Factors Associated with Choice and Success of One- Versus Two-Stage Revision Arthroplasty for Infected Hip and Knee Prostheses

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Abstract *Background:* Prosthetic joint infections (PJI) of hip and knee arthroplasties are becoming increasingly common with an aging population and an increasing demand for these procedures. Despite attempts at standardization, medical and surgical approaches vary widely among practitioners. *Questions/Purposes:* We first sought to determine if there were specific factors associated with choice of one- versus two-stage revision. Then we investigated whether the type of revision approach influenced clinical treatment success. Finally, among two-stage revisions, we assessed if an antibiotic holiday prior to the second procedure affected clinical treatment success. *Methods:* We retrospectively reviewed patients who had revision surgery for infection of a hip or knee arthroplasty between January 1, 2000, and December 31, 2013, at the Sunnybrook Health Sciences Centre and the Holland Orthopedic and Arthritic Centre.

Level of Evidence: Level 3

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PJI cases were identified using the Ontario Joint Replacement Registry. Infection was defined by gross intraoperative evidence of infection, positive intraoperative culture(s), and/or sinus tract prior to operation. The primary outcome was treatment failure at 1 year after revision surgery based on requirement for further surgery, ongoing infection, and/or continuous suppressive antibiotics. *Results:* Of 110 eligible patients identified, 35 patients had a one-stage and 75 patients had a two-stage revision. Choice of a one-stage approach was most influenced by particular surgeon preference and was more likely for hip revision versus knee revision (OR 3.39 (95%CI 1.85–6.23). There was no statistical difference in clinical treatment success rate between one-stage (33/35; 94.2% success) and two-stage revision (63/75; 84%; $p = 0.13$). *Enterococcus* spp. (21 versus 3%; $p = 0.027$) and *Peptostreptococcus* spp. (14 versus 1%; $p = 0.042$) were more common among clinical treatment failures than successes, with a trend towards the same for *Staphylococcus aureus* (29 versus 9%; $p = 0.06$). Additionally, treatment success was not influenced by whether the patient had an antibiotic holiday with a two-stage revision. *Conclusion:* Our findings confirm the uncertainty of surgical strategy for treatment of PJI in hip and knee arthroplasty. Superiority of one- versus two-stage revision and the value of antibiotic-free periods prior to definitive revision remain unclear. Large prospective studies or randomized controlled trials are needed to inform best practice for treatment of these complex clinical problems.

Keywords prosthetic joint infection · one-stage revision · two-stage revision · antibiotic holiday

Introduction

Prosthetic joint infection (PJI) has been a recognized complication of joint replacement since these procedures were developed over 100 years ago. Despite the rates of infection diminishing over time due to improvement in preventative practices, the absolute numbers of prosthetic joint infections are climbing owing to an increased number of replacement surgeries [3]. PJIs cause substantial morbidity for patients and avoidable costs for health-care systems.

Management of PJI consists of a combination of surgical intervention and antimicrobial therapy. Attempts to standardize these practices have been published in the form of treatment guidelines, yet the approach still varies between different practitioners and locations [14–16]. This is in part owing to a paucity of strong evidence to support specific guidelines [14, 16].

Approaches to surgical revision vary geographically whereby North American surgeons tend towards a staged (commonly referred to as two-stage) revision while European surgeons more frequently consider a one-stage approach [16, 17]. However, it is not clear what patient and pathogen characteristics are actually considered in choosing a one- versus two-stage procedure in real-world practice.

Similarly, there is inadequate evidence to guide antibiotic approaches to PJI management. In particular among patients undergoing staged revisions, it is not clear whether an antibiotic-free period is helpful prior to the second stage surgery [1, 13].

Practice varies at our institution with some surgeons choosing one-stage revision strategies and others more often proceeding with a two-stage approach. In our retrospective cohort, we first sought to determine if there were specific factors associated with choice of one- versus two-stage revision. Then we investigated whether the type of revision approach influenced clinical treatment success. Finally, among two-stage revisions, we assessed if an antibiotic holiday prior to the second procedure affected clinical treatment success.

Patients and Methods

We conducted a retrospective cohort study of patients from the Holland Orthopedic and Arthritic Centre and Sunnybrook Health Sciences Centre who underwent revision of a hip or knee arthroplasty for prosthetic joint infection between January 1, 2000, and December 31, 2013. Patients were identified from the Ontario Joint Replacement Record registry. We included any patient undergoing a revision surgery for the diagnosis of prosthetic joint infection.

Prosthetic joint infection was defined as having any of gross intraoperative findings of infection, positive intraoperative culture(s), or sinus tract prior to operation. Patients were excluded if they did not have PJI based on the above criteria or if they already had septic arthritis prior to their original joint arthroplasty. Patients who had debridement and implant retention plus or minus liner exchange were also excluded from this analysis. Patients were followed for at least 1 year after surgery.

The primary outcome was treatment failure at 1 year after revision surgery. Treatment failure was defined as requirement

for further revision surgery, ongoing treatment with antibiotics and/or ongoing signs of infection including persistent wound drainage, sinus tract, or systemic symptoms.

A two-stage or staged revision refers to the surgical approach involving an index procedure that includes irrigation and thorough debridement of the infected joint along with removal of the prosthesis and placement of a spacer or temporary arthroplasty; this is followed later by a second procedure for placement of the new prosthetic joint. The one-stage revisions involved an extensive irrigation and debridement with removal of components. This was immediately followed by re-implantation of new definitive components with a new set of sterile instruments under the same anesthetic.

Antibiotic holiday or antibiotic-free period refers to a period of time without antibiotics for at least 2 weeks prior to the second procedure of a two-stage revision.

A chart review was performed using paper and electronic charts. Data including patient demographic information (age, gender), prior joint surgeries and reason for initial replacement, joint location, timing from first joint replacement to PJI, surgeon, and comorbidities including American Society of Anesthesiology Physical Status Classification System (ASA) score, diabetes, hypertension, chronic kidney disease (CKD), rheumatoid arthritis, corticosteroid use, immunosuppression, smoking, coronary artery disease, cancer, osteoporosis, asthma, COPD, obstructive sleep apnea, hypothyroidism, and BMI were recorded. (Table 1) We also reviewed microbiological data including whether culture was obtained, culture positivity, and specific organism(s) identified (Table 2).

Univariate analysis was used to assess differences in patient and pathogen characteristics among patients undergoing one- versus two-stage revisions, with Fischer's exact test for categorical variables and Mann-Whitney *U* test for continuous variables. Similar testing was performed to assess the association of patient and pathogen characteristics and the choice of surgical approach, with clinical treatment success/failure. Additionally, among patients who underwent a two-stage revision, the chi-square test was performed to test for an association between use of an antibiotic holiday and clinical success/failure. Multivariable logistic regression was performed to assess the patient and pathogen characteristics associated with one- versus two-stage procedure selection with inclusion of all variables with $p < 0.2$ on univariate testing, followed by backward stepwise selection for variable reduction until only variables with $p < 0.05$ were retained. Generalized estimating equations were utilized to account for clustering within surgeons. A similar modelling approach was then performed to test the association of one- versus two-stage surgery selection with the outcome of clinical treatment success/failure, after adjusting for other patient and pathogen characteristics. All analyses were performed in the Microsoft excel or SAS version 9.3 (Cary, NC).

Results

Among 154 patients identified in the joint replacement database, 139 were noted to have a prosthetic joint infection undergoing revision arthroplasty, whereas 15 were

Table 1 Demographic comparison of patients undergoing one- versus two-stage revision

Demographic characteristics	Demographics comparison of patients treated with one- vs. two-stage procedure		
	One stage, <i>n</i> = 35 (%)	Two stage, <i>n</i> = 75 (%)	<i>p</i> value
Age (at initial OR)	68 (IQR 61–79)	63 (IQR 57–74)	0.089
Gender			
Female	19 (54; CI 38–70)	43 (57; CI 46–68)	0.838
Male	16 (46; CI 30–61)	32 (43; CI 32–54)	
Comorbidities			
ASA			0.328
P1	6 (17; CI 8–33)	9 (12; CI 6–21)	
P2	23 (66; CI 49–79)	59 (79; CI 68–86)	
P3	6 (17; CI 8–33)	7 (9; CI 5–18)	
P4	0	0	
Diabetes	6 (17; CI 8–33)	14 (19; CI 11–29)	1.00
Hypertension	19 (54; CI 38–70)	18 (24; CI 16–35)	<i>0.003</i>
Chronic kidney disease (Cr > 90)	4 (11; CI 5–26)	1 (1; CI 0–7)	<i>0.035</i>
Rheumatoid arthritis	4 (11; CI 5–26)	5 (7; CI 3–15)	0.462
Corticosteroid	0 (0)	1 (1; CI 0–7)	1.00
Immunosuppressant	1 (3; CI 1–15)	4 (5; CI 2–13)	1.00
Smoking	1 (3; CI 1–15)	13 (17; CI 10–27)	<i>0.035</i>
Coronary artery disease	13 (37; CI 23–54)	15 (20; CI 13–30)	0.064
Cancer	3 (9; CI 3–22)	4 (5; CI 2–13)	0.677
Osteoporosis	2 (6; CI 2–19)	1 (1; CI 0–7)	0.237
Asthma	1 (3; CI 1–15)	11 (15; CI 8–24)	0.099
COPD	0 (0)	7 (9; CI 5–18)	0.095
Obstructive sleep apnea	0 (0)	3 (4; CI 1–11)	0.550
Hypothyroid	2 (6; CI 2–19)	8 (11; CI 6–20)	0.498
BMI	24 (IQR 24–24)	24 (IQR 24–30)	<i>0.006</i>
Prosthesis			
Primary	26 (74; CI 58–86)	53 (71; CI 60–80)	0.821
Revision	9 (26; CI 14–42)	22 (29; CI 20–40)	
Joint location			
Knee	14 (40; CI 26–56)	52 (69; CI 58–79)	<i>0.006</i>
Hip	21 (60; CI 44–74)	23 (31; CI 21–42)	
Time from 1st joint replacement			
<12 weeks	3 (9; CI 3–22)	2 (3; CI 0–9)	0.324
12 weeks–1 year	3 (9; CI 3–22)	16 (21; CI 14–28)	0.113
>1 year	29 (83; CI 67–92)	57 (76; CI 65–84)	0.468

p value results in italic represent variables that are $p < 0.05$

excluded because of septic arthritis prior to initial joint replacement ($n = 5$), duplicate chart ($n = 5$), patient did not have PJI ($n = 4$), or had native joint septic arthritis ($n = 1$). An additional 29 patients underwent incision and

Table 2 Microbiological data from initial one- versus two-stage revision procedure for PJI

	Microbiological data from initial surgery		
	One stage, <i>n</i> = 35 (%)	Two stage, <i>n</i> = 75 (%)	<i>p</i> value
Total cultures done	33 (94; CI 8–98)	73 (97; CI 91–99)	0.591
Avg number of cultures	3 (IQR 1.75–6.25)	5 (IQR 3–6)	<i>0.011</i>
Cultures positive	16 (46; CI 30–62)	47 (63; CI 51–73)	0.103
Monomicrobial	13 (37; CI 23–54)	31 (41; CI 31–53)	0.350
Polymicrobial	3 (9; CI 3–22)	16 (21; CI 15–32)	
CNST	11 (31; CI 19–48)	32 (43; CI 32–54)	0.299
<i>Staphylococcus aureus</i>	4 (11; CI 5–26)	9 (12; CI 6–21)	1.00
<i>Staphylococcus lugdenensis</i>	0 (0)	5 (7; CI 3–15)	0.176
Beta hemolytic streptococci	1 (3; CI 1–15)	3 (4; CI 1–11)	1.00
Other <i>Streptococcus</i> spp.	1 (3; CI 1–15)	3 (4; CI 1–11)	1.00
<i>Enterococcus</i> spp.	1 (3; CI 1–15)	5 (7; CI 3–15)	0.662
Gram-negative bacilli	1 (3; CI 1–15)	4 (5; CI 2–13)	1.00
<i>Peptostreptococcus</i> spp.	0 (0)	3 (4; CI 1–11)	0.550
<i>Bacteroides fragilis</i>	0 (0)	1 (1; CI 0–7)	1.00
<i>Candida albicans</i>	0 (0)	1 (1; CI 0–7)	1.00

p value results in italic represent variables that are $p < 0.05$

Fig. 1. Proportion of procedures in percentage done as one-stage revision by surgeon. The *diamond* represents the percentage and the *corresponding line* represents the confidence interval of 95%.

drainage plus or minus liner exchange and were thus excluded from further analyses, leaving 110 patients who underwent one- or two-stage revision arthroplasty. Among the 110 patients included, 35 patients (32%)

Table 3 Comparison of patients with clinical treatment success versus failure after revision for PJI

Demographic characteristics	Comparison of patients with successful and unsuccessful PJI treatment		
	Success, <i>n</i> = 96 (%)	Failure, <i>n</i> = 14 (%)	<i>p</i> value
Age (at initial OR)	66 (IQR 58–75)	64 (IQR 52–73)	0.772
Gender			
Female	56 (58; CI 48–68)	6 (42; CI 21–67)	0.388
Male	40 (42; CI 32–52)	8 (57; CI 33–79)	
Comorbidities			
ASA			
P1	13 (14; CI 8–22)	2 (14; CI 4–40)	1.00
P2	71 (74; CI 64–81)	11 (79; CI 52–92)	1.00
P3	12 (13; CI 7–21)	1 (7; CI 1–31)	1.00
P4	0 (0; CI 0–4)	0 (0; CI 0–22)	
Diabetes	16 (17; CI 11–25)	4 (29; CI 12–55)	0.280
Hypertension	49 (51; CI 41–61)	8 (57; CI 33–79)	0.778
Chronic kidney disease (Cr > 90)	5 (5; CI 2–12)	0 (0; CI 0–22)	1.00
Rheumatoid arthritis	7 (7; CI 4–14)	2 (14; CI 4–40)	0.321
Corticosteroid	0 (0; CI 0–4)	1 (7; CI 1–31)	0.127
Immunosuppressant	4 (4; CI 1–10)	1 (7; CI 1–31)	0.501
Smoking	11 (11; CI 7–19)	3 (21; CI 7–48)	0.383
Coronary artery disease	26 (27; CI 19–37)	2 (14; CI 4–40)	0.512
Cancer	7 (7; CI 4–14)	0 (0; CI 0–22)	0.592
Osteoporosis	3 (3; CI 1–9)	0 (0; CI 0–22)	1.00
Asthma	9 (9; CI 5–17)	3 (21; CI 7–48)	0.180
COPD	5 (5; CI 2–12)	2 (14; CI 4–40)	0.218
Obstructive sleep apnea	1 (1; CI 0–6)	2 (14; CI 4–40)	0.042
Hypothyroid	8 (8; CI 4–16)	2 (14; CI 4–40)	0.613
BMI	24 (IQR 24–28)	24 (IQR 24–26)	0.426
Prosthesis			
Primary	70 (73; CI 63–81)	9 (64; CI 39–84)	0.532
Revision	26 (27; CI 18–37)	5 (36; CI 16–61)	
Joint location			
Knee	56 (58; CI 48–68)	10 (71; CI 45–88)	0.398
Hip	40 (42; CI 32–52)	4 (29; CI 12–55)	
Reason for initial surgery			
Osteoarthritis	66 (69; CI 59–77)	11 (79; CI 52–92)	0.547
Post-traumatic arthritis	6 (6; CI 3–13)	0 (0; CI 0–22)	1.00
Acute fracture	4 (4; CI 2–10)	1 (7; CI 1–31)	0.501
Rheumatoid arthritis	7 (7; CI 4–14)	2 (14; CI 4–40)	0.321
Inflammatory arthritis	2 (2; CI 1–7)	0 (0; CI 0–22)	1.00
Other	4 (4; CI 2–10)	0 (0; CI 0–22)	1.00
Unknown	7 (7; CI 2–10)	0 (0; CI 0–22)	0.592
Time from 1st joint replacement to PJI surgery			
<12 weeks	3 (3; CI 1–9)	2 (14; CI 4–40)	0.121
12 weeks–1 year	17 (18; CI 11–27)	2 (14; CI 4–40)	1.00
>1 year	76 (79; CI 70–86)	10 (71; CI 45–88)	0.501

had a one-stage while 75 patients (68%) had a two-stage procedure.

Surgeon preference and hip joint were the main factors associated with patients undergoing a one- rather than two-stage revision. The baseline characteristics between those undergoing one- and two-stage procedures were similar in terms of age, gender, and time since previous surgery (Table 1). Patients who underwent single stage revision were more likely to have hypertension or chronic kidney disease, and less likely to smoke or have asthma (Table 1). A single-stage revision was more often chosen for hip (47%) than knee (21%) procedures ($p = 0.006$). Of the nine surgeons who performed the procedures, six surgeons performed single-stage revisions at a rate between 20 and 30%. There were three outlier surgeons; one performing over 60% one-stage revisions and 2 performing less than 10% one-stage revisions (Fig. 1). The most commonly cultured organism was coagulase negative staphylococci in both one-stage (31%; CI 19–48) and two-stage (43%; CI 32–54) surgical patients. There was no significant difference in the causative organisms identified between one- and two-stage revisions (Table 2). After multi-variable analysis, only chronic kidney disease (OR 10.48; 95%CI 2.7–40.6), hip joint (OR 3.39; 95%CI 1.85–6.23) and negative culture (OR 2.23; 95%CI 1.27–3.93) were predictive of a patient undergoing a one-stage procedure.

There was no difference in clinical treatment success or failure between one- and two-stage procedures. Among the surgical patients, there were 96 treatment successes (87%) and 14 failures (13%). Among patients with clinical success and failure, there was no difference in age, sex, joint, and history of previous joint revision (Table 3). Of patient comorbidities, obstructive sleep apnea was more common among those with clinical treatment failure (Table 3). With respect to microbiologic etiology, *Enterococcus* spp. (21 versus 3%; $p = 0.027$) and *Peptostreptococcus* spp. (14 versus 1%; $p = 0.042$) were more common among those with clinical treatment failure (Table 4). There was a trend towards clinical treatment failure associated with *Staphylococcus aureus* (29 versus 9%; $p = 0.06$). Multivariable analysis again revealed only

obstructive sleep apnea (OR 15.37; 95%CI 1.43–164.99) as a significant predictor of clinical treatment failure. The choice of one-stage revision (OR 0.58; 95%CI 0.02–1.99) was not associated with clinical treatment success or failure (Table 5).

There was no difference in the primary outcome of treatment failure among those receiving an antibiotic-free period and those not receiving an antibiotic-free period. Of the 75 patients who had a two-stage revision, 19 (25%) patients had an antibiotic-free period prior to the second procedure and their treatment failure rate was not significantly different from patients that did not receive an antibiotic-free period (Table 6).

Discussion

Our retrospective review of patients with revision for hip/knee PJI adds to the growing literature supporting similar outcomes regardless of one- versus two-stage treatment approach. Of the 110 patients in our analysis, the predictors for having a one-stage versus a two-stage revision included the hip joint versus knee joint, negative culture, and chronic kidney disease. This difference was associated with surgeon-specific preferences. Our primary outcome was clinical treatment success at 1 year. Our data revealed obstructive sleep apnea as the only statistically significant predictor of failure. The biologic rationale for this is unclear and a spurious result due to low patient numbers is possible. Interestingly, no statistical difference in clinical success was detected between choice of surgical approach (one versus two stage). Additionally, an antibiotic holiday among the patients who underwent a two-stage revision was not associated with clinical success rates.

There are a number of limitations inherent in our retrospective cohort study design. We may have been over-inclusive in our inclusion criteria by not using the Musculoskeletal Infection Society (MSIS) criteria. This is partially balanced because all patients were assessed by an orthopedic surgeon and had an operation for PJI. Also, we could not account for unmeasured variability in specific surgical techniques and devices among cases. Specifically, we did not

Table 4 Microbiological data from initial revision procedure for PJI for patients with clinical treatment success versus failure

	Microbiological data—initial surgery		
	Success, $n = 96$ (%)	Failure, $n = 14$ (%)	p value
Total cultures done	92 (96; CI 90–98)	14 (100; CI 78–100)	1.00
Cultures positive	52 (54; CI 44–64)	11 (79; CI 52–92)	0.146
Monomicrobial	37 (39; CI 29–49)	7 (50; CI 27–73)	0.561
Polymicrobial	15 (16; CI 10–24)	4 (29; CI 12–55)	0.258
CNST	38 (40; CI 30–50)	5 (36; CI 16–61)	1.00
<i>Staphylococcus aureus</i>	9 (9; CI 5–17)	4 (29; CI 12–55)	0.06
<i>Staphylococcus lugdenensis</i>	5 (5; CI 2–12)	0 (0)	1.00
Beta hemolytic <i>Streptococcus</i>	4 (4; CI 2–10)	0 (0)	1.00
Other <i>Streptococcus</i> spp.	3 (3; CI 1–9)	1 (7; CI 1–31)	0.425
<i>Enterococcus</i> spp.	3 (3; CI 1–9)	3 (21; CI 8–48)	0.027
Gram-negative bacilli	3 (3; CI 1–9)	2 (14; CI 4–40)	0.121
<i>Peptostreptococcus</i>	1 (1; CI 0–6)	2 (14; CI 4–40)	0.042
<i>Bacteroides fragilis</i>	0 (0)	1 (7; CI 1–31)	0.127
<i>Candida albicans</i>	0 (0)	1 (7; CI 1–31)	0.127

p value results in italic represent variables that are $p < 0.05$

Table 5 Clinical treatment success versus failure for one- versus two-stage revision

	1-year outcome post revision		<i>p</i> value
	Success, <i>n</i> = 96 (%)	Failure, <i>n</i> = 14 (%)	
One-stage revision	33 (94, CI 81–98)	2 (6, CI 2–19)	0.132
Two-stage revision	63 (84, CI 74–91)	12 (16, CI 9–26)	

account for differences in one-stage technique between different surgeons. Additionally, in a non-randomized study, there will always be bias-by-indication, in that surgeons likely select a procedural approach based on complex characteristics that might not be completely captured by our covariates. For example, a one-stage revision may be reserved for those patient scenarios that are more likely to result in a successful outcome. Other unmeasured surgical factors that may contribute to both procedure selection and patient outcome would include the quality of patient bone stock and soft tissue. Also, our antimicrobial description did not include complete treatment details including preoperative antibiotic use when patients were transferred from other hospitals. Additionally, our study follow-up was shorter at 1 year rather than two as used in some other studies [4, 11]. Finally, even though our study involved a large orthopedic centre over an extended patient accrual period, the data were underpowered to exclude potentially important differences in outcomes among the PJI treatment strategies.

According to guidelines, the decision to consider a one-versus two-stage procedure may be guided by certain clinical variables, such as hip versus knee joint involvement, chronicity of symptoms, presence of a sinus tract or unstable prosthesis, and type of pathogen [14, 15]. In our study, there were both expected and unexpected findings. The hip joint being more common than knee joint for one-stage revision was expected given its endorsement in guidelines and a recent systematic review [8, 14].

A consistent guideline-recommended requirement for choosing a one- over two-stage is that the organism is identifiable and treatable with oral antibiotics [14]. Thus, it would have been expected that a negative culture would have been more common among two-stage revision patients. In our cohort, this was in fact the opposite. One reason could be that the decision to perform a one-stage procedure was pre-determined prior to the surgery based on other clinical factors. Additionally, negative cultures often reflect the use of preoperative antibiotics, which patients could have received prior to presentation without our knowledge given the referral nature of our tertiary hospital.

It has been proposed that a one-stage procedure should be considered for patients who would be poor candidates for multiple surgeries as required for a two-stage approach [4, 17]. However, in our study population, most comorbidities and overall comorbidity burden (as reflected by the ASA score) were not associated with selection of surgical strategy.

One of the main findings in our study was the variability in performing one-stage (32%) versus two-stage revision (68%) among surgeons. Specifically, our cohort included one surgeon who was much more likely to perform a single-stage revision (67%) over a staged approach. Comparatively, two surgeons were more likely to choose two-stage strategies (10% or less). This suggests that choice of surgical strategy may depend on an individual surgeon's experience and interpretation of the literature.

Despite the variability in practice in our cohort, there appeared to be no difference in clinical treatment success or failure based on the specific surgeon. In fact, this held true regardless of what surgical approach was chosen. The majority of the literature focuses on a two-stage approach and suggests its superiority, especially in those with knee PJI [4, 11, 17]. However, as with the hip PJIs, a more recent systematic review showed no difference in treatment outcome for knee PJI regardless of single or staged revision [9]. This is based on cumulative evidence from small non-randomized studies and no robust comparative studies. Our retrospective cohort shows a non-statistically significant ($p = 0.13$) advantage for one-stage revision (94 vs. 84% success) and supports the claim that there may not be a substantial difference in clinical treatment success between one- and two-stage revisions. In fact, adopting a standardized one-stage approach has been shown to be 100% effective in one institution [5, 6]. The ability to avoid a second surgery and a prolonged functional deficit from a temporary prosthesis are attractive advantages for a one-stage approach. However, robust evidence is still lacking to recommend one approach over the other.

Table 6 Clinical treatment success versus failure for patients depending on whether they had an antibiotic-free period or not

	Antibiotic-free period		<i>p</i> value
	Success, <i>n</i> = 63 (%)	Failure, <i>n</i> = 12 (%)	
Holiday >0 day	47 (75; CI 63–84)	9 (75; CI 47–91)	1.000
No holiday	16 (25; CI 16–37)	3 (25; CI 9–53)	

In regard to microbiological data, we did find that *Enterococcus* spp. and *Peptostreptococcus* spp. were associated with treatment failure, which is similar to prior studies [12]. Unlike previous studies, we did not detect a statistically significantly higher rate of treatment failure with *S. aureus* [10].

There is debate as to the best approach to antimicrobial treatment after a two-stage revision procedure. One approach is to stop antibiotics after a defined time and observe for recurrence of infection prior to the second stage. The reason for stopping antibiotics is that recurrence of infection is anticipated to manifest, prompting another debridement procedure. Some clinicians choose to perform an arthrocentesis prior to the second stage to increase certainty that the infection has been cured [13]. Among one group of patients undergoing a two-stage revision, those patients who had re-aspiration prior to the second step had no subsequent clinical failure [13]. Another rationale for this approach is the presumption that source control has been achieved with the first stage. In fact one group showed good treatment success after only 2 weeks of post-first stage antibiotics [7].

The alternative approach is to treat with antibiotics up to the subsequent procedure. This was supported by a study of patients undergoing two-stage revision that showed no difference in re-implantation culture positivity or outcome regardless of whether an antibiotic-free period was instituted [2]. Also, in that study, the majority of re-revisions were required prior to the antibiotic-free period [2]. In fact, since the pathogenesis of PJI is thought to involve the formation of a biofilm and is thus usually paucibacillary, an antibiotic-free period and/or re-aspiration may not be sufficient to rule out persistent infection prior to the second stage, whereas ongoing antibiotics may potentially maximize suppression of organisms in the biofilm and thereby aid eradication at the time of the second stage procedure [2]. This may also make more sense in the context of the modern practice of placing an articulating temporary prosthesis in the joint, rather than a cement spacer, for the period between the first and second step. Our study did not detect a difference in clinical treatment success/failure with or without an antibiotic-free period, suggesting that either approach is reasonable until a larger prospective study can address this question.

This retrospective cohort reviewing patients from our program revealed some important details regarding practice surrounding PJI. The decision to perform one- versus two-stage revision was influenced by the presence of a hip rather than an infected knee prosthesis, particular surgeon preference as well as some limited patient characteristics. There was no statistically significant improvement in success rate between one- and two-stage revision strategies or either medical approach (continuous antibiotic versus antibiotic-free window). Large prospective studies, and ideally randomized controlled trials, are needed to definitively assess the ideal surgical and medical approaches to hip and knee PJI.

Compliance with Ethical Standards

Conflict of Interest: Lucas Castellani, MBBS, FRCPC, Richard Jenkinson, MD, Samira Mubareka, MD and Nick Daneman, MD, MSc have declared that they have no conflict of interest.

Human/Animal Rights: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 [5].

Informed Consent: Informed consent was waived from all patients for being included in the study.

Required Author Forms Disclosure forms provided by the authors are available with the online version of this article.

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