Low Rate of Infection Control in Enterococcal Periprosthetic Joint Infections

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Abstract

Background Enterococcal periprosthetic joint infections (PJIs) are rare after joint arthroplasty. These cases are usually reported in series of PJIs caused by other pathogens. Because few studies have focused only on enterococcal PJIs, management and control of infection of these cases have not yet been well defined.

Questions/Purposes We asked (1) what is the proportion of enterococcal PJI in our institutes; and (2) what is the rate of infection control in these cases?

Methods We respectively identified 22 and 14 joints with monomicrobial and polymicrobial PJI, respectively, caused by enterococcus. The diagnosis of PJI was made based on the presence of sinus tract or two positive intraoperative cultures. PJI was also considered in the presence of one

positive intraoperative culture and abnormal serology. We determined the proportion of enterococcal PJI and management and control of infection in these cases. Minimum followup was 1.5 years (mean, 3.2 years).

Results The proportion of monomicrobial enterococcal PJI was 2.3% (22 of 955 cases of PJI). Mean number of surgeries was two (range, 1–4). Initial irrigation and débridement was performed in 10 joints and eight patients needed reoperation. Seven of the 16 joints were initially managed using two-stage exchange arthroplasty and did not need further operation. Six patients had a definitive resection arthroplasty. Salvage surgeries (fusion and above-knee amputation) were performed in three cases (8%). The infection was ultimately controlled in 32 of the 36 patients.

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Conclusions Management of enterococcal PJI is challenging and multiple operations may need to be performed to control the infection.

Level of Evidence Level IV, therapeutic study. See Guidelines for Authors for a complete description of levels of evidence.

Introduction

Periprosthetic joint infection (PJI) is one of the most challenging complications of joint arthroplasty [17]. PJI with an incidence of 1% to 4% after primary TKA [2, 15, 16] and 1% to 2% after primary THA [10, 11] is one of the main causes of failure after joint arthroplasty [1, 4]. Given the increasing number of primary joint arthroplasties being performed annually, an increasing number of joint arthroplasties complicated by PJI has been reported [5, 7, 19].

Although in patients with PJI the most frequently cultured microorganisms are coagulase-negative Staphylococci and *Staphylococcus aureus*, which are seen in 30% to 43% and 12% to 23% of cases, respectively [21], it is estimated that *Enterococcus* species are responsible for approximately 3% of all PJIs [3]. *Enterococcus* is a Gram-positive, facultatively anaerobic organism, which used to classify as Group D Streptococcus. *Enterococcus* species cause various types of infections, mainly nosocomial infection, endocarditis, urinary tract infection as well as intraabdominal and pelvic infections [8]. Although it is not a common pathogen for orthopaedic infections, there is a growing number of reports showing an increase in frequency of orthopaedic infection caused by *Enterococcus* [14, 18]. Probably as a result of the low frequency of enterococcal PJIs, these cases are usually reported in series of PJIs caused by other pathogens [3]. Two studies [3, 18] focused on the treatment of patients with enterococcal PJI. The first study was performed by El Helou et al. [3] in which 50 episodes of enterococcal PJI were evaluated. They found no difference between outcome of patients with enterococcal PJIs receiving combination therapy and those receiving monotherapy [3]. They also estimated survival free of treatment failure for various surgical approaches in the studied patients at 2 and 5 years [3]. In the second study, management and control of infection in two vancomycin-resistant enterococcal PJIs were reported [18]. Studied patients had a complex course; one needed joint fusion and the other underwent resection arthroplasty. Despite these two studies, frequency, management, and control of infection in patients with enterococcal PJI have not yet been well known.

In the present study, we therefore asked (1) what is the proportion of enterococcal PJI in our institutions; and (2) what is the rate of infection control in these cases?

Patients and Methods

We retrospectively reviewed the electronic infection databases of two institutes to identify patients with a diagnosis of enterococcal PJI. The study covered the time period from 2000 to 2010. PJI diagnosis was considered based on the new definition of PJI provided by the Musculoskeletal Infection Society [13]. Briefly, a diagnosis of PJI was made based on presence of sinus tract or two positive intraoperative cultures. PJI was also considered in the presence of one positive intraoperative culture and abnormal serology including erythrocyte sedimentation rate and C-reactive protein. Usually three to five intraoperative samples are taken in patients with suspicious PJI undergoing surgery in our institutes. During the study period we identified 955 joints with PJI. For this study we included patients who met the definition for PJI and had at least one positive intraoperative culture for any species of *Enterococcus* isolated either from solid medium or broth. Patients with positive culture for methicillin-resistant *S. aureus* (MRSA) were excluded. According to the definition, we identified 36 total joint arthroplasties (19 hips and 17 knees) with a diagnosis of PJI from two institutions. *Enterococcus* had been isolated at least from one culture in all patients. In 22 of the 36 cases, *Enterococcus* was the only isolated microorganism. Vancomycin-resistant *Enterococcus* (VRE) was found in 12 cases (33%) (Table 1).

The cohort consisted of 22 females and mean age of the studied patients at the time of first revision surgery was 66.1 years (range, 34–85 years). The minimum followup was 1.5 years (mean, 3.2 years; range, 1.5–10.5 years). No patients were lost to followup. No patients were recalled specifically for this study; all data were obtained from medical records. Institutional Review Boards of both institutes approved the protocol for this study.

Initial irrigation and débridement was performed in 11 joints, one-stage revision in six joints, and two-stage exchange arthroplasty in 16 joints. Two more joints were scheduled to undergo two-stage exchange arthroplasty; however, at the time of the study, the reimplantation stage was not performed. Definitive resection arthroplasty was performed in one patient as the initial treatment.

In all patients, appropriate intravenous antibiotics were administered based on sensitivity test results for 4 to 6 weeks. Ampicillin, gentamicin, and vancomycin were antibiotics prescribed for non-VRE PJIs. Linezolid and daptomycin were administered for management of cases with VRE. In some patients we did not have details on chronic antibiotic suppression therapy and local antibiotic administration (Table 2).

Patients were followed at 4 to 6 weeks, 6 months, and 1 year. AP and lateral radiographs of the joint were routinely obtained at each followup session. Patients were

Table 1. Comorbidities, preoperative workup, and microbiology results of studied patients

Patient number	Joint	Comorbidities	Positive cultures for Enterococcus (broth) [†]	Preoperative		Synovial fluid WBC count (% neutrophil)	Enterococcus (VRE)	Polymicrobial
				ESR (mm/hr)	CRP (mg/dL)			
1	Hip	Morbid obesity, previous PJI (MRSA)	3 (–)	70	7.3	–	E faecalis (–)	+ (Streptococci)
2	Knee	DM	5 (–)	93	5.8	25,500 (91%)	E faecalis (+)	–
3	Knee	Asthma, anemia	2 (–)	103	7.9	–	E faecalis (–)	+ (Escherichia coli)
4	Hip	RA	3 (–)	37	3.2	–	E faecalis (+)	–
5	Knee	DM, previous PJI	3 (–)	12	32.8	–	E faecalis (+)	–
6	Knee	Gout	2 (–)	68	1.1	–	Both E faecium and E faecalis (+)	–
7	Hip	CAD, hepatitis C, liver transplant	3 (–)	96	7.1	–	E faecalis (–)	+ (coagulase-negative staphylococcus)
8	Knee	–	1 (–)	92	23	–	E faecalis(–)	–
9	Hip	RA, osteoporosis	1 (+)	36	1.6	23,500 (95%)	E faecium (–)	–
10	Hip	Obesity, anemia, asthma, DVT	1 (–)	89	8.1	–	E faecalis (+)	+ (Acinobacter baumannii)
11	Hip	–	2 (–)	78	1.6	–	E faecalis (–)	+ (E coli)
12	Knee	Previous PJI with Staphylococcus aureus	2 (–)	73	5.3	307,500 (92%)	E faecalis (–)	–
13	Hip	–	1 (–)	105	1.6	–	E faecium (+)	–
14	Knee	Asthma, breast cancer, peripheral neuropathy	1 (–)	75	10	89,000 (86%)	E faecalis (–)	–
15	Hip	Asthma, DM, CVA, CHF	3 (+/–*)	105	1.6	–	E faecium (–)	–
16	Knee	Osteoporosis, valvular heart disease	3 (–)	49	1.6	–	E faecalis (–)	–
17	Hip	–	2 (+/–)	37	9.3	–	E faecalis (–)	–
18	Knee	Anemia, atrial fibrillation	2 (–)	82	11.8	2970 (58%)	E faecalis (–)	+ (Enterobacter, Bacteroid fragilis, Pseudomonas aeruginosa)
19	Hip	CHF, atrial fibrillation, postoperative DVT	1 (–)	76	7.8	–	E faecalis (–)	+ (coagulase-negative staphylococcus)
20	Hip	COPD, atrial fibrillation, previous PJI of the same joint	3 (–)	93	7.6	–	E faecium (+)	–
21	Hip	RA	3 (–)	97	9.2	–	E faecalis (–)	–
22	Hip	DM	1 (–)	42	3.2	–	E faecalis (–)	–

Table 1. continued

Patient number	Joint	Comorbidities	Positive cultures for Enterococcus (broth) [†]	Preoperative		Enterococcus (VRE)	Polymicrobial
				ESR (mm/hr)	CRP (mg/dL)		
23	Hip	COPD, atrial fibrillation	2 (–)	60	2.5	E faecalis (–)	–
24	Knee	Previous PJI of the same joint	2 (–)	46	4.2	E faecalis (–)	+ (coagulase-negative Staphylococcus, Corynebacterium species)
25	Hip	–	1 (–)	87	2.8	E faecium (+)	–
26	Knee	–	2 (–)	80	0.8	E faecalis (–)	–
27	Hip	–	5 (–)	26	1.9	E faecium (+)	–
28	Hip	–	5 (–)	48	4	E faecalis (–)	–
29	Hip	Atrial fibrillation, CHF	1 (–)	101	22.5	E faecium (+)	+ (Clostridia)
30	Knee	COPD, anemia, asthma	2 (–)	51	14.3	E faecium (+)	+ (E coli)
31	Knee	RA, DM, asthma	2 (–)	38	9.5	E faecalis (–)	+ (Proteus mirabilis, Bacteroides fragilis)
32	Knee	Asthma, DM, CAD	3 (–)	19	8.7	E faecalis (–)	+ (Candida albicans)
33	Hip	CAD, RA, melanoma	4 (–)	63	5.8	E faecalis (–)	–
34	Knee	RA	1 (–)	12	0.6	E faecalis (–)	+ (coagulase-negative staphylococci)
35	Knee	CHF	1 (–)	65	5.2	E faecalis (–)	+ (Peptostreptococcus magnus)
36	Knee	Gout, ovarian cancer	1 (–)	21	–	E faecium (+)	–

* Microorganism isolated from both one time; [†]all cultures were taken intraoperatively; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; WBC = white blood cell count; VRE = vancomycin-resistant enterococcus; PJI = periprosthetic joint infection; MRSA = methicillin-resistant S aureus; DM = diabetes mellitus; RA = rheumatoid arthritis; CAD = coronary artery disease; DVT = deep venous thrombosis; CVA = cerebrovascular accidents; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; CAD = coronary artery disease.

Table 2. Management, followup, and control of infection in studied patients

Patient number	Initial surgery	Reoperation (number)	Spacer antibiotic	Wound management	Followup (years)	AB for Enterococcus PJI (side effect)	AB suppression	Infection controlled
1	I&D	Polyethylene/head exchange (1)	N/A	I&D, VAC	5.7	Vancomycin	–	Y (disability)
2	Two-stage exchange	Two-stage exchange (1)	Vancomycin, tobramycin	–	6.7	Linezolid	–	Y
3	Two-stage exchange	–	+ (NR)	MF, SG	1.5	Vancomycin	–	Y
4	One-stage exchange	–	N/A	–	1.6	Linezolid	+	Y
5	Resection arthroplasty	Fusion, AKA (2)	N/A	I&D, MF, SG	1.5	Linezolid	–	AKA
6	Two-stage exchange	–	Vancomycin, tobramycin	MF, SG	1.6	Linezolid	+ (Stevens-Johnson syndrome)	Persistent drainage from sinus tract (candidate for salvage surgery)
7	One-stage exchange	–	N/A	–	2.1	Vancomycin	–	Y
8	I&D	Resection arthroplasty (1)	N/A	–	1.5	Vancomycin (Clostridium difficile colitis)	–	Y
9	Two-stage exchange	–	Vancomycin, tobramycin	–	6	Vancomycin	–	Y
10	Two-stage exchange	Resection arthroplasty (1)	Vancomycin, tobramycin	I&D	1.5	Daptomycin	–	Y
11	I&D	–	–	–	1.5	Ampicillin	–	Y
12	Two-stage exchange	–	Tobramycin	–	6.3	Linezolid	–	Y
13 [†]	Two-stage exchange	–	Vancomycin, tobramycin	–	1.5	NR*	–	Y
14	I&D	Two-stage exchange (1)	+(NR)	–	2	Vancomycin	–	Y
15	Two-stage exchange	Resection arthroplasty (1)	Vancomycin, tobramycin	–	1.6	Ampicillin, gentamicin	–	Y
16	Two-stage exchange	–	NR*	–	2	Vancomycin, ampicillin	–	Y
17	I&D	Cup revision (1)	N/A	–	10.5	Vancomycin	–	Y
18	Two-stage exchange	Spacer exchange (1)	Vancomycin, tobramycin	I&D, VAC, MF	2	Ertapenem, Vancomycin	+	Y
19 [‡]	Two-stage exchange	Spacer exchange (1)	NR*	–	4.6	Vancomycin, Linezolid	+	Y

Table 2. continued

Patient number	Initial surgery	Reoperation (number)	Spacer antibiotic	Wound management	Followup (years)	AB for Enterococcus PJI (side effect)	AB suppression	Infection controlled
20	Resection arthroplasty	–	–	–	3.2	Daptomycin	+	Y
21	Two-stage exchange	–	Vancomycin, tobramycin	–	1.5	Vancomycin	–	Y
22	One-stage exchange	–	–	–	7.1	Vancomycin	–	Y
23	One-stage exchange	–	–	–	1.7	Ampicillin, gentamicin	–	Y
24	Two-stage exchange	Spacer exchange, AKA (2)	Vancomycin, tobramycin	I&D, VAC, MF	1.5	Vancomycin	–	AKA
25	I&D	Resection arthroplasty (1)	N/A	Hematoma evacuation	1.5	Linezolid	+	Y
26	Two-stage exchange	–	Vancomycin, tobramycin	–	1.8	Vancomycin, gentamicin	–	Y
27	Two-stage exchange	Spacer exchange (1)	Tigecycline	–	1.5	NR§	–	Y
28	I&D	I&D/cup revision (1)	N/A	–	1.6	Ampicillin, gentamicin	–	Y
29	One-stage exchange	I&D (1)	N/A	–	2.8	Daptomycin, metronidazole	+	Y
30	I&D	Twice pacer exchanges, resection (3)	Vancomycin, tobramycin	Multiple I&D, VAC, SG	2.8	Linezolid	+	Later PJI with coagulase-negative staphylococcus and Proteus
31	Two-stage (spacer exchanged)	Twice I&D, exchange of modular part (3)	+	MF, SG, VAC	2.5	Vancomycin, ertapenem	+	Later PJI with MRSA and Enterobacter
32	Two-stage exchange	I&D/liner exchange (1)	Vancomycin, tobramycin	I&D	6.2	Vancomycin, ampicillin	–	Later PJI with MRSA
33	I&D	–	N/A	–	3.4	Vancomycin	–	Y
34	One-stage exchange	–	N/A	–	6	Vancomycin	–	Later PJI with MRSA resulted in AKA
35	Two-stage exchange	Spacer exchanged (1)	Vancomycin, tobramycin	–	1.9	Vancomycin	–	Y
36	I&D	Two-stage, fusion (2)	Vancomycin, tobramycin	MF	5.2	Linezolid	–	Fusion

* Name of antibiotic not mentioned in patient notes; † the reimplantation was not performed during the study period; AB = antibiotic; PJI = periprosthetic joint infection; I&D = irrigation and débridement; AKA = above-knee amputation; N/A = not applicable; NR = not reported; VAC = vacuum-assisted closure; MF = muscle flap; SG = skin graft; Y = yes; MRSA = methicillin-resistant *Staphylococcus aureus*.

followed up by serology and if necessary aspiration and bone scan performed.

Results

Of 955 joints with PJI, 36 patients had at least one culture with isolated *Enterococcus* spp. In 22 patients, the PJI was monomicrobial. The overall proportion of monomicrobial enterococcal PJI in the studied cohort was 2.3% (22 patients of 955 joints with PJI in both institutions).

The mean number of operations for management of PJI without considering number of operations performed for management of wound problems was 1.6 (range, 1–4). Irrigation and débridement was performed in 11 patients as the initial treatment; however, eight of these 11 patients needed reoperation to control the infection. In the six patients in whom a one-stage revision was the initial treatment, the components were still in place at latest followup but one patient needed later irrigation and débridement. Seven of the 16 patients initially managed using two-stage exchange arthroplasty did not need further surgery to control the infection. Two more patients were scheduled for two-stage exchange arthroplasty in that the second stage (reimplantation) was not performed during the study period. One of these patients needed spacer exchange. Definitive resection arthroplasty was performed as the initial management in one joint because the patient was not considered to be an appropriate candidate for two-stage exchange. Five more patients ultimately needed definitive resection arthroplasty because the initial treatment failed to control the infection. Three patients had salvage surgery after failure of the initial treatment, including one fusion and two above-knee amputations (Table 2). Three patients (8%) had died at the time of latest followup. Mean time from first revision to death was 4.4 years (range, 1.9–6.2 years). In one patient, *Clostridium difficile* colitis developed as a result of antibiotic therapy. One patient developed Stevens-Johnson syndrome resulting from chronic antibiotic suppression therapy.

Discussion

PJI is one of the major causes of failure after joint arthroplasty [17]. Although *S. aureus* and coagulase-negative Staphylococci are traditionally the main pathogens for PJI, there are other microorganisms that can result in PJI. *Enterococcus* species are among the infrequent pathogens that are known to result in orthopaedic infections including PJI. *Enterococcus* is a Gram-positive, facultatively anaerobic organism, which used to be classified as Group D Streptococcus. *Enterococcus* causes

various types of infections, mainly nosocomial infection, endocarditis, urinary tract infection as well as intraabdominal and pelvic infections [8]. As mentioned earlier, there are only two studies that merely focused on management and control of infection in patients with enterococcal PJI [3, 18] and frequency, management, and control of this type of PJI has not yet been well known in these patients. Our experience suggested that patients with enterococcal PJI were challenging to manage and the rate of infection control was lower in patients infected with nonenterococcal infections compared with other infections. This study aimed to determine the proportion of enterococcal PJI and to assess management and control of this type of PJI in two referral institutes.

Before discussing our results, it should be stated that this study has a few limitations. First, we encountered missing data on chronicity of PJIs (acute versus chronic), symptoms of patients at the time of first presentation, and antibiotic suppression therapy. Second, given the complex course of these patients and lack of a universally accepted definition for success of surgical treatment of PJI, we did not perform survival analysis in our cohort. The majority of the patients in this study had multiple surgeries and depending on the definition, survival free of failure was low in our study and much lower than the cohort reported by El Helou et al. [3]. In the majority of patients in our cohort, PJI was ultimately controlled but at the expense of performing a considerable number of resection arthroplasties and salvage surgeries with or without chronic suppression antibiotic therapy that cannot be considered a favorable outcome.

The overall proportion of monomicrobial enterococcal PJIs in our cohort was in agreement with the reported incidence for enterococcal PJIs in the literature, which varies from 2.5% to 3% [3]. To be able to compare the proportion of enterococcal PJI with a previous study [3], we considered only monomicrobial enterococcal PJIs to calculate the proportion of enterococcal PJI in our institutions. However, we included polymicrobial PJIs in the final report on management and control of infection in these patients. We believe excluding patients with polymicrobial infections gives the opportunity for more accurate evaluation of enterococcal PJIs; it results in missing some polymicrobial PJIs in which *Enterococcus* is the major isolated pathogen. Moreover, it seems a considerable number of enterococcal PJIs are indeed polymicrobial PJIs [17].

There are a number of treatment options available for patients with PJI in general that also apply to patients with enterococcal infections. These include a combination of medical (antibiotic therapy) and surgical treatments [12]. Regarding the antibiotic therapy, intravenous ampicillin, gentamicin, or vancomycin is sufficient for non-VRE species [8]. However, medical management of infected cases

with VRE is more challenging and needs to be treated by either linezolid or daptomycin [20]. Irrigation and débridement, one-stage exchange arthroplasty, two-stage exchange arthroplasty, and salvage surgeries (fusion and amputation) are available surgical options for management of PJI. Among these options, two-stage exchange arthroplasty is the preferred method of treatment of patients with chronic PJI in North America [12]. The exact success rate of these interventions is not well known and varies widely depending on what is considered a success. One study from the Mayo Clinic evaluated the outcome of treatment for 50 episodes of enterococcal PJI in 47 patients [3]. Among them, two-stage exchange arthroplasty was performed in 17 (34%) and irrigation and débridement with retention of prosthesis in five patients (10%). There was a relatively large cohort of patients (23 patients [46%]) who underwent resection arthroplasty without reimplantation. One patient in that series required amputation. They estimated 2-year survival free of treatment failure as 94% for patients treated with two-stage exchange arthroplasty, 76% for patients treated with resection arthroplasty, and 80% for patients treated with débridement and retention of the components. In another study, management and control of infection in two PJIs after TKA were reported [18]. The outcome in this small case series was poor because one patient needed resection arthroplasty and the other underwent fusion to control the infection.

There are a number of reasons that may explain the results of our study that is less optimal than a previous report by El Helou et al. [3]. We included patients with polymicrobial PJI, which may have confounded the outcome because some of these patients could have had sinus tract [6] and soft tissue defects, compromising outcome [21]. To minimize the effect of confounders, we excluded all patients in whom MRSA had been isolated at the same time because control of infection in patients with MRSA PJI is so challenging [9]. The other reason for higher failure is that fewer patients in our cohort underwent resection arthroplasty as the initial treatment. Nearly half of the patients in the Mayo Clinic series had resection arthroplasty as their original operation [3]. The latter indicates those investigators had a higher threshold and were more selective in subjecting patients to two-stage exchange arthroplasty. Another explanation for our low rate of infection control may be the high percent of VRE-positive cases (33%) in our series because control of infection in these cases reportedly is so difficult [18]. Finally, the difference in the medical management between our institutions and the Mayo Clinic [3] may have also influenced the outcome.

Surprisingly, the six patients in our series who underwent one-stage exchange all had the prostheses in place at the last followup with infection well controlled. We assume that these patients had acute PJI with a short interval from

development of PJI and performing the surgery, although we do not have accurate data in this regard to confirm our hypothesis.

Our data suggest that although enterococcal PJI is not frequent, management of these patients is challenging. These patients usually require multiple operations to control their infection and a considerable number of cases will ultimately undergo salvage surgery or resection arthroplasty. Performing more studies to determine the incidence of enterococcal PJI and to determine best management and control of infection in these patients is recommended. The current study highlights the shortcomings of the current treatment strategy and the desperate need for future developments.

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