Outcomes of endovascular treatment for aortic pseudoaneurysm in Behcet's disease

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Objective: **To evaluate the effectiveness of endovascular stent grafting for surgical management of aortic pseudoaneurysm in patients with Behcet's disease (BD).**

Methods: **We present a single-institution retrospective cohort of patients with aortic pseudoaneurysm and BD treated with aortic stent grafting. Computed tomography imaging was obtained preoperatively in all patients and once within 2 weeks postoperatively, and then annually. Clinical follow-up and erythrocyte sedimentation rate were used to follow BD activity. Immunosuppressant therapy was instituted prior to endovascular treatment unless a contraindication existed.**

Results: **From 1998 to 2012, 10 patients (eight male, two female; median age, 39) with BD and aortic pseudoaneurysm were treated with endovascular stent grafting at this institution. Ninety percent of these patients received immunosuppressive therapy before and after surgical treatment. The median follow-up period was 57 months (interquartile range, 43-72). The locations of the 12 pseudoaneurysms treated in this cohort were infrarenal abdominal aorta (seven), descending thoracic aorta (four), and aortic arch (one). Median pseudoaneurysm size was 4.5 cm (interquartile range, 3.4-5.9). At long-term follow-up, complete resolution of the aortic pseudoaneurysm was noted in all patients. No endoleaks occurred. Newly developed pseudoaneurysm at the distal margin of the stent graft was noted in one patient 17 months after the stent graft procedure. One patient required a subsequent stent graft placement for an expanding pseudoaneurysm of the subclavian artery. No patient deaths occurred during the follow-up period.**

Conclusions: **Endovascular treatment of aortic pseudoaneurysm with stent-grafting in patients with BD is safe and effective with long-term durability. (J Vasc Surg 2014;59:608-14.)**

Behcet'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. Venous lesions range from superficial thrombophlebitis to occlusive lesions of the vena cava, and stenosis and/or pseudoaneurysms may occur in the peripheral arteries and the aorta. Venous thrombosis is the most frequent vascular complication of this disease, but pseudoaneurysm and rupture of the large arteries or the aorta, while less frequent, are of greater concern, since these events are a major cause of mortality in this condition.[2]

In the surgical treatment of vasculo-BD, anastamotic dehiscence has been one of the major reported complications. Pseudoaneurysms of anastomotic sites may occur in 30% to 50% of them.[3] At the time of reoperation in the setting of an anastomotic dehiscence, arterial reconstruction may be difficult to achieve. In an effort to reduce complications, endovascular treatment has been proposed as an alternative to open surgery in BD. Several studies have reported successful treatment of abdominal aortic pseudoaneurysm with the use of endovascular stent grafts in BD.[4-7] However, there exist few reports describing the long-term outcomes of endovascular treatment for pseudoaneurysm in these patients. The purpose of this study was to investigate the long-term effectiveness and safety of endovascular treatment for aortic pseudoaneurysm in patients with BD.

METHODS

Clinical database and patient characteristics. This study was approved by the Institutional Review Board. To identify subjects for enrollment in this retrospective series, records from all patients who underwent endovascular stent graft aortic pseudoaneurysm repair at this institution between 1998 and 2012 were reviewed to find patients with a coexistent diagnosis of BD. With regard to diagnosis, all patients satisfied the International Study Group Criteria for BD, which requires the presence of oral ulceration plus any two of genital ulceration, typical defined eye lesions, typical defined skin lesions, or a positive pathergy test.[8] All the patients had taken negative results for the blood culture to rule out mycotic aneurysm. The final study cohort consisted of 10 patients.

Stent graft technical description. All patients underwent preprocedure computed tomography (CT) imaging

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Table I. Patient characteristics

Patient	*Gender*	*Age*	*Anatomic distribution*	*Max. diameter of aneurysm, mm*	*Elapsed time from initial diagnosis, months*	*Combined arterial involvement*	*Previous operation history*
1	M	38	AA	25	90	None	Bypass graft due to aortic dissection[a]
2	M	39	AA	45	50	Right SFA pseudoaneurysm, left popliteal artery occlusion	Graft replacement from left CFA to right SFA due to left iliac artery occlusion
3	M	52	AA	45	154	None	None
4	M	35	AA	141	0	Right CFA pseudoaneurysm, right SCA pseudoaneurysm	None
5	M	44	AA	104	134	Right popliteal artery occlusion, segmental occlusion of right SFA	Left total hip replacement and right hip bone graft due to bilateral AVN
6	M	52	AA	33	69	None	None
7	M	49	AA	45	173	None	None
8	F	38	DT (multiple)	63	92	None	None
9	M	36	DT	27	2	Left SCA aneurysm	None
10	F	38	Aortic arch (including left SCA orifice)	36	21	Left SCA occlusion	None

AA, Infrarenal abdominal aortic; *AVN,* avascular necrosis; *CFA,* common femoral artery; *DT,* descending thoracic; *SCA,* subclavian artery; *SFA,* superficial femoral artery.
[a]Graft-interposition surgery (from infrarenal aorta to aortic bifurcation) for aortic dissection.

to guide the individual selection of a stent graft implant. The diameter of the stent graft used was chosen to be 10% to 15% larger than the diameter of the aorta measured on CT. We placed the stent graft 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. In this series, the implants selected consisted of self-expandable SEAL stent-grafts (S&G Biotech, Gyeonggi-do, South Korea), Excluder stent-graft (W. L. Gore & Associates, Flagstaff, Ariz), and custom-designed Z-type stent-graft (Tae Woong Medical, Seoul, South Korea). Deployed stent-grafts were subsequently dilated with an Equalizer occlusion balloon catheter (Boston Scientific, Natick, Mass) with 10% to 20% oversize.

Percutaneous access (n = 9) or cut-down technique (n = 1) was obtained through either the right or bilateral common femoral arteries, and each stent graft was inserted through the opening of the arterial puncture site. Technical success of the procedure was defined as complete exclusion of the inlet of the saccular pseudoaneurysm from the circulation and the absence of perigraft leakage on aortography.

Medical management. Immunosuppressive therapy was administered before and after surgical intervention. The dose of prednisolone (Yuhan, Seoul, South Korea) was adjusted between 5 and 60 mg/day, according to each patient's clinical condition, and azathioprine (50-100 mg/day; Myungmoon Pharm, Seoul, South Korea) and/or colchicines (1.2 mg/day; Korea United Pharm, Seoul, South Korea) were added if needed according to clinical condition and disease activity. Each patient's immunosuppressive regimen was adjusted based on serial measurement of the erythrocyte sedimentation rate (ESR) using the Westergren method (Espette, Korea; reference range <20 mm/h).

Follow-up evaluation. Follow-up clinical evaluation and CT imaging was obtained preoperatively in all patients and once within two weeks postoperatively, and then annually. CT images were reviewed for stent graft placement, diameter of the aorta, complete obliteration and thrombosis of the pseudoaneurysm sac, and the occurrence of complications, specifically pseudoaneurysm.

Statistical analysis. Quantitative variables were expressed as median and interquartile range, and qualitative variables were expressed as absolute and relative frequencies. The Wilcoxon matched-pairs signed-rank test (two-tailed probability) was used for intergroup comparisons. A *P* value of less than 0.05 was chosen as the threshold for indicating a statistically significant difference. Statistical analysis was performed with SPSS software (version 17.0; SPSS, Chicago, Ill).

RESULTS

The final study cohort consisted of 10 patients (eight men, two women; median age, 39 years [interquartile range (IQR), 38-48 months]). Patient demographics are given in Table I. In this cohort, aortic pseudoaneurysm was detected a median of 80 months (IQR, 28-124 months) after the initial diagnosis of BD. In these 10 patients, 12 pseudoaneurysms were identified, and all were saccular pseudoaneurysms: seven in the infrarenal abdominal aorta (Fig 1), four in the descending thoracic aorta, and one in the aortic arch. One patient had multiple

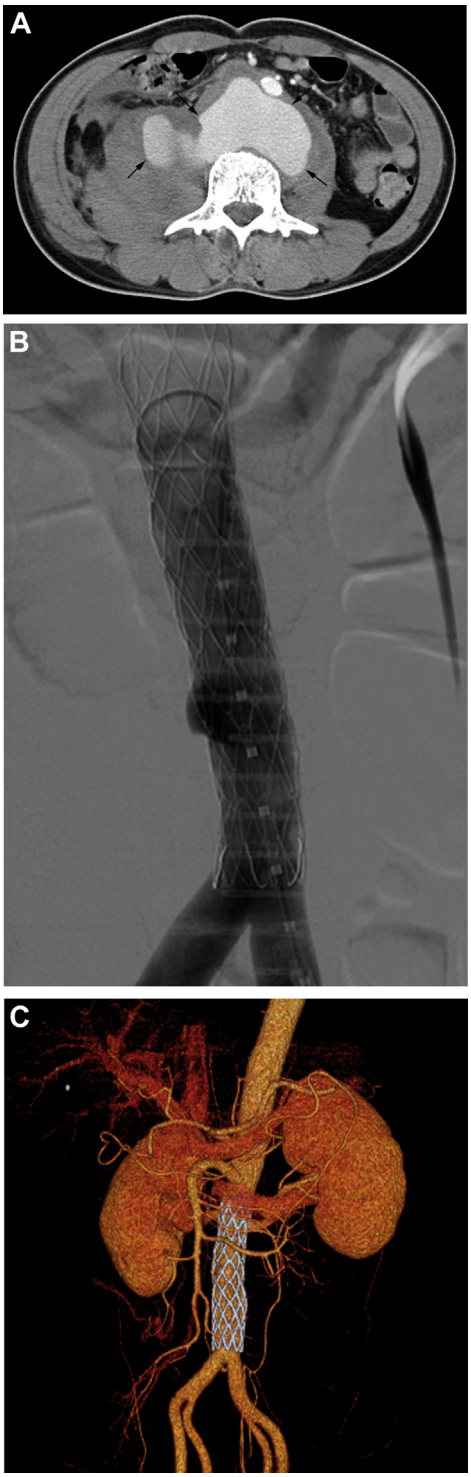

Fig 1. A 35-year-old male with ruptured abdominal aortic aneurysm. **A,** Axial image demonstrates a ruptured aortic aneurysm and subsequent retroperitoneal hemorrhage (*arrows*). **B,** Abdominal aortogram following stent graft placement demonstrates that the aneurysm has almost disappeared. **C,** At the 52-month follow-up, three-dimensional volume rendering computed tomography (CT) image reveals the aneurysm has completely regressed.

aortic pseudoaneurysms requiring treatment, with three pseudoaneurysms located in the descending thoracic aorta (Fig 2). Five patients (50%) had other associated arterial pathologies, including pseudoaneurysm and/or occlusion of the femoral, popliteal, or subclavian arteries.

Technical success was achieved in all patients with no immediate complications from the stent graft procedures. One patient required additional endovascular procedures for the treatment of arterial pseudoaneurysms of the right common femoral artery and the right subclavian artery, 10 days after the initial treatment of the patient's abdominal aortic lesion.

Clinical follow-up. Median follow-up duration was 57 months (IQR, 43-72 months). Imaging studies revealed complete resolution of the aortic pseudoaneurysms in all patients, and the median diameter of the aorta was significantly reduced from 4.5 cm (IQR, 3.4-5.9 cm) to 2.3 cm (IQR, 2.1-2.5 cm; $P = .005$). No patients experienced complications from the initial procedure requiring reintervention. In one patient treated for an abdominal aortic pseudoaneurysm, a new pseudoaneurysm developed at the distal margin of the stent graft that was diagnosed 17 months after the first procedure. This new lesion was followed by serial imaging for 5 years. This pseudoaneurysm was noted to slowly increase in size over the course of the first 3 years following its identification, up to a diameter of 28 mm, but its size has been stable in the subsequent 2 years leading up to the time of this report, so no further intervention has yet been performed.

During the follow-up, one patient, who had initially been treated for a pseudoaneurysm in the descending thoracic aorta, required further treatment for an arterial pseudoaneurysm of the left subclavian artery that had expanded to 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.

Nine (90%) patients in this cohort received immunosuppressive therapy at the time of their endovascular procedure and continued this treatment during follow-up. The one patient not on immunosuppressive therapy had previously received steroid therapy for 3 years and had developed bilateral femoral head avascular necrosis (AVN). Steroid therapy was considered to be contraindicated in this individual. At the time of endovascular treatment, six patients had ESR values in the normal range, and four patients demonstrated persistently elevated ESR values.

For all patients except the individual who had been diagnosed with AVN, immunosuppressive medications were continued during the follow-up period, with medication doses adjusted based on disease activity as measured by ESR. Three patients were noted on follow-up to have ESR elevations. One of these patients was the patient with AVN,

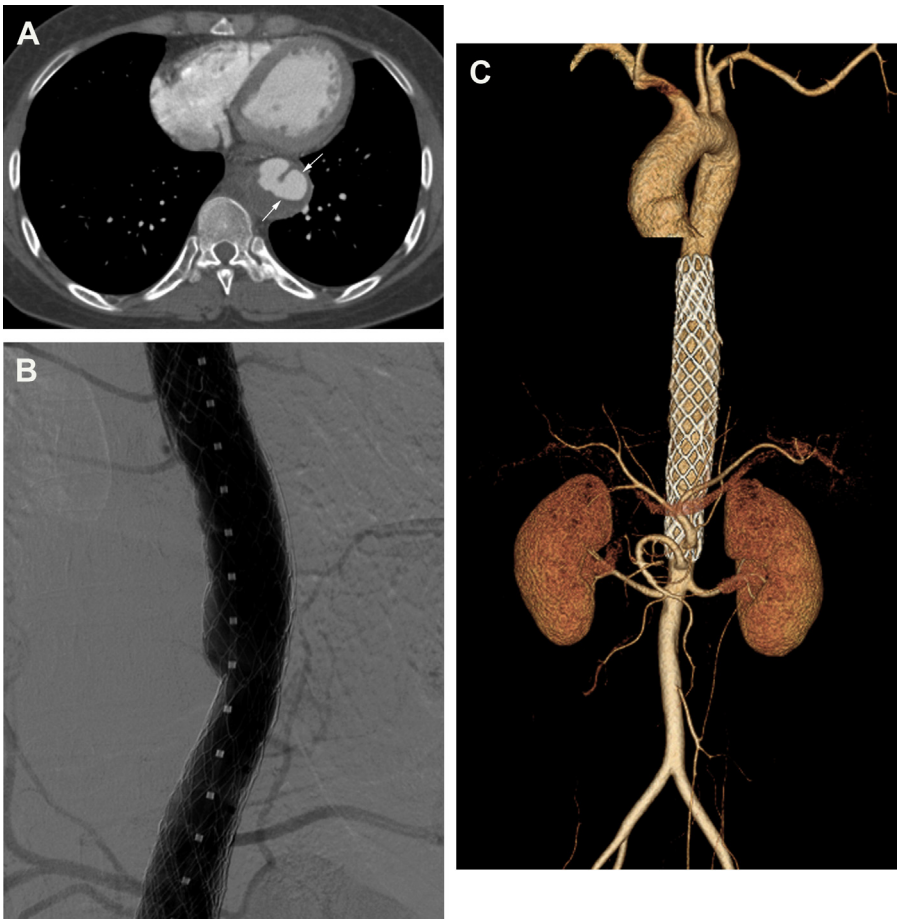

Fig 2. A 38-year-old female with multiple descending thoracic aortic aneurysms. **A,** Axial image reveals thoracic aortic pseudoaneurysm (*white arrows*). **B,** Aortogram demonstrates that the aneurysm is no longer visualized after stent graft placement. **C,** The aneurysm in the descending thoracic aorta has completely regressed after 70 months.

whose pseudoaneurysm nonetheless resolved following endovascular intervention and who has not demonstrated any recurrence or complications after 52 months of follow-up. In the second patient with an elevated ESR, during the follow-up, the patient had stopped medication several times of his own will and skipped periodic outpatient visiting. So appropriate dose control was not possible, and he was noted to have large fluctuations of his ESR (36 ± 30 mm/h [mean ± standard deviation]) during follow-up. At 17-month follow-up, he was found to have a new aortic pseudoaneurysm that developed at the distal margin of the stent graft. The third patient in elevated ESR had been in low compliance with medication but, with the increase of her compliance, ESR level was nearly normalized. On follow-up, her pseudoaneurysm has completely resolved.

DISCUSSION

Aortic pseudoaneurysm is a rare complication of BD, but this complication is associated with high morbidity and mortality if rupture occurs. Outcomes of endovascular or surgical treatment have been described (Table II). 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. Ozeren et al[9] reported that following 12 primary operations for arterial occlusion or aneurysm in BD, 12 reoperations on seven patients were required due to complications including graft thrombosis, bleeding, graft infection, aortoenteric fistula, and anastomotic pseudoaneurysm. Similarly, Liu et al[10] 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. Since the first successful outcome of endovascular stent grafting by Vasseur et al,[4] many investigators have reported endovascular procedures are effective in reducing postoperative complications compared with open surgical treatments.[11-14] One criticism

Table II. Recent studies concerning Behcet's disease (BD) in vascular patients

First author	*Year*	*Case, No.*	*Involvement*	*Vascular symptom*	*Preoperative medication*
Ozeren[9]	2000	12	Arterial aneurysm or occlusion	Abdominal pain, pain in extremities, pre-shock	CS, CCC
Park[12]	2001	7	Aortic or arterial aneurysm	NA	NA
Koo[14]	2003	9	Arterial pseudoaneurysm	NA	ST, AZA
Iscan[21]	2005	20	Arterial aneursym (19), occlusion (1)	Visceral pain, abdominal pain	NA
Kalko[15]	2005	16	Arterial aneurysm	NA	ST, CPM
Hosaka[22]	2005	10	Arterial aneurysm	NA	ST, CCC
Ohshima[23]	2008	1	CCA aneurysm	Swelling, pulsatile mass	NA
Kwon[16]	2008	12	Abdominal aortic pseudoaneurysm	NA	ST, AZA, CCC, CPM
Liu[10]	2009	10	Arterial pseudoaneurysm	Abdominal pain, back pain	ST, CPM
Kim[17]	2009	16	Arterial pseudoaneurysm	NA	ST, AZA, CCC
	2009	7	Arterial pseudoaneurysm	NA	NA
Saadoun[24]	2012	101	Arterial aneurysms, occlusions, stenosis, aortitis	NA	ST (86.1%), IMM (CPM, AZA) (78.2%)
Tuzun[25]	2012	25	Nonpulmonary arterial aneurysm (23), occlusion (2)	NA	ST, CPM
Unal[26]	2013	11	Arterial pseudoaneurysm (responsed to medication)	NA	IMM

AZA, Azathioprine; *CCC,* colchicines; *CPM,* cyclophosphamide; *CS,* cyclosporine; *EV,* endovascular intervention; *IMM,* immunosuppressant; *NA,* not available; *SG,* surgery; *ST,* corticosteroids.

of these reports, however, is that the short duration of follow-up reported for endovascular treatments in BD prevents a fair comparison with outcomes for open surgical procedures.[15] In support of this concern, Kwon et al[16] reported a relatively high rate of recurrent pseudoaneurysm at the margins of endovascular stent grafts in a patient cohort with a mean follow-up duration of 45.5 months. However, their work only describes stent grafting on four patients, which is too small of a sample size to have a statistically meaningful discussion. Additionally, three of those four cases were follow-up treatments for pseudoaneurysms caused by a previous interposition surgery or a patchy-closure surgery, which cannot be strictly considered as complication of stent grafting. In contrast, Kim et al[17] have reported follow-up results of stent grafting of 20 arterial aneurysms in 16 BD patients. In this case series with a mean follow-up duration of 47.6 months, only three patients were found to have complications. It should be noted, though, that this study included a heterogeneous group of lesions affecting vessels ranging in size from small arteries to the aorta.

While BD may affect vessels of a range of sizes, involvement of the large arteries or aorta particularly places the patient at risk for significant morbidity and mortality. As for follow-up duration, a prolonged monitoring is required in vascular BD patients, since recurrence of pseudoaneurysm at the site of surgery is possible. In this study, we investigated long-term outcomes of endovascular stent graft treatment for aortic pseudoaneurysm in patients with BD. We conclude from our results that endovascular treatment of aortic pseudoaneurysm in BD patients is safe and effective based on our data and long-term follow-up results. In this study, all aortic pseudoaneurysms were completely resolved at a median follow-up duration of 57 months. In a cohort of 10 patients, only one patient (10%) developed a new pseudoaneurysm at the distal margin of the stent graft, and this newly developed pseudoaneurysm has been stable in size on follow-up for the last 2 years. Our complication rate (10%) is lower than the previously published rates of postoperative pseudoaneurysm for open surgical interposition, which are reportedly between 30% and 50%,[3,18] and lower than the published rates of postoperative pseudoaneurysm occurring after endovascular intervention, which range from 14.3% to 22.2%.[10,12,14]

In the treatment of arterial pseudoaneurysm in BD, endovascular interventions have also been found to have higher survival rates compared with open procedures.[10,12,14] In this study, all patients survived until the time of last follow-up. In addition, no primary lesions have required reintervention following stent grafting.

Another aspect of the surgical management of BD that has received recent attention is the use of immunosuppressive agents.[9] Ando et al[19] have proposed that steroids should be given to BD patients pre- and postoperatively in order to modulate inflammation and thereby reduce complications. This practice is supported by the results of Koo et al[14] and Liu et al,[10] who reported, although with a small number of patients, that patients without taking immunosuppressant had a higher recurrence rate.

The standard immunosuppressive regimen for BD is steroid, and optionally azathioprine and colchicines can be used.[18] In this study, patients were prescribed prednisolone and optionally colchicines and azathioprine before and after their procedures according to each patient's clinical condition and ESR values to measure BD activity.[20]

Although endovascular procedures are less invasive than open surgery, stents and/or stent grafts may provoke inflammation within the aortic wall by foreign body

Table II. Continued.

Surgery, No. (%)	*Endovascular, No. (%)*	*Intervention-related death, No. (%)*	*Recurred pseudoaneurysm, No. (%)*	*Occlusion, No. (%)*	*Follow-up, mean*
12 (100)	None	0 (0)	3 (25)	3 (25)	36 months
none	7 (100)	0 (0)	1 (14)	1 (14)	28 months
none	9 (100)	0 (0)	1 (11)	1 (11)	24.1 months
20 (100)	None	2 (10)	10 (50)	9 (45)	44 months
16 (100)	None	0 (0)	2 (13)	NA	17 months
10 (100)	None	1 (10)	5 lesions (10)	5 lesions (24)	133 months
None	1 (100)	0 (0)	0 (0)	0 (0)	12 months
11 (92)	4 (33)	0 (0)	SG: 5 (45), EV: 2 (50)	NA	45.5 months
None	10 (100)	0 (0)	2 (20)	NA	25.8 months
None	16 (100)	0 (0)	2 (13)	2 (13)	47.6 months
7 (100)	None	1 (14)	2 (29)	NA	NA
47 (47)	1 (1)	NA	NA	9 (19)	7.6 years
22 (88)	None	1 (5)	2 (9)	10 lesions (40)	7.4 years
None	None	NA	6 (55)	NA	20 months

reaction and mechanical irritation, and this may contribute to the recurrence of pseudoaneurysm after endovascular treatments, especially at the both margins of the stent. Thus, immunosuppressive therapy may reduce the risk of these complications by decreasing and modulating these inflammatory reactions. Not only was the postprocedural medication important, but also the preprocedural remission of the disease activity. The establishment of the remission before the surgical intervention decreases the incidence of postoperative complications as suggested by Kalko et al[15] In terms of establishment of remission of BD before the surgical treatment, we have experienced only four graft replacement surgeries for aortic pseudoaneurysms in BD patients. Three patients achieved normal range of ESR level before surgery, whereas one patient with elevated ESR presented as ruptured aortic pseudoaneurysm and expired during emergent surgery. Among three patients who survived, one patient was lost to follow-up. The remaining two patients had no complication or recurred pseudoaneurysm until the follow-up, 57 and 47 months, respectively. Thus, we believe that ESR levels are important during pre- and postoperative periods, but further large study should be mandatory.

In this study, we tried to normalize every patient's ESR to achieve BD remission prior to the endovascular procedure. However, four patients still had elevated ESR at the time of the endovascular procedure, and we could not wait for the remission to occur. Specifically, the first two already had ruptured pseudoaneurysm, the third patient could not use corticosteroids due to his bilateral femoral head AVN, and the last one showed an aggravation of abdominal pain.

Immunosuppressant therapy was continued following endovascular treatment and serial ESR values were obtained for all patients at follow-up evaluations. At follow-up, three patients were noted to have elevated ESR levels despite being on immunosuppressant medication, and as discussed in the results section above, the one patient who developed a new pseudoaneurysm at the distal margin of his stent graft was noted to have an elevated ESR (preprocedure ESR, 23 mm/h; mean postprocedure ESR, 36 mm/h). Further studies are needed to establish if ESR elevation is associated with a greater risk of pseudoaneurysm recurrence, and if more aggressive immunosuppression is effective in preventing this complication.

In this study, a more sophisticated data analysis such as a multivariate analysis was not possible due to the small sample size of the dataset. We aim to initiate a multi-center study to collect a larger number of samples for this rare disease as future work. Also, we are considering a possible extension to this study such as analyzing any association between BD and hyperhomocysteinemia and/or integrating statin therapy data.

CONCLUSIONS

In summary, we conclude that endovascular stent grafting for aortic pseudoaneurysm in BD is safe and effective on long-term follow-up. We suggest that BD activity should be modulated before and after the procedure with the use of immunosuppressive therapy. Further investigations are needed to determine the specific dosing and duration of immunosuppressant therapy that is most effective for the prevention of recurrence of aortic pseudoaneurysm in these cases.

AUTHOR CONTRIBUTIONS

Conception and design: DL, MK
Analysis and interpretation: MK, SK

Data collection: SK
Writing the article: SK
Critical revision of the article: SL, JW
Final approval of the article: DC, YK, YN
Statistical analysis: SK
Obtained funding: DL
Overall responsibility: MK

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