Ann Vasc Dis Vol. 11, No. 4; 2018; pp 520–524

Online November 7, 2018
doi: 10.3400/avd.oa.18-00058

Original Article

Polyester Grafts Are a Risk Factor for Postimplantation Syndrome after Abdominal Endovascular Aneurysm Repair: Retrospective Analysis for Polyester Graft, Excluder®, and Endologix Powerlink®/AFX®

Eisaku Ito, MD,[1] Naoki Toya, MD, PhD,[1] Soichiro Fukushima, MD,[1] Ryosuke Nishie, MD,[1] Tadashi Akiba, MD, PhD,[2] and Takao Ohki, MD, PhD[3]

Objective: Postimplantation syndrome (PIS) is a postoperative syndrome that occurs after endovascular aneurysm repair (EVAR), accompanied by high fever, leukocytosis, and high serum C-reactive protein (CRP). Its pathogenesis and clinical meaning are still under discussion. Here, we evaluate the relationship between postoperative fever after EVAR and graft fabric focusing on Endologix Powerlink® and AFX® (EPL/AFX).

Materials and Methods: From January 2015 to July 2017, data on elective EVAR for abdominal aortic aneurysm (AAA) using mainbody were retrospectively collected. The primary endpoint was maximal postoperative fever.

Results: We identified 128 patients who underwent elective EVAR for AAA (105 males, 82%; aged 57–90, median: 74 years). The median maximal postoperative fever was 37.8°C (36.6–39.7°C): polyester graft, 38.2°C (37.1–39.7°C); Excluder®, 37.8°C (36.6–39.2°C); and EPL/AFX, 37.7°C (37–38.7°C). The maximal postoperative fever with a polyester graft was significantly higher than that with an expanded polytetrafluoroethylene (ePTFE) graft (p<0.001). However, there was no difference between Excluder® and EPL/AFX (p=0.214).

Conclusion: In this study, it was found that polyester grafts are significantly associated with PIS after elective EVAR for AAA. If patient anatomy is permitted, it may be better to choose the ePTFE graft, especially for patients with a poor general condition.

Keywords: endovascular aneurysm repair, abdominal aortic aneurysm, postimplantation syndrome

[1] *Division of Vascular Surgery, The Jikei University Kashiwa Hospital, Kashiwa, Chiba, Japan*
[2] *Department of Surgery, The Jikei University Kashiwa Hospital, Kashiwa, Chiba, Japan*
[3] *Department of Vascular Surgery, The Jikei University School of Medicine, Tokyo, Japan*

Received: May 22, 2018; Accepted: September 11, 2018
Corresponding author: Naoki Toya, MD, PhD. Division of Vascular Surgery, The Jikei University Kashiwa Hospital, 163-1 Kashiwashita, Kashiwa, Chiba 277-0004, Japan
Tel: +81-4-7164-1111, Fax: +81-4-7163-3488
E-mail: toyanaoki@gmail.com

Introduction

Endovascular aneurysm repair (EVAR) for abdominal aortic aneurysms (AAAs) is less invasive and is associated with a significant reduction in operative mortality and morbidity compared with conventional open surgery.[1–3] Postimplantation syndrome (PIS) is a postoperative syndrome characterized by high fever, leukocytosis, and high serum C-reactive protein (CRP) following EVAR.[4–7] There are some reports on PIS associated with acute hepatic dysfunction and multiple-organ failure.[8,9] However, the pathogenesis and clinical meaning of PIS are still under discussion.[4,8,9] Compared with expanded polytetrafluoroethylene (ePTFE) grafts, polyester grafts have been reported to be a risk factor for PIS. However, there are many reports on PIS associated with Gore Excluder® (Excluder®, W. L. Gore & Associates, Flagstaff, AZ, USA), which is one of the most famous ePTFE grafts, but there is no report on PIS associated with Endologix Powerlink® (Endologix Inc., Irvine, CA, USA) and AFX® (Endologix Inc., Irvine, CA, USA) (EPL/AFX), which is an ePTFE graft. Here, we evaluated the relationship between postoperative fever after EVAR and graft fabric focusing on EPL/AFX.

Methods

Study design

We performed a retrospective review of patients who

underwent EVAR using a Zenith Flex® stent graft (Cook Medical, Bloomington, IN, USA), an Excluder® stent graft, an Endurant® stent graft (Medtronic, Minneapolis, MN, USA), an Aorfix® stent graft (Lombard Medical Technologies, Didcot, UK), or a Powerlink® and AFX® stent graft at The Jikei University Kashiwa Hospital, Chiba, Japan, between January 2015 and July 2017. The patients included in this study underwent elective EVAR for AAA using a bifurcated mainbody stent graft. Patients with ruptured AAAs were excluded. The primary endpoint was maximal postoperative fever.

The Jikei University Kashiwa Hospital's Institutional Review Board approved this study, and informed consent was waived because it is a retrospective observational study using a deidentified database, 29-205(8821).

Patients

Patients with AAAs and a minimum external diameter of 5.5 cm (short axis) or saccular morphology were deemed eligible for EVAR. The exclusion criteria for elective EVAR included acute myocardial or cerebral infarction within three months before the surgery and/or a recent symptomatic blue toe syndrome. All patients were classified according to the American Society of Anesthesiologists system (grades 1–4). EVAR was performed under local or epidural anesthesia in patients with severe and extremely severe chronic obstructive pulmonary disease (COPD) with a forced expiratory volume in one second (FEV1) of 50% [stage III or IV according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification]. Patients with end-stage renal disease were considered eligible for EVAR.

Data analysis

The body temperature of all patients was evaluated every eight hours after EVAR, and it was confirmed that their serum CRP levels normalized before discharge. If the body temperature was higher than 38.5°C, the patient received ice cooling and oral acetaminophens (400 mg/8 h). Postoperative hepatic failure was defined when the level of aspartate aminotransferase (AST) or alanine aminotransferase (ALT) rose to more than double compared with preoperative data.

Statistical analysis

Patient characteristics and operative variables were analyzed using the Chi-square test, analysis of variance (ANOVA), and the Kruskal–Wallis test. Univariate analyses were performed in order to identify patient- and procedure-related risk factors for postoperative fever using linear progression models. ANOVA was used when continuous data exhibited a normal distribution. For comparison of nonparametric data, the Kruskal–Wallis test was used. Categorical data were evaluated using the Chi-square or Fisher's exact test. Then, only factors that achieved a level of $p<0.05$ after univariate testing were entered in the logistic regression analysis. All statistical analyses were performed using Stata/IC (STATA statisti-

Table 1 Patient characteristics and operative details (univariate analysis)

Variables	Polyester graft (n=59)	Excluder (n=33)	EPL/AFX (n=36)	p value
	n (%) or median (range)			
Preoperative factors				
Age (years)	74 (57–89)	77 (58–89)	74 (59–90)	0.233*
Male	49 (83.1%)	24 (72.7%)	32 (88.9%)	0.209†
Hypertension	39 (66.1%)	23 (69.7%)	18 (51.4%)	0.236†
Coronary artery disease	11 (18.6%)	7 (21.2%)	6 (17.1%)	0.910†
Dyslipidemia	19 (32.2%)	11 (33.3%)	6 (17.1%)	0.223†
Stroke	8 (13.6%)	3 (9.1%)	2 (5.7%)	0.464†
Diabetes	7 (11.9%)	4 (12.1%)	6 (17.1%)	0.745†
COPD	3 (5.1%)	3 (9.1%)	4 (11.4%)	0.520†
Chronic renal failure	20 (33.9%)	13 (39.4%)	8 (22.9%)	0.324†
Aneurysm size (mm)	50 (34–67)	48.5 (33–100)	43 (28–79)	0.002**
Saccular aneurysm	9 (15.3%)	4 (12.1%)	13 (37.1%)	0.015†
Operative factors				
Internal iliac artery embolization	21 (35.6%)	8 (24.2%)	16 (44.4%)	0.213†
Surgery duration (min)	132 (80–276)	131(81–306)	126 (63–264)	0.420**
Blood loss (mL)	40 (10–1000)	40 (0–6800)	50 (10–800)	0.328**
Fluoroscopy time (min)	25 (12–147)	25.5 (10–65)	21.5 (9–104)	0.230**
Contrast media (mL)	140 (37–320)	130 (82–395)	98 (46–239)	<0.001**

† Chi-square test; * ANOVA; ** Kruskal–Wallis test

EPL: Endologix Powerlink; COPD: chronic obstructive pulmonary disease

cal software, version 14.0; Stata Corp., College Station, TX, USA). Two-sided probability p values of <0.05 were considered significant.

Results

Baseline characteristics and operative details (Table 1)

We identified 128 patients who underwent elective EVAR for AAA using mainbody (105 males, 82%; aged 57–90, median: 74 years). Excluder® was used on 33 patients (25.8%), EPL/AFX was used on 36 patients (28.1%), Aorfix® was used on 32 patients (25%), Endurant® was used on 26 patients (20.3%), and Zenith Flex® was used on one patient (0.8%). There were no hospital deaths, major adverse effects, multiple-organ failure, or hepatic failure. The rate of saccular aneurysm with EPL/AFX was significantly higher than with the other devices ($p=0.015$), smaller aneurysms ($p=0.002$), and lower-contrast media ($p<0.001$).

Outcomes

The median maximal postoperative fever was 37.8°C (36.6–39.7°C): polyester graft, 38.2°C (37.1–39.7°C); Excluder®, 37.8°C (36.6–39.2°C); and EPL/AFX, 37.7°C (37–38.7°C).

Univariate analysis for postoperative fever (logistic regression analysis) (Table 2)

Univariate analyses were performed using logistic regression analysis for postoperative fever. The cut-off of fever was 38°C. The contrast media and polyester graft were significantly associated with maximal postoperative fever ($p=0.010$, $p=0.001$).

Table 2 Univariate analysis for postoperative fever (≧38°C) (logistic regression analysis)

Variables	OR	(95%CI)	p value
Preoperative factors			
Age (years)	0.983	(0.938–1.030)	0.480
Male	1.469	(0.585–3.689)	0.413
Hypertension	0.898	(0.436–1.847)	0.770
Coronary artery disease	1.408	(0.577–3.435)	0.452
Dyslipidemia	1.594	(0.733–3.466)	0.240
Stroke	0.399	(0.078–1.147)	0.079
Diabetes	0.991	(0.356–2.759)	0.987
COPD	1.750	(0.469–6.527)	0.405
Chronic renal failure	0.708	(0.334–1.502)	0.368
Aneurysm size (mm)	1.001	(0.975–1.045)	0.593
Saccular aneurysm	0.551	(0.223–1.363)	0.197
Operative factors			
Internal iliac artery embolization	1.133	(0.548–2.343)	0.737
Surgery duration (min)	1.003	(0.995–1.011)	0.480
Blood loss (mL)	0.999	(0.997–1.001)	0.445
Fluoroscopy time (min)	1.017	(0.996–1.038)	0.115
Contrast media (mL)	1.010	(1.002–1.016)	0.010
Polyester graft	3.364	(1.625–6.961)	0.001

OR: odds ratio; CI: confidence interval; COPD: chronic obstructive pulmonary disease

Table 3 Subgroup analysis for postoperative fever in each graft (liner regression analysis)

Variables	Polyester graft* (n=59)	ePTFE graft** (n=69)	Excluder® (n=33)	EPL/AFX (n=36)	P1	P2	P3	P4
	Median (range)							
Post-operative maximal fever (°C)	38.2 (37.1–39.7)	37.7 (36.6–39.2)	37.8 (36.6–39.2)	37.7 (37.0–38.7)	<0.001	0.027	<0.001	0.214
Serum CRP (mg/dL)								
POD1	2.9 (0.3–9.2)	1.1 (0.1–27.7)	1.3 (0.1–27.7)	1.1 (0.1–3.9)	0.038	0.404	<0.001	0.148
POD3	11.9 (0.8–24.7)	5.6 (0.1–26.1)	5.7 (0.1–26.1)	4.9 (0.2–12.9)	<0.001	<0.001	<0.001	0.110
White blood cell count (/μL)								
POD1	11000 (4700–28700)	7900 (1200–15900)	8100 (1200–15900)	7550 (4700–14200)	<0.001	<0.001	<0.001	0.600
POD3	8500 (4100–18600)	7400 (3000–14100)	8350 (4100–14100)	7000 (3000–11000)	0.009	0.378	0.001	0.019
Postoperative hepatic failure	8 (13.6%)	6 (8.7%)	4 (12.1%)	2 (5.6%)	0.740	0.836	0.445	0.384
Admission duration after EVAR (days)	6 (2–17)	5 (2–34)	4.5 (2–19)	5 (3–34)	0.959	0.934	0.986	0.970

*Polyester grafts included Zenith Flex®, Endurant®, and Aorfix®. **ePTFE grafts included Excluder® and EPL/AFX.

CRP: C-reactive protein; POD: postoperative day; EVAR: endovascular aneurysm repair; ePTFE: expanded polytetrafluoroethylene; EPL/AFX: Endologix Powerlink® and AFX®

P1: polyester graft versus ePTFE graft; P2: polyester graft versus Excluder®; P3: polyester graft versus EPL/AFX; P4: Excluder® versus EPL/AFX.

Subgroup analysis for postoperative fever in each grafts (liner regression analysis) (Table 3)

Subgroup analysis was performed using linear regression analysis for fever in each graft. It was found that the maximal postoperative fever with polyester grafts was significantly higher than that with ePTFE grafts ($p<0.001$). However, there was no difference between Excluder® and EPL/AFX ($p=0.214$). There were 14 patients with postoperative hepatic failure. However, there was no significant difference between polyester grafts and ePTFE grafts. ePTFE grafts tended to reduce postoperative hepatic failure (13.6% versus 8.7%, $p=0.740$).

Discussion

Although the inflammatory responses after EVAR are defined in PIS, the diagnostic criteria are not confirmed. High fever, leukocytosis, and elevated serum CRP and interleukin (IL)-6 are known to be symptoms and signs for PIS. The rate of PIS was reported to be 14%–60%.[4–7] Although PIS is usually treated conservatively, it occasionally induces acute hepatic failure and multiple-organ failure.[4,6–9] Moreover, it was reported that PIS is associated with a 30-day cardiovascular event after EVAR.[4,6] Therefore, postoperative surveillance is thought to be necessary.[4,6,7]

The pathogenesis of PIS is unknown.[4,8,9] Compared with ePTFE grafts, polyester grafts have been reported to be a risk factor for PIS.[7] In general, after enhanced computerized tomography scans, percutaneous coronary angioplasty, or endovascular therapy for limb revascularization, inflammatory responses are uncommon. Therefore, contrast media and stent structure are not related to postoperative fevers.[4] In this study, it was shown that polyester grafts are associated with postoperative fevers. This phenomenon is known to occur after open graft repair using a polyester graft. Polyester grafts are comprised of gelatin, and gelatin is thought to be associated with postoperative fevers.[10–12] However, polyester grafts used as stent grafts do not contain sealed gelatin. It is thought that the pathogenesis of PIS differs between EVAR and open surgeries. There are some reports proposing that polyester triggers higher release of inflammatory biomarkers (tumor necrosis factor-α, IL-6, IL-10, and CRP) than ePTFE in vitro.[7,13,14] We hypothesize that these inflammatory biomarkers promote PIS.

Limitations

Our study had several limitations. First, in this study, due to the fact that EPL/AFX tended to be chosen for saccular and smaller aneurysms, there might be some biases. Second, we were not able to perform multivariate analyses because of the sample size. Finally, this study was retrospective in nature and had a relatively small number of patients from a single center. A prospective, blinded clinical trial is required in order to establish the mechanism and physiology of PIS and aneurysm prognosis.

Conclusion

In this study, it was shown that ePTFE grafts (Excluder® and EPL/AFX) are associated with a lower probability of postoperative fever. If patient anatomy is permitted, it may be better to choose ePTFE grafts, especially for patients with a poor general condition.

Disclosure Statement

Takao Ohki is a paid consultant of W. L. Gore & Associates. The other authors do not have any conflicts of interest or financial ties to disclose.

Author Contributions

Study conception: EI
Data collection: EI, NT, SF, RN
Analysis: EI, NT
Investigation: EI, NT, SF, RN
Writing: EI
Critical review and revision: all authors
Final approval of the article: all authors
Accountability for all aspects of the work: all authors

References

1) De Bruin JL, Baas AF, Buth J, et al. Long-term outcome of open or endovascular repair of abdominal aortic aneurysm. N Engl J Med 2010; **362**: 1881-9.
2) United Kingdom EVAR Trial Investigators; Greenhalgh RM, Brown LC, Powell JT, et al. Endovascular versus open repair of abdominal aortic aneurysm. N Engl J Med 2010; **362**: 1863-71.
3) Chaikof EL, Blankensteijn JD, Harris PL, et al. Reporting standards for endovascular aortic aneurysm repair. J Vasc Surg 2002; **35**: 1048-60.
4) Arnaoutoglou E, Kouvelos G, Papa N, et al. Prospective evaluation of post-implantation inflammatory response after EVAR for AAA: influence on patients' 30 day outcome. Eur J Vasc Endovasc Surg 2015; **49**: 175-83.
5) Syk I, Brunkwall J, Ivancev K, et al. Postoperative fever, bowel ischaemia and cytokine response to abdominal aortic aneurysm repair—a comparison between endovascular and open surgery. Eur J Vasc Endovasc Surg 1998; **15**: 398-405.
6) Arnaoutoglou E, Papas N, Milionis H, et al. Post-implantation syndrome after endovascular repair of aortic aneurysms: need for postdischarge surveillance. Interact Cardiovasc Thorac Surg 2010; **11**: 449-54.
7) Moulakakis KG, Alepaki M, Sfyroeras GS, et al. The impact of endograft type on inflammatory response after endovas-

cular treatment of abdominal aortic aneurysm. J Vasc Surg 2013; **57**: 668-77.
8) Ohara N, Miyata T, Oshiro H, et al. Adverse outcome following transfemoral endovascular stent-graft repair of an abdominal aortic aneurysm in a patient with severe liver dysfunction: report of a case. Surg Today 2000; **30**: 764-7.
9) Blum U, Voshage G, Lammer J, et al. Endoluminal stent-grafts for infrarenal abdominal aortic aneurysms. N Engl J Med 1997; **336**: 13-20.
10) Utoh J, Goto H, Hirata T, et al. Postoperative inflammatory reactions to sealed Dracon prostheses: a comparison of Gelseal and Hemashield. J Cardiovasc Surg (Torino) 1997; **38**: 287-90.
11) Lacroix H, Boel K, Nevelsteen A, et al. Early inflammatory response to gelatin- and collagen-sealed Dacron prostheses. Ann Vasc Surg 1995; **9**: 152-4.
12) Shindo S, Motohashi S, Katsu M, et al. Coated prostheses are associated with prolonged inflammation in aortic surgery: a cost analysis. Artif Organs 2008; **32**: 183-7.
13) Swartbol P, Truedsson L, Pärsson H, et al. Tumor necrosis factor-α and interleukin-6 release from white blood cells induced by different graft materials in vitro are affected by pentoxifylline and iloprost. J Biomed Mater Res 1997; **36**: 400-6.
14) Voûte MT, Bastos Gonçalves FM, van de Luijtgaarden KM, et al. Stent graft composition plays a material role in the postimplantation syndrome. J Vasc Surg 2012; **56**: 1503-9.