Ann Vasc Dis Vol. 11, No. 2; 2018; pp 191–195

Online March 22, 2018
doi: 10.3400/avd.oa.17-00128

Original Article

Efficacy of Preoperative Antibiotic Therapy for the Treatment of Vascular Graft Infection

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Objective: We aimed to assess the efficacy of preoperative antibiotic therapy for the treatment of prosthetic graft infection.

Materials and Methods: We retrospectively analyzed the treatment strategies used for managing patients with prosthetic vascular graft infections between 2000 and 2016. The patients were divided into two groups: early antibiotic (EA) group, those who were administered with antibiotics ≥2 weeks preoperatively and late antibiotic (LA) group, those who were administered with antibiotics <2 weeks preoperatively. We evaluated the outcomes including surgical procedures, length of hospital stay, and surgical revision.

Results: All the surgical procedures performed in the EA group were elective surgeries. Three of the 11 surgeries performed in the LA group were emergency surgeries (P=0.16). No significant differences were observed in the operative procedure (P=0.64), operation time (P=0.37), and blood loss (P=0.63) of the two groups. Although the length of postoperative hospital stay did not significantly differ (P=0.61), the total length of hospital stay was longer in the EA group (P=0.02). Surgical revisions were performed for five patients in the LA group and for none in the EA group (P=0.04).

Conclusion: Preoperative antibiotic therapy provided excellent outcomes in terms of avoiding surgical revisions in the treatment of vascular graft infection.

Keywords: vascular graft infection, antibiotic therapy

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Introduction

Although systemic prophylactic antibiotics and successful revascularization are effective treatment methods, prosthetic vascular graft infection is a serious and life-threatening complication with 1%–5% of patients treated in clinical practice. The frequency of the infection varies, depending on the anatomical implantation site, the graft biomaterial used, and the patient's comorbidities. This disease is associated with a high mortality rate (approximately 75%) and a high amputation rate (estimated to be as high as 70%).[1–5] The current recommendations for treating vascular graft infection are primarily based on the findings reported by small case series and expert opinions.[6,7]

The basic principle of surgical treatment involves the removal and replacement of the infected graft; this is the standard approach used for most patients presenting with a graft infection. Antimicrobial therapy is an essential addition to the surgical management of graft infection. The duration of antimicrobial therapy can range from several weeks to more than a year or lifelong suppressive therapy.[8–10] However, few studies have described the role and usefulness of preoperative antibiotic administration for treating graft infection.

We aimed to assess the efficacy of preoperative antibiotic administration in terms of infection recurrence and/or the need for reoperation.

Materials and Methods

Patients and data collection

We retrospectively analyzed the treatment strategies used for managing prosthetic vascular graft infection and their outcomes over 17 years between January 2000 and November 2016 in patients diagnosed with prosthetic vascular graft infection. We excluded patients with vascular access graft infection of end-stage renal disease. Patients were divided into two groups: early antibiotic (EA) group, those administered with antibiotics ≥2 weeks preoperatively and late antibiotic (LA) group, those administered with antibiotics <2 weeks preoperatively. We evaluated

the outcomes including surgical procedures, length of hospital stay, and surgical revision. Patients with vascular graft infection were identified from the database maintained by the University of Tokyo Hospital. The patients' clinical and laboratory data were obtained from the medical records of the hospital. In cases where the patient's follow-up data were unavailable, the patient or the attending doctor was contacted through telephone to obtain the necessary missing information.

Definitions

Patients were diagnosed with graft infection if at least one of the following criteria were met: 1) Microorganisms were detected in the area surrounding the graft, 2) Histopathological or radiological examination indicated graft infection, or 3) The patients experienced consistent bacteremia following graft implantation without any other focus of infection. We generally administered empiric antibiotic therapy. Thereafter, specific antibiotic treatment that was known to be effective against the detected organism according to sensitivity testing was initiated.

We considered the graft infection as cured if the patient was stable and fulfilled the following conditions: 1) No clinical signs of infection (normal body temperature, normal inflammatory marker levels, and no local inflammation), 2) Normal graft function (no graft-related bleeding and no ischemia distal to the graft), and 3) No histopathological or radiological evidence of infection. Treatment failure was defined as the presence of the abovementioned signs of infection without an alternative underlying cause.

Statistical analyses

The patients' baseline characteristics, concurrent medical conditions, surgical procedures, and antimicrobial treatments were compared using the Chi-Square test or the Fisher's exact test for categorical variables and the Mann–Whitney test for continuous variables. Numerical values are indicated as mean ± standard deviation values in each table. We used Microsoft® Excel 2016 (Microsoft Corporation, Redmond, WA, USA) statistical software for all analyses. $P \leq 0.05$ was considered significant.

Results

Patient's characteristics and clinical presentations

During the entire study period, 17 patients (six from the EA group and 11 from the LA group) were diagnosed with a graft infection. **Table 1** shows the patient characteristics. No significant differences were observed in the baseline characteristics of the two groups. In the EA group, aneurysmectomy with Y-graft replacement was performed as the initial surgery in two patients with abdominal aortic aneurysm (AAA), femoropopliteal (FP) bypass was performed in two patients with arteriosclerosis obliterans (ASO), and femorofemoral (FF) crossover bypass was performed in one patient with ASO and one patient with Takayasu arteritis. In the LA group, aneurysmectomy with Y-graft replacement was performed as the initial surgery in one patient with AAA, FP bypass was performed in three patients with ASO, iliofemoral (IF) bypass in two patients with ASO and one patient with Buerger disease, axillofemoral (AxF) bypass in one patient with ASO, FF crossover bypass in one patient with acute thromboembolism, and aneurysmectomy with graft replacement in two patients with peripheral arterial aneurysm (Behcet disease). Dacron prosthetic grafts were implanted in all the patients in both groups. The average duration until the development of graft infection after implantation was 59.1 months in the EA group and 99.8 months in the LA group ($P = 0.28$). In the EA and LA groups, five and nine patients developed peripheral graft infection, whereas one and two patients developed abdominal graft infection, respectively (**Table 2**, $P = 0.94$). The average duration of preoperative antibiotic treatment was 33.8 days in the EA

Table 1 Patient characteristics

	EA group (n=6)	LA group (n=11)	P value
Age	71.3±9.9	65.2±11.5	0.43
Sex (male/female)	4/2	10/1	0.21
Hypertension	4 (66.7%)	7 (63.6%)	0.90
Diabetes mellitus	1 (16.7%)	6 (54.5%)	0.13
Dyslipidemia	0 (0%)	4 (36.4%)	0.09
Coronary artery disease	0 (0%)	3 (27.3%)	0.16
Cerebrovascular disease	1 (16.7%)	1 (9.1%)	0.64
End-stage renal disease	1 (16.7%)	3 (27.3%)	0.62
Smoking	4 (66.7%)	9 (81.8%)	0.48
Steroid	1 (16.7%)	0 (0%)	0.16
Primary disease	AAA 2, ASO 3, Takayasu arteritis 1	AAA 1, ASO 6, Buerger disease 1, Behcet disease 2, acute thromboembolism 1	

EA: early antibiotic; LA: late antibiotic; AAA: abdominal aortic aneurysm; ASO: arteriosclerosis obliterans

Table 2 Clinical presentation

		EA group (n=6)	LA group (n=11)	P value
	Duration for developing graft infection (months)	59.1 (0.4–100.7)	99.8 (2.6–29.4)	0.28
	Prosthetic graft	Dacron 6 (100%)	Dacron 11 (100%)	—
Infection site	Peripheral	5 (83.3%)	9 (81.8%)	0.94
	Abdominal	1 (16.7%)	2 (18.2%)	
Microorganism	Antibiotic resistant	3 (50.0%)	3 (27.3%)	0.34
Laboratory data	WBC >9,000 or <4,000/mL	3 (50.0%)	8 (72.7%)	0.35
	CRP (mg/dL)	10.5±13.6	9.2±9.6	0.81

EA: early antibiotic; LA: late antibiotic; CRP: C-reactive protein; WBC: white blood cells

Table 3 Surgical and antimicrobial therapy

		EA group (n=6)	LA group (n=11)	P value
Unstable vital signs		0 (0%)	1 (9.1%)	0.45
Emergency operation		0 (0%)	3 (27.3%)	0.16
Surgical procedure	Graft removal with revascularization	3 (50.0%)	8 (72.7%)	0.64
	Graft removal alone	2 (33.3%)	2 (18.2%)	
	Debridement with graft retention	1 (16.7%)	1 (9.1%)	
Operation time (min)		248±188	341±219	0.37
Blood loss (mL)		472±636	936±2111	0.63
Length of postoperative hospital stay		46.2±41.3	39.0±15.6	0.61
Total length of hospital stay		99.5±66.4	45.6±15.4	0.02
Surgical revision		0 (0%)	5 (45.5%)	0.04
Duration of antibiotic therapy (months)		4.4±2.8	8.7±12.5	0.46

EA: early antibiotic; LA: late antibiotic

group and 5.0 days in the LA group.

Microbiological data

The infecting microorganism was identified in all the patients in both groups. In the EA group, the following pathogens were identified: *Enterococcus faecalis*, 2; methicillin-susceptible *Staphylococcus aureus* (MSSA), 1; and methicillin-resistant *Staphylococcus aureus* (MRSA), 3. In the LA group, the following pathogens were identified: Staphylococcus species, 1; *Streptococcus agalactiae*, 1; *Enterobacter aerogenes*, 1; *E. faecalis*, 1; MSSA, 4; MRSA, 2; and extended spectrum β-lactamase (ESBL), 1. No significant difference was detected in the ratio of drug-resistant bacteria (i.e., MRSA or ESBL) between the two groups (**Table 2**, P = 0.34).

Surgical and antimicrobial therapy

Only elective surgeries performed in the EA group, whereas three of the 11 surgeries performed in the LA group were emergency surgeries (P = 0.16). In the EA group, graft removal with arterial reconstruction was performed in three patients, graft removal alone in two patients, and debridement with graft retention in one patient. In the LA group, graft removal with arterial reconstruction was performed in eight patients, graft removal alone in two patients, and debridement with graft retention in one patient (**Table 3**). No significant differences were observed with respect to the operative procedure (P = 0.64), operation time (P = 0.37), and blood loss (P = 0.63) between the groups. No postoperative or in-hospital death was reported in either group. Although no difference was observed in the length of postoperative hospital stay (P = 0.61), the total length of hospital stay was higher in the EA group (P = 0.02). The mean duration of postoperative antimicrobial therapy was 4.4 months in the EA group and 8.7 months in the LA group (P = 0.46). Surgical revisions were performed for treatment failure in five patients of the LA group (two patients underwent drainage for recurrent infection, one underwent repair for infected anastomotic aneurysm, and two underwent removal of the occluded infected graft and additional revascularization), whereas no patient from the EA group required surgical revision (P = 0.04). There was one infection-related death in the LA group (5.9%) in 7 months postoperatively.

Discussion

Vascular graft infection is a serious health issue associated with a high risk of mortality, amputation, and reinfection. The fundamental principles of surgical treatment involve

debridement of the infected graft and revascularization; however, surgical intervention for vascular graft infection continues to be challenging.

Pre- and intra-operative antibiotic prophylaxis is largely beneficial for reducing surgical site infection associated with vascular surgery. Antibiotic therapy plays a vital role in patients presenting with prosthetic graft infection; broad-spectrum antibiotics are initiated at the onset of graft infection, followed by the administration of culture-specific antibiotics after the causative microorganisms have been identified during the treatment period.[11] The duration of antimicrobial treatment in patients with prosthetic graft infection following radical surgery is controversial in the absence of relevant standard guidelines. While some authors recommend lifelong antibiotic treatment, few recommend a 6-month treatment period and others recommend a 6-week treatment period. Based on our experience, we recommend that antibiotic administration should be continued for at least 6 weeks after radical surgery and the treatment should be discontinued in patients with no clinical, radiological, and/or laboratory evidence of infection.

According to a previous study, the type of surgical intervention used for managing infections (graft retention versus graft replacement) did not affect the primary outcome, whereas a rifampicin-based antimicrobial regimen was associated with a high cure rate.[12] Among 61 patients who presented with graft infection, 12 (19.7%) did not undergo any surgical intervention and were treated using only antibiotics. Rifampicin might be useful primarily against bio-film producing gram-positive pathogens, and a recent study has demonstrated the potential benefit of rifampicin-containing regimens against Staphylococcus-induced prosthetic vascular graft infection.[13] Both in vitro and animal studies have shown that rifampicin-coated grafts are effective treatments for in-situ graft replacement and the prevention of graft infection; however, clinical studies have reported inconclusive results.[14–23]

Few studies have described the role of preoperative antibiotics for the management of vascular prosthetic graft infection. Sugimoto et al. reported that the preoperative administration of systemic antibiotics effectively controlled sepsis in patients with infected AAAs and that timely surgical intervention with sepsis control provided excellent outcomes.[24] Another study reported a rat model wherein the infection was established subcutaneously in the back of rats by implanting a Dacron graft that was then topically inoculated with MSSA or MRSA.[25] Teicoplanin showed greater efficacy than vancomycin and cefazolin in this study. A daily decline in the bacterial count was observed with complete bacterial eradication following a 3-day regimen of this antibiotic. This animal study suggested that preoperative antibiotic therapy can decrease the bacterial counts before surgical intervention and may also reduce recurrent postoperative infections.

Graft-preserving strategies have also been proven successful in recent studies, particularly in patients with poor physiological reserve and thoracic graft infection.[26–28] In contrast, another study reported a high mortality rate (59%) associated with abdominal vascular graft infection treated using graft retention.[29] The contraindication of conservative treatment is valid, and surgical treatment should be performed as soon as possible in patients with anastomotic aneurysm, suture line hemorrhage, and systemic sepsis. Other cases can take some time to extend effective antibiotic therapy to decrease the bacterial count and avoid reinfection following surgical treatment.

There are some limitations to our study. The present study had a retrospective design. A direct between-group comparison revealed that they were heterogeneous; moreover, the relatively smaller sample size did not permit adequate statistical analyses. In addition, several advances may have been made in the surgical management of vascular graft infection during the study period, owing to rapid technological advancements with a higher tendency toward graft-preserving techniques.

Conclusion

Our results showed that preoperative antibiotic therapy provided excellent outcomes that prevented the need for surgical revisions and helped treat vascular graft infection. Following the detection of a graft infection, a treatment strategy should be designed after careful evaluation of the potential benefits to the patient in terms of life expectancy and operative risk. An individualized approach is necessary. Thus far, no well-defined guidelines have been established for managing graft infections. Further large-scale, multicenter trials and meta-analyses are warranted for establishing clear guidelines that enable effective management of graft infection.

Disclosure Statement

All authors declare no conflict of interest.

Author Contributions

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

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