14	1.04±0.13	0.24
3-month postoperative	0.95±0.16	0.91±0.15	0.49
6-month postoperative	0.89±0.17	0.9±0.12	0.93
1-year postoperative	0.83±0.14	0.87±0.12	0.4
2-year postoperative	0.8±0.14	0.87±0.12	0.24
ICU admission [*n* (%)]	9 (31.0)	2 (8.7)	0.05
Hospital stay (days) [median (IQR)]	5.0 (4.0–6.5)	3.0 (2.0–4.0)	< 0.001
Time to foot wound healing (m) [median (IQR)]	2.0 (1.0–3.0)	2.0 (1.0–3.0)	0.97
Wound infection and seroma [*n* (%)]	5 (17.2)	2 (8.7)	0.37
Primary patency [*n* (%)]	18 (62.1)	14 (60.9)	0.93
Primary-assisted patency [*n* (%)]	22 (75.9)	16 (69.6)	0.61
Primary patency duration (years) [mean (95% CI)]	3.34 (2.77–3.9)	3.26 (2.62–3.9)	0.87
Secondary patency [*n* (%)]	25 (86.2)	20 (87.0)	0.94
Secondary patency duration (years) [mean (95% CI)]	4.16 (3.61–4.55)	4 (3.66–4.52)	0.93
Major amputation [*n* (%)]	4 (13.8)	3 (13.0)	0.94
Mortality [*n* (%)]	3 (10.3)	1 (4.3)	0.42
Peak systolic velocity at ankle in cm/s (mean±SD)			
Immediate postoperative	74±4	72±5	0.34
3-month postoperative	68±3	69±3	0.45
6-month postoperative	68±2	67±2	0.23
1-year postoperative	67±3	65±4	0.31
2-year postoperative	57±3	58±2	0.22

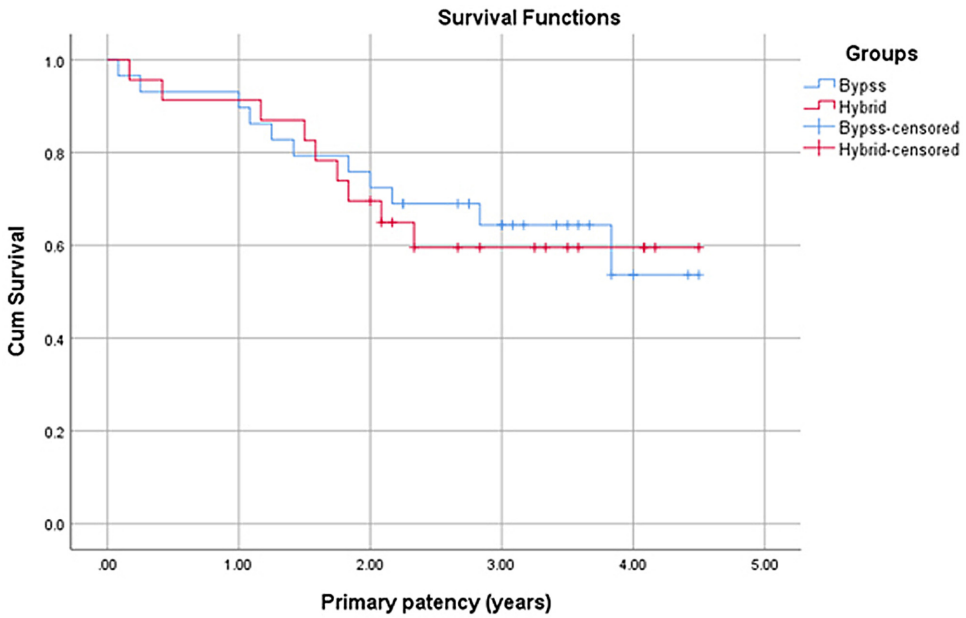
ABI, ankle-brachial pressure index; CI, confidence interval.

[mean (95% confidence interval): 3.34 (2.77–3.9) vs. 3.26 (2.62–3.9) years, *P*=0.87] and secondary patency duration [4.16 (3.61–4.55) vs. 4 (3.66–4.52) years, *P*=0.93] (Table 2 and Figs. 2 and 3).

Discussion

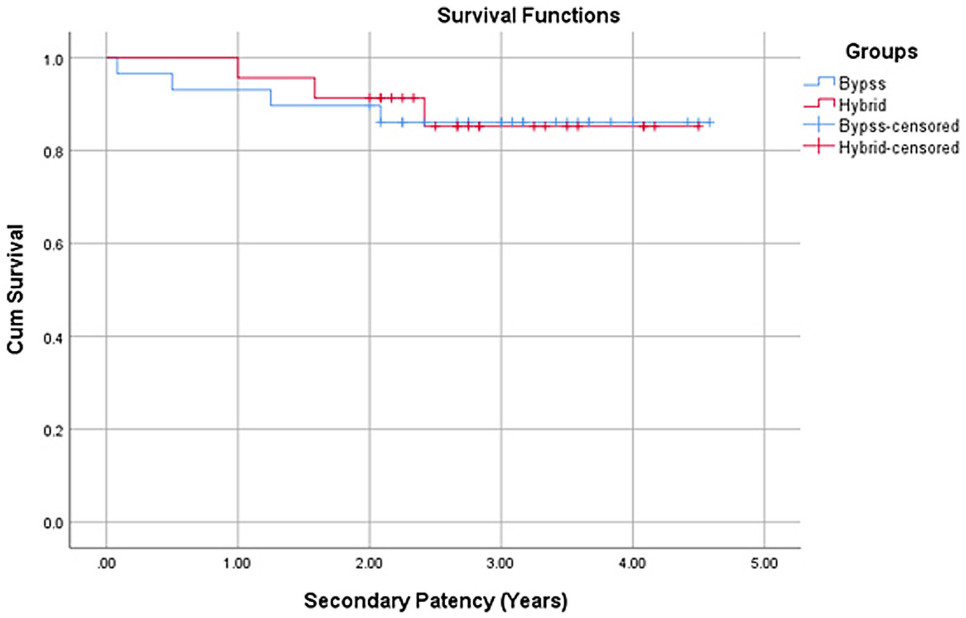
The present randomized study reported the outcome of open surgical bypass in comparison with hybrid interventions for management of multilevel critical limb ischemia. In the hybrid approach, the reported primary, primary-assisted, and secondary patency rates were 60.9, 69.6, and 87.0%, respectively. The value of hybrid interventions for critical limb ischemia was highlighted by many retrospective studies. In the study of Balaz *et al.* [16], the technical success rate was 99.3% and the 1-year primary, assisted-primary, and secondary patency rates were 60, 61, and 64%, respectively. In another study, the reported technical success rate was 100%, whereas the 1-year primary,

Figure 2



Primary patency.

Figure 3



Secondary patency.

primary assisted, and secondary patency rates were 39, 66, and 81%, respectively [6]. In comparison, the 1-year primary, primary-assisted, and secondary patency rates in the study of Soares *et al.* [8] were 78.28, 85.12, and 90.19%, respectively.

In contrast, the 18-month primary and primary-assisted patency rates in the multicentric study of Lee *et al.* [7] were 63.9 and 90.0%, respectively, whereas the study by Jung *et al.* [17] on patients with multilevel critical limb ischemia subjected to hybrid surgery reported 2-year primary and secondary patency rates of 67.3 and 72.1%, respectively, and the 5-year follow-up study of Barilla *et al.* [18] reported primary and secondary patency rates of 65 and 68%, respectively. The notable variation of the patency rates among the different studies reflects the heterogenous nature of

the underlying vascular pathology in the studied populations and the different interventions utilized.

The present study showed comparable technical success, patency, amputation, and mortality rates in the two surgical approaches. These findings are in accordance with the conclusions of previous two retrospective studies. In the study of Joh *et al.* [15], the primary patency rates of the open and hybrid approaches were 90.9 and 100%, respectively (P=0.44). Likewise, the retrospective study of Zhou *et al.* [14] reported comparable 3-year patency rates in the open and hybrid groups.

In the present study, the hybrid approach provided shorter hospital stay and less frequency of ICU admission in line with previous report [14]. In addition, patients subjected to the hybrid intervention experienced significantly lower rate of postoperative wound infection and seroma formation. The shorter length of hospital stay and lower frequency of ICU admission in the hybrid group are expected and are attributed to the less invasive nature of the procedure.

In conclusion, the present randomized study showed that hybrid intervention is a reliable option in treatment of multilevel critical limb ischemia. It provides patency and limb salvage rates equivalent to open surgery. Considering its less invasive nature, the hybrid approach is associated with lower need of ICU admission and shorter hospital stay, which can reduce the clinical resource utilization. However, these conclusions are not without limitations. The study was conducted on a relatively small sample size. This is attributed to the low rate of cases presented even to a large tertiary hospital like ours. It is common to see published studies conducted on similar number of patients.‘

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Nil.

Conflicts of interest
There are no conflicts of interest.

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