10-1-2012

Low rate of infection control in enterococcal periprosthetic joint infections.

Mohammad R Rasouli

Mohan S Tripathi

Robert Kenyon

Nathan Wetters

Craig J Della Valle

See next page for additional authors

Authors
Mohammad R Rasouli, Mohan S Tripathi, Robert Kenyon, Nathan Wetters, Craig J Della Valle, and Javad Parvizi

Low Rate of Infection Control in Enterococcal Periprosthetic Joint Infections

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 follow-up 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 de´bridement 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.

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% to2% 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, facultativel y 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 de´bridement 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 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 de´bridement 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 de´bridement. 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 twostage 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 oagulasenegative 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 de´bridement, one-stage exchange arthroplasty, two-

168 stage exchange arthroplasty, and salvage surgeries (fusion and amputation) are available surgical
169 options for management of PJI. Among these options, two-stage exchange arthroplasty is the
170 preferred method of treatment of patients with chronic PJI in North America [12]. The exact
171 success rate of these interventions is not well known and varies widely depending on what is
172 considered a success. One study from the Mayo Clinic evaluated the outcome of treatment for 50
173 episodes of enterococcal PJI in 47 patients [3]. Among them, two-stage exchange arthroplasty
174 was performed in 17 (34%) and irrigation and de´bridement with retention of prosthesis in five
175 patients (10%). There was a relatively large cohort of patients (23 patients [46%]) who
176 underwent resection arthroplasty without reimplantation. One patient in that series required
177 amputation. They estimated 2-year survival free of treatment failure as 94% for patients treated
178 with two-stage exchange arthroplasty, 76% for patients treated with resection arthroplasty, and
179 80% for patients treated with de´bridement and retention of the components. In another study,
180 management and control of infection in two PJIs after TKA were reported [18]. The outcome in
181 this small case series was poor because one patient needed resection arthroplasty and the other
182 underwent fusion to control the infection.

183 There are a number of reasons that may explain the results of our study that is less
184 optimal than a previous report by El Helou et al. [3]. We included patients with polymicrobial
185 PJI, which may have confounded the outcome because some of these patients could have had
186 sinus tract [6] and soft tissue defects, compromising outcome [21]. To minimize the effect of
187 confounders, we excluded all patients in whom MRSA had been isolated at the same time
188 because control of infection in patients with MRSA PJI is so challenging [9]. The other reason
189 for higher failure is that fewer patients in our cohort underwent resection arthroplasty as the
190 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.

References

1. Callaghan JJ, O'Rourke MR, Saleh KJ. Why knees fail: lessons learned. *J Arthroplasty*. 2004;19:31–34.
2. Della Valle CJ, Zuckerman JD, Di Cesare PE. Periprosthetic sepsis. *Clin Orthop Relat Res*. 2004;420:26–31.
3. El Helou OC, Berbari EF, Marculescu CE, El Atrouni WI, Razonable RR, Steckelberg JM, Hanssen AD, Osmon DR. Outcome of enterococcal prosthetic joint infection: is combination systemic therapy superior to monotherapy? *Clin Infect Dis*. 2008;47:903–909.
4. Jafari SM, Coyle C, Mortazavi SM, Sharkey PF, Parvizi J. Revision hip arthroplasty: infection is the most common cause of failure. *Clin Orthop Relat Res*. 2010;468:2046–2051.
5. Kurtz SM, Lau E, Schmier J, Ong KL, Zhao K, Parvizi J. Infection burden for hip and knee arthroplasty in the United States. *J Arthroplasty*. 2008;23:984–991.
6. Marculescu CE, Cantey JR. Polymicrobial prosthetic joint infections: risk factors and outcome. *Clin Orthop Relat Res*. 2008;466:1397–1404.
7. Moyad TF, Thornhill T, Estok D. Evaluation and management of the infected total hip and knee. *Orthopedics.* 2008;31:581–588; quiz 589–590.
8. Murray BE. The life and times of the Enterococcus. *Clin Microbiol Rev*. 1990;3:46–65.
9. Parvizi J, Azzam K, Ghanem E, Austin MS, Rothman RH. Periprosthetic infection due to resistant staphylococci: serious problems on the horizon. *Clin Orthop Relat Res*. 2009;467:1732–1739.
10. Parvizi J, Ghanem E, Azzam K, Davis E, Jaberi F, Hozack W. Periprosthetic infection: are current treatment strategies adequate? *Acta Orthop Belg*. 2008;74:793–800.
11. Parvizi J, Jacovides C, Zmistowski B, Jung KA. Definition of periprosthetic joint infection: is there a consensus? *Clin Orthop Relat Res*. 2011;469:3022–3030.
12. Parvizi J, Zmistowski B, Adeli B. Periprosthetic joint infection: treatment options. *Orthopedics.* 2010;33:659.
13. Parvizi J, Zmistowski B, Berbari EF, Bauer TW, Springer BD, Della Valle CJ, Garvin KL, Mont MA, Wongworawat MD, Zalavras CG. New definition for periprosthetic joint infection: from the Workgroup of the Musculoskeletal Infection Society. *Clin Orthop Relat Res*. 2011;469:2992–2994.
14. Pasticci MB, Baldelli F, Malincarne L, Mancini GB, Marroni M, Morosi S, Stagni G. Vancomycin-resistant Enterococcus faecium osteoarthritis following Staphylococcus aureus hip infection. *Orthopedics.* 2005;28:1457–1458.
15. Peersman G, Laskin R, Davis J, Peterson M. Infection in total knee replacement: a retrospective review of 6489 total knee replacements. *Clin Orthop Relat Res*. 2001;392:15–23.
16. Phillips JE, Crane TP, Noy M, Elliott TS, Grimer RJ. The incidence of deep prosthetic infections in a specialist orthopaedic hospital: a 15-year prospective survey. *JBone Joint Surg Br*. 2006;88:943–948.
17. Pulido L, Ghanem E, Joshi A, Purtill JJ, Parvizi J. Periprosthetic joint infection: the incidence, timing, and predisposing factors. *Clin Orthop Relat Res*. 2008;466:1710–1715.
18. Ries MD. Vancomycin-resistant Enterococcus infected total knee arthroplasty. *J Arthroplasty*. 2001;16:802–805.

19. Spangehl MJ, Masri BA, O'Connell JX, Duncan CP. Prospective analysis of preoperative and intraoperative investigations for the diagnosis of infection at the sites of two hundred and two revision total hip arthroplasties. *J Bone Joint Surg Am*. 1999;81:672–683.
20. Twilla JD, Finch CK, Usery JB, Gelfand MS, Hudson JQ, Broyles JE. Vancomycin-resistant Enterococcus bacteremia: an evaluation of treatment with linezolid or daptomycin. *J Hosp Med*. 2012;7:243–248.
21. Zimmerli W, Trampuz A, Ochsner PE. Prosthetic-joint infections. *N Engl J Med*. 2004;351:1645–1654.