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A History of Treated Periprosthetic Joint Infection Increases the Risk of Subsequent Different Site Infection

Hany Bedair MD, Nitin Goyal MD, Mathew J. Dietz MD, Kenneth Urish MD, PhD, Viktor Hansen MD, Jorge Manrique MD, William Hamilton MD, Greg Deirmengian MD

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Abstract

Background After the successful treatment of periprosthetic joint infection (PJI), patients may present with degenerative joint disease in another joint with symptoms severe enough to warrant arthroplasty. However, it is not known whether patients with a history of treated PJI at one site will have an increased risk of PJI in the second arthroplasty site.

Questions/purposes The primary objective of this study is to determine if there is a difference in the risk of developing a PJI after a second total hip arthroplasty (THA) or total knee arthroplasty (TKA) in patients who have had a previous PJI at another anatomic site compared with patients who have had no history of PJI. The secondary objective is to determine other potential risk factors that may predict PJI at the site of the second arthroplasty.

Methods A retrospective matched cohort study was performed to identify all patients at four academic institutions successfully treated for PJI who subsequently underwent a second primary THA or TKA (n = 90), constituting our study group. Patients were matched (one-to-one) to control subjects who had no history of PJI after their first arthroplasty (n = 90); they were matched based on age, sex, diabetic status, BMI, American Society of Anesthesiologists, institution, joint of interest, and year of surgery (± 2 years). We compared the case and control groups to determine whether a prior infection increased the relative risk of a subsequent PJI at another anatomic site. To identify other potential risk factors for subsequent PJI, a subgroup univariate analysis of our study group (n = 90)

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Each author certifies that his or her institution approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.
This work was performed at the Massachusetts General Hospital, Boston, MA, USA; Anderson Orthopaedic Clinic, Alexandria, VA, USA; West Virginia University, Morgantown, WV, USA; and Thomas Jefferson University, Philadelphia, PA, USA.

H. Bedair, V. Hansen
Department of Orthopaedics, Massachusetts General Hospital, Boston, MA, USA

N. Goyal, W. Hamilton
Anderson Orthopaedic Clinic, Alexandria, VA, USA

M. J. Dietz
Department of Orthopaedics, West Virginia University, Morgantown, WV, USA

K. Urish
Department of Orthopaedics, University of Pittsburgh, Pittsburgh, PA, USA

J. Manrique, G. Deirmengian
Department of Orthopaedics, Thomas Jefferson University, Philadelphia, PA, USA

J. Manrique (✉)
The Rothman Institute at Thomas Jefferson University, 125 S 9th Street, Suite 1000, Philadelphia, PA 19107, USA
e-mail: jorgemanriquemd@gmail.com

was performed. To identify other potential risk factors for subsequent PJI, a subgroup univariate analysis of our study group (n = 90) was performed.

Results Patients with a history of PJI had a greater risk of developing PJI in a subsequent THA or TKA (10 of 90 versus zero of 90 in the control group; relative risk, 21.00; 95% confidence interval [CI], 1.25–353.08; p = 0.035). Excluding PJI, we identified no other factors associated with a second joint infection. In patients with a history of PJI, a second PJI occurred more frequently in female patients (female: nine of 10 [90%] versus female: 40 of 80 [50%]; odds ratio [OR], 8.83; 95% CI, 1.13–403.33; p = 0.02) and in those whose initial infection was a staphylococcal species (subsequent PJI seven of 10 [70%] versus no subsequent PJI 28 of 80 [35%]; OR, 4.26; 95% CI, 0.89–27.50; p = 0.04).

Conclusions A history of PJI predisposes patients to subsequent PJI in primary THA or THA. Patients and surgeons must be aware of the higher risk of this devastating complication before proceeding with a second arthroplasty.

Level of Evidence Level III, prognostic study.

Introduction

It is common for patients to have several prosthetic joints, ranging in some studies from approximately 30% to approximately 45% for TKAs [8]. In the setting of multiple joint arthroplasties, the problem of infection may be further magnified, because the morbidity of multiple infected joint replacements can be devastating [1–3, 9, 11]. Murray et al. [6] reported that when a patient presents with periprosthetic joint infection (PJI) at a single site, there is an approximately 15% risk of PJI in a second site of a preexisting prosthetic joint [4]. This risk of PJI in a preexisting site is much greater than the infection risk in primary THA and TKA commonly reported to be approximately 1% [5, 7].

There are patients, however, who have developed and have been treated for PJI at a single site who then undergo a primary THA or TKA at another anatomic site. Although previous reports focused on second-site PJI in preexisting joint arthroplasties, it is unclear what the risk is of PJI at this subsequent second site. Also, it is unclear whether these patients who have subsequent primary joint arthroplasty have a different risk of PJI in the second replaced joint compared with patients with no history of PJI.

The primary objective of this study is to determine whether there is a difference in the risk of PJI after a second THA or TKA in patients who have had a previous PJI at another anatomic site compared with patients who have had no history of PJI. The secondary objective is to determine any potential risk factors that are associated with increased PJI risk at the site of the second arthroplasty.

Patients and Methods

A multicenter, institutional review board-approved, retrospective matched cohort study was performed. All patients at four high-volume academic centers from 1989 to the present time who had a primary THA or TKA that subsequently developed a PJI were identified using the respective institutional databases.

Ninety patients who were treated for PJI and then underwent a second primary THA (n = 35) or TKA (n = 55) at another anatomic site at the same institution were identified. The institutional databases for each site were then queried to identify patients who had a primary THA or TKA that was not complicated by PJI and then underwent a second primary THA or TKA at another anatomic site. These control patients were matched by age at the time of the initial surgery (± 2 years), sex, history of diabetes mellitus, body mass index (BMI; < 30, 30–35, > 35 kg/m^2), American Society of Anesthesiologists (ASA), joints replaced, institution, and year of second arthroplasty surgery (before 2000, 2000–2005, 2005–2010, after 2010) (Table 1). If in the rare occasion that the matching algorithm generated more than one match, one patient was randomly selected from the pool for a one-to-one ratio. Patients with less than 2 years of followup were excluded from both groups. Patients who had a recurrence of PJI in the initial joint at any time were also excluded to avoid reporting on patients with either known failure of PJI or secondary infection in a preexisting joint. Patients' overall medical status as represented by Charlson Comorbidity Index was also collected but not included in the matching algorithm. Continuous variables were reported as mean ± SD and compared using nonpaired t-tests; proportions were reported for categorical variables and compared using Fisher's exact tests (SAS Institute Inc, Cary, NC, USA). Threshold for significance was set at p < 0.05.

In our study population (n = 90) who had prior PJI, we investigated if age, sex, history of diabetes mellitus, BMI, ASA, and/or Charlson Comorbidity Index were risk factors for developing infection at a subsequent arthroplasty site. Details regarding PJI were collected including time from diagnosis of PJI in the initial joint to the time of the second arthroplasty, type of surgical treatment (irrigation and débridement with component retention, single-stage exchange, two-stage exchange, or more than one of these techniques), infecting organism, resistance patterns, and the use of chronic suppressive antibiotics. These variables were also compared between those with and without

Table 1. Demographic and data used in matching algorithm (with the exception of Charlson Comorbidity Index)

Parameter	Study group (n = 90)	Control croup (n = 90)	p value
Age (years) (mean ± SD)	65 ± 12	64 ± 12	0.74
Female sex (%)	49 (54%)	47 (52%)	0.88
Body mass index (kg/m^2) (mean ± SD)	32 ± 7	32 ± 7	0.99
Diabetes (%)	(12/81) 15	(17/90) 19	0.54
American Society of Anesthesiologists			Fisher's exact or chi-square p value
1	1	0	
2	28	31	
3	39	49	
4	0	0	
Charlson Comorbidity Index (mean ± SD)	4 ± 1	4 ± 2	0.57

secondary PJI. Continuous variables were reported as mean ± SD and compared using nonpaired t-tests; proportions were reported for categorical variables and compared using Fisher's exact tests (SAS Institute Inc). Threshold for significance set at $p < 0.05$.

Results

Patients with a history of PJI had a greater risk of developing PJI in a subsequent THA or TKA (10 of 90 versus control zero of 90; relative risk, 21.00; 95% confidence interval [CI], 1.25–353.08; $p = 0.04$). The Charlson Comorbidity Index was not different between the groups (cases 3.59 ± 1.2 versus controls 3.54 ± 1.5, $p = 0.57$).

In patients with a history of PJI, a second PJI occurred more frequently in female patients (female: nine of 10 [90%] versus female: 40 of 80 [50%]; odds ratio [OR], 8.83; 95% CI, 1.13–403.33; $p = 0.02$) and in those whose initial infection was a staphylococcal species (subsequent PJI seven of 10 [70%] versus no subsequent PJI 28 of 80 [35%]; OR, 4.26; 95% CI, 0.89–27.50; $p = 0.04$; Table 2).

Discussion

It is known that a patient who develops a PJI in one joint is at risk for PJI in another, preexisting prosthetic joint. However, the risk of infection in subsequent arthroplasties in other joints after treatment of an earlier PJI is unknown. Therefore, we aimed to determine if subsequent joints are at greater risk compared with those who had an infection-free first joint, and we also aimed to determine other risk factors, if any, that may contribute to any observed differences.

The limitations of this study mainly stem from its relatively small sample size, retrospective nature, and heterogeneity in the accepted treatment practices for PJI, the study's matching algorithm, and patients who may have been lost to followup. Although PJI is a devastating complication, it is fortunately relatively rare. It is even more rare to have a second primary arthroplasty after treatment for PJI as demonstrated by this study in which only 90 patients were identified over a 25-year period at four high-volume arthroplasty centers. These types of rare situations may best be identified and studied through large national registries that might be able to capture a larger sample size. As a result of similar limitations regarding the sample size, study of these rare problems does not lend itself to prospective randomized studies and is best investigated through case-control studies. Despite the inherent limitations of case-control studies including the inability to generate true incidence rates, biases, and inconsistent records, this study design, although not able to establish causations, can establish associations, like in this case.

The heterogeneity in the diagnosis and treatment of PJI is a limitation in most studies concerning this topic. A consistent and accepted criterion for the diagnosis for PJI has only recently become widely adopted, and a consistent treatment and the definition of a "successful" treatment of PJI remain elusive. There may also be an inherent treatment bias whereas patients with a previous PJI may not seek a second arthroplasty despite possibly being clinically indicated. Finally, patients lost to followup may be a weakness of this study. Patients reported in both groups in this study as well as patients who did meet inclusion criteria may have been treated at other institutions and may alter the observed risk of subsequent PJI. It appears that patients who have experienced PJI in one joint are at substantially increased risk of developing PJI in subsequent arthroplasties performed on other joints, even if the

Table 2. Univariate analysis of data collected from patients with a history of PJI after their initial arthroplasty

Factors	No secondary PJI (n = 80/90)	Secondary PJI (n = 10/90)	Mean/percent difference		p value
Age (years) (mean ± SD)	61 ± 11	59 ± 12	2.2		0.623
Female sex (%)	40/80 (50%)	9/10 (90%)	OR = 8.83	(95% CI, 1.13–403.33)	0.02*
Body mass index (kg/m^2) (mean ± SD)	32 ± 7	34 ± 6	1.9		0.402
Diabetes (%)	14%	20%	6%		0.622
American Society of Anesthesiologists					0.093
1	1	0			
2	28	0			
3	32	7			
4	0	0			
Charlson Comorbidity Index (mean ± SD)	4 ± 1	3 ± 1	0.2		0.604
Time from diagnosis of initial PJI to second arthroplasty (months) (mean ± SD)	35 ± 33	22 ± 23	13 months		0.218
Treatment of initial PJI with I&D	19% (n = 15)	20% (n = 2)	1%		0.640 (all treatments compared)
Treatment of initial PJI with single-stage exchange	11% (n = 9)	10% (n = 1)	1		0.640 (all treatments compared)
Treatment of initial PJI with two-stage exchange	56% (n = 45)	70% (n = 7)	14%		0.640 (all treatments compared)
Treatment of initial PJI with more than one technique	14% (n = 11)	0% (n = 0)	14%		0.640 (all treatments compared)
Patients treated with chronic suppressive antibiotics before second arthroplasty	0% (n = 0)	0% (n = 0)	0%		1.00
Initial infecting organism (staphylococcus species)	35% (n = 28)	70% (n = 7)	OR = 4.26	(95% CI, 0.89–27.50)	0.032*
Initial infecting organism (resistant staphylococcus species)	15% (n = 12)	20% (n = 2)	5.0%		0.681
Second PJI infecting organism (staphylococcus species)	N/A	80% (n = 8)	N/A		N/A
Second infecting organism (resistant staphylococcus species)	N/A	10% (n = 1)	N/A		N/A
Initial and subsequent PJI on ipsilateral limb	N/A	0% (n = 0)	N/A		N/A
Date of initial PJI (> year 2000)	898% (n = 71)	100% (n = 10)	11.2%		0.590

* Significant; PJI = periprosthetic joint infection; I&D = irrigation and débridement; OR = odds ratio; CI = confidence interval; N/A = not applicable.

index PJI was treated. Although others have reported on the incidence of PJI in multiple preexisting joints [4, 6], we are unaware of any studies that have specifically investigated the clinical scenario of interest of this study. Direct correlations cannot, therefore, be made to other studies on this topic. In the situation in which more than one existing joint develops PJI, one might assume that a bacteremic state could contribute to multiple joints being seeded in close temporal proximity. By contrast, in this study all of the patients with a history of PJI who underwent a second arthroplasty that became infected were deemed to have been treated successfully for their

previous PJI. None of these patients were being chronically suppressed by antibiotics at the time of the second arthroplasty. The average time from PJI treatment to the second arthroplasty was approximately 33 months, which is beyond the accepted standards in the peer-reviewed literature of the demonstration that infection control beyond 24 months is being regarded as successful. The infecting organisms were the same species in the first and second PJI in 40% (four of 10 cases) and all four of these were staphylococcal species.

These rates are similar to those in patients with failed treatment of PJI in a single joint and certainly raises the concern that perhaps the initial PJI in these patients was not fully treated, there may have existing a chronic, subclinical infection, or that these patients may be otherwise colonized [12]. In addition, certain host factors may play a role in subsequent infections because some patients may have subclinical immune deficiencies that predispose them to PJI, as observed in other types of musculoskeletal infections [3]. The only observed predictors of a second joint PJI in another joint or patients is an initial infection with a staphylococcal species. Although the rate of secondary PJI in this cohort was 11%, it only represents 10 actual cases. This sample size is likely underpowered to detect more predictors of PJI. This does, however, raise the concern that there may exist some underlying predisposition to infection in this cohort that may not be readily detected that may include subclinical immune deficiencies or malnutrition [10].

Patients should be counseled and caregivers should recognize that despite having been adequately treated for PJI in the past, patients are at an extremely high risk of developing PJI after future joint arthroplasties. Future studies incorporating more consistent definitions, treatments, and control of PJI may help to elucidate those factors that place these patients at high risk for subsequent infections.

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