

# Predictors of recurrence of arterial lesions after surgical repair in Behçet's disease

Mohamed Sabry, Sayed Younis, Hany A. Mohamed

Department of Vascular and Endovascular Surgery, Faculty of Medicine, Cairo University, Cairo, Egypt

Correspondence to Mohamed Sabry, MD, Department of Vascular and Endovascular Surgery, Faculty of Medicine, Cairo University, Cairo 12511, Egypt. Mob: +966577420178; e-mail: drsabry955@yahoo.com

**Received:** 18 October 2022

**Revised:** 21 November 2022

**Accepted:** 4 December 2022

**Published:** 28 April 2023

The Egyptian Journal of Surgery 2023, 41:1532–1538

## Background

Behçet's disease (BD) is an aggressively devastating systemic vasculitis that involves multiple systems and is characterized by unexpected periods of exacerbations and remissions. When vascular complications dominate the clinical presentation, the term vasculo-BD is used. This study aimed to present our experience in the surgical management of vasculo-BD arterial lesions, the recurrence rate, and the factors associated with this recurrence.

## Patients and method

This is a retrospective study that included an analysis of a prospectively maintained database of patients with vasculo-BD who underwent surgical repair for arterial lesions. Patients' data and outcome after 2-year follow-up were recorded.

## Results

This study included 16 patients with vasculo-BD. Three (18.75%) patients indicated surgery owing to arterial thrombosis, and 13 (81.25%) patients had arterial aneurysms. The aorta was affected in five (31.25%) patients and the peripheral arteries in 11 (68.75%) patients. Immediate technical success was obtained in all cases (100%). Minor complications were shown in four (25%) patients. A total of 10 (62.5%) patients had postoperative recurrence. The recurrence occurrence decreased significantly with the use of sleeve protection ( $P=0.039$ ) and immunosuppressive drugs ( $P=0.039$ ). The recurrence-free survival was significantly longer in patients who underwent sleeve protection and received immunosuppressive therapy.

## Conclusion

The surgical approach for arterial lesions in patients with BD is associated with a high recurrence rate. Sleeve protection and considering the immunosuppressive therapy influenced the recurrence rate and recurrence-free survival.

## Keywords:

arterial lesions, Behçet's disease, recurrence, surgical management, vasculo-Behçet's disease

Egyptian J Surgery 41:1532–1538

© 2023 The Egyptian Journal of Surgery

1110-1121

## Introduction

Behçet's disease (BD) is a complex inflammatory disorder with significant morbidity and mortality. It usually has a middle-aged onset and is characteristically prevalent in the 'Silk Route' regions, which extend from Japan to the Mediterranean and Middle Eastern countries [1].

BD is an aggressively devastating systemic vasculitis that involves multiple systems and is characterized by unexpected periods of exacerbations and remissions. BD etiology remains unclear, but a multifactorial pathogenetic mechanism triggered by immunologic and environmental factors in genetically predisposed individuals has been proposed [2].

The cardiovascular system is frequently involved in BD, and when vascular complications dominate the clinical presentation, the term vasculo-BD is used [3].

The disease affects small, medium, and large-sized arteries or veins, and all layers of the heart. In the affected vessels, an endovascular and perivascular inflammatory process occurs and leads to vascular narrowing, thrombus formation, and aneurysms [4].

Vasculo-BD is a disease that is continuously challenging vascular surgeons. It carries a high risk of postoperative recurrence of primary disease, even with a successful operation. Surgical bypass has been used with confirmed safety and efficacy [5]. However, it may be complicated by anastomotic pseudoaneurysm recurrence [6].

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

The outcomes of surgical repair have been studied in patients with vasculo-BD. Nevertheless, there is scarce evidence addressing the predictors of disease recurrence. This study aimed to present our experience in the surgical management of vasculo-BD arterial lesions, the recurrence rate, and the factors associated with this recurrence.

## Patients and methods

This is a retrospective study that was done in a specialized vascular center in Saudi Arabia and included an analysis of a prospectively maintained database of patients with vasculo-BD who underwent surgical repair for arterial lesions during the period from April 2018 to April 2020 and had follow-up data till April 2022. The study was conducted after the approval of the regional Research Ethics Committee and per the Helsinki Declaration. Patients were diagnosed with BD according to the international classification criteria for BD [7]. Patients were eligible for the study if they attended the Department of Vascular Surgery with aortic or peripheral arterial lesions indicating surgical repair. The arterial lesions were diagnosed by Doppler ultrasound and computed tomography angiography. The indications for surgical repair were symptomatic thrombosis or aneurysms, an aortic aneurysm with a diameter exceeding 5 cm, or increasing by more than 0.5 cm per 6 months, rapidly expanding peripheral artery aneurysms, or when they are four to five times the normal artery or a pseudoaneurysm of a diameter exceeding 2 cm. Symptomatic arterial thrombosis was offered initial conservative management unless there was critical limb ischemia. Patients with previous arterial intervention, patients indicating emergency intervention, and those with coronary or cranial artery affection were excluded from the study. Patients with other autoimmune diseases, granulomatous infection, or atherosclerosis were also excluded. Informed written consent was obtained from each patient included.

Patients presenting in an acute inflammatory phase of the disease underwent preoperative immunosuppressive treatment. The bypass surgery was performed, as usual, using a prosthetic graft or the saphenous vein as the conduit. The graft type was selected based on the surgeon preference according to the size of the affected artery and the size and quality of the saphenous vein. Preoperative dedicated assessment of the used autogenous veins was performed to exclude disease-related vein changes. During the positioning of the graft, the apparently disease-free arterial segment was the site of reconstruction. In some cases, sleeve

protection was used, which is defined as a piece of Dacron graft that was taken and wrapped around the anastomosis to reinforce the anastomosis site and prevent a potential recurrence. All anastomoses were made using polypropylene suture thread in a wide-bite running suture technique, which is considered one of the most important methods of prevention of recurrence.

Patients with aneurysms postoperatively received dual-antiplatelet therapy in the form of aspirin 81 mg daily plus clopidogrel 75 mg daily for 3 months and then aspirin was stopped but clopidogrel continued indefinitely. Those with arterial thrombosis postoperatively received anticoagulant treatment in the form of enoxaparin therapeutic dose according to the body weight for 2 weeks and then were shifted to oral apixaban 5 mg once daily. All patients received a clinical examination and were treated accordingly by the hospital rheumatologist. The patients were instructed to attend the hospital if there were any adverse events.

Follow-up visits were scheduled initially postoperatively after 2 weeks, then 1 month, and then regular visits every 6 months. During each visit, patients underwent history taking, clinical examination, and Doppler or computed tomography angiography scanning.

## Study outcomes

The primary outcome was the rate of recurrence till 2 years of follow-up, and the secondary outcome was the potential predictors of postoperative recurrence.

A recurrence was considered when an aneurysm or pseudoaneurysm reappeared at the site of operation, or when thrombosis occurred at the bypass graft.

## Statistical analysis

The patients' data was analyzed using the statistical software SPSS (IBM, Armonk, New York, USA), version 26. After normality testing, expression of variables and comparison were performed using the appropriate tests. A Kaplan–Meier analysis was used to assess the cumulative recurrence-free survival rates. A Cox regression analysis was performed to identify predictors for recurrence-free survival. *P* values less than 0.05 were considered statistically significant.

## Results

The present study included 16 patients with vasculo-BD, comprising nine (56.25%) males and seven

(43.75%) females. The patients' age ranged from 28 to 66 years, with a mean of  $47.3 \pm 13.1$  years. A total of 10 (62.5%) patients had hypertension, six (37.5%) patients had diabetes mellitus, seven (43.7%) patients had dyslipidemia, and 11 (68.75%) patients were smokers (Table 1).

Concerning clinical data, the duration from disease diagnosis to surgery ranged from 0.2 to 6 years, with a mean of  $3.1 \pm 1.8$  years. At the time of surgery, 14 (87.5%) patients had oral ulcers, 10 (62.5%) patients had genital ulcers, seven (43.75%) patients had skin lesions, four (25%) patients had eye affection, two (12.5%) patients had neurological affection, and 10 (62.5%) patients had venous affection (Table 2).

Three (18.75%) patients indicated surgery owing to arterial thrombosis, and 13 (81.25%) patients had arterial aneurysms. The aorta was affected in five (31.25%) patients and the peripheral arteries in 11 (68.75%) patients. The peripheral arterial lesions were all in the lower limb. Those were in the iliac artery (four patients, 25%), superficial femoral artery (six patients, 37.5%), and popliteal artery (one patient, 6.25%) (Table 2).

Immunosuppressive drug administration was indicated in eight (50%) patients. Synthetic graft (expanded polytetrafluorethylene; ePTFE) was used in nine (56.25%) patients, and autogenous graft in seven (43.75%) patients. Sleeve protection was added to eight (50%) patients (Table 2).

Immediate technical success was obtained in all cases (100%). Minor complications were shown in four (25%) patients who had been managed accordingly; two (12.5%) had surgical site hematoma, and the other two had wound infection. Graft occlusion occurred in three (18.75%) patients, and an anastomotic pseudoaneurysm was seen in six (37.5%) patients.

**Table 1 Sociodemographic data of the study patients**

	Study patients (N=16) Mean±SD (minimum–maximum)
Age (years)	$47.3 \pm 13.1$ (28–66) n (%)
Sex	
Female	7 (43.75)
Male	9 (56.25)
Comorbidities	
Diabetes mellitus	6 (37.5)
Hypertension	10 (62.5)
Dyslipidemia	7 (43.75)
Smoking	11 (68.75)

One (6.25%) patient had an aneurysm in the contralateral iliac artery. A total of 10 (62.5%) patients had postoperative recurrence (Table 3); two (12.5%) cases were diagnosed at the 3-month follow-up, four (25%) cases at the 9-month follow-up, two (12.5%) cases at the 18-month follow-up, and another two (12.5%) cases at the 24-month follow-up. One mortality case was encountered 10 months after aortic surgery (one of the cases having a recurrence at the 3-month follow-up). The cause of death was a ruptured cerebral aneurysm.

The effects of patient baseline data and clinical and surgical data on the occurrence of recurrence were analyzed. The recurrence occurrence decreased

**Table 2 Clinical and surgical data of the study patients**

	Study patients (N=16) Mean±SD (minimum–maximum)
Duration from the disease diagnosis to surgery (years)	$3.1 \pm 1.8$ (0.2–6) n (%)
Disease manifestations	
Oral ulcers	14 (87.5)
Genital ulcers	10 (62.5)
Skin lesions	7 (43.75)
Eye affection	4 (25)
Neurological affection	2 (12.5)
Venous affection	10 (62.5)
Indication of surgery	
Arterial thrombosis	3 (18.75)
Arterial aneurysm	13 (81.25)
Site of affection	
Aorta	5 (31.25)
Iliac artery	4 (25)
Superficial femoral artery	6 (37.5)
Popliteal artery	1 (6.25)
Preoperative immunosuppressive therapy	8 (50)
Graft	
Synthetic	9 (56.25)
Autogenous	7 (43.75)
Sleeve protection	8 (50)

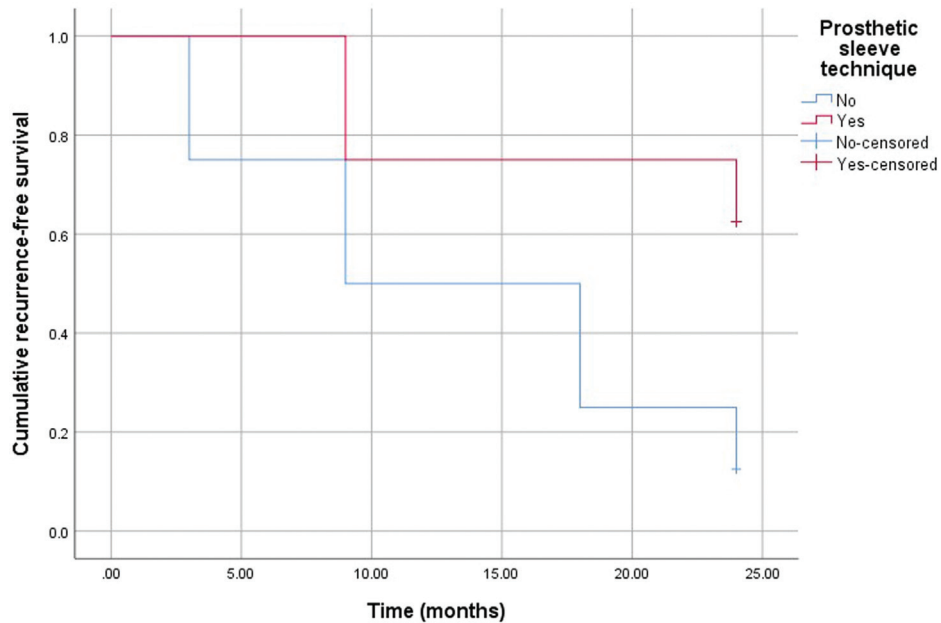
**Table 3 The patients' outcome**

	Study patients (N=16) n (%)
Immediate technical success	16 (100)
Minor complications	
Surgical site hematoma	2 (12.5)
Wound infection	2 (12.5)
Major complications/recurrence	
Graft occlusion	3 (18.75)
Anastomosis pseudoaneurysm	6 (37.5)
New aneurysm	1 (6.75)

significantly with the use of sleeve protection ( $P=0.039$ ) and immunosuppressive drugs ( $P=0.039$ ). The recurrence-free survival was significantly longer in patients who underwent sleeve protection (Fig. 1), with a mean recurrence-free survival of 20.24 months compared with 13.5 months in patients without sleeve protection (log-rank  $P=0.033$ ). Moreover, the use of immunosuppressive drugs was associated with a significantly longer recurrence-free survival (Fig. 2),

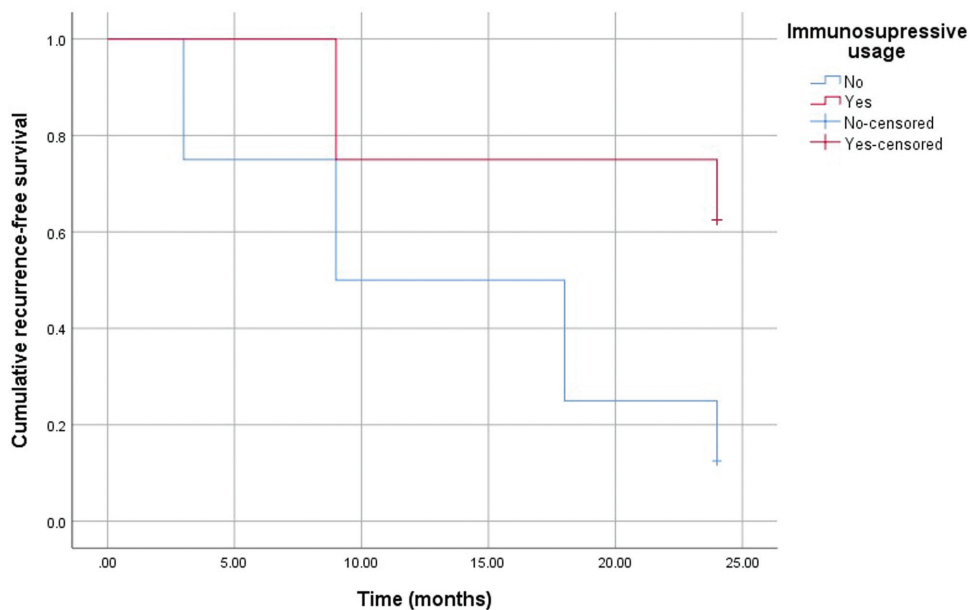
with a mean recurrence-free survival of 22.5 months compared with 11.25 months in patients who did not receive immunosuppressive therapy (log-rank  $P=0.012$ ). The use of autogenous graft was associated with a longer recurrence-free survival (Fig. 3), with a mean recurrence-free survival of 21 months compared with 13.7 months in patients who had synthetic graft. However, the difference lacked statistical significance (log-rank  $P=0.1$ ).

**Figure 1**



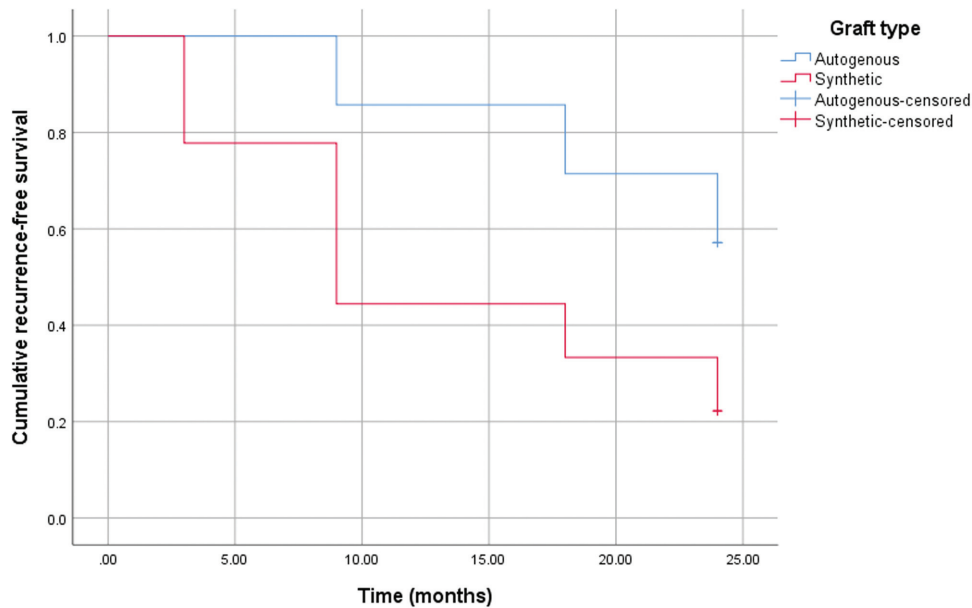
The effect of using sleeve protection on the recurrence-free survival.

**Figure 2**



The effect of using immunosuppressive drugs on the recurrence-free survival.

Figure 3



The effect of graft type on the recurrence-free survival.

Cox regression analysis showed that the use of immunosuppressive therapy was a significant predictor of recurrence-free survival ( $P=0.033$ ).

### Discussion

Treatment of BD remains perplexing and of low evidence level [5]. Arterial thrombosis and aneurysm management is particularly challenging, with surgical interference being associated with a high rate of recurrence and postoperative complications [6]. A few studies presented experience in the surgical management of arterial lesions in BD [6–11]. Moreover, the clinical profile and disease course vary among different geographic regions and ethnic clusters, and there is still a lack of data concerning vasculo-BD in North Africa. Some Egyptian studies described BD-associated vascular manifestations [12–14]. However, the present study is the first to address the surgical management of arterial lesions in vasculo-BD, the recurrence rate, and the factors associated with this recurrence in Egyptian patients.

In the current work, the duration from disease diagnosis to surgery ranged from 0.2 to 6 years, with a mean of  $3.1 \pm 1.8$  years. This was relatively shorter than the previously reported data. Saadoun *et al.* [9] reported a median period of 4 years, and other studies found the interval between the onset of BD and the occurrence of arterial lesions indicating surgery to be 5 years or more [6,10]. This difference is likely

attributable to the late diagnosis of BD, in part due to the reluctance of patients to seek medical consultation and, in another part, due to the unpopularity of the disease among general physicians.

This study showed male predominance, which is consistent with other studies that reported higher prevalence of BD-related vascular complications among males [6,8–11,14–17]. The physiologic and genetic variations are acknowledged to result in a sex-related difference in the inflammatory process. In particular, estrogen hormone has been reported to reduce oxidative stress and the apoptotic process, and downregulate the inflammatory markers [18,19]. The sex difference in the prevalence of smoking could be another contributing factor.

In the present study, most of the lesions were aneurysms. Similar findings were previously reported [6,8–11]. This is rather expected given that arterial occlusion tends to proceed in a rather benign course, whereas BD-associated aneurysms are disposed to show rapid enlargement and more frequently indicate surgical interference [17].

In our cohort, the arterial lesions indicating surgery were encountered in the aorta and lower limb arteries. This is congruent with reports from Turkey, China, and Korea, which defined the lower extremity arteries and the abdominal aorta as the most frequently attacked locations in BD [20–22].

We found that 62.5% of the patients had postoperative recurrence during the follow-up period. This is comparable with the previously reported postoperative relapse rates. Gaudric *et al.* [11] described that 51% of patients experienced recurrence. Koksoy *et al.* [10] and Saadoun *et al.* [9] reported relapse rates of 62 and 61.5%, respectively. This high recurrence rate is not surprising as the postoperative frequent recurrence of arterial lesions has been established. The anastomotic healing process is assumed to be improper in patients with BD. Pseudoaneurysms may develop in incompletely healed regions that represent mechanical defects or may be induced by vasculitis [8]. The site of anastomotic recurrence underwent histological investigations that explored leukocytoclastic arthritis changes, which are the same as those found in genital ulcers [23]. As for graft thrombotic occlusion, the inflammatory process, with resultant intimal thickening, and the systemic condition of pro-coagulative tendency may explain the frequent postoperative graft thrombosis.

Immunosuppressive therapy was administered to 50% of the study patients. It is still a matter of debate whether immunosuppressive therapy can influence postoperative recurrence [23]. In our experience, the use of immunosuppressive drugs was associated with a significantly less recurrence rate and a significantly longer recurrence-free survival. It was a significant predictor of recurrence-free survival. This is likely owing to their inhibitory effect on arterial wall inflammation [24].

The grafts used in our study were either synthetic grafts (ePTFE) or autogenous grafts (saphenous vein). Some authors preclude using autogenous grafts for fear of being affected by the disease and being predisposed to postoperative relapse [11]. In our experience, using a saphenous vein after a proper dedicated examination to ensure its healthiness was associated with lower rates of recurrence. However, without statistical significance. This was partially supported by the series of Koksoy *et al.* [10] that disclosed that choosing synthetic or autogenous graft did not affect the patient's outcome. Saphenous vein superiority to PTFE grafts was previously recognized, and it was presumed that when it is appropriate, it should always be chosen for bypass [25].

Sleeve protection was used in half of this study's patients. The sleeve protection technique is the reinforcement of the arterial anastomosis sites by casing them with a prosthetic graft. It is a simple and effective method, but its influence on postoperative recurrence has only been assessed in a

single study [11]. The described study, as well as the current one, found that the protected anastomoses were less frequently encountered by relapse. This enhanced reinforcement mechanically supports the anastomotic site and reduces the risk of failure.

We acknowledge that this work is limited by the small sample size, the retrospective design, being a single-center study, and the limited follow-up period. However, our study is one of a few studies addressing the outcome of surgical management for arterial lesions, and the first one was conducted on Egyptian patients with BD.

---

## Conclusion

The surgical approach for arterial lesions in patients with BD is associated with a high recurrence rate. Sleeve protection and the considered immunosuppressive therapy influenced the recurrence rate and recurrence-free survival. Using a saphenous vein as the bypass graft, after ensuring its appropriateness, appears to be associated with a longer recurrence-free survival. Further multicentric studies investigating a larger cohort of patients are needed to provide a more consolidated conclusion.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

---

## References

- Alpsoy E. Behçet's disease: a comprehensive review with a focus on epidemiology, etiology and clinical features, and management of mucocutaneous lesions. *J Dermatol* 2016; 43:620–632.
- Zeidan MJ, Saadoun D, Garrido M, Klatzmann D, Six A, Cacoub P. Behçet's disease physiopathology: a contemporary review. *Auto Immun Highlights* 2016; 7:4.
- Kechida M, Salah S, Kahloun R, Klii R, Hammami S, Khochtafi I. Cardiac and vascular complications of Behçet disease in the Tunisian context: clinical characteristics and predictive factors. *Adv Rheumatol* 2018; 58:32.
- Ishibashi H. What Is Vascular Behçet's Disease?. *Ann Vasc Dis* 2018; 11:52–56.
- Hatemi G, Silman A, Bang D, Bodaghi B, Chamberlain AM, Gul A, *et al.* EULAR recommendations for the management of Behcet disease. *Ann Rheum Dis* 2008; 67:1656–1662.
- Hosaka A, Miyata T, Shigematsu H, Shigematsu K, Okamoto H, Ishii S, *et al.* Long-term outcome after surgical treatment of arterial lesions in Behcet disease. *J Vasc Surg* 2005; 42:116–121.
- International Team for the Revision of the International Criteria for Behçet's Disease (ITR-ICBD). The International Criteria for Behçet's Disease (ICBD): a collaborative study of 27 countries on the sensitivity and specificity of the new criteria. *J Eur Acad Dermatol Venereol* 2014; 28:338–347.
- Chung SW, Bae M, Lee CW, Huh U, Jin M, Kim MS, *et al.* Surgical experience of Behcet's disease involving the peripheral artery. *Ann Vasc Surg* 2020; 69:246–253.
- Saadoun D, Asli B, Wechsler B, Houman H, Geri G, Desseaux K, *et al.* Long-term outcome of arterial lesions in Behçet disease: a series of 101 patients. *Medicine (Baltimore)* 2012; 91:18–24.

- 10 Koksoy C, Gyedu A, Alacayir I, Bengisun U, Uncu H, Anadol E. Surgical treatment of peripheral aneurysms in patients with Behçet's disease. *Eur J Vasc Endovasc Surg* 2011; 42:525–530.
- 11 Gaudric J, Jayet J, Saadoun D, Couture T, Ferfar Y, Davaine JM, *et al.* Factors influencing the recurrence of arterial involvement after surgical repair in Behçet disease. *J Vasc Surg* 2020; 72:1761–1769.
- 12 Badr Eldin A, Ibrahim A. Assessment of the relationship between vascular endothelial growth factor and cardiovascular involvement in Egyptian patients with Behçet's disease. *Egypt Rheumatol* 2014; 36:131–137.
- 13 Hassan S, Gheita T, Ghoneim S, Nasr L. Subclinical atherosclerosis in Behçet's disease. *Turk J Rheumatol* 2012; 27:109–114.
- 14 Morshedy NA, Mohammed DF, Badr FM. Teama MAE monem. The pattern of cardiovascular manifestations in Egyptian Behçet's patients and its relation to disease activity. *Egypt J Intern Med* 2021; 33:12.
- 15 Tohmé A, Aoun N, El-Rassi B, Ghayad E. Vascular manifestations of Behçet's disease. Eighteen cases among 140 patients. *Joint Bone Spine* 2003; 70:384–389.
- 16 Sarica-Kucukoglu R, Akdag-Kose A, Kayaball M, Yazganoglu KD, Disci R, Erzenegin D, Azizlerli G. Vascular involvement in Behçet's disease: a retrospective analysis of 2319 cases. *Int J Dermatol* 2006; 45:919–921.
- 17 Fei Y, Li X, Lin S, Song X, Wu Q, Zhu Y, *et al.* Major vascular involvement in Behçet's disease: a retrospective study of 796 patients. *Clin Rheumatol* 2013; 32:845–852.
- 18 Chen RY, Fan YM, Zhang Q, Liu S, Li Q, Ke GL, *et al.* Estradiol inhibits Th17 cell differentiation through inhibition of ROR $\gamma$ T transcription by recruiting the ER $\alpha$ /REA complex to estrogen response elements of the ROR $\gamma$ T promoter. *J Immunol* 2015; 194:4019–4028.
- 19 Xiang D, Liu Y, Zhou S, Zhou E, Wang Y. Protective effects of estrogen on cardiovascular disease mediated by oxidative stress. *Oxid Med Cell Longev* 2021; 2021:e5523516.
- 20 Melikoglu M, Kural-Seyahi E, Tascilar K, Yazici H. The unique features of vasculitis in Behçet's syndrome. *Clin Rev Allergy Immunol* 2008; 35:40–46.
- 21 Kwon TW, Park SJ, Kim HK, Yoon HK, Kim GE, Yu B. Surgical treatment result of abdominal aortic aneurysm in Behçet's disease. *Eur J Vasc Endovasc Surg* 2008; 35:173–180.
- 22 Maldini C, Lavalley MP, Cheminant M, de Menthon M, Mahr A. Relationships of HLA-B51 or B5 genotype with Behçet's disease clinical characteristics: Systematic review and meta-analyses of observational studies. *Rheumatology (Oxford)* 2012; 51:887–900.
- 23 Iscan ZH, Vural KM, Bayazit M. Compelling nature of arterial manifestations in Behçet disease. *J Vasc Surg* 2005; 41:53–58.
- 24 Yazici H, Barnes CG. Practical treatment recommendations for pharmacotherapy of Behçet's syndrome. *Drugs* 1991; 42:796–804.
- 25 Klinkert P, Post PN, Breslau PJ, van Bockel JH. Saphenous vein versus PTFE for above-knee femoropopliteal bypass. A review of the literature. *Eur J Vasc Endovasc Surg* 2004; 27:357–362.