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Aortic aneurysm in Behcet's disease, management options: Single-center experience

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Abstract--This study aims to review contemporary lines of endovascular management of Aortic aneurysm in bechet's disease illustrating the pros and cons of each treatment modality. This is a retrospective cohort study of all consecutive Aortic aneurysms in patients diagnosed bechet's disease treated between 2018-2021. The aim of this study is to evaluate efficacy & outcome of endovascular stent graft implantation for the treatment of Aortic aneurysm in Bechet's disease. From feb 2018 to august 2021, 11 Aortic aneurysms were diagnosed in 10 patients with Bechet's disease. All patients were male. The patients ranged in age from 33 to 66 years (median, 41 years). There were three infrarenal abdominal aortic aneurysm, two supra celiac aneurysm, three descending thoracic, one Aortic arch aneurysm, and one patient had both pararenal & descending thoracic aneurysm. All patients received immunosuppressive therapy before intervention to induce remission. After hospital discharge, all patients were followed up regularly at 3 months intervals. The mean duration of follow-up was 22.6 months (range, 1-39 months). A straight tube graft was implanted in nine patients and a bifurcated graft in one patient. Two stage procedures (debranching before endovascular therapy) were performed in three patients. endovascular aortic stent

graft was successful in all patients, the overall survival was 80%, one patient died day 1 post-operative due to MI, 2nd patient died one month after stent graft due to mediastinitis, two patients developed access site pseudoaneurysm, graft migration and type Ib endoleak occurred in one patient and one patient needed bilateral CIA kissing stent for bilateral CIA stenosis. Endovascular stent graft and adjunctive immunosuppressive therapy seems to be safe and effective in the treatment of aortic aneurysm or pseudoaneurysm in Behçet's disease.

Keywords--Behçet's syndrome, Behçet's disease, immunosuppressive therapy, endovascular techniques, aortic aneurysm, pseudoaneurysm.

Introduction

Behçet's disease (BD) is a multisystem chronic inflammatory condition with neurologic, cardiovascular, pulmonary, and musculoskeletal manifestations. Vascular involvement, termed vasculo-BD, has been reported to occur in 7% to 29% of affected patients.¹ In vasculo-BD, both veins and arteries may be affected. stenosis and/or pseudoaneurysms may occur in the peripheral arteries and the aorta. pseudoaneurysm and rupture of the large arteries or the aorta are of greater concern, since these events are a major cause of mortality in this condition.¹ The abdominal aorta is the most common site of arterial involvement in Behçet's disease, followed by the pulmonary, femoral, popliteal, and carotid arteries in that order. Conventional open surgery is the most frequently used treatment for the arterial lesions in Behçet's disease patients.² Pseudoaneurysm at the site of the anastomosis is one of the most serious complications after open repair. Recent studies have shown that endovascular stent graft may offer an alternative treatment for arterial aneurysms in Behçet's disease.³⁻⁴ Endovascular treatment combined with immunosuppressive therapy has been reported to be associated with better post-operative results and lower recurrence rates than open repair.⁵

Materials and Methods

This is retrospective analysis of collected data for patients treated at KasrAlainy medical school vascular surgery department, with endovascular approach for aortic aneurysm or pseudoaneurysm due to behcet's disease between February 2018 and August 2021.

Inclusion criteria

Ten Patients were included with a diagnosis of Behçet's disease according to the criteria of the International Study Group of Behçet's Disease (These criteria require the presence of recurrent oral ulceration in association with at least two of the following: characteristic ocular lesions, characteristic skin lesions, genital ulceration and a positive pathergy test result).⁶ All patients have An aortic aneurysm with aortic morphology compatible with endograft placement.

Exclusion criteria

- Atherosclerotic aortic aneurysm.
- Patient with active disease.
- Patients with unsuitable anatomy for Endovascular management.
- Infected aneurysm.
- Patients with renal impairment or allergy to contrast.
- Traumatic aneurysm.
- Other vasculitic aneurysms

Preoperative preparations

- Patient's demographic data and medical records (associated comorbidities, family history of AAA, and any previous surgical procedures) were collected. All patients underwent routine preoperative laboratory and radiological investigations including CBC, coagulation profile, liver functions, kidney functions, ESR, CRP, ECG, ECHO cardiograph, CXR.
- Contrast enhanced multi-slice CT, with 1 mm axial cuts, whole aorta to lower extremities.
 - The output DICOM files were transferred to DICOM viewer software application like (3mensio Pie Medical Imaging, Osirix DICOM viewer) .
- The operative risk was assessed by a cardiologist, anaesthesiologist, and chest physician.
- Debranching procedures were performed before the deployment of the stent grafts. In case of insufficient proximal landing zone, Endovascular repair was performed in the same operating setting or staged procedure.
- Adjunctive debranching procedure were performed in three cases with insufficient proximal landing zone, one patient needed aortic arch debranching for arch aneurysm, and one needed carotid subclavian bypass for descending thoracic aortic aneurysm, and total visceral debranching for pararenal aneurysm.
- Prophylactic use of cerebrospinal fluid drainage to prevent spinal cord ischemia was used. Spinal drains were placed the day prior to TEVAR in the intensive-care unit (ICU). Target CSF pressure intra and postoperatively should be between 8 and 12 mmHg.⁷

Immunosuppressive treatment

- Patients who had symptomatic pseudoaneurysms and imaging evidence of life-threatening aortic rupture, received intravenous glucocorticoids (hydrocortisone, 200mg/d), and cyclophosphamide (200 mg/d) was commenced once the diagnosis was made, immediately before endovascular therapy.
- Patients with nonruptured pseudoaneurysms were administered immunosuppressive treatment with oral prednisone (60mg/d) combined with cyclophosphamide (200 mg/d) for 1 to 3 weeks until the esr and crp values were within the normal range. Once their inflammatory markers normalized, they underwent endovascular stent graft implantation.

- After the endograft procedure, intravenous hydrocortisone (200 mg/d) combined with cyclophosphamide (200 mg/d) was continued for at least 3 days.
- Patients then began receiving oral prednisone (60 mg/d). This drug regimen was tapered intermittently, adjusted in conjunction with the individual patient's response and guidelines provided by the consulting rheumatologists. All patients were advised to maintain immunosuppressive therapy for at least 2 years.

Endovascular Repair

The endovascular devices were delivered via the common femoral artery, either open or percutaneous access. In case of percutaneous approach for endovascular stent delivery we use preclose technique using Percloses ProGlide® 6F Suture-Mediated Closure System (Abbott Vascular, CA, USA). Initial Angiography through a 5F pigtail catheter advanced above aneurysm sac, Controlled hypotension was used for precise deployment. The stent graft is placed with at least 2 cm safety margin of healthy aorta. However, a healthy aortic wall cannot be easily differentiated from the BD-involved segment of aorta in many cases. For these, we placed the stent graft as long as possible to cover the possible BD involved segment. A completion angiogram was performed after stent-graft deployment to confirm proper position of the stent graft and exclusion of any endoleak. Postoperatively, care for the surgical site with daily dressing till removal of stitches two weeks later.

Follow-up

Was performed for all patients with a CTA scan at 30 days, followed by color DUS imaging between 3 to 6 months and CTA at 1 year and yearly thereafter. If an endoleak is detected on color DUS imaging or there is an increase in sac size at any time, the patient will undergo CTA scanning and management accordingly. Complications which occurred during or after the Endovascular procedure were reported and managed accordingly.

Statistical Methods

Data were coded and entered using the statistical package SPSS (Statistical Package for the Social Sciences) version 24. Data was summarized using mean, standard deviation, median, minimum and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data.

Results

This study reviewed the pre-operative, intra-operative, and post-operative data of 10 patients underwent endovascular management for aortic aneurysm due to Behçet's disease. The age of the studied patients ranged from 33 to 66 years with a median age of 41 years. All the patients were males. Mean follow up period was 22.6 months (range, 1-39 months). Patient demographics are given in Table 1.

Table 1
Patient demographic data

Patient no.	Gender	Age	Associated comorbidities	Special habits	Other vascular involvement	Follow up mon.
1	M	33	NA	Smoker	NA	35
2	M	45	Hypertension	Smoker	LT lower limb old DVT, RT subclavian artery aneurysm	34
3	M	66	NA	NA	NA	19
4	M	41	diabetic	NA	NA	1
5	M	37	NA	NA	NA	18
6	M	42	NA	Smoker	NA	30
7	M	36	NA	NA	NA	39
8	M	38	NA	Smoker	Lt lower limb old DVT, RT CFA pseudoaneurysm	38
9	M	45	CAD,history of CABG	NA	NA	0
10	M	46	Hypertension	smoker	NA	12

Clinical presentation

All patients fulfilled the International Study Group criteria for the diagnosis of Behcet disease, All patients gave history of orogenital ulcers, two patients gave history of DVT , positive family history of behchet's disease was found in four patients, Five patients presented to rheumatology clinic by oral and genital ulcers ,and after investigations aortic aneurysm was identified, two patients presented by abdominal pain referred to the back ,One patient presented by groin swelling for associated CFA aneurysm, One patient presented by hematemesis due to pressure ulcer in the esophagus (thoracic aneurysm) ,One patient presented by RT neck swelling for RT subclavian aneurysm.

aneurysm symptoms

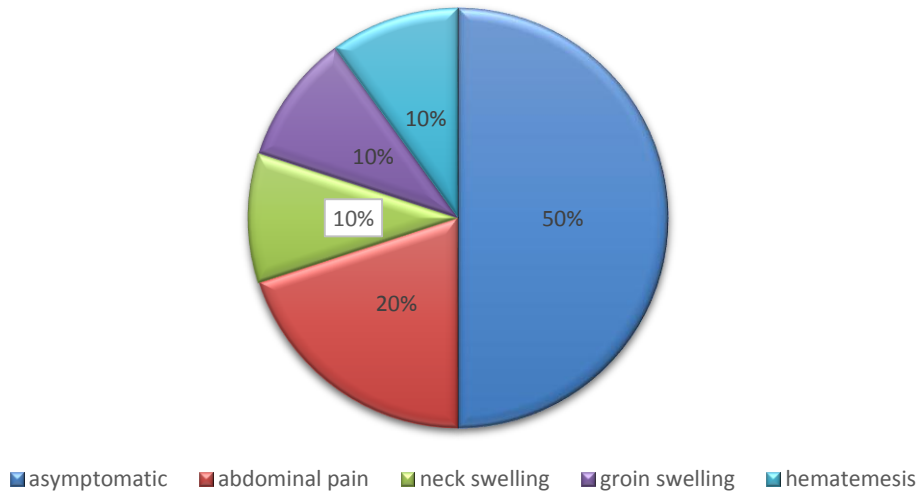


Fig 1. Aneurysm symptoms

Preoperative CTA assessment showed 8 saccular Aortic aneurysm in 8 patient, and 3 fusiform aneurysm in 2 patients (one patient has pararenal fusiform aneurysm and descending thoracic aneurysm), two patients had other associated arterial pathologies, including RT SCA aneurysm & RT CFA aneurysm. Aneurysm characteristics are given in Table 5.

Table 2
Aneurysm characteristics

Patient no.	Type	Anatomic distribution	Max diameter(mm)	Combined arterial involvement	Vascular symptom
1	Saccular	Infrarenal	60	NA	NA
2	Saccular	Aortic arch	82	RT SCA aneurysm	Neck swelling
3	Saccular	Supraceliac	100	NA	Abdominal pain
4	Saccular	Descending thoracic	73	NA	Hematemesis
5	Fusiform	Descending thoracic	58	NA	NA
6	Saccular	Supraceliac	82	NA	NA
7	Saccular	Infrarenal	59	NA	NA
8	Saccular	Infrarenal	33	RT CFA aneurysm	Groin swelling
9	Fusiform	Pararenal & descending thoracic	75	NA	NA
10	saccular	Descending thoracic	46	NA	NA

Aneurysm distribution

Three patients had infrarenal aneurysm, two had supra celiac aneurysm, one had Aortic arch aneurysm, three had descending thoracic, and one patient had both pararenal & descending thoracic aneurysms. Maximum diameter of aneurysms ranged between 33 to 100 mm with mean Max. Diameter 66.8 mm.

ANEURYSM DISTRIBUTION

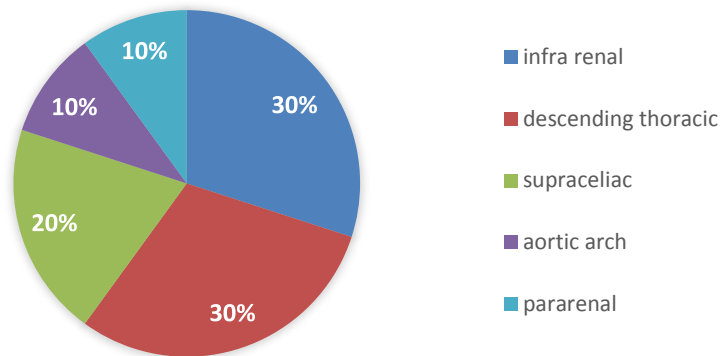


Fig 2. Aneurysm distribution

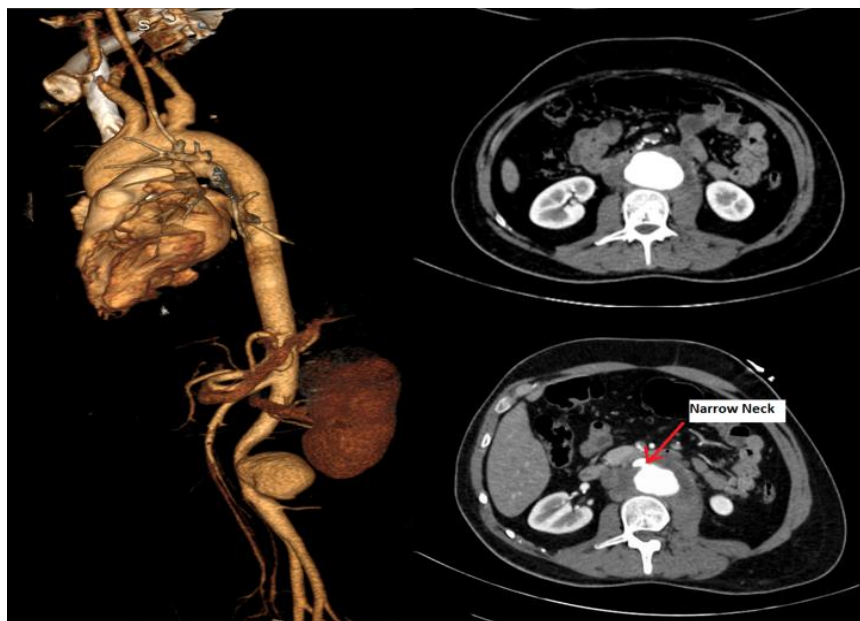


Fig 3. CTA shows infrarenal saccular aneurysm

Nine (90%) patients in this study received immunosuppressive therapy (prednisolone & cyclophosphamide) before their endovascular procedure and

continued immunosuppressive treatment in the form of prednisolone during follow-up. one patient with ruptured saccular aneurysm received pulse steroid therapy (hydrocortisone, 200mg/d) before procedure and cyclophosphamide for 3 days after procedure. All patients continued immunosuppressive treatment in the form of prednisolone during follow-up. Adjunctive debranching procedure were performed in three cases with insufficient proximal landing zone, one patient needed aortic arch debranching for arch aneurysm, and one needed carotid subclavian bypass for descending thoracic aortic aneurysm (fig.4), and total visceral debranching for pararenal aneurysm



Fig 4. Angiography shows left CCA to left subclavian artery bypass & stent graft deployed in aortic arch

All patients received general anesthesia, open CFA access was obtained in eight patients, and two patients had percutaneous CFA access.

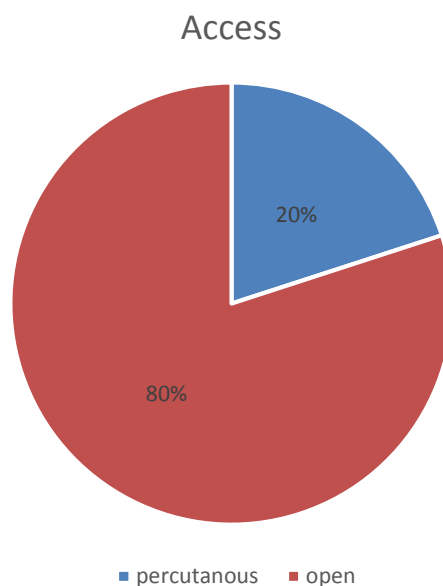


Fig 5. Femoral access

Endovascular stent grafts were deployed successfully in all patients 100%, the choice of the stent graft design was based on the individual patient's anatomy, especially the proximity of the lesion(s) to aortic branch vessels. Nine tubular stent grafts were implanted to repair pseudoaneurysms with sufficient proximal and distal aortic neck segments of healthy vessel appropriate for anchoring the graft. In this group, three stent grafts were placed in the infrarenal aorta, and six stent grafts in descending thoracic Aorta (three in supraceliac Aorta & three distal to Lt subclavian artery), and one in Aortic Arch, One bifurcated stent grafts was deployed for abdominal aortic aneurysms adjacent to the aortic bifurcation and one patient needed bilateral CIA covered stent in addition to tube graft, coiling of aneurysmal sac was done in one patient. Two patients needed further management for associated arterial aneurysm, first patient had Rt subclavian artery aneurysm treated by covered stent, second patient had RT CFA aneurysm treated by surgical interposition between CFA & SFA by 8 mm PTFE graft.

Table 3
Reported procedure related Complications

Patient no.	30-day mortality	Graft related complications	endoleak	Access site complication	Need for further intervention	Renal insufficiency
1	X	X	X	NA	NO	X
2	X	X	X	RT CFA pseudoaneurysm	RT subclavian aneurysm & RT CFA pseudo aneurysm	X
3	X	X	X	NA	NO	X
4	X	X	X	NA	No	X

9	X	X	X	NA	NO	X
6	X	X	X	LT CFA pseudoaneurysm	LT CFA pseudoaneurysm	X
7	X	Graft migration	√ Type 1B	NA	Aorto uni iliac EVAR& fem -fem bypass	X
8	X	X	X	NA	Bilateral CIA stenting	X
5	√	X	X	NA	NO	X
10	X	X	X	NA	NO	X

Overall survival was 80 % with mortality of 20% as 2 cases died during follow -up period, one of them during first 30 day (10%). First patient died 1st day post-operative, patient had history of CAD & previous CABG operation, he had pararenal & descending thoracic Aortic aneurysm, carotid subclavian bypass was done followed by stent graft in thoracic aorta , then after 6 months total visceral debranching was done followed by 2 stent graft insertion in abdominal Aorta (1 tube & 1 bifurcated graft) with no intraoperavtive complication. Patient developed chest pain 1st day after endovascular procedure, he was diagnosed. Acute MI by ECG & cardiac enzymes & unfortunately patient died shortly after. Second patient presented by hematemesis due to oesophageal ulcer due to presseure by saccular aortic aneurysm , CTA shows leaking descending thoracic Aortic aneurysm, stentgraft to thoracic Aorta was done , conservative mangment to oesophageal tear was done by total parentral nutrition & follow up , oesophageal tear didn` t respond to conservative treatment which mandate insertion of oesophageal stent ,then patient developed mediastinitis and died by septic shock 40 days after endovascular procedure .

Access site complication

There were 2 cases (20%) complicated with CFA pseudoaneurysm both after surgical cut-down. First patient treated by ligation of CFA due to ruptured pseudoaneurysm & the limb was adequately perfused so no futher manegment was needed, 2nd patient treated by primary repair of CFA by prolene 5-0 sutures with no post-operative complications.



Fig6 CTA shows LT CFA pseudoaneurysm after open femoral access.

Graft related complications

During follow up period , no evidence graft occlusion , graft infection or sac size expansion , but graft migration & type IB endoleak occurred in one patient after 15 mon. of stent graft to infra renal Aorta ,this complication was managed by insertion of Aorto unifemoral stent graft & fem -fem bypass.

Re- intervention

two patients needed re-intervention during follow up period , one patient for management of migrated stent graft ,and one patient developed bilateral CIA stenosis after 1 year of stent graft deployment so bilateral CIA kissing stent was performed (fig. 7) .

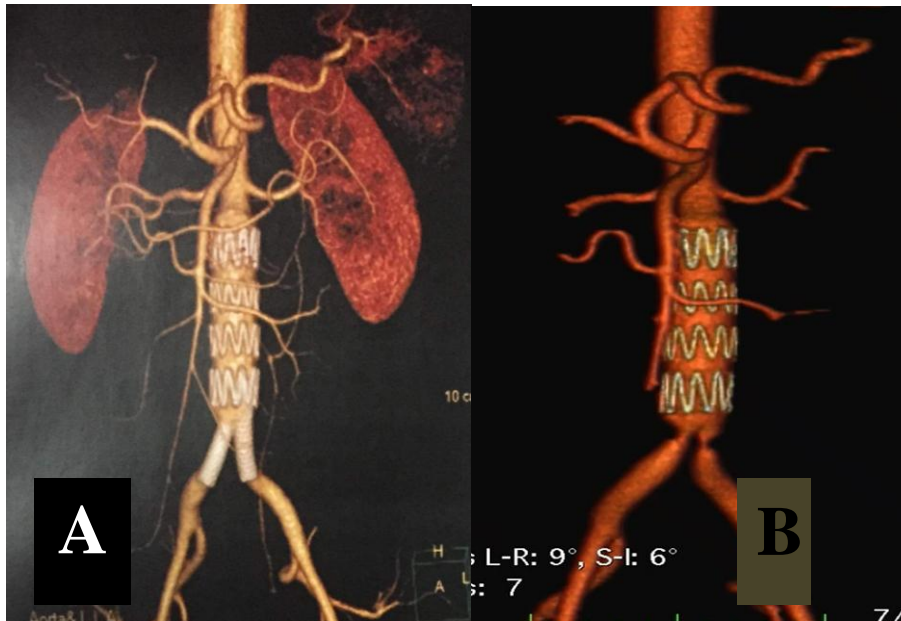


Fig 7. (A)CTA shows bilateral CIA stenosis, (B) kissing stent to bilateral CIA

Discussion

BD is a chronic inflammatory disease of unknown origin. Although arterial involvement is not common, it can complicate the clinical picture and cause potentially fatal complications. The expression of vasculitis due to Behçet's disease may be in many clinical forms as stenosis, occlusion and aneurysm formation. Although, aneurysm and pseudoaneurysm are mostly seen in the arterial system, thrombosis occurs in the venous system.⁸ Arterial aneurysms are the most serious ones because of the inherited high risk of rupture. The abdominal aorta is the most common location of aneurysms in Behçet's disease, followed by the pulmonary and femoral arteries.⁹ Aortic pseudoaneurysm is a rare complication of BD (1.5%-2.7%), but this complication is associated with high morbidity and mortality if rupture occurs. Surgical treatment of aortic pseudoaneurysm in the setting of BD has been frequently reported to be unsuccessful, with high rates of occlusion and postoperative anastomotic pseudoaneurysm.¹⁰⁻¹¹

Liu et al., reported the results of a meta-analysis that found that pseudoaneurysm-related mortality with surgery was 10% to 30%, and that recurrent pseudoaneurysm developed at an anastomotic site in 10% to 50% of patients with BD. The shared conclusion of these authors was that surgical treatment of arterial complications in BD was unsatisfactory.³ In 1998 Vasseur et al., first reported endovascular treatment of a BD patient with aortoiliac false aneurysms using a bifurcated stent graft. This showed that endovascular treatment could provide a feasible, less invasive alternative to surgery for patients with aortic pseudoaneurysm due to BD.¹² Since the first successful outcome of endovascular stent grafting by Vasseur et al., many investigators have reported endovascular procedures are effective in reducing postoperative complications compared with open surgical treatments.¹³

In this study, we evaluated efficacy & outcome of endovascular stent graft implantation for the treatment of aortic pseudoaneurysm in 10 patients with Behçet's disease. In our study all patients were males with a median age of 41 y (range 33-66 y), similar demographic features were reported in other studies as liu et al., study included 9 males patients and one female with median age of 35.5 years (range, 24-54 years), kim et al., study included 8 male & one female patient with a median age of 39 years, in shen et al., study, all patients were males- and The median age was 41 years (from 29 years to 56 years).¹³⁻¹⁴ In our study Nine (90%) patients received immunosuppressive therapy (prednisolone & cyclophosphamide) before their endovascular procedure. one patient with ruptured saccular aneurysm received pulse steroid therapy (hydrocortisone, 200mg/d) before procedure and cyclophosphamide for 3 days after procedure. All patients continued immunosuppressive treatment in the form of prednisolone during follow-up, this drug regimen was tapered intermittently, adjusted in conjunction with the individual patient's response and guidelines provided by the consulting rheumatologists according to EULAR guidelines.¹⁵

Our strategy was similar to balcioglu et al., as all Patients received immunosuppressive therapy with oral prednisolone and cyclophosphamide for 2 weeks or more before the procedure, and intravenous hydrocortisone combined with cyclophosphamide for 3 days after the procedure. Thereafter, oral immunosuppressive therapy was continued for 2 years.⁹ Kim et al., reported that only one patient in their cohort did not receive preoperative immunosuppressive medication due to a delayed diagnosis after intervention and exhibited comorbid bilateral femoral head avascular necrosis, in which prednisone was contraindicated, while in shen et al., study 6 out of 10 patients (60%) didn't receive preoperative immunosuppressive medication because their diagnosis of BD was made after EVAR.¹³⁻¹⁴ In our study, Adjunctive debranching procedure were performed in three cases with insufficient proximal landing zone, one patient needed aortic arch debranching for arch aneurysm, and one needed carotid subclavian bypass for descending thoracic aortic aneurysm and total visceral debranching for pararenal aneurysm.

In balcioglu et al., study total visceral debranching was performed to three patients before stent graft implantation for type 4 TAAA, while in both kim et al., and liu et al., studies no adjunctive debranching procedure were performed.⁹ In our 10 patients, all endovascular stent grafts were deployed successfully (100%), with complete exclusion of 8 saccular Aortic aneurysms & 3 fusiform aneurysms, similar results were obtained in liu et al., & kim et al., and balcioglu et al., studies in which Technical success was achieved in all patients 100% with no immediate complications from the stent graft procedures.^{3-9, 13} In shen et al., study the overall success rate was 90% after 8 endovascular & 2 surgical repair and the only failed case involved the use of the chimney technique to reach a suprarenal location.¹⁴

Mean follow-up period in our study was 22.6 months (range, 1-39 months), while mean follow up in liu et al., study was 25.8 months (range, 6-50 months) and in balcioglu et al., study it was 40 months (range, 12-60 months).³⁻⁹ The overall survival rate is 80% in our series. With 30-day mortality of 10%, in liu et al., study the overall survival was 90%, while in kim et al., study the overall survival

rate was 100%.³⁻¹³ In shen et al., study Four aneurysm-related deaths occurred within the follow-up period. The overall 1-year, 3-year and 5-year survival rates were 80%, 64% and 48%, respectively. All deaths due to rupture of recurrent aneurysm, three of them after endovascular treatment and 1 after surgical repair.¹⁴ In our study, surgical cut down for femoral access was performed in 8 patients and percutaneous access was obtained in 2 patients, there were 2 cases (20%) complicated with CFA pseudoaneurysm both after surgical cut-down. First patient treated by ligation of CFA due to ruptured pseudoaneurysm & the limb was compensated so no further manegment was needed, 2nd patient treated by primary repair of CFA by prolene 5-0 sutures with no post-operative complications.

In liu et al., study all the stent grafts were introduced through surgical cutdown, At 6 months after the procedure one patient has pseudoaneurysm at the femoral artery access site and another pseudoaneurysm at the proximal edge of the aortic stent graft, and patient died due to ruptured aortic pseudoaneurysm.³ While in kim et al., study Percutaneous access was obtained in all patients except in one case surgical cut-down technique 10% was obtained, with no reported access site complications.¹³ In our study 2 patients 20% needed reintervention, one patient need bilateral CIA stenting for bilateral CIA stenosis, and one patient need aorto uni iliac STENT graft & fem fem bypass. In balcioglu et al., study two patients needed abdominal exploration: one for seroma around the debranching grafts and the other for a fistula between the duodenum and the debranching graft.⁹

In kim et al., study One patient required a subsequent stent graft placement for an expanding pseudoaneurysm of the subclavian artery (6.4 cm). This was treated with a hybrid endovascular procedure, in which “right common carotid artery to left common carotid artery bypass grafting with ligation of left common carotid and left subclavian artery” was performed first, followed by a stent graft insertion from the aortic arch to the descending thoracic aorta. This pseudoaneurysm resolved following this procedure in 13 months of subsequent follow-up.¹³ In our study, graft migration & type IB endoleak occurred in one patient after 15 mon. of stent graft to infra renal Aorta, this complication was managed by insertion of Aorto unifem stent graft & fem -fem bypass., while in other studies they didn't report any stent graft related complication. We reported recurrence of aneurysm in one of our patients due to graft migration & type Ib endoleak after 15 months of follow up, that was similar to recurrence rate in kim et al., study in which Newly developed pseudoaneurysm at the distal margin of the stent graft was noted in one patient 17 months after the stent graft procedure.¹³

shen et al., had high recurrence rate 50%, Further analysis demonstrated that the absence of systemic immunosuppressive medication prior to intervention in several patients might account for the abnormally high rate of recurrence in his study as 6 out of 10 patients (60%) didn't receive preoperative immunosuppressive medication, and 4 out of these 6 patients (66.7%) experienced recurrence.¹⁴ In liu et al., study one patient 10 % had recurrent aneurysmal disease at the distal margin of the primary stent was successfully treated with an additional stent graft.³ Our single-center study had a small sample size due to the low prevalence of BD patients with aortic pseudoaneurysm, a more sophisticated data analysis such as a multivariate

analysis was not possible due to the small sample size. On the basis of limited experience, endovascular stent graft implantation combined with immunosuppressive therapy appears to be an effective treatment for aortic aneurysms in Behçet's disease. The endovascular approach is less invasive than open surgery, and immunosuppressive therapy may help to prevent recurrence of aneurysms. Further, prospective studies on a larger scale are recommended.

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