# Is endovascular therapy effective in acute femoropopliteal bypass graft failure?

# Akut femoropopliteal bypass greft obstrüksiyonlarında endovasküler tedavi etkin bir yöntem mi?

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Dergiye Ulaşma Tarihi: 28.01.2019 Dergiye Kabul Tarihi: 31.01.2019 Doi: 10.5505/aot.2019.03064

## ÖZET

**GİRİŞ ve AMAÇ:** Çalışmamızda FPBG obstrüksiyonlarında endovasküler tedavinin (EVT) etkinliğini araştırmayı amaçladık.
**YÖNTEM ve GEREÇLER:** Çalışmaya 39'u tromboze, 18'i stenoz olmak üzere toplam 57 femoropopliteal bypass greft obstrüksiyonu dahil edilmiştir. Uygulanan EVT işlemleri intra-arteriyel trombolitik tedavi, perkütan translüminal anjiyoplasti ve stentlemeden oluşmaktadır. İşlem sonrası greft açık kalım oranları Kaplan Meier analizi ile tespit edilmiş ve gruplar arasındaki farklılıklar Log-Rank metodu ile değerlendirilmiştir.
**BULGULAR:** Tromboze greftlerin %74.3'ünde, stenozlu greftlerin % 100'ünde EVT sonrası patensi sağlanmıştır. EVT sonrası teknik başarı PTFE greftlerde %78, SV greftlerde %90 olarak hesaplanmıştır. Tromboze PTFE greftlerde primer patensi (p = 0.01) ve asiste primer patensi (p = 0.03) oranları SV greftlerden daha anlamlı olarak daha yüksektir. Stenozlu PTFE ve SV greftlerin patensi oranları arasında anlamlı farklılık bulunmamıştır. Tromboze greftlerde trombolitik ajanların greft patensi oranları arasında anlamlı farklılık bulunmamıştır. Total komplikasyon oranı tromboze greftlerde %23, stenozlu greftlerde %11.1'dir. Sonuç: EVT, uygun maliyete sahip olması, kolay uygulanabilir olması ve işlem sonrası inatçı obstrüksiyonlara kolaylıkla tekrar müdahele edilebilmesi gibi avantajları nedeniyle tromboze veya stenozlu greftlerin tedavisinde önemli bir role sahiptir. EVT, tromboze PTFE greftlerde SV greftlere göre daha uzun patensi sağlamaktadır. Bu nedenle özellikle cerrahi açıdan yüksek risk taşıyan hastalarda gelişen PTFE greft trombozlarında EVT'nin etkin bir tedavi yöntemi olduğunu düşünmekteyiz.
**TARTIŞMA ve SONUÇ:** EVT, uygun maliyete sahip olması, kolay uygulanabilir olması ve işlem sonrası inatçı obstrüksiyonlara kolaylıkla tekrar müdahele edilebilmesi gibi avantajları nedeniyle tromboze veya stenozlu greftlerin tedavisinde önemli bir role sahiptir. EVT, tromboze PTFE greftlerde SV greftlere göre daha uzun patensi sağlamaktadır. Bu nedenle özellikle cerrahi açıdan yüksek risk taşıyan hastalarda gelişen PTFE greft trombozlarında EVT'nin etkin bir tedavi yöntemi olduğunu düşünmekteyiz.
**Anahtar Kelimeler:** Femoropopliteal bypass grefti, intra-arteriyel trombolitik tedavi, perkütan translüminal anjiyoplasti, stent

## ABSTRACT

**INTRODUCTION:** The purpose of this study was to evaluate the role of endovascular therapy in femoropopliteal bypass graft failure.
**MATERIAL and METHODS:** Fifty seven (39 thrombosed grafts, 18 stenosed grafts) endovascular interventions were performed to 40 grafts. Endovascular treatment (EVT) options were catheter directed intra-arterial thrombolytic therapy, percutaneous transluminal angioplasty and stent placement. After EVT, the duration of patency was analyzed with Kaplan-Meier analysis and statistical significance of differences between groups was evaluated with Log-Rank method.

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**RESULTS:** The initial successes of EVT in the thrombosed and stenosed grafts were 74.3 % and 100%, respectively. The initial success rates of EVT in the SV grafts and PTFE grafts were 90% and 78.5%, respectively. The primary patentcy (p = 0.01), assisted primary patency rates (p = 0.03) were significantly higher in thrombosed polytetrafluoroethylene (PTFE) grafts than saphenous vein (SV) grafts. There was no significant difference between patency rates of stenosed PTFE and SV grafts. We found no significant difference between patency rates among thrombolytic agents. The total complication rates were 23% in thrombosed grafts and 11.1% in stenosed grafts.

**DISCUSSION AND CONCLUSION:** EVT plays an important role in the treatment of thrombosed and stenosed grafts due to advantages of being cost-effective, having an easy application and being available for serial interventions for refractory lesions. Furthermore, EVT is more effective in thrombosed PTFE grafts than SV grafts, thus we consider that EVT is the best alternative for thrombosed PTFE grafts, especially in the high surgical risk patients.

**Keywords:** Femoropopliteal bypass grafts, intra-arterial thrombolytic therapy, percutaneous transluminal angioplasty, stent.

## INTRODUCTION

Chronic peripheral arterial disease of the lower limbs may present either as intermittent claudication or as critical limb ischemia which may lead to significant morbidity and mortality. Besides the conservative therapy and endovascular interventions, the implantation of femoropopliteal bypass graft (FPBG) is an effective procedure for infrainguinal artery occlusive disease. By placing a graft in the threatened area, the blocked arterial segment is bypassed and the patency is established in the distal arterial system. The greater saphenous vein (SV) is the most preferred graft material for infrainguinal artery occlusions. The prosthetic grafts including polytetrafluoroethylene (PTFE) and Dacron, are the widely accepted conduits if saphenous vein is not proper. Following femoropopliteal bypass grafting, 5-year patency rates for autologous SV grafts and PTFE grafts were 70% and 50%, respectively (1). Although most studies indicated the better patency rates for SV grafts as compared to prosthetic grafts, few studies revealed that PTFE grafts has been more durable than SV grafts (1-3). The treatment approaches for FPBG failure including thrombosis and symptomatic stenosis are conservative management, surgical thrombectomy, graft replacement and endovascular treatment (EVT), including intra-arterial thrombolytic therapy (IATL), percutaneous transluminal angioplasty (PTA) and stent placement. In recent years, despite the long patency rates of surgery, EVT has become an initial therapeutic option for thrombosed or stenosed FPBG (2) to maintain the patency. Previous studies reported that initial success rate of EVT was high while long term patency was not as durable as surgery in both thrombosed and stenosed grafts (1-6). A definitive consensus about treatment approach regarding the efficacy and duration of the treatment options for FPBG failure remains unclear. This study evaluated the efficacy and duration of EVT of the threatened FPBG, by using post-procedural initial success rates, primary and assisted primary patency rates and complication rates in our experience.

## MATERIAL and METHODS

A total of 51 grafts of 46 patients with acute limb ischemia who were diagnosed by Doppler ultrasound or multislice imaging modalities, between April 1997 and March 2012, were evaluated. Seven cases with irreversible acute limb ischemia which was classified by the Rutherford scale (7) and manifesting as ischemia with major tissue loss or permanent nerve damage and 4 cases who had absolute and relative contraindications for IATL, including stroke or gastrointestinal hemorrhage in the previous 3 months and poorly controlled hypertension, were excluded from this study. Patients with acute limb ischemia (< 14 days) were included in this study. Thirty five patients (28 males, 7 females) with 40 acute thrombosed or symptomatic stenosed above-knee FPBGs, treated with EVT options such as IATL, PTA and stent placement at our department, were enrolled in this study. Patient ages ranged from 31 to 86 years. 57 endovascular interventions were performed to 40 grafts. The common comorbidities of the subjects were hyperlipidemia (12.5%), diabetes mellitus (47.5%), chronic renal failure (20%),

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hypertension (30%) and coronary artery disease (55%).

Failure of FPBG was verified with color Doppler ultrasound (US) (Siemens Acuson Antares PE, Hitachi EUB-6500, Germany), computerized tomography angiography (CTA) (Siemens Somatom Sensation, 16, Germany), magnetic resonance angiography (MRA) (Siemens Magnetom Avanto, 1,5T, Germany) or digital subtraction angiography (DSA) (Siemens Artis Zee Ceiling, Siemens Multistar TOP, Germany). All of the patients, included to this study, had patent run off vessels which had been evaluated before the procedure by DSA, CTA or MRA. All patients had angiographic evidence of the popliteal artery with one to three runoff vessels.

The FPBG was usually cannulated by means of either the contralateral or ipsilateral femoral artery approach. The other access sites were femoro-femoral cross over graft in two cases and the axillary artery in two cases. Arterial access was maintained under sonography guidance with single-wall puncture technique. After 4-French or 5-French vascular sheath placement, vascular access was secured. A guide wire (Amplatz super stiff™, Boston Scientific, Costa Rica) was passed through the occluded graft. Then 4 or 5-French vascular sheath was removed and 6-French Balkin (Terumo, Terumo Corporation, Belgium) or 6-French Terumo (Terumo, Terumo Medical Corporation, USA) vascular sheaths were placed in place of these sheaths. After these procedures, 4 or 5-French Mc Namara infusion catheters (Cragg Mc Namara™, Micro Therapeutics, Inc. USA) were positioned within the thrombus for thrombolytic therapy and lytic agents including tissue plasminogen activator (tPA), streptokinase (STK) and urokinase (UK) were delivered via the catheter. Lytic therapy dosages were 0.05 mg/kg/hr for up to 12 hours for tPA, a bolus loading dose of 2000U/kg over 30 minutes followed by a maintenance dose of 100,000 units/hour for 72 hours for STK and 250,000 units bolus followed by 4000 units/min for 4 hours, followed by 2000 units/min for up to 36 hours for UK. During the procedure, unfractioned heparin treatment (250-500 IU/h) was delivered through infusion catheter, vascular sheath or peripheral veins. After the procedure, hemoglobin values were analyzed twice a day. For PTA treatment, in proximal lesions, contralateral retrograde access was used, but for more distal lesions, ipsilateral antegrad puncture was preferred. PTA treatment was performed after replacement of guide wire with a stiff wire and the sheath with an appropriate-sized sheath. Stent placement was performed in 17 cases. The deployed stents were non-drug eluting and self-expandable nitinol stents (Bard Life Stent, Ev3 Protege Everflex, and Terumo Misago Rx). Stent placement was accomplished in lesions after refractory to PTA and stenting was also preferred for complications that were occurred after PTA such as dissection and pseudoaneurism. Because of the deployed stents were self-expanding, the diameter of stent was chosen as equal or 1 mm larger than that of the balloon to ensure stent conformation to the graft wall efficiently.

After the EVT, the patients were followed by cardiovascular surgeon. Physical examination, Doppler ultrasound and ABI evaluations were performed at 30 days, 3 months, 6 months, and 12 months after the procedure. One year after EVT, the follow-ups were performed once per 6 months. This follow-up programme was also assessed after femoropopliteal bypass graft surgery in our hospital. If graft failure was suspected with physical examination, Doppler ultrasound and ABI measurements, computerized tomography angiography, magnetic resonance angiography or DSA were performed.

The technical success of lytic therapy was defined as the restoration of antegrad blood flow with complete or near complete (95%) lysis of the thrombus and patency should continue least one month. The treatment with PTA and stent placement was defined as technically successful if there was less than 30% residual stenosis. The clinical success of EVT was denoted as relief of acute ischemic symptoms. Primary patency was defined as the time interval from the initial procedure to the first reintervention. Assisted primary patency was defined as the interval from the first intervention to permanent occlusion. The data including endovascular procedures, technical and clinical success, primary and assisted primary patency rates, complication rates and type of graft material, was obtained through the database of the department of interventional radiology at Baskent Hospital. We analyzed the duration of patency rates by using Kaplan-Meier analysis. We tested statistical

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significance of differences between groups with Log-Rank method. All analyses were performed by using SPSS 20.0 software.

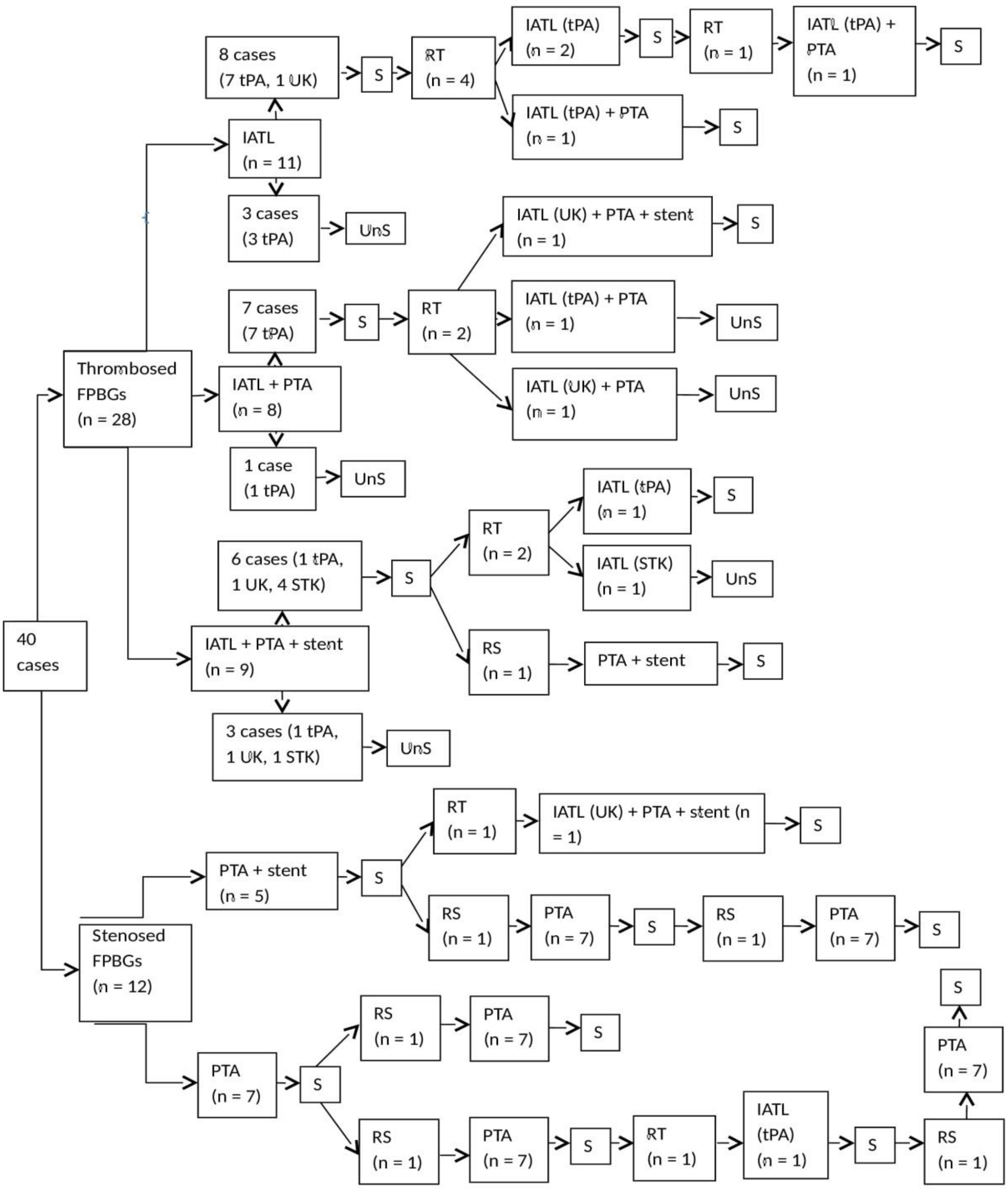


**Fig 1.** Flowchart of participants and interventions performed to the subjects in this study (FPBGs, femoropopliteal bypass grafts; tPA, tissue plasminogen activator; UK, urokinase; STK, streptokinase; IATL, intra-arterial thrombolytic therapy; PTA, percutaneous transluminal angioplasty; RT, rethrombosis; RS, restenosis; S, successful procedure; UnS; unsuccessful procedure.

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## RESULTS

Both technical and clinical successes were achieved in forty seven procedures. The initial successes of EVT in the thrombosed and stenosed grafts were 74.3 % (29/39) and 100% (18/18), respectively. In the stenosed grafts, the stenosis were found at the distal anastomosis in 7 grafts, proximal anastomosis in 5 grafts and both proximal and distal anastomosis in 6 grafts. Stenosis were also observed in 23 thrombosed grafts which were placed at the distal anastomosis in 14 grafts, proximal anastomosis in 1 graft and both proximal and distal anastomosis in 8 grafts. In thrombosed grafts, the initial success was achieved in 12 grafts with IATL (11 tPA and 1 UK), 9 grafts with IATL (9 tpA) and PTA, and 8 grafts with IATL (1 tPA, 5 STK and 2 UK), PTA and stenting. In 10 thrombosed grafts, the patency coud not been maintained by EVT. These unsuccessful procedures were 4 grafts with IATL (3 tPA, 1 STK), 3 grafts with IATL (2 tPA and 1 UK) and PTA, and 3 grafts with IATL (1 tPA, 1 STK and 1 UK), PTA and stenting. The EVT procedures, performed to the thrombosed and stenosed grafts, were demonstrated in flowchart (Fig 1). The initial success rates of EVT in the SV grafts and PTFE grafts were 90% and 78.5%, respectively. Fig 2 and Fig 3 show representative images of interventions.

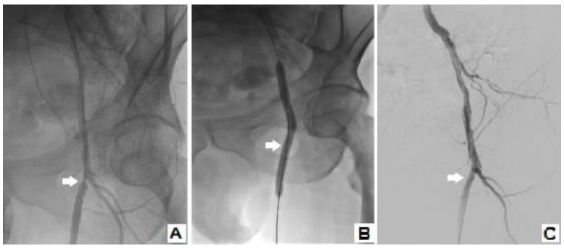


**Fig 2.** Digital subtraction angiography images. A. Image showed prominent stenosis in the origin of the femoropopliteal bypass graft (arrow). B. Percutaneous transluminal angioplasty treatment was performed to the stenosis (arrow). C. The patency of bypass graft was established without any residual stenosis (arrow).

The primary and assisted primary patency of all grafts were 24.2 ± 3.8 (95% CI: 16.8-31.6) months and 29.4 ± 4.2 (95% CI: 21.2-37.5) months, respectively. The primary and assisted primary patency of the thrombosed and stenosed grafts were featured in Table 1. The thrombolytic therapy with tPA was performed in 27 grafts while 12 grafts were treated with the other thrombolytic agents, such as STK and UK. The initial success of IATL with tPA (80.8%) was higher than STK and UK (66.7%). The lytic therapy with STK and UK was more effective in the short period, however tPA treatment was more durable in the long period (Table 2). Nevertheless, no statistically significant difference was found between the primary and assisted primary patency rates of those thrombolytic agents (Table 2).

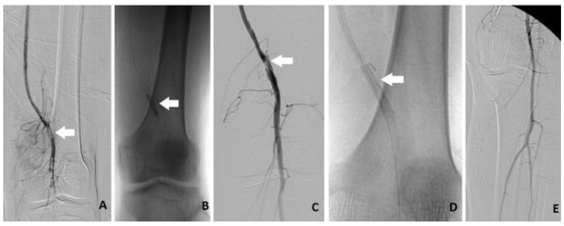


**Fig 3.** Digital subtraction angiography images. A. Image showed residual thrombus (arrow) in the distal segment of the femoropopliteal bypass graft following thrombolytic therapy. B. Percutaneous transluminal angioplasty treatment (arrow) was performed to the residual thrombosis in the bypass graft. C. Dissection (arrow) was developed after percutaneous transluminal angioplasty. D. Stent placement was accomplished at the dissected segment (arrow). E. The patency was maintained following stent placement.

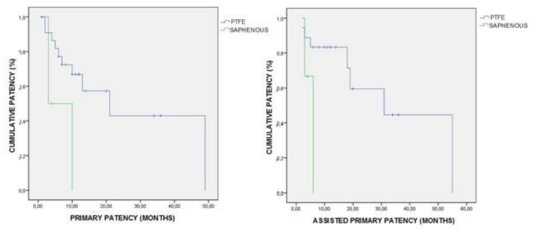


**Fig 4**. Primary and Assisted Primary Patency of Thrombosed PTFE Grafts and SV grafts.

The thrombosis (79.3%) has been observed more than stenosis (20.6%) significantly in the PTFE grafts ($p = 0.002$). Although, the stenosis rate (66.6%) was higher than thrombosis (33.3%) in the SV grafts, we found no significant correlation between those rates ($p = 0.157$). The primary and assisted primary patency rates were significantly higher in the thrombosed PTFE grafts as compared to SV grafts ($p<0.05$) (Fig 4). The primary and assisted primary patency rates of the thrombosed grafts were featured in Table 3. The initial success was 78.5% in the PTFE grafts, 90% in the SV grafts. There was no statistically significant difference between the primary and

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assisted primary patency of the stenosed PTFE and SV grafts (Table 4). After the graft placement surgery, the mean occlusion time of the PTFE and SV grafts were 18.9 ± 6.7 and 23.4 ± 7 months, respectively.

**Table 1.** The Primary and Assisted Primary Patency of Thrombosed and Stenosed Grafts

| | Thrombosed Grafts | Stenosed Grafts |
|---|---|---|
| Estimated primary patency (month) | 23 ± 4.9 (95% CI: 13.3-32.5) | 25.1 ± 6 (95% CI: 13.2-37) |
| 1. year primary patency rate (%) | 53.7 ± 10 | 51.9 ± 12.4 |
| 2. year primary patency rate (%) | 34.5 ± 13 | 38.9 ± 14.6 |
| 4. year primary patency rate (%) | 0 | 19.4 ± 15.6 |
| Estimated assisted primary patency (month) | 31.4 ± 6.3 (95% CI: 19-43.7) | 30.5 ± 5.7 (95% CI: 19.3-41.6) |
| 1. year assisted primary patency rate (%) | 75.6 ± 9.5 | 91.7 ± 8 |
| 2. year assisted primary patency rate (%) | 54 ± 14.6 | 60 ± 15.9 |
| 4. year assisted primary patency rate (%) | 40.5 ± 16 | 18 ± 15.1 |

At 6-month follow up, the major amputation rates were 2.5% and 5.5% in the thrombosed and stenosed grafts, respectively. The complications, occured after EVT, were featured in Table 5. Both major hemorrhage and one-month mortality rates were 10.2% in the thrombosed grafts and all of those were treated with tPA. On day 2 post-procedure, three patients died from major hemorrhage including 2 cases with retroperitoneal hemorrhage and 1 patient with intraabdominal hemorrhage. On day 5 post-procedure, 1 patient died from massive gastrointestinal hemorrhage. Minor hemorrhage such as groin hematoma was observed in 3 patients following İATL (1 tPa, 1 UK and 1 STK). No death or major hemorrhage was detected in the stenosed grafts. During the procedure, dissection was observed in three patients and pseudoaneurism has developed in one patient. The total complication rates, including major and minor complications were 23% and 11.1% in thrombosed and stenosed grafts, respectively.

## DISCUSSION

The FPBG surgery is a treatment option for patients who are at risk of losing limb by placing graft in the affected area to improve blood flow in the lower limb. The great SV and PTFE grafts are considered as the most acceptable conduits for arterial bypass. The patency of graft differs due to the type of graft material and comorbidities such as chronic

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diseases. The surgery and EVT are the main treatment options for the failed FPBG. However, there is no consensus about the treatment approach of the FPBG failure (2, 4, 8-17).

Previous studies indicated that initial success rates of EVT ranged from 70% to 90% and 85% to 95% in the thrombosed and stenosed grafts, respectively, which is consistent with our study (1, 6, 14, 18, 19). Some studies showed that the long term patency rate of EVT, was below the expectations in the thrombosed and stenosed grafts in spite of the high initial success rates (1, 11, 12, 20-22). In our study the primary and assisted primary patency rates were higher in the thrombosed grafts when compared with previous studies (1, 12, 20). The patency rates of the stenosed grafts were also similar to the previous reports (4, 21, 22).

**Table 2.** The Primary and Assisted Primary Patency of the Thrombolytic Therapy with tPA and STK or UK.

| | tPA | STK or UK | p value |
|---|---|---|---|
| Estimated primary patency (month) | 20.7 ± 3.7 (95% CI: 13.5-28) | 19.5 ± 7.4 (95% CI: 5.1-34) | 0.794 |
| 1. year primary patency rate (%) | 49.7 ± 12.3 | 62.5 ± 17.1 | |
| 2. year primary patency rate (%) | 49.7 ± 12.3 | 20.8 ± 17.9 | |
| Estimated assisted primary patency (month) | 23.9 ± 4.3 (95% CI: 15.5-32.3) | 29.5 ± 10.1 (95% CI: 9.6-49.3) | 0.649 |
| 1. year assisted primary patency rate (%) | 72.2 ± 11.9 | 83.3 ± 15.2 | |
| 2. year assisted primary patency rate (%) | 54.2 ± 18 | 55.6 ± 24.8 | |

**Table 3.** The Primary and Assisted Primary Patency of the Thrombosed PTFE and SV Grafts.

| | Thrombosed PTFE Grafts | Thrombosed SV Grafts | p value |
|---|---|---|---|
| Estimated primary patency (month) | 27.1 ± 5.8 (95% CI: 16-38.3) | 6.5 ± 1.6 ay (95% CI: 3.3-9.6) | 0.013 |
| 1. year primary patency rate (%) | 66.9 ± 10.3 | 19 ± 16.8 | |
| 2. year primary patency rate (%) | 43 ± 15.6 | 0 | |
| Estimated assisted primary patency (month) | 34.1 ± 6.7 (95% CI: 21-47.3) | 5 ± 1.1 ay (95% CI: 2.7-7.2) | 0.038 |
| 1. year assisted primary patency rate (%) | 83.3 ± 8.8 | 0 | |
| 2. year assisted primary patency rate (%) | 75 ± 21.7 | 0 | |

**Table 4.** The Primary and Assisted Primary Patency of the Stenosed PTFE and SV grafts.

| | Stenosed PTFE Grafts | Stenosed SV Grafts | p value |
|---|---|---|---|
| Estimated primary patency (month) | 17.6 ± 4.6 (95% CI: 8.5-26.8) | 24.3 ± 7.4 (95% CI: 10 ± 39) | 0,850 |
| 1. year primary patency rate (%) | 50 ± 20.4 | 53.6 ± 15.6 | |
| 2. year primary patency rate (%) | 50 ± 20.4 | 35.7 ± 17.9 | |
| Estimated assisted primary patency (month) | 22.7 ± 7.6 (95% CI: 7.7-37.7 | 31 ± 6.7 (95% CI: 17.7-44.1) | 0.988 |
| 1. year assisted primary patency rate (%) | 75 ± 21.7 | 87.5 ± 11.7 | |
| 2. year assisted primary patency rate (%) | 75 ± 21.7 | 54.7 ± 20.1 | |

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Previous studies revealed that initial success of EVT ranged from 76% to 98% in the thrombosed PTFE grafts, similar to our study (1, 14, 19). However, our initial success rates of EVT were higher in the thrombosed SV grafts, as compared to the previous studies which have reported the initial success rates were ranging from 66% to 78% (1, 12, 14, 19).

**Table 5.** Complications Following Endovascular Therapy in Femoropopliteal Bypass Graft Failure

| Complications | Thrombosed Grafts | Stenosed Grafts |
|---|---|---|
| Major Complications | | - |
| • Major Hemorrhage | 4 | - |
| ➢ Retroperitoneal hemorrhage | 2 | - |
| ➢ Gastrointestinal hemorrhage | 1 | - |
| ➢ Intraabdominal hemorrhage | 1 | - |
| Minor Complications | | |
| • Minor Hemorrhage | 3 | - |
| • Dissection | 1 | 2 |
| • Pseudoaneurysm | 1 | - |

The majority of the previous studies indicated that the patency of thrombosed SV grafts was more durable than prosthetic grafts after successful lysis (14, 23). Conrad et al. (14) reported that the functioning endothelium could protect against the prothrombotic potential in thrombosed SV grafts after successful lysis, as compared to prosthetic grafts which have not this endothelium protection. And also, Jackson et al. (24) revealed that the incidence of limb-threatening ischemia was found to be higher after the occlusion of PTFE grafts than SV grafts which have a potential for forming the collateral circulatory to maintain limb viability in case of graft failure. However, few studies demonstrated that thrombosed prosthetic grafts had better patency rates after lytic therapy than SV grafts which is consistent with our study (1, 3, 25). Although, the endothelium shows a protective potential against the thrombosis in the SV grafts, the intimal injury which can develop due to the arterial pressure, leads to the platelet adherence and intimal hyperplasia which may result in graft thrombosis in the SV grafts. And also, PTFE grafts are more durable to the blood pressure and have a lower risk of complications such as aneurysm or dissection. As a result of these advantages of PTFE grafts, we consider that following successful lytic therapy, thrombosed PTFE grafts also presents better patency rates in contrast to several previous studies (14, 23).

In the SV grafts, symptomatic stenosis may develop owing to the intimal hyperplasia, technical errors as well as dysplastic post-phlebitic veins. Several studies stated that 1 year patency rates of the stenosed SV grafts following EVT, has ranged from 54% to 62%, which is similar to our study (4, 21). Although, SV graft is considered as the most acceptable conduit, we found no statistical difference between the patency rates of the stenosed SV grafts and PTFE grafts after EVT (23, 24).

In both thrombosed and stenosed grafts, self-expandable nitinol stents were accomplished in the stenosis after refractory to the PTA in this study. We believe that self-expandable nitinol stents conforms to the graft wall efficiently. The size discrepancy between graft and native vessel in the anastomotic site might lead to dissection or extravasation while stent placement. As a result of this, we chose self-expandable stents to provide safer stent conformation to the graft. Also self-expandable stents are more resistive to the stent fractures which may generally occur at the anastomotic sites.

The catheter-directed intra-arterial thrombolysis has become the most preferable treatment option and reduces the need of surgery for bypass graft thrombosis. Direct delivery of the lytic agent inside the thrombosed segment of the graft produces increased plasmin activity locally, protects this plasmin from the circulating antiplasmin. Therefore, the effective therapy can be achieved with low dose lytic therapy. IATL may also lyse the thrombus in the collateral vessels and distal small arteries which is beneficial if a new bypass graft must be

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replaced. In addition, after successful lysis, underlying causative lesions can be identified and treated with PTA or stent placement. However, the risks of complications including minor and major hemorrhage, distal embolization as well as the mortality risk have limited the usage of thrombolytic agents (2, 3, 11, 14, 26, 29). Several studies reported that the lower risk of major hemorrhage and mortality and the higher rates of the technical and clinical success have been observed in IATL with UK as compared to tPA (27, 28). In contrast, some studies found no statistical significant difference in the efficacy and safety between tPA and UK treatments in the thrombosed grafts (15, 29). In our study, the initial success rate was higher in the tPA group when compared with UK and STK. We also detected that STK and UK treatment was more effective in the short period, but in the long period the efficacy of tPA treatment was better. However, there was no statistically significant difference between the primary and assisted primary patency of thrombosed grafts, treated with tPA and STK or UK. Additionally, in this study, complications such as major hemorrhage, mortality and amputation were observed in the patients who have treated with tPA and these complication rates were similar to the previous studies, except amputation rate which was lower as compared to the previous reports (27, 28, 30).

The treatment approach of FPBG failure is still controversial (3-6, 11-15, 19-21, 25-30). In a study performed by Abu Rahma et al., where lysis/PTA therapy and thrombectomy/open patch angioplasty were compared, the higher 2 years patency rates were detected in the surgery as compared to lysis/PTA therapy and these rates were reported as 87% for surgery, 26% for EVT (13). However, they found no statistically significant difference of mortality and morbidity rates between surgery and EVT (13). In another study by Berridge et al., in which thrombolytic therapy and surgery were compared, no statistically difference was found limb salvage and death rates at 1, 6 and 12 months between surgery and thrombolysis, but they showed major hemorrhage and distal embolization had been more likely in thrombolysis when compared with surgery (16). STILE Investigators reported that thrombolysis in patients with acute ischemia and surgery in patients with chronic ischemia was more likely to provide better patency rates and limb salvage (29). In the present study, we have not compared our results with surgery however we consider that thrombolytic therapy can be the first choice for FPBG thrombosis due to the advantages of having easy application, being less invasive and inexpensive, ability to lyse collateral vessels near graft and being available for high surgical risk patients.

Previous studies revealed that surgery has been superior to the EVT in stenosed grafts by comparison the patency rates and limb salvage (4, 5, 17, 22). Nehler et al. showed that 1, 2 years patency rates and mortality rate were 99%, 97% and 0.9% following surgery in the stenosed bypass grafts, respectively (17). In this study, the initial success rate of PTA and stent placement was high in the stenosed grafts, however the long term patency rates were not as good as surgery (17, 22). Although surgery has better patency rates, EVT is a good alternative for high surgical risk patients and also can be used in patients who have deeply placed grafts, resulting in difficulties for surgical revision.

This study has some limitations which have to be pointed out. First, it was designed as a retrospective study. Second, we did not compare our results with surgery to determine the best treatment approach for FPBG failure. Finally, the sample size was relatively small to generalize the results.

In conclusion, we consider that EVT including IATL, PTA and stent placement for FPBG failure is effective procedure. Although EVT is not as durable as surgery, it may offer advantages superior to surgery such as being less invasive and available for serial interventions for refractory lesions following EVT or surgery and it is also a good alternative for high surgical risk patients to maintain limb salvage. In contrast to the majority of previous studies, we found that the patency rates of thrombosed PTFE grafts following EVT, were significantly higher than thrombosed SV grafts owing to the inflammatory changes that may develop in the vein graft wall during the thrombosis.

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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