

Comparison of short- and mid-term outcomes of antiplatelet versus anticoagulant use in peripheral artery disease patients with synthetic grafts

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ABSTRACT

Objectives: This study aimed to compare the short- and mid-term outcomes of graft patency in patients receiving anticoagulant or antiplatelet therapy during the postoperative period.

Patients and methods: A total of 109 patients (103 males, 6 females; mean age 69.5±7.9 years; range 44 to 80 years) were included in this retrospectively study between January 2015 and January 2022. Of these, 46 patients were receiving anticoagulant therapy, while 63 were on antiplatelet therapy. The graft patency rates were evaluated during outpatient follow-ups at one-, three-, six-, and 12 months through physical examinations and imaging methods (Doppler ultrasonography or computed tomographic angiography).

Results: The efficacy of anticoagulant and antiplatelet therapy was similar after femoropopliteal bypass using a synthetic graft.

Conclusion: We believe that treatment plans should be individualized for each patient in the postoperative period.

Keywords: Antiagregan therapy, anticoagulant therapy, peripheral artery disease, synthetic graft usage.

Considering its past, present, and future, many unanswered questions remain regarding peripheral artery disease (PAD). Addressing some of these questions, particularly in the context of femoropopliteal occlusive artery disease, constitutes the main objective of our study. Peripheral artery disease is one of the major causes of morbidity that negatively affects patients' quality of life.^[1] Atherosclerosis is the primary cause of most lower extremity vascular issues. As a result of atherosclerosis, stenosis or narrowing occurs in the main arteries supplying the lower extremities, leading to symptoms in patients. In addition to atherosclerosis, PAD also includes thrombosis, arterial inflammation, arterial dilation, aneurysm formation, or external compression leading to arterial stenosis or occlusion.^[2,3]

The most common site for the development of atherosclerotic occlusive lesions in the lower extremities is the femoropopliteal artery segment. When occlusive disease occurs in these arteries, a wide range of clinical manifestations can arise, from claudication to amputation, depending on the severity of the lesion. The severity of clinical symptoms in PAD is

determined by the degree of arterial narrowing, the ability of collateral circulation to provide sufficient tissue perfusion, blood viscosity, and the presence of comorbid conditions in the patient.^[4]

Several classic cardiovascular risk factors, such as diabetes mellitus (DM), dyslipidemia, smoking, hypertension (HT), and advanced age, play a role in the etiology of PAD.^[2,3] The signs and symptoms of PAD reflect the degree of circulatory impairment, indicating whether this deterioration occurs gradually over a long period or acutely and irreversibly. Proper clinical assessment is critical for accurate diagnosis and for determining the most appropriate treatment strategy.

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After deciding on surgical intervention for PAD, two main treatment options are available: endovascular procedures and surgical intervention. The burden of calcification in femoropopliteal lesions has been proven to affect both the success of the procedure and the mid-term restenosis rate. Ketenciler et al.^[5] and Fanelli et al.^[6] reported that an increased cross-sectional calcification burden observed on computed tomography angiography, along with a longitudinal calcification burden observed on digital subtraction angiography, is associated with a progressive decline in clinical success. Moreover, this study demonstrated that the cross-sectional calcification burden was a stronger predictor of poor outcomes compared to the longitudinal calcification burden.

Additionally, the severity of ischemia in the patient, the need for revascularization, and the suitability for revascularization should be evaluated through objective tests. When planning treatment after an objective assessment, factors such as comorbidities, prior medical history, and the necessity of surgical treatment should be considered.^[7-9]

For symptomatic patients, single antiplatelet therapy is recommended, whereas dual antiplatelet therapy is suggested for patients undergoing percutaneous intervention. In patients undergoing surgical intervention, the choice between dual antiplatelet therapy or a combination of antiplatelet and anticoagulant therapy should be made based on graft patency and bleeding risk.^[10]

In this study, we aimed to determine the short and medium term results on graft patency in patients who received anticoagulant and antiaggregant treatment in the postoperative period and their advantages and disadvantages over each other.

PATIENTS AND METHODS

This single-center, retrospective, observational cross-sectional study included adult patients who underwent surgery using a synthetic graft due to PAD at the Eskişehir Osmangazi University Faculty of Medicine between January 2015 and January 2022. A total of 109 patients (103 males, 6 females; mean age 69.5 ± 7.9 years; range 44 to 80 years) were included in the study. All patients were symptomatic, presenting with complaints such as claudication, pain, difficulty walking, and early

fatigue. For patients scheduled for surgery, any ongoing antiplatelet and anticoagulant treatments were discontinued one week prior to the procedure, and low-molecular-weight heparin was administered at a therapeutic dose based on body weight. Patients' demographic data (age and sex) and general health information (HT, DM, atrial fibrillation [AF], hyperlipidemia, chronic kidney disease, coronary artery disease, and smoking status) were retrieved from the hospital database. Written informed consent was obtained from all participants. The study protocol was approved by Eskişehir Osmangazi University Faculty of Medicine Ethics Committee (date: 19.10.2023, no: 45425468-42). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Surgical technique

Under general anesthesia, incisions were made in the femoral and supragenicular medial tibial regions. Proximally, the common femoral artery was dissected and suspended. Through the incision in the supragenicular medial tibial region, the supragenicular popliteal artery was similarly dissected and suspended. Heparin was administered at a dose of 100 IU/kg.

An arteriotomy was performed on the popliteal artery. A synthetic graft of appropriate diameter was anastomosed end-to-side in a continuous manner to the popliteal artery. The graft was then tunneled through a subcutaneous passage and delivered to the femoral region. An arteriotomy was also performed on the common femoral artery, and the proximal end of the graft was anastomosed end-to-side in a continuous fashion. Adequate flow was observed in both the proximal and distal sections of the graft. After confirming hemostasis, the surgical layers were closed in an appropriate manner.

Postoperative period

All patients were monitored in an intensive care unit for 24 h postoperatively. During this period, heparin infusion was administered at a dose adjusted to body weight. On the first postoperative day, 46 patients were started on anticoagulant therapy, while 63 patients received antiplatelet therapy (acetylsalicylic acid [ASA] and clopidogrel).

Patient data were obtained from follow-up examinations and hospital record systems. After discharge, patients underwent physical examinations,

Doppler ultrasonography, and, when necessary, computed tomography angiography to assess graft patency and complications at one-, three-, six-, and 12-month follow-up visits.

Statistical analysis

Data were analyzed using SPSS version 15.0 software (SPSS Inc., Chicago, IL, USA). Descriptive statistics were expressed as frequency, percentage, and mean \pm standard deviation (SD). Categorical data were analyzed using the chi-square test and Fisher exact test. A p -value <0.05 was considered statistically significant.

RESULTS

The most common systemic disease was HT, observed in 63 (57.7%) patients, followed by hyperlipidemia in 61 (55.9%) patients. Coronary artery disease was present in 53 (48.6%) patients, DM in 50 (45.8%), smoking in 46 (42.2%), chronic kidney disease in eight (7.3%), and AF in five (4.5%) patients. The demographic and clinical data of the study population are summarized in Table 1.

The postoperative outcomes of the patients are presented in Table 2. A total of five (4.5%) patients

Table 1
Demographic and clinical data of the study population

	Anticoagulant (n=46)		Antiaggregant (n=63)		<i>p</i>
	n	%	n	%	
Sex					
Male	45	97.8	58	92.1	0.398 ^a
Female	1	2.2	5	7.9	
Hypertension	29	63	34	54	0.34 ^b
Hyperlipidemia	25	54.3	36	57.1	0.77 ^b
Coronary artery disease	23	50	30	47.6	0.80 ^a
Smoker	20	43.5	26	41.3	0.81 ^a
Chronic kidney failure	4	8.7	4	6.3	0.71 ^a
Diabetes mellitus	17	37	33	52.4	0.11 ^b
Atrial fibrillation	5	8.7	0	0	0.12 ^c

a Fisher exact test; b Pearson Chi-square test; c Chi-square test.

Table 2
Operative and postoperative outcomes

	Anticoagulant		Antiaggregant		Total		<i>p</i>
	n	%	n	%	n	%	
Number of patients (postoperative period)	47	43.1	62	56.9	109		0.96 ^a
Postoperative early stage bleeding-hematoma (first 24 h)	2	4.2	3	4.8	5	4.5	0.64 ^b
1 st month patency	45	95.7	60	96.7	105	96.3	0.32 ^b
3 th month patency	44	93.6	59	95.1	103	94.4	0.50 ^a
6 th month patency	44	93.6	58	93.5	102	93.5	0.85 ^a
1 st year patency	43	91.4	56	90.3	99	90.8	0.36 ^b
Wound infection	4	8.7	8	12.7	12	11	0.36 ^b
Amputation	4	8.7	6	9.5	10	9.1	0.58 ^b

a Chi-square test; b Fisher exact test.

required revision due to early bleeding or hematoma within the first 24 h. Twelve (11%) patients experienced wound infections, and 10 (9.1%) patients required amputation of the lower extremity.

DISCUSSION

In this study, we analyzed patency and survival outcomes in the postoperative period for patients who underwent femoropopliteal bypass procedures due to PAD. According to the literature, PAD is more prevalent in males.^[10] Factors such as higher rates of smoking, elevated low-density lipoprotein levels, and reduced high-density lipoprotein levels in males are thought to contribute to this trend. Similarly, in our study, PAD was more frequently observed in males, consistent with previous findings. Among our patients undergoing femoropopliteal bypass with synthetic grafts, 94.5% were male, and 5.5% were female.

Studies by Selvin et al.^[11] and Menke et al.^[12] reported a higher prevalence of PAD in patients with chronic kidney disease. In our study, femoropopliteal bypass was performed in eight patients with chronic kidney disease. Another subgroup characterized by poor survival and graft patency outcomes was those with AF. Previous studies have demonstrated a strong association between AF and major cardiac events, morbidity, and mortality.^[13] Among the five AF patients in our study, one required amputation, and another underwent reoperation due to graft thrombosis.

Amputation is a critical endpoint in the postoperative period following femoropopliteal bypass surgery for PAD. In a study conducted by Rahman and Özkısacık,^[14] the amputation rate was reported as 7.6%. Similarly, our study identified an amputation rate of 9.1%, aligning with the literature. Regarding antithrombotic therapy in patients undergoing femoropopliteal bypass with synthetic grafts, different treatment modalities have been reported in the literature.^[15] Additionally, various surgical clinics apply different treatment protocols, and optimization of these therapies remains an ongoing area of research. A meta-analysis of 16 studies evaluated the effect of antiplatelet therapy after femoropopliteal bypass.^[16] The analysis revealed that antiplatelet therapy with ASA or a combination of ASA and dipyridamole generally yielded positive effects on primary vessel patency rates after 12 months. Subgroup analysis suggested that antiplatelet

therapy might provide greater benefits in patients with synthetic grafts compared to those with vein grafts.^[16] A study comparing ASA plus placebo with ASA plus clopidogrel found that the latter combination did not increase overall efficacy in the peripheral bypass population but demonstrated statistically significant benefits in patients with prosthetic grafts.^[17] Furthermore, combined therapy was not associated with an increased bleeding risk.

In our study, based on previous findings, we administered dual antiplatelet therapy with ASA and clopidogrel in the postoperative period. In the follow-up of patients receiving dual antiplatelet therapy in this group beyond the first 24 h postoperatively, no major bleeding was observed. The majority of studies, as highlighted above, have focused on ASA and clopidogrel. However, there is insufficient data regarding the use of other antiplatelet agents in patients with synthetic grafts, emphasizing the need for further extensive studies.

The use of ASA, vitamin K antagonists (VKAs), and dual antiplatelet therapy after lower extremity bypass surgery was compared,^[15] and ASA use significantly improved graft patency compared to placebo. While VKAs did not affect graft patency rates, they were associated with approximately a two-fold increase in bleeding complications. Similar to the literature, our study found no significant difference in graft patency rates between the anticoagulant and antiplatelet groups (one-year patency rates of 84.8% for the anticoagulant group and 93.7% for the antiplatelet group).

The most common anticoagulation protocol in Türkiye involves initiating therapy with low-molecular-weight heparin and VKA, followed by transitioning to VKA monotherapy once the target international normalized ratio (INR) level of 2 is achieved and maintained for 24 h. However, Sargin et al.^[18] reported that patients spent only 34.3% of their follow-up time within the therapeutic INR range of 2 to 3. Moreover, the mean INR value remained below 2 in 52.03% of patients.^[18]

The multicenter prospective Bypass Oral Anticoagulants or Aspirin study randomized patients undergoing lower extremity bypass surgery to receive either anticoagulant therapy or antiplatelet therapy (ASA 80 mg/day).^[19] While overall graft patency rates did not differ significantly, subgroup analysis indicated that oral

anticoagulant therapy might improve venous graft patency rates compared to ASA, whereas ASA was more effective in improving synthetic graft patency compared to anticoagulants.^[19] These findings underscore the importance of medication-related health considerations, particularly in the elderly population.^[20] In our clinical follow-up, achieving and maintaining target INR levels remained a significant challenge in the anticoagulant group. Among our patients, 10 required rehospitalization due to elevated INR levels, yet no major bleeding events were detected. The low socioeconomic and awareness levels of our patients were identified as key factors influencing their adherence. Therefore, we believe that patients prescribed warfarin, as well as their caregivers, should receive comprehensive education on the importance of regular INR monitoring and its dietary and drug interactions.

This study had certain limitations. First, patency rates were assessed using Doppler ultrasonography in the postoperative period, which is more subjective and operator-dependent compared to computed tomography angiography. Second, the relatively small sample size was another limitation.

In conclusion, our findings indicate that short- and mid-term graft patency rates were comparable across both treatment groups. Consequently, we emphasize the necessity of considering patient demographics, procedural specifics, and adherence to treatment regimens when initiating postoperative medical management.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Idea/concept, data collection and/or processing: M.Ç.; Design, analysis and/or interpretation, literature review, writing the article, references and fundings, control/supervision, critical review: M.Ç., A.Ş.

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