

Original Article

Mid-term results of combined medical and popliteal artery endarterectomy treatment in Buerger's disease

Umit Kahraman¹, Sedat Karaca¹, Karya Islamoglu², Aysen Yaprak Engin¹, Fatih Islamoglu¹

¹Ege University, Faculty of Medicine, Department of Cardiovascular Surgery, İzmir, Türkiye

²Ege University School of Medicine, 6th grade, İzmir, Türkiye

Received: September 08, 2023 Accepted: October 15, 2023 Published online: October 22, 2023

Content of this journal is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License



Abstract

Aim: Our aim in this article is to present the mid-term results of the best preoperative and postoperative medical treatment and analgesia treatment in patients with advanced Buerger's disease who underwent saphenous patchplasty and saphenous distal bypass after endarterectomy to the popliteal artery or trifurcation area.

Material and Methods: Between 2015 and 2023, we operated on 83 patients, diagnosed with Buerger's disease, who were in the chronic stage of the disease, and whose advanced imaging was performed. Preoperative, postoperative, and 1st year control evaluations were determined according to Rutherford, Fontaine classification, and Ankle-Brachial Indexes. Medical treatments of the patients were organized by the vascular surgery team and algology department. After determining the surgical approach strategy according to the imaging of the patients, saphenous patchplasty and anatomical bypass were performed.

Results: The mean preoperative ankle-brachial index was 0.305, the mean postoperative ankle-brachial index was 0.644, and the mean 1-year ankle-brachial index was 0.629 in 83 patients included in the study. Statistically significant improvements were observed in the Rutherford and Fontaine classifications. (p-value < 0,001) Amputation was performed in 9.6% of patients within 1 year.

Conclusion: Good clinical results and limb salvage can be achieved with a combined medical and surgical treatment approach in advancedstage patients who do not respond despite optimal medical treatment. Provided that patients quit smoking, good determination of the target surgical site, Saphenous patchplasty, and Saphenous distal bypass applied after endarterectomy in suitable patients are supported with good medical and analgesia treatment, the results will improve further.

Keywords: Buerger's Disease, thromboangiitis obliterans, saphenous patchplasty, popliteal bypass

INTRODUCTION

Buerger's disease (Thromboangiitis Obliterans) is an inflammatory occlusive disease involving primarily small and medium-sized arteries and veins of the extremities [1]. Although the etiology of the disease is not known exactly, active smoking and male gender are predisposing factors for the disease [2]. After the granulomatous infiltrative process in the acute phase of Buerger's disease, lesions become chronic and lead to fibrotic

band formations [3]. These bands especially affect the perfusion of distal arteries. Although lesions are seen in different anatomical regions, the infra-genicular level is usually affected [4]. Although intermittent claudication is mostly seen in the physical examination of patients diagnosed with Buerger's disease, rest pain due to circulatory disturbance, and minor and major tissue destruction may be observed in the long term. Treatment options for advanced Buerger's disease with this clinical presentation are still controversial. In the literature, there are medical treatments,

CITATION

Kahraman U, Karaca S, Islamoglu K, Engin AY, Islamoglu F. Mid-term results of combined medical and popliteal artery endarterectomy treatment in Buerger's disease. Turk J Vasc Surg. 2023;32(3):174-80.



Corresponding Author: Umit Kahraman, Ege University, Faculty of Medicine, Department of Cardiovascular Surgery, İzmir, Türkiye
Email: umitkahraman81@gmail.com

sympathectomy, and experimental surgical interventions like stem cell applications [2,5-7].

Although the prognosis was poor after previous surgical interventions, especially in the acute phase, today, combined treatment with advanced medical treatment and a multidisciplinary approach may lead to favorable results [8,9]. In this article, we presented the mid-term results of patients who underwent saphenous patchplasty and saphenous distal bypass after endarterectomy to the popliteal artery or trifurcation region, followed by good preoperative and postoperative medical treatment. We excised the fibrin band caused by the chronic inflammation due to Buerger's disease with endarterectomy and performed saphenous patchplasty and saphenous distal bypass.

MATERIAL AND METHODS

Ethics Statement and Informed Consent

Ethics committee approval for this study was granted by the ethics committee of our university at the ethics committee meeting held on 17.05.2022 with the letter numbered E99166796-050.06.04-693052. Informed consent forms were obtained from all patients included in the study.

Study Design, Patient and Data Collection

The study included 83 patients who received combined medical and surgical treatment in our clinic between 2015 and 2023. Patients were included based on the presence of distal vascular bed involvement on routinely performed computed tomography angiography images in hospitalization, a previous diagnosis of Buerger's disease, being in the chronic stage of Buerger's disease, and being in the advanced stage according to the international Rutherford and Fontaine classification and also the patients were determined according to the diagnostic criteria of Shionoya. All patients had critical ischemic pain in spite of painkiller regimens. Ankle-brachial indexes were measured by Ankle Brachial Index Screening Device (ABPIMD) device (MESI Inc. Slovenia). Patients were screened retrospectively after ethics committee approval and informed consent forms were obtained.

Medical Therapy

Medical Therapy was started first for every hospitalized patient including the following:

Platelet Inhibitors

Acetyl Salicylic Acid: In our study, patients whose antiplatelet treatment regimen was continued with acetylsalicylic acid in the postoperative period used 100 mg per oral (PO) 1x1. Patients started the antiplatelet treatment regimen on postoperative day 1.

Clopidogrel: In our study, patients who continued their antiplatelet treatment regimen with clopidogrel in the postoperative period used 75 mg PO 1x1. Patients started the antiplatelet treatment regimen on postoperative day 1.

Anticoagulation

In our study, all patients used low molecular weight heparin (LMWH) in the early postoperative period until the mobilization process. The treatment regimen of the patients was 100 Units/kg subcutaneous (SC) injection 2x1.

Rivaroxaban: In our study, in patients whose anticoagulant treatment was continued with rivaroxaban after mobilization in the postoperative period, the treatment regimen was started as 15 mg (PO) 2x1 and adjusted to 20 mg PO 1x1 in the first week of treatment.

Prostacyclin Analogues

Iloprost: In all patients included in the study, prostacyclin analogs treatment was completed in 5 days in the preoperative period and 3 days in the postoperative period. Patients received iloprost at a dose of 1 ng/kg as a 6-hour infusion per day.

Cilostazol

All patients included in the study were treated with 2x100 mg Cilostazol after iloprost treatment. The patients were discharged with Cilostazol treatment.

Synthetic polysaccharides with anticoagulant activity

Dextran: Postoperative Dextran infusion was 20 ml/h on the first postoperative day in all patients included in the study.

Analgesia

Preoperative and postoperative analgesia treatment of the patients was organized by the algology team. The treatment regimen was divided into 3 subgroups 1- No use of analgesic drugs, 2- Paracetamol, non-steroidal antiinflammatory (NSAID), synthetic opioid derivatives, and 3- Gabapentinoids, and opioid derivatives.

Surgical Therapy

Surgical treatment planning was based on preoperative computed tomography angiography imaging. According to the computed tomography, we evaluated the patients with organized thrombus and blood vessel fibrosis in the end-stage lesions as chronic buerger patients. There was no significant increase in acute phase reactants of these patients. C-reactive protein values above the normal reference value (0-5) were detected in 10 mg/L (12.04 %) patients preoperatively, while 3 mg/L (3.6%) patients with sedimentation values above 20 mg/L were observed. Patients in the chronic process were operated on.

All patients had medical treatment before with unsatisfied results leading to limb amputation starting with toes. Below knee inflammatory occlusion of trifurcation arteries of these patients was making it impossible success or chance to make classical angioplasty or endovascular techniques. Two procedures were performed in this technique.

Saphenous Patchplasty

Saphenous patchplasty was performed for patients whose occlusion was confined to infragenicular popliteal artery and trifurcation branches. The popliteal artery, tibioperoneal trunk, and anterior tibial artery were found at the infragenicular level in patients and prepared for clamping. After the clamping, a longitudinal incision was performed from the popliteal artery through to the tibioperoneal trunk and, anterior tibial artery (Figure 1). Then excision of the fibrin band was performed that developed secondary to chronic inflammation in the background of Buerger's disease (Figure 2). The operation was completed by patchplasty and anatomic bypass with saphenous vein graft which was prepared after fibrin band excision.

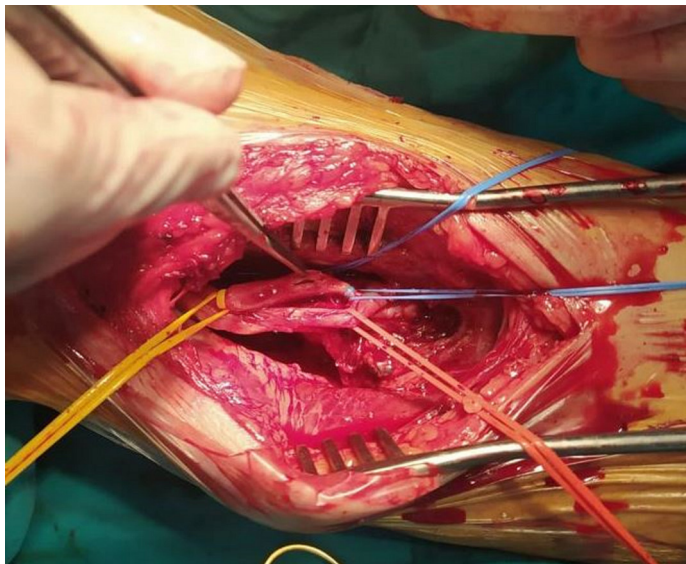


Figure 1. A longitudinal incision was performed from the popliteal artery through to the tibioperoneal trunk and, anterior tibial artery

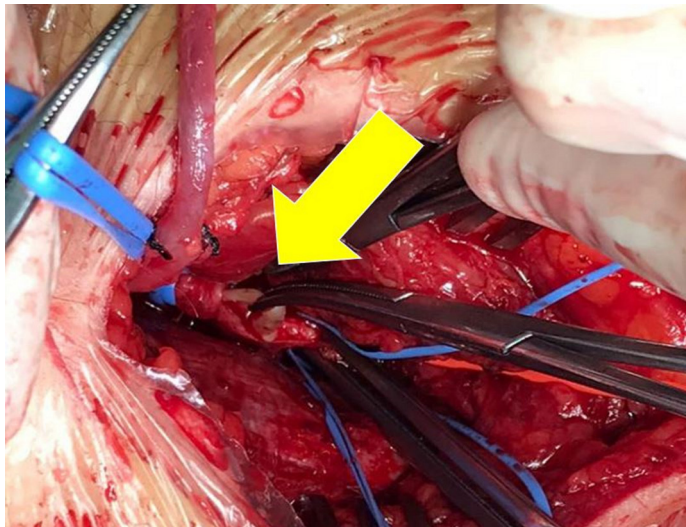


Figure 2. Excision of the fibrin band was performed that developed secondary to chronic inflammation in the background of Buerger's disease

Anatomic Bypass

Anatomic bypass procedures were performed for patients whose occluding disease affected both supragenicular and infragenicular popliteal arteries. The operation was performed by using a saphenous vein graft from appropriate levels based on preoperative computed tomography (CT) evaluation in addition to total excision of fibrin band causing high-grade stenosis of Buerger's disease starting from the supragenicular level and reaching the infragenicular level. Proximal anastomosis was performed on the common femoral artery in some patients and on the suprafragenicular popliteal artery in some patients. All distal anastomoses were made to the infragenicular popliteal artery.

The saphenous vein was used as a graft in all patients. The saphenous vein was prepared above the knee in all patients according to the graft size.

Statistical Analysis

Data analysis was performed in IBM SPSS (version 25). When summarizing the data of the patients, frequencies, and percentages were given for categorical variables and means and standard deviations were given for continuous variables. Friedman's analysis was performed in the analyses related to scoring of the stage according to the international Rutherford and Fontaine classification and Wilcoxon Signed Ranks Test was applied for significant variables. Bonferroni adjustment was made to avoid erroneous p values in multiple comparisons and the results were reported. A chi-square test was applied for independent group comparisons. Spearman correlation was used for the relationship between variables and a p-value less than 0.05 was considered statistically significant for each test.

RESULTS

Patient Characteristics

The study consists of 83 patients who were treated at Ege University Faculty of Medicine, Department of Cardiovascular Surgery between 2015 and 2023. Twenty (24.1%) of the patients were female, and 63 (75.9%) were male. The mean age was 41.86 ± 4.5 years. Hypertension was observed in 42 patients (50.6%), diabetes and hyperlipidemia with high cholesterol levels were not observed in any of the patients, and chronic renal failure-dialysis free was observed in 2 (2.9%) patients. Smoking was recorded in 63 (75.9%) of the patients in the sample before the operation. All patients had previously smoked. C-reactive protein values above the normal reference value (0-5) were detected in 10 (12.04%) patients preoperatively, while 3 (3.6%) patients with sedimentation values above 20 were observed. 77 patients (92.8%) had no motor deficiency, and 71 patients (85.5%) had no sensorial deficiency (Table 1).

Table 1. Demographic data of patients

Variables (n: 83)		Mean±standard deviation/N (percentile)
Sex	Female	20 (24.1 %)
	Male	63 (75.9 %)
Comorbidities	HT	42 (50.6%)
	DM	-
	Hyperlipidemia	-
	Chronic renal disease	2 (2.9%)
Smoker		63 (75.9%)
CRP (mg/L)		5.58±14.6
Sedimentation (>22 mm/hr)		3 (3.6%)
Motor deficiency		6 (7.2%)
Sensorial deficiency		12 (14.5%)

HT: hypertension, DM: diabetes mellitus

Shionoya's Diagnostic criteria

According to the diagnostic criteria of Shionoya in our patients, the mean age was 41.86 ± 4.5 years, although 68.8 % quit, all of them were smokers and only hypertension (50.6%) was observed in atherosclerotic factors. All the patients had popliteal artery and trifurcation involvement at an operable level.

International Classifications and Ankle-Brachial Index

While the mean preoperative ankle-brachial index (ABI) of 83 patients was 0.305 ± 0.081 , the mean postoperative ankle-brachial index was 0.644 ± 0.092 , and the mean 1-year ankle-brachial index was 0.629 ± 0.101 (Figure 3).

According to Rutherford's classification (class 1,2,3,4,5,6), the class of the number of patients was (1, 1, 4, 29, 39, 9; mean class: 4.901 ± 0.803) in the preoperative period, (16, 19, 26, 9, 5, 8; mean class: 2.361 ± 1.606) in the postoperative period, and (17, 19, 18, 17, 3, 9; mean class: 2.404 ± 1.718) in the 1st year postoperatively, respectively preoperative versus postoperative $p=0.002$, 95% CI: 1.119–3.005; preoperative versus postoperative 1st year $p=0.006$, 95% CI: 0.189–3.246, $p<0.05$ significant) (Figure 4).

According to Fontaine staging (2a,2b,3,4), the stages of the patients were (0, 0, 30, 53) in the preoperative period, (16, 50, 10, 7) in the postoperative period, and (17, 46, 13, 7) in the postoperative 1st year, respectively. preoperative versus postoperative $p=0.028$, 95% CI: 0.183–0.916; preoperative versus postoperative 1st year $p=0.036$, 95% CI: 0.105–1.299, $p<0.05$ significant) (Figure 5).

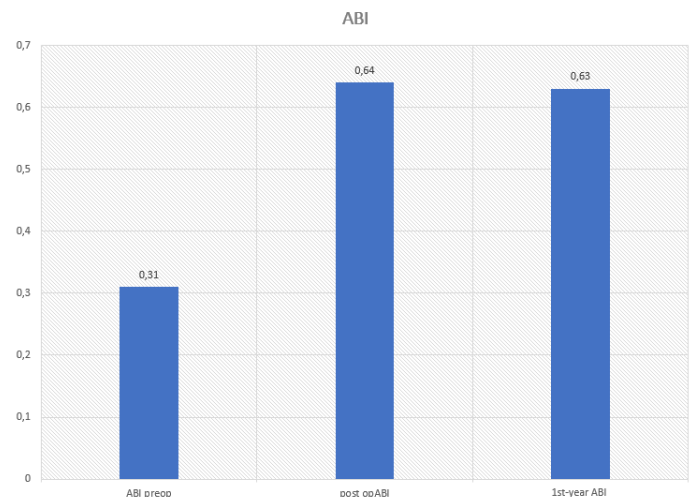


Figure 3. The mean preoperative, postoperative, and postoperative 1st-year ABI's (ankle-brachial indexes) patients. (pre-op: preoperative, post-op: postoperative; preoperative versus postoperative $p<0.001$, 95% CI: 1.009–3.102; preoperative versus postoperative 1st-year $p<0.001$, 95% CI: 1.271–4.545, $p<0.05$ significant)

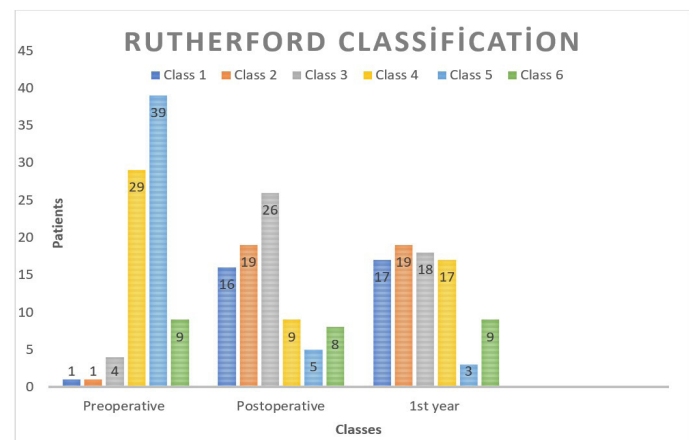


Figure 4. Rutherford's classification

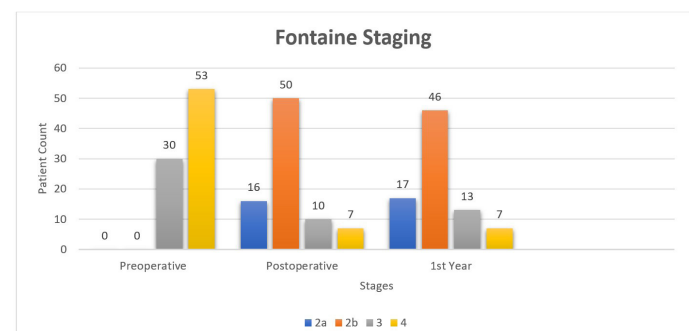


Figure 5. Fontaine Staging

The univariate statistical comparative analyses showed that both preoperative versus postoperative and preoperative versus postoperative 1st year Rutherford and Fontaine classifications of patients improved significantly, but no difference between postoperative and postoperative 1st-year results (Table 2).

Table 2. The univariate statistical comparative analyses

Friedman analysis				Wilcoxon Signed ranks tests			
Preoperative vs postoperative (1st year)	p	Fontaine	p	Rutherford	p	ABI	p
Rutherford classification	<0.001*	Pre-op. vs Post-op.	<0.001*	Pre-op. vs Post-op.	<0.001*	Pre-op. vs Post-op.	<0.001*
Fontaine staging	<0.001*	Pre-op. vs 1st year.	<0.001*	Pre-op. vs 1st year.	<0.001*	Pre-op. vs 1st year.	<0.001*
ABI assessments	<0.001*	Post-op. vs 1st year	0.266	Post-op. vs 1st year	0.345	Post-op. vs 1st year	0.349

pre-op: preoperative, post-op: postoperative, ABI: ankle-brachial index

Surgical Treatment

The popliteal artery, tibioperoneal trunk, and anterior tibial artery were found at the infragenicular level in patients, and a longitudinal incision was performed from the popliteal artery through to the tibioperoneal trunk and, anterior tibial artery. Then excision of the fibrin band was performed that developed secondary to chronic inflammation in the background of Buerger's disease. The operation was completed by patchplasty and anatomic bypass with saphenous vein graft which was prepared after fibrin band excision.

Patchplasty and anatomic bypass were seen in all patients. Proximal anastomosis was performed on the common femoral artery in 38 (45.8%) patients and on the supragenicular popliteal artery in 45 (54.2%) patients. Distal anastomosis was performed on the infragenicular popliteal artery in 83 patients. The saphenous vein was used as a graft in all patients. However, in 6 patients, polytetrafluoroethylene (PTFE) synthetic graft bypass was performed again due to early occlusion of the saphenous graft. In all patients whose saphenous graft was replaced with a PTFE graft, the PTFE graft was placed over the saphenous patchplasty.

Medical Treatment

Preoperatively, 2 (2.4%) patients received Novel oral anticoagulants (NOACs) for anticoagulant therapy, 65 (78%) patients received acetylsalicylic acid (ASA), 15 (18%) received ASA+Clopidogrel and 1 patient received Clopidogrel for antiaggregant therapy. In the early postoperative period, all patients received low molecular weight heparin and dextran treatment until mobilization. Following this, 58 patients (69%) received NOACs, 24 patients (28%) received low molecular weight heparin (LMWH), and 1 patient received Warfarin for anticoagulant therapy. For antiaggregant therapy, 60 patients (72%) received Clopidogrel and 19 patients (22%) received ASA. 4 patients (4.8%) received ASA+Clopidogrel.

For pain treatment, in the preoperative period, 52 (62.6%) patients received non-steroidal anti-inflammatory drugs (NSAIDs) and/or tramadol Hydrochloride, and 31 (37.3%) patients received Gabapentin and Derivatives. In the postoperative period, 19 (22.8%) patients received nothing, 48 (57.8%) received NSAIDs and/or Tramadol Hydrochloride, and 16 (19.2%) received

Gabapentin and Derivatives.

Limb Salvage and Smoking

63 of the patients (75.9%) were smokers. 20 patients did not smoke before the operation. 57 (68.6%) patients did not smoke after the operation. Accordingly, 37 (44.5%) patients did not smoke after the operation. 5 (6.2%) patients underwent reoperation in the early period, 3 patients had ankle amputation, 1 patient was amputated below the knee, and 1 patient had trans metatarsal amputation. Within 1 year, 3 (3.6%) patients had phalangeal, and one patient had trans metatarsal amputation. Amputation was performed in 9.6% of patients within 1 year. All patients who underwent amputation were active smokers.

No mortality was observed in our sample.

DISCUSSION

In peripheral arterial disease, factors such as hyperlipidemia, diabetes mellitus, and hypertension are seen to predispose to atherosclerotic occlusion, whereas, in Buerger's disease, the absence of

atherosclerotic risk factors other than smoking constitutes one of Shinoya's diagnostic criteria [4]. According to the diagnostic criteria of Shionoya in our patients, the mean age was 41.86 ± 4.5 years, although 68.8% quit, all of them were smokers and only hypertension (50.6%) was observed among atherosclerotic factors. All of the patients had popliteal artery and trifurcation involvement at an operable level.

Peripheral arterial disease is more common after the 5th decade, whereas Buerger's disease is more common in young adult males [10]. In our patients, the mean age was 41.86 ± 4.5 years, and 75.9% were male.

It is a known fact that surgical interventions due to active vasculitis in the acute period of Buerger's disease give negative results [11]. We think that the active vasculitis period should come to an end in Buerger's disease and should be intervened after fibrin band formation is seen in advanced imaging. It is noteworthy that the disease is in the chronic stage in previously reported successful surgical case reports. The chronic phase of the disease shows a decrease in the hypercellularity and frequent recanalization of the vessel lumen. End-stage lesions demonstrate organized thrombus and blood vessel fibrosis [12]. We did not operate

our patients in the acute phase of Buerger's disease. According to the computed tomography, we evaluated the patients with organized thrombus and blood vessel fibrosis in the end-stage lesions as chronic buerger patients. There was no significant increase in acute phase reactants of these patients. C-reactive protein values above the normal reference value (0-5mg/L) were detected in 10 mg/L (12.04%) patients preoperatively, while 3 (3.6%) patients with sedimentation values above 20mg/L were observed. Patients in the chronic process were operated on. In all patients, excision of the fibrin band that developed secondary to chronic inflammation in the popliteal artery, tibioperoneal trunk, and anterior tibial artery was performed at the infragenicular level, and endarterectomy was performed at the appropriate levels. After the fibrin band excision, patchplasty and anatomic bypass was performed with the Saphenous vein graft prepared, and the operation was completed. Although this is a place that is difficult to reach surgically and an operation that is technically difficult to perform, our results are satisfactory. The mean preoperative ankle-brachial index (ABI) of 83 patients was 0.305, the mean postoperative ankle-brachial index was 0.644, and the mean 1-year ankle-brachial index was 0.629. According to Rutherford's classification (according to class 1,2,3,4,5,6), the class of the number of patients were (1, 1, 4, 29, 39, 9) in the preoperative period, (16, 19, 26, 9, 5, 8) in the postoperative period, and (17, 19, 18, 17, 3, 9) in the 1st year postoperatively, respectively. According to Fontaine staging (2a,2b,3,4), the stages of the patients were (0, 0, 30, 53) in the preoperative period, (16, 50, 10, 7) in the postoperative period, and (17, 46, 13, 7) in the postoperative 1st year, respectively. As seen in our reports, there was an increase in the number of patients whose ABI increased after the operations and the number of patients whose complaints and lesions decreased after the operation according to the Rutherford and Fontaine classification. In the 1-year follow-up of these patients, the results in the postoperative period are almost the same.

We suggest that if there are no contraindications in the medical treatment of the disease, iloprost should be used. It is known that iloprost increases wound healing, reduces pain at rest, and consequently, decreases amputation rates [13]. In all patients included in the study, prostacyclin analogs treatment was completed in 5 days in the preoperative period and 3 days in the postoperative period.

Platelet aggregability is enhanced in smokers, and long-term smoking might enhance the sensitivity of platelets to epinephrine or ADP [14]. Anticoagulant therapy may alleviate the inflammation and symptoms of Buerger's disease [15]. We believe that the combination of anticoagulant and antiaggregant therapy leads to better outcomes in patients, especially when bypass with a saphenous vein graft is considered. The fact that Buerger's disease is characterized by spasms unlike atherosclerotic occlusion led us to think that patients may benefit from anticoagulant therapy during spasm attacks. In

Our Publication in the postoperative period, 58 patients (69%) received

NOACs, 24 patients (28%) received low molecular weight heparin (LMWH), and 1 patient received Warfarin for anticoagulant therapy within a 1st year period. For antiaggregant therapy, 60 patients (72%) received Clopidogrel, and 19 patients (22%) received ASA. 4 patients (4.8%) received ASA+ Clopidogrel in the postoperative period. Post-operative dual or single anti-aggregant treatment was determined for patients with very thin crural artery structure, atherosclerotic basis, and patients undergoing revision.

Heparin-dextran combined therapy has a significant role in the alleviation of agonizing rest pain, increasing claudication distance, and healing of ischemic ulcers in patients of Buerger's disease [16]. Postoperative Dextran infusion was 20 ml/h on the first postoperative day in all patients included in the study.

Patients with nonatherosclerotic arterial occlusive disease also benefit from cilostazol, but patients with Buerger disease or diabetic angiopathy seem to benefit less. Combining cilostazol with anticoagulant or antiaggregant agents and closer monitoring of these patients may produce better results [17]. In our study, all patients were treated with 2x100 mg Cilostazol after iloprost treatment. The patients were discharged with Cilostazol treatment.

We think that the management of pain, which is the most important symptom of Buerger's disease, with the support of algology provides a positive effect in terms of early mobilization of patients and graft patency in the postoperative period. In our study for pain treatment, in the preoperative period, 52 (62.6%) patients received non-steroidal anti-inflammatory drugs (NSAIDs) and/or tramadol hydrochloride, and 31 (37.3%) patients received gabapentin and derivatives. In the postoperative period, 19 (22.8%) patients received nothing, 48 (57.8%) received NSAIDs and/or tramadol hydrochloride, and 16 (19.2%) received gabapentin and derivatives.

In one study, 94% of patients who quit smoking avoided limb amputation. Of the patients who continued to smoke, 43% had at least one amputation [18]. In another publication where revascularization was performed on 60 patients, the limb salvage rate was 80% [19]. In our study, 5 patients underwent reoperation (6.2%) in the early period, 3 patients had ankle amputation, 1 patient was amputated below the knee, and 1 patient had trans metatarsal amputation. Within 1 year, 3 (3.6%) patients had phalangeal, and one patient had trans metatarsal amputation. Amputation was performed in 9.6% of patients within 1 year. All patients who underwent amputation were active smokers. In our study, 1-year amputation rates appear to be lower or the same compared to other publications. Although smoking is of course seen as a significant effect on amputation rates, we think that our surgical technique and the medical treatment we applied reduced amputation rates.

CONCLUSION

Good clinical results and limb salvage can be achieved with a combined medical and surgical treatment approach in advanced-stage patients who do not respond despite optimal medical treatment.

Provided that patients quit smoking and advanced imaging in the preoperative period, good determination of the target surgical site, Saphenous patchplasty, and Saphenous distal bypass applied after endarterectomy in suitable patients is supported with good medical and analgesia treatment, the results will improve further.

Limitations

The fact that this study was conducted in a single center with a limited number of patients constitutes a limitation in terms of evaluating the effects of the study. The results on this subject will become more meaningful over time, with multicenter studies that will include more patients.

Ethics Committee Approval: Ethics committee approval for this study was granted by the ethics committee of our university at the ethics committee meeting held on 17.05.2022 with the letter numbered E99166796-050.06.04-693052.

Patient Consent for Publication: Patients were screened retrospectively after ethics committee approval and informed consent forms were obtained.

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

Author Contributions: All authors contributed equally to the article.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

Acknowledgment: We thank Duygu Karakaya for conducting the statistical studies of this study.

REFERENCES

1. Igari K, Kudo T, Toyofuku T, Inoue Y. Endothelial dysfunction in patients with Buerger disease. *Vasc Health Risk Manag.* 2017;13:317-23.
2. Ghoneim BM, Karmota AG, Abuhadema AM, Shaker AA, Abdelmawla HM, Nasser MM, et al. Management of Buerger's disease in endovascular era. *Int J Angiol.* 2019;28:173-81.
3. Qaja E, Muco E, Hashmi MF. Buerger's Disease. 2022 Feb 16. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; 2022.
4. Shionoya S. Diagnostic criteria of Buerger's disease. *Int J Cardiol.* 1998;66:S243-5.
5. Cacione DG, Macedo CR, do Carmo Novaes F, Baptista-Silva JCC. Pharmacological treatment for Buerger's disease. *Cochrane Database Syst Rev.* 2016;3:CD011033. Update in: *Cochrane Database Syst Rev.* 2020;5:CD011033.
6. Cacione DG, Moreno DH, Nakano LC, Baptista-Silva JC. Surgical sympathectomy for Buerger's disease. *JRSM Open.* 2017;8:2054270417717666.
7. Cacione DG, do Carmo Novaes F, Moreno DH. Stem cell therapy for treatment of thromboangiitis obliterans (Buerger's disease). *Cochrane Database Syst Rev.* 2018;10:CD012794.
8. De Caridi G, Massara M, Villari S, Martelli E, Spinelli F, Grande R, et al. Extreme distal bypass to improve wound healing in Buerger's disease. *Int Wound J.* 2016;13:97-100.
9. Kodama A, Takahashi N, Sugimoto M, Niimi K, Banno H, Komori K. Three cases of dorsal metatarsal artery bypass in patients with Buerger disease. *J Vasc Surg Cases Innov Tech.* 2018;4:185-8.
10. Fazeli B, Ligi D, Keramat S, Maniscalco R, Sharebiani H, Mannello F. Recent updates and advances in Winiwarter-Buerger disease (Thromboangiitis Obliterans): biomolecular mechanisms, diagnostics and clinical consequences. *Diagnostics (Basel).* 2021;11:1736.
11. Shionoya S, Ban I, Nakata Y, Matsubara J, Hirai M, Kawai S. Surgical treatment of Buerger's disease. *The Journal of Cardiovascular Surgery*, 01 Jan 1980, 21(1):77-84 PMID: 7358786.
12. Qaja E, Muco E, Hashmi MF. Buerger Disease. 2023 Feb 19. In: *StatPearls [Internet]*. Treasure Island (FL): StatPearls Publishing; 2023.
13. Fiessinger JN, Shafer M. Trial of iloprost versus aspirin treatment for critical limb ischemia of thromboangiitis obliterans. *The TAO study. Lancet.* 1990;335:555-7.
14. Fusegawa F, Handa S. Platelet aggregation induced by ADP or epinephrine is enhanced in habitual smokers. *Thromb Res.* 2000;97:287-95.
15. Gao J, Huang L, Wang J. Outcomes of anticoagulant therapy with low-molecular-weight heparin (LMWH) and warfarin for thromboangiitis obliterans (TAO). *Curr Vasc Pharmacol.* 2021;19:655-62.
16. Bag S, Behera A, Khandelwal N, Bapuraj JR, Vasishta RK. Improvement in blood supply after "Heparin-Dextran" therapy in patients of Buerger's disease with critical limb ischemia. *Indian J Surg.* 2013;75:462-8.
17. Can Depboylu B, Yazman S, Harmandar B, Funda Tetik M, Istar H, Arslan K, et al. Do patients with arterial occlusive disease of different etiologies benefit equally from cilostazol?. *Tex Heart Inst J.* 2023;50:e217747.
18. Olin JW. Thromboangiitis obliterans (Buerger's disease). *N Engl J Med.* 2000;343:864-9.
19. Sambandam MT, Boologapandian V, Amalorpavanathan J. Limb salvage in critical limb ischemia in thromboangiitis obliterans patients- revascularisation- a study. *J Evolution Med Dent Sci.* 2018;7:3679-83.