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Original research

Risk of Periprosthetic Joint Infection in Patients With Ipsilateral Infected Arthroplasties

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ABSTRACT

Background: The risk of periprosthetic joint infection (PJI) subsequently developing at a second site after an initial PJI has been documented to be approximately 18%-20%. To the best of our knowledge, only a single study has evaluated the incidence in ipsilateral joints and if the risk of infection would be different. While this was the only other study to evaluate this specific subfield, we set to re-evaluate and confirm the incidence of developing a second PJI in the setting of an ipsilateral prosthesis and possible associated risk factors.

Methods: We retrospectively reviewed all patients treated surgically for lower-extremity PJI at our institution by 5 surgeons from 2015 to 2021. Patients with multiple arthroplasties on the ipsilateral extremity were included. Time between initial and subsequent infection, risk factors for infection, bacterial source, and bacteremia were identified.

Results: Of 392 patients treated for PJI, 179 (45.6%) had multiple prosthetic joints. Forty-seven of those 179 patients had ipsilateral extremity prosthesis, which made up our study population. Three patients (6.4%) developed a separate infection at an ipsilateral TJA. In total, 10 patients (21.3%) developed a separate PJI. Patients on immunosuppressants had a higher likelihood of developing second PJI on the ipsilateral extremity ($P = .02$).

Conclusions: Our study identified the risk of developing an ipsilateral PJI to not be any greater than that in patients with contralateral TJAs. It appears that sharing an extremity with an infected TJA does not pose substantially increased risk of subsequent infection of the un-involved prosthesis. Furthermore, immunosuppressant use may increase the risk of a separate ipsilateral PJI.

Introduction

Periprosthetic joint infections (PJI) is one of the most devastating complications of total joint arthroplasty (TJA). Despite this feared complication, TJA is still considered one of the most successful surgeries in medicine, with yearly procedural volumes of hip and knee arthroplasty volume expected to hit 3.4 million by 2030 [1]. Furthermore, it is estimated that 45% of patients with a joint arthroplasty have >1 joint replaced [2]. The population with multiple joints replaced is likely to rise in the future.

It has been demonstrated that remote infections have been shown to increase the risk of bacterial seeding and PJI [3-5]. It is well known that patients with multiple prosthetic joints can have infections in multiple joints, a so-called synchronous infection. Murray et al. (1991) defined infection moving from one prosthesis to another as metachronous spread [6]. They found the risk of infection in patients with multiple prosthesis to be 18%. Similar work by Luessenhop et al. and Jafari et al. showed a risk of 19% and 20%, respectively [7,8]. In all 3 of these studies, rheumatoid arthritis (RA) was associated with higher infection risk of multiple joints [6-8]. Abblitt et al. (2018) found the risk to be slightly less, with their cohort showing 13% of patients with multiple arthroplasties at risk of a separate site becoming infected [9]. Lastly, Akkaya et al. (2023) looked at patients with hip and knee arthroplasties on the same side who experience a PJI and assessed the factors that contributed to the development of subsequent PJI. The authors

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reported an incidence of up to 20% within the first 2 years postoperatively [10].

All of the aforementioned studies assessed multiple sites of TJA and PJI. Given that patients with multiple arthroplasties on the same extremity share an intramedullary canal, lymphatic flow, and blood flow, they may have an even higher incidence of infection. Therefore, it is important to define this risk. Our study is one of the few to solely evaluate the incidence of infection in patients with multiple TJA on the same extremity and reports on a subject where high numbers are hard to achieve without a more complex, multicenter study or registry [11]. We sought to delineate if having an arthroplasty on an ipsilateral extremity poses an increased or neutral risk of subsequent infection compared to prior studies on the subject. We also sought to evaluate if any identifiable risk factors were associated with developing an ipsilateral PJI.

Material and methods

Institutional review board approval at our institution was obtained for this retrospective study. Institutional total joint database was utilized to identify patients treated for PJI by our 5 fellowship-trained arthroplasty surgeons between 2015 and 2021. International Classification of Diseases codes 9 and 10 were used to identify these patients. Periprosthetic infection was defined using the Musculoskeletal Infection Society criteria. Inclusion criteria were set to include (1) patients treated for PJI from institutional joint database and (2) patients with another ipsilateral extremity arthroplasty at the time of treatment for PJI. Therefore, arthroplasties included hip, knee, and ankle. Patients were excluded if no ipsilateral joint arthroplasty was identified, or the second ipsilateral joint arthroplasty was performed after PJI.

A retrospective chart review was performed on included patients. The medical record, including clinical notes, radiographs, and operative reports, was reviewed. Basic demographic data including age, gender, and body mass index were gathered. Basic information on the joint arthroplasties was collected including anatomic sites of the surgery, laterality, and the date of surgery. Dates of initial and subsequent infections were recorded. Patient factors were also recorded including the comorbidities diabetes, autoimmune disease, end-stage renal disease, and tobacco use.

Data about the PJI were collected including infectious organisms at both the initial and subsequent PJI. Culture-negative infections were also recorded. In addition, bacteremia was documented as noted in the medical record.

During the time interval, 392 patients were treated for PJI. A total of 179 (46%) had another prosthetic joint on the ipsilateral or contralateral extremity. Lastly, a total of 47 of those 179 had ipsilateral joint replacements (26%) which made up our study population. The average age of patients in the cohort was 68 ± 10 years, and 22 (47%) were male (Table 1).

Continuous variables were reported as means and standard deviations, and categorical variables were reported as percentages. Comparisons between categorical variables were carried out using chi-square test or Fisher's exact test, and continuous variables were analyzed using either independent *t*-test or Mann-Whitney test. Significance was set at alpha 0.05.

Results

Ten patients developed a new infection (21%). Three patients (6.4%) had infections at an ipsilateral joint location, 5 patients (10.6%) had infections at a contralateral location, and 2 patients (4.1%) had infections of the same joint with a different bacteria (Fig. 1, Table 1).

Table 1
Population demographics.

Variable	Single joint PJI (n = 37)	Ipsilateral PJI (n = 3)	*P* value
Age	69.9 ± 8.9	64.6 ± 9.2	.443
Male gender	18 (48%)	1 (33.3%)	.609
BMI	31.6 ± 5.5	26.5 ± 3.1	.122
Diabetes	10 (26.3%)	2 (66.7%)	.189
Chronic renal failure	4 (10.5%)	0 (0%)	.548
Tobacco use	5 (13.2%)	0 (0%)	.552
Autoimmune disease	11 (28.9%)	2(66.7%)	.189
Immunosuppressants[a]	5 (13.2%)	2(66.7%)	.02[b]
Bacteremia	7 (18.4%)	1 (33.3%)	.360
Average infection-related surgeries	1.8 ± 1.1	3.3 ± 1.2	.019[b]

BMI, body mass index.
[a] Immunosuppressants include steroid use, disease-modifying anti-rheumatic drugs, and biologics.
[b] Significance, averages, and standard deviations are reported.

The 37 patients who did not develop secondary infections were compared to the 3 patients that developed secondary ipsilateral infections (Table 2). The average body mass index, average age, and gender for the 2 groups were not statistically different. Diabetes, chronic renal failure, tobacco use, and autoimmune disease were no different between the 2 groups. An association was established between the use of immunosuppressant medications (steroids, biologics) and development of a secondary infection at an ipsilateral location ($P = .02$). Lastly, patients with a secondary infection underwent infection-related surgeries with a higher frequency ($P = .019$).

All 3 patients in the ipsilateral group also had at least one contralateral arthroplasty. There were 10 patients in the cohort in total with only 2 arthroplasties, indicating the majority had contralateral and ipsilateral prosthesis. None of the patients with 2 arthroplasties developed a secondary infection.

A breakdown of the 3 patients who did sustain an ipsilateral infection showed the following: patient one—TKA primary infection, THA secondary infection 16 months apart, different bacteria; patient 2—TKA primary infection, THA secondary infection 15 years apart, unknown primary bacteria; patient 3—total ankle primary infection, TKA secondary infection 10 days apart, same bacteria. Interestingly, all primary infections were in the distal extremity first, followed by the proximal.

Discussion

The reported incidence of PJI involving a second joint ranges from 13% to 20% [6-9]. Previous studies have evaluated patients with joints at all locations. Using similar studies previously published as a framework, our goal was to evaluate the risk of

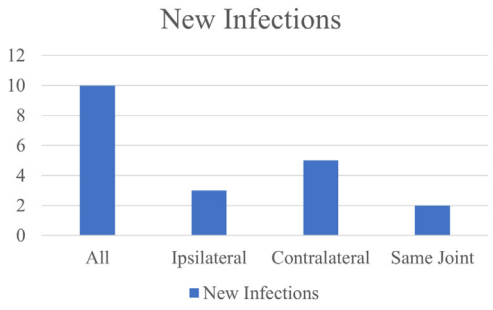

Figure 1. The total amount of patients who developed a new infection was 21.3% (10/47). Three patients (6.4%) had infections at an ipsilateral joint location, 5 patients (10.6%) had infections at a contralateral location, and 2 patients (4.1%) had infections of the same joint with a different bacterium.

Table 2
Comparison of patients that did not develop secondary infections and those who developed secondary ipsilateral infections.

Variable	Single joint PJI (n = 37)	All multiple PJI (n = 10)	All multiple PJI (n = 10)		
			Ipsilateral PJI (n = 3)	Contralateral PJI (n = 5)	Same joint different pathogen (n = 2)
Age	69.9 ± 8.9	62.3 ± 9.3	64.6 ± 9.2	60.5 ± 6.3	63.5 ± 20.6
Male gender	18 (48%)	4 (40%)	1 (33.3%)	3 (60%)	0 (0%)
BMI	31.6 ± 5.5	30.1 ± 6.9	26.5 ± 3.1	30.6 ± 8.8	34.4 ± 5.6
Number of joint replacements					
2 Arthroplasties	10	0	0	0	0
3 Arthroplasties	19	7	2	3	2
4 Arthroplasties	8	3	1	2	0
Second infection location					
Ipsilateral hip	-	-	2	-	2
Ipsilateral knee	-	-	1	-	0
Ipsilateral ankle	-	-	0	-	0
Diabetes	10 (26.3%)	2 (20%)	2 (66.7%)	0 (0%)	0 (0%)
Chronic renal failure	4 (10.5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Tobacco use	5 (13.2%)	2 (20%)	0 (0%)	2 (40%)	0 (0%)
Autoimmune disease	11 (28.9%)	5 (50%)	2(66.7%)	2 (40%)	1 (50%)
Immunosuppressants[a]	5 (13.2%)	3 (30%)	2(66.7%)	0 (0%)	1 (50%)
Bacteremia	7 (18.4%)	0 (0%)	1 (33.3%)	0 (0%)	0 (0%)
Average infection-related surgeries	1.8 ± 1.1	3.6 ± 1.4	3.3 ± 1.2	4.0 ± 1.7	3.0 ± 1.4

[a] Immunosuppressants include steroid use, disease-modifying anti-rheumatic drugs, and biologics.

developing a second PJI in an ipsilateral prosthetic joint. Our study is the first to evaluate this risk in isolation. We identified the risk of an ipsilateral prosthesis becoming infected after a prosthesis on that same extremity had already been infected to be 6.4%. This rate appears to be lower than all-comers in the literature. Furthermore, when adding the patients in our cohort who also suffered a PJI of a contralateral TJA, our numbers compared to previously published data with 21.3% of the entire cohort having another site become infected.

This study has several limitations. First, it is a retrospective review of a database with a small patient population (n = 48). Jafari et al. published in 2012 the risk of PJI on all patients with TJA with similar numbers (55 patients), which communicates to the difficulty in obtaining large numbers for a study of this nature [8]. Second, we attempted to capture all PJIs in patients with multiple ipsilateral TJAs, but patients may have sought care at outside institutions.

Patients with ipsilateral prosthetic joints share an intramedullary canal, blood flow, lymph flow, and encounter trauma when operated on during debridement of an infected prosthesis. Direct seeding of the proximal or distal prosthesis could occur during debridement of the canal and infected arthroplasty site. Bacterial metastasis via lymphatics can often drive systemic infection [12]. It would therefore be a valid hypothesis to believe that infection could be spread to the other prosthesis preoperatively, during the procedure, or during the postoperative course, creating a higher risk to patients with ipsilateral TJA than to patients with contralateral TJA. The results of this study do not seem to suggest this to be the case given that the occurrence was not any higher than all-comers. This study is unique in that it specifically evaluates only patients who have ipsilateral TJAs. All 3 of our patients had at least one contralateral arthroplasty.

Previous studies have evaluated the risk factors in patients with multiple TJAs to develop a PJI in a separate joint. Jafari et al. (2012) demonstrated a trend toward increased risk with increased Charlson Index [8] while Murray et al. (1991) [6] demonstrated no association with host risk factors. Luessenhop et al. (1996) [7] demonstrated an increased risk in patients with RA. Ablitt et al. (2017) [9] showed increased risk in patients with bacteremia at the time of PJI. Komnos et al. (2020) [13] also showed increased risk in patients with RA, female gender, bacteremia at presentation, and infection with Methicillin-resistant Staphylococcus Aureus. Cordtz et al. (2018) [14] showed that patients with RA seem to have an increased 10-year risk of PJI compared to patients with osteoarthritis when undergoing hip or knee arthroplasty. Our data did not show a statistically significant difference with respect to gender, diabetes, RA, or smoking history. We did however see a statistically significant difference in patients who are on immunosuppressant medications showing a higher likelihood of developing ipsilateral PJI. It is possible that this immunocompromised state allows bacteria to seed the subsequent joint via the lymphatic or vascular systems, or perhaps directly through the canal.

Knowing that patients with multiple TJAs are at increased risk of subsequent infection is important. What is equally important to the clinician is how to treat these patients. As published by Komnos et al. (2020) [13], patients with multiple arthroplasties should undergo clinical evaluation of the other prosthetic joints. When broken down into ipsilateral extremity vs contralateral extremity, it does not appear that a higher index of suspicion is warranted for the ipsilateral joint.

Present study is not without limitations inherent to retrospective studies on the topic. Namely, reported sample size may be too small to drive definitive inferences on optimal treatment. However, this work reports on the experience with PJI of 5 high-volume surgeons over a 6-year period. This study suggests several questions for future research. First, a study with higher numbers to confirm these findings would be prudent. Given how PJIs only account for a small proportion of patients with TJAs, it is difficult to obtain studies with large numbers. Second, all 3 of our patients who developed ipsilateral infections did so after the distal extremity was infected first. While the bacteria found at the time of second infection was not always the same, this may represent a biological phenomenon that is occurring, which could be an area for future research.

Conclusions

Evaluation of this patient population demonstrates that the risk of developing a second PJI at a separate site, an extremity that has a previously infected TJA, does not appear to be higher (6.3%) than that at all sites of TJA previously reported in the literature (13%-20%) [6-9]. It also adds to the limited work that has been published in this area recently, and that future, larger-scale studies should be undertaken [11]. Lastly, it appears that patients on

immunosuppressant medications may be at higher risk of developing infection at a separate ipsilateral location.

Conflicts of interest

C.W.G. is a paid consultant for Stryker and Ortho Development Corporation. S.L. receives royalties from, is in the speakers' bureau of, is a paid consultant for, and receives research support from Zimmer Biomet and is a member of the Hillsborough County Medical Society. M.A.M. is in the speakers' bureau of/paid presentations for Corin U.S.A., is a paid consultant for Corin U.S.A., and receives research support from Corin U.S.A., Smith & Nephew, and Stryker. P.S. receives research support from CoreLink, receives financial or material support from Enovis, and is a board member/makes committee appointments for American Shoulder and Elbow Surgeons. G.A.A. and R.W. declare no conflicts.

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CRediT authorship contribution statement

Robert M. Wetzel: Writing – review & editing, Writing – original draft, Methodology, Investigation, Data curation. **Giovanni A. Ayala:** Writing – review & editing, Writing – original draft, Validation, Methodology, Investigation, Data curation. **Christopher W. Grayson:** Writing – review & editing, Writing – original draft, Supervision, Resources, Methodology, Investigation, Conceptualization. **Michael A. Miranda:** Writing – review & editing, Writing – original draft, Resources, Methodology, Investigation, Funding acquisition, Conceptualization. **Peter Simon:** Writing – review & editing, Writing – original draft, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation. **Steven T. Lyons:** Writing – review & editing, Writing – original draft, Validation, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization.

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References

[1] Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. J Bone Joint Surg Am 2007;89:780–5. https://doi.org/10.2106/JBJS.F.00222.

[2] Shao Y, Zhang C, Charron KD, Macdonald SJ, McCalden RW, Bourne RB. The fate of the remaining knee(s) or hip(s) in osteoarthritic patients undergoing a primary TKA or THA. J Arthroplasty 2013;28:1842–5. https://doi.org/10.1016/j.arth.2012/10/008.

[3] Wilson MG, Kelley K, Thornhill TS. Infection as a complication of total knee-replacement arthroplasty. Risk factors and treatment of in sixty-seven cases. J Bone Joint Surg Am 1990;72:878–83.

[4] Jupiter JB, Karchmer AW, Lowell JD, Harris WH. Total hip arthroplasty in the treatment of adult hips with current or quiescent sepsis. J Bone Joint Surg Am 1981;63:194–200.

[5] Fitzgerald R, Nolan D, Ilstrup D, Van Scoy R, Washington J, Coventry M. Deep wound sepsis following total hip arthroplasty. J Bone Joint Surg Am 1977;59:847–55.

[6] Murray RP, Bourne MH, Fitzgerald RH. Metachronous infections in patients who have had more than one total joint arthroplasty. J Bone Joint Surg Am 1991;73:1469–74.

[7] Luessenhop CP, Higgins LD, Brause BD, Ranawat CS. Multiple prosthetic infections after total joint arthroplasty. Risk factor analysis. J Arthroplasty 1996;11:862–8. https://doi.org/10.1016/S0883-5403(96)80189-6.

[8] Jafari SM, Casper DS, Restrepo C, Zmistowski B, Parvizi J, Sharkey PF. Periprosthetic joint infection: are patients with multiple prosthetic joints at risk? J Arthroplasty 2012;27:877–80. https://doi.org/10.1016/j.arth.2012.01.002.

[9] Abblitt WP, Chan EW, Shinar AA. Risk of periprosthetic joint infection in patients with multiple arthroplasties. J Arthroplasty 2018;33:840–3. https://doi.org/10.1016/j.arth.2017.10.024.

[10] Akkaya M, Vles G, Sangaletti R, Zanna L, Gehrke T, Citak M. What is the safe distance between hip and knee implants to reduce the risk of ipsilateral metachronous periprosthetic joint infection? Clin Orthop Relat Res 2023;481:1597–606. https://doi.org/10.1097/CORR.0000000000002598.

[11] Kurmis AP. CORR Insights®: what is the safe distance between hip and knee implants to reduce the risk of ipsilateral metachronous periprosthetic joint infection? Clin Orthop Relat Res 2023;481:1607–9. https://doi.org/10.1097/CORR.0000000000002617.

[12] Siggins MK, Sriskandan S. Bacterial lymphatic metastasis in infection and immunity. Cells 2021;11:33. https://doi.org/10.3390/cells11010033.

[13] Komnos GA, Manrique J, Goswami K, Tan TL, Restrepo C, Sherman MB, et al. Periprosthetic joint infection in patients who have multiple prostheses in place: what should be done with the silent prosthetic joints. J Bone Joint Surg Am 2020;102:1160–8. https://doi.org/10.2106/JBJS.18.01500.

[14] Cordtz RL, Zobbe K, Højgaard P, Kristensen LE, Overgaard S, Odgaard A, et al. Predictors of revision, prosthetic joint infection and mortality following total hip or total knee arthroplasty in patients with rheumatoid arthritis: a nationwide cohort study using Danish healthcare registers. Ann Rheum Dis 2018;77:281–8. https://doi.org/10.1136/annrheumdis-2017-212339.