ABSTRACT

Background: Ischemic rest pain occurs when the blood flow to the foot is decreased to the point where ischemia of the sensory nerves occurs. As the ischemia becomes advanced, the pain is present constantly and tissue loss occurred. This affects patient morbidity and quality of life. Aim of the work: to compare the results (limb salvage rate, patency, improvement of clinical outcome according to Rutherford criteria, hospital stay, morbidity and mortality) of revascularization in infrainguinal arterial occlusive disease using femoro-distal bypass surgery either by reversed saphenous graft versus saphenous in-situ graft. Study Design: randomized controlled trail Methodology: thirty patients with infrainguinal femoro-popliteal occlusive disease. Patients were scheduled for limb revascularization using femoro-distal bypass surgery either by reversed saphenous graft or saphenous in-situ graft. Results: The present study was conducted on 30 patients, 19 males (63.33%) and 11 females (36.67%). Demographic and Clinical Characteristics are shown in table 1. Age mean was 58.2±12.33 and 57.2±11.24 for ‘Reversed’ technique and in-situ’ techniques respectively. The pre-intervention mean ABPI for the 30 patients was 0.29±0.2, which improved to 0.58±0.17 immediately post-intervention (P<0.001). When evaluated after 1 month post-procedure, it improved to 0.62±0.19 (P<0.001), after 3 months to 0.70±0.20, after 6 months to 0.75±0.20 and 0.63±0.31 after 12 months. (P< 0.001). There was statistically significant improvement in the type of wave pattern by duplex scan pre-operative and post-operative. Morbidity and mortality: 1 year duration postoperatively, morbidity occurred in 9 patients (30 %): 5 of 15 patients (33.33 %) underwent major amputations in Reversed’ technique group and 4 in the other group: Above knee amputation (AKA), below knee amputation (BKA) and forefoot amputation. Mortality occurred in two patients (13.3 %); one of them due to myocardial infarction and the other one due to cerebral infarction. No other patients were lost during the period of follow-up. Mortality were not related to the procedure, but were attributed to the associated co-morbidities.

Conclusion: Femoro-distal bypass performed by ‘in-situ’ technique has better outcome after 1 year of follow-up regarding limb salvage and amputation rate. Diabetes and preoperative smoking did not significantly affect late patency regardless of the technique. Continuation of smoking after operation significantly decreased late patency rate in both groups. There was no significant difference in early thrombectomy rate between groups. Early thrombectomy, however, significantly reduced late patency rate in both. Therefore we consider important more frequent physical and Doppler ultrasonographic control in patients that were early thrombectomized. No significant difference in early reoperations rate between these two techniques.

Key Words: limb ischemia, Femoro-distal bypass, saphenous graft.
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INTRODUCTION

Autologous great saphenous vein (GSV) has always been considered the gold standard conduit for infrainguinal revascularization. Autologous vein bypass is associated with excellent patency rates,
and limb salvage in CLI patients and decreased rates of operative mortality (Santo et al., 2014). Autogenous vein may be used in 1 of 3 primary configurations: reversed greater saphenous vein, nonreversed translocated great saphenous vein, and in-situ (Slovtzoff et al, 2012). In-situ saphenous vein bypass, which was performed first by Rob in 1959, but introduced by Hall in 1962, has been widely applied as an alternative to the reversed bypass (Connolly, 2005). The procedure was performed with a reversed vein conduit, which remained the standard of practice in vascular surgery for nearly three decades (Norman et al, 2011). In the early 1960s, Hall, as well as May, DeWeese and Rob introduced the in-situ technique in which the saphenous vein was left in its bed, the valves were cut, and side branches ligated. Some vascular surgeons continued to use a reverse saphenous vein bypass from the groin to the ankle or foot, but the results were not comparable to the distal in-situ procedure (Connolly, 2011).

**PATIENTS AND METHODS**

**Study Population:** randomized controlled trail was conducted on thirty patients with infrainguinal femoro-popliteal occlusive disease. Patients were scheduled for limb revascularization using femoro-distal bypass surgery either by reversed saphenous graft or saphenous in-situ graft.

**Patients: Inclusion criteria:** Patients with infrainguinal arterial occlusive disease who were diagnosed with the clinical presentations of incapacitating claudication or critical limb ischemia with angiographic confirmation of femoro-popliteal occlusion.

**Exclusion criteria:** All lesions associated with A/V malformation, All lesions associated with aneurysmal dilatation, Patients with contraindication to anticoagulant therapy or anti-platelet, Patients unfit for surgery, Patients with useless limb (paraplegic, knee joint spasticity, bed ridden patients ...etc.), Patients with inconvenient saphenous vein (small caliber, severe varicosities, previously harvested bilateral saphenous veins) or Patients with DVT or Chronic venous insufficiency.

**Methods:** All patients were subjected to full clinical detailed history, full clinical assessment including cardio respiratory evaluation. Cerebrovascular evaluation, Echocardiogram and thallium study to be done if needed.

(a) Routine lab tests (complete blood count, fasting and post prandial blood sugar level, kidney function tests, liver function tests, and coagulation profile).

(b) Ankle pressure and ankle/brachial index (APBI).

(c) Duplex study detecting great saphenous vein caliber, tributaries, deep venous system and ankle peak systolic velocity (APSV).

(d) Computerized tomographic angiography for the aorta both iliacs and both lower limb arterial tree to detect femoro-popliteal occlusion.

(e) Consent for intervention: consent was taken from the patient, discussing with him the surgical procedure and possible complications during and after the procedures.

**Procedure:** Femoro-distal bypass surgery using saphenous in-situ graft. General or Spinal anesthesia, groin incision to identify the saphenous vein and the common femoral artery then another below knee incision according to the target distal artery then introducing the valvotome (metal or disposable ) retrograde after finishing the proximal anastomosis then accomplishing the distal anastomosis and finally ligation of the marked tributaries.
reversed saphenous graft: General or Spinal anesthesia, groin incision to identify the saphenous vein and the common femoral artery then another below knee incision according to the target distal artery plus an incision over the distal saphenous and stab incisions over the great saphenous vein course with ligation of the tributaries then preparation of the vein and accomplish the anastomosis in reversed manner.

FOLLOW UP AND ASSESSMENTS: The clinical improvement of the patients were evaluated post-operatively or post intervention according to Rutherford criteria, change in APBI or APSV and limb salvage rate. Hemodynamic end point (The patency or restenosis), the patients underwent duplex ultrasound at 1, 3, 6 and 12 months follow up to insure the patency and rule out restenosis. The length of hospital stay was evaluated and the thirty days morbidity and mortality rates.

Follow up: The patients were evaluated at 1, 3, 6 and 12 months. The patients with recurrent symptoms, disappearance of distal pulse or evidence of restenosis were evaluated with duplex and CT angiography.

The results obtained were statistically evaluated by SPSS 20. The study was approved by the Ethics Board of Al-Azhar University.

RESULTS
The present study was conducted on 30 patients, 19 males (63.33%) and 11 females (36.67%). Demographic and Clinical Characteristics are shown in table 1. Age mean was 58.2±12.33 and 57.2±11.24 for ‘Reversed’ technique and in-situ technique respectively.

Table 1 Distribution of the studied patients regarding their sex.

<table>
<thead>
<tr>
<th>Sex</th>
<th>‘Reversed’ technique</th>
<th>‘In-situ’ technique</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>9 (60%)</td>
<td>10 (66.67%)</td>
</tr>
<tr>
<td>Female</td>
<td>6 (40%)</td>
<td>5 (33.33%)</td>
</tr>
</tbody>
</table>

The associated comorbidities are shown in the following chart.

Figure 1: Associated comorbidities and risk factors
Symptoms and signs of patients included in this study included Rest pain, Ischemic Ulcers, Gangrene of Toe, Heel or Forefoot as shown below.

Table 2 Symptoms and signs of patients included in this study.

<table>
<thead>
<tr>
<th>Symptoms &amp; signs</th>
<th>‘Reversed’ technique</th>
<th>‘In-situ’ technique</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest pain</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Ischemic Ulcers</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Gangrene:</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>Toe</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Heel</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Forefoot</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

Lesion characterization (Pre-procedure evaluation):
Results of CTA: According to inclusion criteria, all patients had infra-inguinal arterial occlusive disease with angiographic confirmation of femoropopliteal occlusion. Table below shows the associated infra-genicular lesions.

Table 3: Localization, number of the affected infra-genicular arteries.

<table>
<thead>
<tr>
<th>Artery</th>
<th>No (%)</th>
<th>Stenosis (n)</th>
<th>Occlusions (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TP Trunk</td>
<td>6</td>
<td>20 %</td>
<td>4</td>
</tr>
<tr>
<td>ATA</td>
<td>9</td>
<td>30%</td>
<td>5</td>
</tr>
<tr>
<td>PTA</td>
<td>8</td>
<td>26.67%</td>
<td>5</td>
</tr>
<tr>
<td>PA</td>
<td>10</td>
<td>33.33%</td>
<td>7</td>
</tr>
</tbody>
</table>

Most of the lesions were in the peroneal and anterior tibial arterial territories (33 % and 30 %, respectively).
Indications for operative treatment were based on subjective complaints, clinical findings, CW Doppler ultrasonography (Doppler index and waveform spectral analysis) and angiography.

**Procedure (Technical) outcome:**
The procedure time was estimated from the time of infiltration of local anaesthesia to the end of the procedure. It ranged from 60 min to 125 minutes in Reversed group and from 51 min to 103 minutes in in-situ group.

<table>
<thead>
<tr>
<th>Table 4: procedure time</th>
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</thead>
<tbody>
<tr>
<td>procedure time</td>
</tr>
<tr>
<td>Mean</td>
</tr>
</tbody>
</table>

The hospital stay ranged from 5 to 21 days in Reversed group and from 6 days to 20 days in in-situ group.

<table>
<thead>
<tr>
<th>Table 5: hospital stay</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital stay (days)</td>
</tr>
<tr>
<td>Mean</td>
</tr>
</tbody>
</table>

**Clinical outcome:**
Early results including Patency, Early thrombectomy, Limb salvage and Amputation rate were followed postoperatively. These findings were shown together between ‘Reversed’ technique and in-situ technique in the table below.

The early patency rate was 96.34% in the group with ‘reversed’ bypass, and 95.93% in the group with ‘in-situ’ bypass.

<table>
<thead>
<tr>
<th>Table 6: The early results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early results</td>
</tr>
<tr>
<td>Patency</td>
</tr>
<tr>
<td>Early thrombectomy</td>
</tr>
<tr>
<td>Limb salvage</td>
</tr>
<tr>
<td>Amputation</td>
</tr>
</tbody>
</table>

Two early major amputations were done in a ‘reversed’ group (13.3%). One of them was performed in cases of graft occlusion and unsuccessful reoperation. The other patient had patent graft, but extensive gangrene could not be stopped after operation.

In a group with ‘in-situ’ bypass one early amputation was carried out (6.06%). He had graft occlusion and unsuccessful reoperation.

The early limb salvage rate was 86.67% in the group with ‘reversed’ bypass technique, and 93.33% in the group with ‘in-situ’ bypass technique.

Late results including redo operations, Limb salvage and Amputation rate were followed up postoperatively. These findings were shown together between ‘Reversed’ technique and in-situ technique in the table below.

There was no mortality in the early postoperative period in both groups. Early thrombectomy was carried out on two cases with ‘reversed’ (13.3%) and, one (6.6%) with ‘in-situ’ bypass. There was no significant difference in early thrombectomy rate between ‘reversed’ and ‘in-situ’ group ($\chi^2 = 1.52, P>0.05$).

Furthermore, statistical analysis revealed that early reoperations significantly decreased late patency rate of both ‘reversed’ ($\chi^2 = 15.87, P 0.01$) and ‘in-situ’ ($\chi^2 = 21.15, P0.01$) bypass reconstructions.

Late reoperations were performed on 2 (13.3%) patients with ‘reversed’ bypass. In one case proximal disease progression occurred. He was treated with ilio-femoral bypass reconstructions. The limb was rescued.

Late reoperations were performed on 1 (6.06%) patients with ‘in-situ’ bypass. The reason was proximal disease progression which was corrected by aorto-bifemoral reconstruction. The limb was rescued.

In one case, distal disease progression occurred with possibility for more distal femoro-crural bypass using contralateral autologous saphenous vein graft. This procedure rescued the extremity in this case.

<table>
<thead>
<tr>
<th>Table 7: The late results (At one month post-operatively)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Late results</td>
</tr>
<tr>
<td>Redo operations</td>
</tr>
<tr>
<td>Limb salvage</td>
</tr>
<tr>
<td>Amputation</td>
</tr>
</tbody>
</table>

Limb salvage was defined as freedom from
major amputation. Toe, ray, or transmetatarsal amputations were considered as minor amputations. During the whole follow-up period 5 (33.33 %) amputations were performed in the group with ‘reversed’ bypass technique, and 4 (26.67 %) in the group with ‘in-situ’ bypass technique.

Table 8: Amputation (At one year post-operatively)

<table>
<thead>
<tr>
<th>Late results</th>
<th>‘Reversed’ technique</th>
<th>‘In-situ’ technique</th>
</tr>
</thead>
<tbody>
<tr>
<td>Limb salvage</td>
<td>66.67 %</td>
<td>73.33 %</td>
</tr>
<tr>
<td>Amputation</td>
<td>5 (33.33 %)</td>
<td>4 (26.67 %)</td>
</tr>
</tbody>
</table>

The late limb salvage rate in the group with ‘reversed’ bypass technique was 66.67 % while in the group with ‘in-situ’ bypass technique 73.33 %.

Factors influencing late results were illustrated as Factors influencing late patency, Technique (‘reversed’ or ‘in-situ’), Diabetes, Preoperative smoking, Postoperative smoking and early thrombectomy.

Table 9: The factors influencing late results

<table>
<thead>
<tr>
<th>Factors influencing late patency</th>
<th>Statistically significant difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technique (‘reversed’ or ‘in-situ’)</td>
<td>No</td>
</tr>
<tr>
<td>Diabetes</td>
<td>No</td>
</tr>
<tr>
<td>Preoperative smoking</td>
<td>No</td>
</tr>
<tr>
<td>Postoperative smoking</td>
<td>Yes</td>
</tr>
<tr>
<td>Early thrombectomy</td>
<td>Yes</td>
</tr>
</tbody>
</table>

The statistical analysis did not show any significant difference in late occlusions rate between groups regarding preoperative smokers ($\chi^2 = 0.94; P>0.05$). However, we found a highly significant statistical difference in the late patency rate of the ‘reversed’ ($\chi^2 = 44.66; P0.01$), and the ‘in-situ’ ($\chi^2 = 22.642; P0.01$) bypass reconstruction in favor of patients who quit smoking after operation.

There was no significant difference in late patency between diabetics and non-diabetics operated by ‘reversed’ ($\chi^2 = 0.01; P>0.05$) or ‘in-situ’ ($\chi^2 = 0.05; P>0.05$) technique.

Clinical successes were defined as relief of rest pain or improve healing of the ulcer and limb salvage, based on Rutherford categories.

Of 3 patients (10 %) suffering from rest pain: ‘Reversed’ technique succeeded in 2 patients (100 %) and became claudicants, in In-situ technique the patient with rest pain was improved, Tissue loss was resolved in 11 patients (78.6 %) in ‘Reversed’ technique and 10 patients (71.4 %) in ‘In-situ technique.

Failed and successful cases received conservative treatment in the form of anticoagulants, antiplatelets and vasodilators.

Post-procedural evaluation:

A- Ankle Brachial Pressure Index (ABPI) evaluation:

The pre-intervention mean ABPI for the 30 patients was 0.29±0.2, which improved to 0.58±0.17 immediately post-intervention ($P<0.001$). When evaluated after 1 months post-procedure, it improved to 0.62±0.19 ($P<0.001$), after 3 months to 0.70±0.20, after 6 months to 0.75±0.20 and 0.63±0.31 after 12 months. ($P<0.001$).

Figure 2: ABI Changes

B-Duplex scan evaluation:

There was statistically significant improvement in the type of wave pattern by duplex scan post- operatively.
Morbidity and mortality:
1 year duration postoperatively, morbidity occurred in 9 patients (30 %):
- 5 of 15 patients (33.33 %) underwent major amputations in Reversed’ technique group and 4 in the other group:
  - Above knee amputation (AKA), below knee amputation (BKA) and forefoot amputation.
Mortality occurred in two patients (13.3 %); one of them due to myocardial infarction and the other one due to cerebral infarction. No other patients were lost during the period of follow-up. Mortality was not related to the procedure, but was attributed to the associated co-morbidities.

DISCUSSION
Autogenous single-segment great saphenous vein (GSV) remains the optimal conduit for infrainguinal revascularization (Ziza et al., 2015).
Patency rate
At 1 year, secondary patency rates of reversed vein graft was 58.3% (Ziza et al., 2015).
Regarding the way of vein harvesting, either open or endoscopic, no significant differences were found between both groups regarding to primary patency or assisted primary patency (Peinado Cebrian et al., 2015).
At 1, 2, and 3 years, primary graft patency of reversed GSV was 84%, 71%, and 71%, respectively (Gessaroli et al., 2015).
Primary patency at 2 and 5 years was estimated at 47% and 32%, respectively, for the reversed GSV group. Primary assisted patency at 2 and 5 years was estimated at 71% and 55%, respectively, for the GSV group. Secondary patency at 2 and 5 years was estimated at 75% and 60%, respectively, for the GSV group (Avgerinos et al., 2015).
The five-year cumulative primary patency rate was 59.8% in in-situ saphenous bypass. The five-year cumulative secondary patency rate was 81.7% (Izumi et al., 2010).
Over a 5-year period, the cumulative patency rate of the <<=in-situ>> grafts amounted to 56.4%, and that by the reversed autovein equaled 47.6 % (Gavrilenko and Skrylev, 2007).
Of the presumed original benefits of the in-situ operation, it is now clear that the hemodynamic flow of converging (in-situ) versus diverging vein (reversed) boundaries plus better vein/artery size match are the main advantages. It is now popular belief that the reversed saphenous vein graft to the popliteal artery has no significant hemodynamic disadvantage because the vein is of comparable diameter at the knee and in the groin. In contrast, vein bypass from the groin to the ankle strongly favors the in-situ procedure because of the convergence of the walls of the vein below the knee and better vein/artery size match (Connolly, 2005).
Our results show better patency of ‘in-situ’ bypass, and no significant difference for other follow-up intervals.
Factors affecting patency
Ejection fraction <45% and dialysis were the most significant factors predicting failure of revascularization (Ziza et al., 2015).

Fransson et al., studied the effect of diabetes on patency rate of in-situ GSV bypass. The 5 year patency did not differ significantly between groups, 68 % in diabetic patients vs. 72 % in non-diabetics (Fransson and Thorne, 2010). The limb salvage was equal in both groups, 86 % after 5 years. Mortality during follow up was significantly higher among diabetics, at two years 31 % for diabetics vs. 14 % for non-diabetic patients.

The main factor exerting a statistically reliable influence on the patency of the femoropopliteal grafts was found to be the level of the establishment of the distal anastomosis. When the distal anastomosis was established, above the knee-joint fissure, no statistically significant differences in the patency of the grafts performed by of the reversed autovein and those carried out according to the <<in-situ>> technique were revealed. Placing the distal anastomosis below the knee-joint fissure appeared to offer apparent advantages of autovenous grafting performed according to the <<in-situ>> technique (Gavrilenko and Skrylev, 2007).

The most controversial facet of the in-situ operation has been the question of valvulotome is superior to lyse valves and whether to perform the operation open as originally described, or closed to avoid skin complications from a long groin to ankle incision (Connolly, 2005).

Associated co morbidities
The cumulative 30-days operative mortality rate of reversed vein graft was 2.9% (Gessaroli et al., 2015).

COMPLICATIONS
Patients with lower limb arterial disease have a high risk for complications related with surgical wounds (Peinado Cebrian et al., 2015).

At 30 days, perioperative death rate was 6.8%, major adverse cardiovascular event rate was 7.6%, and major adverse limb event rate was 11.9% (Ziza et al., 2015).

At 1 year, freedom from major adverse limb event or perioperative death, limb salvage, survival, amputation-free survival, and secondary patency rates were, respectively, 64.9%, 82.5%, 85.4%, 73.3%, and 58.3% (Ziza et al., 2015).

No significant differences were found between both groups regarding to amputation-free survival (Peinado Cebrian et al., 2015).

At 1, 2, and 3 years, limb salvage rate of GSV reversed graft was 84%, 75%, and 75%, respectively and patient survival rate was 87%, 73%, and 65%, respectively; P = 0.86).

Wengerter et al. found no difference in the complication-rate between these two techniques (Gavrilenko and Skrylev, 2007). Also, in this study we found no significant difference in the early complication-rate.

According to our study, in patients with three and two patent crural arteries, there was no difference in late patency between the two techniques. Only in cases where one patent crural artery ‘in-situ’ proved to have better late patency. There are numerous articles in the literature about the negative influence of poor run-off on late patency of femoro-distal bypass reconstructions.

Poor crural vessel status was found to decreases late patency rate of Femoro-distal bypass reconstructions and add that patients with a patent bypass and distal anastomosis placed at ‘blind popliteal artery segment’ have correspondingly high limb-loss rate (Connolly, 2005)

In diabetics, pathological changes
commonly affect small-calibre (crural and pedal) arteries. Arterial wall calcifications which are common in such circumstances reduce their elasticity, disturb compliance and amplify ‘mechanical mismatch’ e.g. they lower capability of pulsatile flow takeover. Frequent time changes exist at microcirculatory level which in all present poor prognostic factor in relation to late patency. In addition to this are other diabetic complications such as delayed wound healing and infective diathesis.

There are some controversial papers which point to diabetes as a significant factor in decreasing the late patency rate (Connolly, 2005), however, others do not agree with this (Ziza et al., 2015). Our results did not show diabetes to substantially influence late patency of Femoro-distal bypass reconstructions considering both techniques together and each for itself. However, we must point out that treatment of gangrenous foot lesions despite successful revascularization contribute to a longer hospital stay of such patients.

In the issue of preoperative smoking our work did not show any significant difference in late patency on ‘reversed’ and ‘in-situ’ bypass. However, we found highly significant statistical difference that reveals much better late patency of both techniques together as an each for itself in patients which have quit smoking after operation.

If no suitable saphenous vein, cold-stored venous allografts may be used for performing infragenicular revascularization with acceptable safety and efficacy results despite poor long-term patency (Ziza et al., 2015).

CONCLUSIONS

Our results revealed no significant difference in early reoperations rate between these two techniques. Nevertheless late patency rate was considerably lower in both groups, together and separately, if early thrombectomy had to be done. Keeping in mind the goals of this work we conclude the following: Femoro-distal bypass performed by ‘in-situ’ technique has better outcome after 1 year of follow-up regarding limb salvage and amputation rate. Diabetes and preoperative smoking did not significantly affect late patency regardless of technique. Continuation of smoking after operation significantly decreased late patency rate in both groups. There was no significant difference in early thrombectomy rate between groups. Early thrombectomy, however, significantly reduced late patency rate in both. Therefore we consider important more frequent physical and Doppler ultrasonographic control in patients that were early thrombectomized.

REFERENCES


