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Comparable outcome of culture-negative and culture-positive periprosthetic hip joint infection for patients undergoing two-stage revision

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Abstract

Purpose Lack of peri-operative microbiological evidence is an unfavourable factor in one-stage revision. The objective of this study was to figure out whether being culture-negative was an unfavourable factor for periprosthetic hip joint infection (PHJI) in patients undergoing two-stage revision.

Methods Records of PHJI patients treated between October 2003 and December 2016 were reviewed at our institution. Information such as microbiological data, clinical outcomes, and other details of patients' clinical courses were recorded.

Results A total of the 58 cases were reviewed. The median follow-up duration was 68.5 months. The infection control rate of PHJI was 93.1% after two-stage revision. Kaplan–Meier analysis showed no significant difference in infection control rates between culture-negative and culture-positive groups. Culture-positive sinus secretions were significantly associated with an increased rate of reinfection ($P = 0.039$).

Conclusions Two-stage revision had a high success rate for eradication of PHJI. Culture-negative PHJI had a comparable outcome with culture-positive PHJI.

Keywords Culture negative · Two-stage revision · Periprosthetic joint infection · Hip

Introduction

Periprosthetic joint infection (PJI) is a catastrophic complication after total joint arthroplasty [1, 2]. The incidence of periprosthetic hip joint infection (PHJI) is approximately 0.57–0.98% [2–4]. The infection control rate for PHJI after two-stage revision approaches 73~100% (total of 499/556, 89.75%) [5].

In prior studies, clinicians have suggested that two-stage revision and post-operative intravenous vancomycin therapy in patients with culture-negative PJI achieves similar rates of infection control as in with patients with culture-positive PJI [6, 7]. For two-stage revision, the five year infection-free survival rate of culture-negative (CN) PJI (including knee and hip) after two-stage revision was 79% compared with 74% in culture-positive (CP) PJIs, without a significant difference ($P = 0.09$) [7].

While a lack of identification of an infecting organism preoperatively is one of the contra-indications of one-stage THA revision [8], in two-stage revision, whether or not being CN is a risk factor for reinfection in PHJI has not been widely studied. Prior studies comparing CN and CP PJIs included both knees and hips, and outcomes of PHJI could not be identified [6, 7]. The purposes of this study were to figure out the infection control rates and risk factors of reinfection in periprosthetic hip joint infection patients who underwent two-stage revision, especially to compare the outcomes between CN and CP PJIs. We hypothesized that CN PJI has a worse outcome than CP PJI.

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Materials and methods

Study design

After approval by the local ethics committee (approval no. 2017–104), a retrospective case cohort study was performed including all patients who underwent an articulating antibiotic two-stage revision for periprosthetic hip joint infection in a single centre.

Enrollment and screening

Between September 1, 2003, and December 31, 2016, all patients with a PJI after THA, aged 18 years and older, with a minimum follow-up of six months after reimplantation or nine months after the antibiotic two-stage revision (some patients did not receive the second stage of reimplantation because of economic factors, general health conditions, or reinfection after the two-stage revision) were included in this study.

Exclusion criteria included the following:

1. Patients received a mixed group of treatments (e.g. arthrodesis, debridement, or one-stage revision) ($n = 3$).
2. Patients underwent not only hip revision and but also knee revision ($n = 1$).
3. Patients with less than six months of follow-up after reimplantation or 9 months after two-stage revision were excluded unless an endpoint event (e.g. reinfection) occurred ($n = 1$).
4. Patients underwent two-stage revision for non-prosthetic hip joint infection ($n = 2$).
5. Patients underwent two-stage revision with only a superficial infection ($n = 0$).

Seven patients were excluded among 65 patients. Finally, we included 58 patients in this study.

PJI diagnosis was finally determined by a clinician after evaluation of all of the available peri-operative information [9] based on the following criteria:

1. A sinus tract communicated with the prosthesis.
2. One micro-organism was isolated from at least two separate samples (tissue, fluid) obtained from the affected joint.
3. At least four of following criteria existed:

   (i) Elevated serum erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP) concentration
   (ii) Synovial leukocyte count was elevated
   (iii) Synovial neutrophil percentage was elevated
   (iv) Presence of purulence in the joint
   (v) Isolation of a pathogen in one culture
   (vi) More than five neutrophils/high-power field in five fields from a histologic analysis at ×400 magnification.

Mandatory pre-operative CT/ultrasound-guided hip aspiration

Pre-operative hip aspiration is essential for two-stage revision. The hip joint is more difficult for clinicians to aspirate than the knee joint without CT/ultrasound guidance. The synovial fluid is used for microbiological identification, antimicrobial susceptibility tests, and synovial cell counts. A prolonged ten day culture time is required for microbiological identification and antimicrobial susceptibility tests. Before hip aspiration, antibiotics are stopped for at least 4 weeks to raise the detection rate [10, 11]. Additionally, secretions from patients with sinus tracts underwent culturing.

The treatment pathway for periprosthetic hip joint patients

The treatment of PJI patients always consists of two parts, surgery and antimicrobial therapy. All revision procedures and antibiotic use followed a standardized protocol. Four experienced surgeons performed all of the two-stage revisions in a standard manner under general anesthesia and using a posterolateral approach. Details are as follows:

1. Intra-operative culture

Intra-operative samples for culture and histopathology were taken of synovial fluid and tissues as prosthetic components were removed. For all patients, at least five tissue samples were taken, and each sample was from a different location. The prosthetic components were put into a sterile jar for ultrasonication. Specimens were transported to the laboratory within 6 h [12].

2. Antibiotic use in spacers

For culture-negative patients, empirical antibiotics in handmold cement were a combination of meropenem and vancomycin, and clinicians should pay attention to the thermal stability and therapeutic dose of the chosen antibiotics in the cement.

3. Antibiotic treatment intervals

The intravenous antibiotics were continued and adjusted post-operatively according to the intra-operative culture and antimicrobial susceptibility tests for two weeks during the stay in the hospital. Discharged patients continued on oral antibiotics for another four weeks, and patients then stopped the

antibiotic therapy. The antibiotics for culture-negative PJI were rifampicin and levofloxacin. Inflammatory markers were tested for every two weeks prior to reimplantation.

Follow-up method and data collection

The first follow-up after revision was at one month, the second was at three months, and then patients were followed up regularly every year. The recurrence of infection and other complications was recorded by the surgeons. The end point of follow-up was defined as recurrence of PJI or death.

One trained doctor recorded all the data. Basic information like age, gender, duration of the procedure, transfusion, length of stay, and readmission was recorded. The pre-operative and intra-operative culture outcomes and associated antimicrobial susceptibility test outcomes were recorded. In addition, outcome of treatment and the last follow-up date, complications, and their time of occurrence were noted.

The definition of a successfully treated PJI is [13] as follows:

1. Eradication of infection (a healed wound without fistula, drainage, no pain, and no infection recurrence caused by the same pathogen)
2. No subsequent surgical procedure for infection after reimplantation
3. No occurrence of PJI-related mortality

Data analysis

The distribution of demographic characteristic data, such as age, gender, American Society of Anesthesiologists (ASA) score, duration of follow-up, length free of infection of the prior THA, duration of infection symptoms, and age of prior implant, was analyzed. The peri-operative culture outcomes and associated antimicrobial susceptibility test results were evaluated. The duration of follow-up, the occurrence of reinfection, and other complications were recorded. The potential risk factors of reinfection were analyzed. The infection-free survival rate and its 95%CI were calculated.

Statistical methods

A chi-squared analysis or a Fisher's exact test was used where appropriate for analyzing categorical data. Shapiro–Wilk test was used to test the normality of the data. An independent t test or the nonparametric Mann–Whitney U test was used for between-group comparisons of numerical data. Analysis of variance (ANOVA) was utilized to analyze the differences among group means and their associated procedures. Continuous data with a normal distribution are expressed as the mean (95% confidence interval (CI), mean − 1.96 × standard error (SE) to mean + 1.96 × SE) and data with a non-normal distribution as the median (interquartile range). A Kaplan–Meier survival analysis was used to analyze the expected duration until events happened.

Statistical significance was defined as $P < 0.05$. All analyses were undertaken using IBM SPSS Statistics for Mac Version 21 (IBM Corporation, 2012).

Results

Demography

Sixty-one patients with periprosthetic hip joint infection treated by articulating two-stage revision were identified. Of them, three patients were ineligible according to the exclusion criteria. Twenty-five patients (43.1%, 25/58) were hospitalized for a two-stage revision between 2003 and 2010. The median duration of follow-up for 58 patients after the two-stage revision was 68.5 months (interquartile range 41.0 to 97.3 months). The length that patients were free of infection after the prior THA was 21 months (median; interquartile range 0.25 to 55.8). The duration of infection symptoms was 12 months (median; interquartile range 6 to 36). At the time of the first stage (spacer) of revision, the mean age of patients was 65.4 years old (range 36 to 86 years old), and 75.9% (44/58) of patients had a pre-operative American Society of Anesthesiologists (ASA) score ≥ 2, with six patients having an ASA score = 3. Thirty-six patients (62.1%, 36/58) were diagnosed with traumatic arthritis (including femoral neck fracture (FNF), avascular necrosis (AVN) following FNF, and acetabular fracture) in association with the prior THA. Of the patients who were on the two-stage treatment pathway, 10 patients (17.2%, 10/58) retained the spacer as a definitive treatment method because of economic factors, general health conditions, psychological factors (afraid of surgical risks such as reinfection), or reinfection after the two-stage revision. For the 48 patients (82.8%, 48/58) who progressed to reimplantation, the median interval between stages was 5.2 months (interquartile range 3.0 to 6.0 months).

There were 19 peri-operative culture-negative (CN) and 39 culture-positive (CP) patients, and demographic characteristics of CN and CP groups were presented (Table 1). The diagnosis for CN PJI Patients without a sinus was listed (Table 2).

Microbiology

Distribution of pathogens

In those PJI patients undergoing two-stage revision who received mandatory pre-operative culture testing, all possible microbiological results are as follows:

Table 1 Demographic characteristics of CN and CP groups

	CN	CP	*P* value	total
Count	19	39	–	58
Age (year)	61 (50–75)	69 (60–76)	0.357	68 (55.75–75.25)
Duration infection free (months)	43 (0.25–108)	12 (0.25–48)	0.160	21 (0.25–55.75)
Duration of symptoms (months)	24 (11–48)	12 (4–24)	0.074	12 (6–36)
Interval between stages (months)	4 (3–6)	4 (3–6.75)	0.630	4 (3–6)
Duration of follow-up (months)	85 (44–113)	63 (25–88)	0.066	68.5 (41–97.25)
Gender (percentage males)	8 (42%)	21 (54%)	0.576	29 (50%)
Re-implanted	17 (89%)	32 (82%)	0.703	49 (84.4%)
Sinus tract	6 (32%)	19 (49%)	0.266	25 (43.1%)
ASA scoring[a]	1.95 (1.69–2.20)	1.87 (1.69–2.06)	0.611	1.90 (1.75–2.04)

Most parametric data are presented as the median (interquartile)

CN culture negative, *CP* culture positive, *FNF* femoral neck fracture

[a] Data are presented as the mean (95% confidence interval)

1. Pre-operative culture-positive:
   (i) Pre-operative culture-positive, intra-operative culture-negative (six cases)
   (ii) Pre-operative culture positive, intra-operative culture matched (three cases, all the pre-operative cultures from hip aspiration)
   (iii) Pre-operative culture positive, intra-operative culture not matched (four cases, all the pre-operative cultures from a sinus secretion)
2. Pre-operative culture-negative, intra-operative culture-positive (26 cases)
3. Peri-operative culture-negative (19 cases)

Table 2 Clinical and para-clinical signs of CN PJI patients without a sinus

Case	i	ii	iii	iv	v	vi	VAS	3p-BS
1	+/−	↑	↑	+	−	>25	6	Null
2	+	↑	↑	−	−	>25	4	Null
3	+	↑	↑	+	−	>25	6	Null
4	+	↑	↑	−	−	>25	3	Null
5	+	↑	↑	+	−	>25	5	Infection
6	+	↑	↑	+	−	10–25	7	Null
7	+/−	↑	↑	−	−	>25	4	Infection
8	+	↑	↑	+	−	>25	4	Infection
9	+	Null	Null	−	−	>25	5	Infection
10	+	↑	↑	+	−	>25	5	Null
11	+	↑	↑	+	−	>25	6	Infection
12	+	↑	↑	−	−	>25	5	Infection
13	+	↑	↑	−	−	10–25	5	Infection

Two patients had one inflammatory marker elevated (+/−), and the others had both CRP and ESR elevated (+). Synovial fluid of five patients was clear, but all of the patients had elevated synovial leukocyte counts (↑) and synovial neutrophil percentages (↑). One patient (case 9) did not have enough synovial fluid sample for both the culture and synovial cell count; the three-phase bone scan indicated a periprosthetic joint infection

i elevated serum erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP) concentration, *ii* synovial leukocyte count elevated, *iii* synovial neutrophil percentage elevated, *iv* presence of purulence in the joint, *v* isolation of a pathogen in one culture, *vi* more than five neutrophils/high-power field in five fields from histological analysis at ×400 magnification, *VAS* visual analogue scale, *3p-BS* three-phase bone scan

Nineteen patients who underwent two-stage revision were peri-operative-culture-negative (PCN) (32.7%, 19/58), and 39 cases had culture-positive outcomes (Fig. 1). Of these 39, 6 with secretion cultures (SCs) had only a sinus secretion culture outcome, and the other 33 patients had hip aspiration/intra-operative culture outcomes; positive outcomes included 14 coagulase-negative *Staphylococcus* (CoNS) cases, 8 *Staphylococcus aureus* (S.A.) cases, 5 multiple microbial infection (MMI) cases (Table 3), and 6 other cases (e.g. infections with *Pseudomonas aeruginosa*, *Mycobacterium tuberculosis* (TB), *Candida*, *Escherichia coli* (*E. Coli*)).

Pre-operative secretion culture (SC) and hip aspiration culture

Six cases had only a sinus secretion culture outcome, while four cases had both a sinus secretion culture outcome and intra-operative/hip aspiration culture outcome, but no sinus secretion culture outcome matched the intra-operative/hip aspiration culture outcome in this study (Table 4).

All the culture outcomes of hip aspirations and those of intra-operative samples were the same (four cases underwent two-stage revision and had positive culture outcomes in both stages).

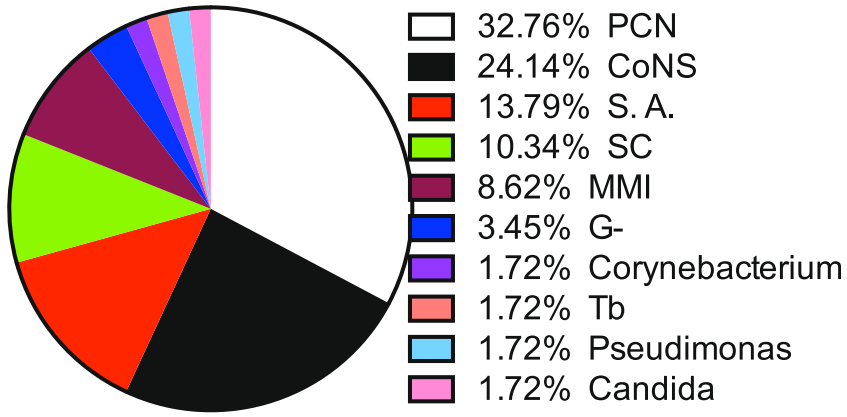

Fig. 1 PCN peri-operative-culture-negative, CoNS Coagulase-negative *Staphylococcus*, S.A. *Staphylococcus aureus*, MMI multiple microbial infection, G− gram-negative microbe, Tb *Mycobacterium tuberculosis*, SC pre-operative secretion culture (from surgical site) positive and hip aspiration/intra-operative culture negative, MMI multiple microbial infection. One patient infected with *Candida tropicalis*

The frequency of pathogens

If SC cases are included, S.A. was the most frequent pathogen (38.5%, 15/39 cases), *Staphylococcus epidermidis* (S.E.) was the second most frequent (28.2%, 11/39 cases), and CoNS (except S.E.) was the third most frequent (17.9%, 7/39 cases). CoNS (including S.E.) accounted for 46.1% of all culture-positive cases.

If SC cases are excluded, the most frequent pathogen was S.E. (33.3%, 11/33 cases), S.A. was the second most frequent (24.2%, 8/33 cases), and CoNS (except S.E.) was the third most frequent (18.1%, 6/33 cases). CoNS (including S.E.) accounted for 51.5% of all hip aspiration/intra-operative culture-positive cases.

Outcome

Reinfection

Four patients (6.9%, 4/58) had a reinfected periprosthetic joint. The infection control rate was 93.1% (54/58). The five year infection-free survival rate was 95.4% (95%CI, 89.1–100%) in patients treated with two-stage revisions (Fig. 2).

A univariate Cox regression was used to identify out factors associated with infection-free survival, and a positive sinus secretion culture was significantly associated with an increased rate of implant failure (HR = 11.1, 95%CI 1.1–108.9, $P = 0.039 < 0.05$, Table 5; HR, adjusted for age and gender, 18.7, 95%CI 1.4–243.1, $P = 0.025 < 0.05$, Table 6). There were ten patients who had positive sinus secretion cultures, and four of them had intra-operative culture outcomes that were all different from the sinus secretion culture outcomes (Table 4). In addition, positive or negative peri-operative cultures were not significantly associated with reinfection (Table 5).

The treatment for reinfection included reoperation with two-stage revision (one case, with PJI finally eradicated) and long-term oral antibiotic suppression (three cases). No amputations were performed.

Table 3 Multiple microbial infection list

MMI	Secretion culture	Hip aspiration	Intraoperative culture
1	*Staphylococcus aureus*	0	*Staphylococcus hominis*
2	G−	0	*Staphylococcus epidermidis*
3	0	0	*Staphylococcus epidermidis*, *Acinetobacter baumannii*
4	*Staphylococcus aureus*	0	*Burkholderia pickettii*
5	*Chryseobacterium meningosepticum*	TB	*Bacteroides ovatus*

MMI multiple microbial infection, *G−* gram-negative microbe

Other complications

Other complications included one spacer fracture and two dislocations. These three patients were not reinfected.

One patient sustained a fracture of the spacer two months after revision during weight-bearing activities, and CRP and ESR values were normal at that time. The patient then underwent a successful reimplantation (Fig. 3). One patient sustained dislocation the night of the two-stage revision, and finally, a closed reduction was performed involving immobilization with traction for two weeks. The patient underwent a successful reimplantation. A 74-year-old patient suffered habitual dislocation after reimplantation; the first dislocation occurred 15 months after reimplantation, and it reoccurred twice with no hematoma formation after the closed reduction. Finally, the patient underwent an open

Table 4 Sinus secretion culture outcome list

Case	Secretion culture	O/M R	MR	Intrao-culture	O/M R	MR	Reinfection
1	*S. aureus*	0	0	*Burkholderia pickettii*	0	0	0
2	*S. aureus*	1	1	*S. hominis*	0	1	0
3	*Escherichia coli*	/	/	*S. epidermidis*	1	1	0
4	*C. meningosepticum*	/	1	*Bacteroides ovatus*	/	0	0
5	*S. aurcularis*	0	0	/	/	/	0
6	*S. aureus*	1	1	/	/	/	1
7	*S. aureus*	0	0	/	/	/	0
8	*S. aureus*	0	0	/	/	/	1
9	*S. aureus*	1	1	/	/	/	1
10	*S. aureus*	1	1	/	/	/	0

No patients had a positive outcome of the hip aspiration culture

S. Staphylococcus, *TB Mycobacterium tuberculosis*, 1 positive, 0 negative, / no data, *MR* multi-antibiotic resistance, *O/M R* oxacillin/methicillin resistance, *Intrao-culture* intraoperative culture, *C. meningosepticum Chryseobacterium meningosepticum*

reduction for cup exchange, and the dislocation did not occur again. No aseptic loosening or venous thromboembolism (VTE)/pulmonary embolism (PE) was observed in this study.

Outcome of CN and CP groups.

Outcome of CN and CP groups is presented in Table 7.

Five-year infection-free survival was 92.8% (95%CI, 83.2%–100%) in CP patients (Fig. 4).

Comparison with other studies

Other studies of two-stage revisions are listed in Table 8.

Discussion

We reviewed 58 cases of periprosthetic hip joint infection managed by two-stage revision, with an overall infection control rate of 93.1% (54/58) over a median follow-up of 68.5 months (5.7 years). There was no significant difference in reinfection rates between culture-negative and culture-positive PJIs.

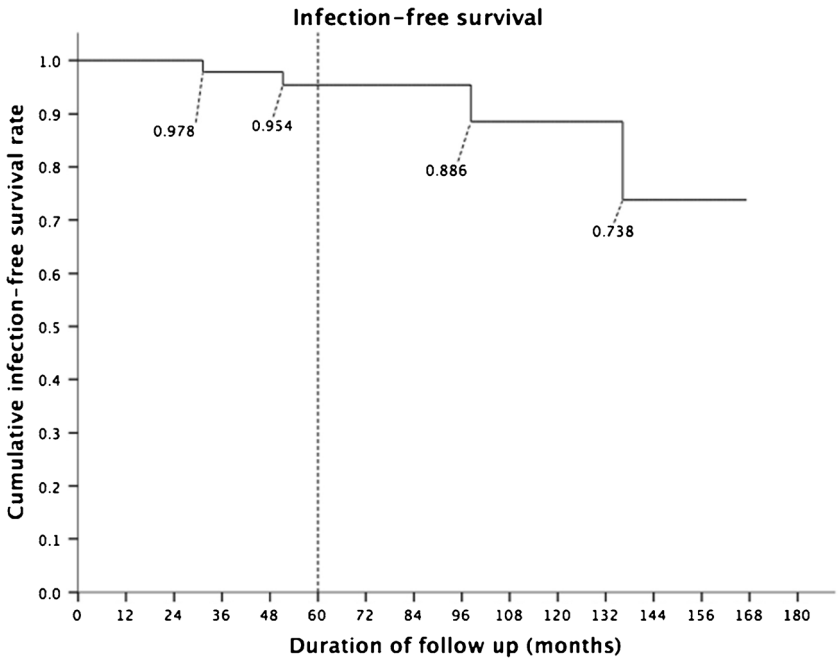

Fig. 2 Cumulative infection-free survival rate in patients with periprosthetic hip joint infections undergoing spacer revision. The five year (60 months) survival rate was 95.4%

Table 5 Risk factors influencing reinfection from univariate Cox regression

Factor	HR	95%CI	*P* value
Age (year)	1.005	0.933–1.084	0.888
Gender	2.089	0.205–21.249	0.534
Duration of symptoms (months)	0.993	0.955–1.034	0.742
Duration infection-free (months)	0.997	0.977–1.018	0.786
Age of implant (months)	0.999	0.989–1.009	0.786
Re-implanted or not	1.274	0.409–3.964	0.676
Interval until spacer revision (month)	0.964	0.678–1.369	0.837
Sinus tract existed	3.497	0.357–34.214	0.282
Pre-operative culture-positive	8.542	0.878–83.09	0.065
Sinus secretion culture-positive*	11.081	1.128–108.886	0.039
Intra-operative culture-positive	0.347	0.036–3.355	0.361
Peri-operative culture-positive	42.936	0.009–201,178.767	0.383
ASA scoring	1.053	0.244–4.537	0.945
Multiple microbial infection	0.04	0–44,734.548	0.65
Gram-positive *Staphylococcus*	84.95	0.024–297,079.277	0.286
Traumatic arthritis or not (primary THA)	1.15	0.14–9.409	0.896
Previous revision	0.028	0–230.315	0.437

HR hazard ratio, *CI* confidence interval

*$P < 0.05$

Prior studies indicated that significant risk factors for reinfection in two-stage revision included a previous revision, younger age [14], lympho-edema, prolonged duration between stages [15], and morbid obesity [16]. In addition, being culture-negative was not a significant risk factor in prior studies that contained both knee and PHJI cases [6, 7]. This study showed that a culture-positive secretion from a sinus tract was a risk factor for reinfection, and there was no significant difference in reinfection rates between CN and CP patients.

In this study, CN patients were defined on the basis of peri-operative culture-negative samples with a strict pre-operative hip aspiration culture, intra-operative culture, and secretion culture if a sinus tract existed. In addition, in a prior study, secretion-culture-positive patients were not considered as CP patients [7]. Secretion-culture-positive patients without aspiration culture outcomes received empirical local antibiotics. In addition, 15.7% (21/134) of CN patients had a sinus tract [7]. In our study, 32% (6/19) of CN patients had a sinus tract, compared with the 48.7% (19/39) of CP patients with a sinus tract. A culture-positive secretion was a risk factor for reinfection.

Table 6 Risk factors influencing reinfection from covariate Cox regression

Factor	HR	95%CI	*P* value
Age (year)	13.332	0.18–990.103	0.239
Gender	0.955	0.856–1.065	0.407
Surgical site/sinus secretion cultures positive	18.669	1.434–243.082	0.025

HR hazard ratio, *CI* confidence interval

Fig. 3 Spacer fracture occurred 2 months after insertion (CRP and ESR were normal at that time). This patient then underwent a successful two-stage exchange

Empirical antibiotic use for culture-negative patients undergoing two-stage revision was comparable to antibiotic use in CP PJI patients according to the known organisms. CN patients received local empirical antimicrobial therapy with vancomycin and/or an aminoglycoside, and the

Table 7 Outcomes of CN and CP groups

Count	CN	CP	*P* value*	Total
Re-infection	0	4 (10.2%)	0.397	4 (6.90%)
Dislocation of spacer	0	1 (2.56%)	0.672	1 (1.72%)
Dislocation after reimplantation	1 (5.26%)	1 (2.56%)	0.448	2 (3.45%)
Dislocation	1 (5.26%)	2 (5.13%)	0.296	3 (5.17%)
Fracture of spacer	0	1 (2.56%)	0.672	1 (1.72%)

CN culture negative, *CP* culture positive

*Exact significance (one-sided, but still no significant difference)

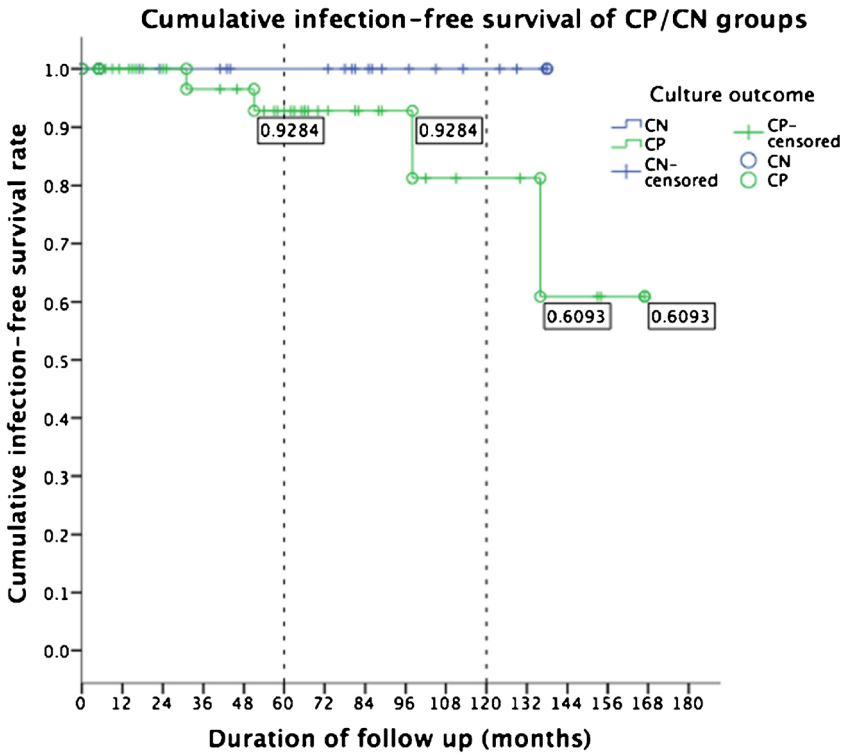

Fig. 4 Kaplan–Meier plot showing the cumulative infection-free survival rate of the culture-positive group versus that of the culture-negative group. The 5-year (60 months) survival rate of the culture-positive group was 92.8%

microbiological eradication rate of PJI (including both knee and hip joints) ranged from 73 to 94% [6, 7, 17]. Another study, which compared the outcome of CN PJI with that of CP PJI after debridement, antibiotics, and implant retention (DAIR), or two-stage revision, suggested that culture negativity may not necessarily be a negative prognostic factor for PJI [18]. In this study, CN PJI patients received local vancomycin with meropenem, and the infection control rate was 100%. The combination of vancomycin and meropenem can treat almost all the microbial organisms (e.g. gram+/gram−/drug-resistant bacteria) except for TB and fungi.

The most common organism identified in intra-operative culture outcomes in this study was oxacillin/methicillin-resistant *Staphylococcus epidermidis* (MRSE), which was different from another study [19]. In addition, the most common sinus secretion pathogen was S.A., and outcomes for sinus secretions were always different from the outcomes for intra-operative cultures; a positive sinus secretion culture was a risk factor for reinfection. The use of a hand-made articulating spacer made sure that surgeons could add the antibiotics they wanted according to the antimicrobial susceptibility test results.

The limitations of this study are its retrospective nature and that the sample size may not be big enough, in addition to the fact that the diagnosis and treatment of PJI have improved over the decade.

In conclusion, this study showed that a two-stage revision was an effective procedure for treatment of periprosthetic hip joint infection, with a high infection control rate (93.1%) over a mid-term follow-up following a standard clinical pathway. Culture-negative PJI was not associated with a worse outcome. Antibiotic use should be determined according to a reliable antimicrobial susceptibility test. A positive sinus secretion culture was a risk factor for reinfection.

Table 8 Comparison of reinfection with other studies of two-stage revision

Count	CP (R)	CN (R)	*P* value*	Total (R)	OR	95%CI
Huang et al. (2012)	172 (33)	33 (8)	0.325	205 (41)	0.781	0.381–1.603
Malekzadeh et al.(2010)	23 (6)	29 (6)	0.447	52 (12)	1.150	0.615–2.149
Subtotal	195 (39)	62 (14)	0.392	257 (53)	0.891	0.533–1.488
In this study	39 (4)	19 (0)	0.194	58 (4)	0.648	0.533–0.789[a]
Total	214 (39)	101 (18)	0.533	315 (57)	1.019	0.669–1.552

CN culture negative, *CP* culture positive, *R* reinfection cases, *OR* odds ratio for cohort CN

*Exact significance (one-sided, but still no significant difference)

[a] Range did not cross 1

Compliance with ethical standards

Conflict of interest No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article. All authors declare that no conflict of interest arises from participation in this study.

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