

ARTHROPLASTY

Short-term results following two-stage revision for periprosthetic joint infection

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Abstract

Background: Hip and knee arthroplasty procedures are successful surgical procedures, with total hip arthroplasty being named the operation of the 20th century. With there being an estimated rate globally of periprosthetic joint infection of 1% for hips and 2% for knees, this minimal infection rate represents a large global concern. The successful management of periprosthetic joint infection remains controversial with multiple proposed strategies. Our aim is to present our short-term data for a two-stage revision protocol.

Methods: A single centre retrospective review of an existing database starting from January 2013 and including April 2019 was conducted looking at patients having undergone two-stage revision for periprosthetic joint infection. The unit utilised a standard approach to two-stage revisions. Data was collected from the existing database to ascertain short-term success based on the Delphi-based international multidisciplinary consensus criteria.

Results: A total of 2 125 entries were reviewed from the database comprising 1 912 primary arthroplasty procedures. From all revision cases 19 patients were identified to have undergone a two-stage revision by our unit. Of these patients we managed to collect sufficient data to gauge treatment success in 12 patients. Of these 12 patients with a mean follow-up of 25.6 months, ten reported complete wound healing, pain improvement and no subsequent surgery. One patient demised from septic complications and one required subsequent arthrodesis which controlled the sepsis.

Conclusion: Our results showed a high infection eradication rate following our two-staged revision protocol despite frequent delays between first and second stages as a result of resource constraints and limitations.

Level of evidence: Level 4

Keywords: revision, arthroplasty, two-stage, periprosthetic joint infection

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Introduction

Hip and knee arthroplasty procedures are considered highly successful surgical procedures, with total hip arthroplasty being named the operation of the 20th century.¹ Globally, there is an increase in the number of these procedures due to an increasing elderly population; an increase in skilled surgeons; and the success rate of the operation.² With an estimated rate globally of periprosthetic infection of 1% for hips and 2% for knees,³ even a minimal infection rate represents a large global concern medically² and financially.⁴

The successful management of periprosthetic joint infection (PJI) remains controversial, with multiple successful treatment options reported in the literature leading to uncertainty as to which is the best approach. The two-staged approach is still regarded as the gold standard⁵ for chronic infections defined as an infection after six to eight weeks from the index procedure.^{6,7} The two-staged approach has reported cure rates of over 90%,^{8,9} ranging from 76% to 100%. This figure depends on the definition of cure which has not been uniform throughout the literature,⁵ with some authors only looking at re-operation and others looking at loosening or combinations thereof.¹⁰ Within the body of literature looking at the two-stage approach to PJI, there is controversy regarding the specific aspects of each stage⁵ in terms of type of cement spacer, antibiotic dose within the spacer, time between stages and the relevance of further investigations such as an alpha-defensin test at the second stage.

The purpose of this study was to assess the short-term success of our two-stage revision protocol in patients presenting with late chronic periprosthetic joint infection as defined by Segawa *et al.*¹¹ and further expanded on by Tsukayama¹² and summarised in *Table 1* following hip and knee arthroplasty at our institution.

Patients and methods

Institutional approval was obtained and a retrospective review conducted of patients managed for chronic deep PJI using a two-stage revision protocol. Information was extracted from a patient database and included patients managed at our institution from January 2013 up to and including April 2019. The database, which was recorded on Apple Numbers (Apple Inc, Cupertino, CA, USA), was analysed and all patients with radiographic evidence of having a cement spacer were included in the initial cohort. All patients with cement spacers were regarded to have been treated for a late chronic PJI as defined by Tsukayama,^{11,12} depicted in *Table 1*. Thereafter patients who had been assessed following reimplantation and had documented outcomes were included. Patients with no record of follow-up following reimplantation were excluded from the cohort.

Demographic data and details of respective surgical procedures were collected onto a spreadsheet using Microsoft Excel (Microsoft, Redmond, WA, USA). We documented the joint involved, the number of surgeries and the dates these were performed as well as the outcome of the most recent available assessment of the patient recorded.

PJI was routinely diagnosed based on the Musculoskeletal Infection Society (MSIS) criteria for PJI of 2011¹³ prior to the initiation

of a two-stage revision. After diagnosis patients were booked for and underwent a two-staged revision. The first stage consisted of a thorough joint debridement of all infected and necrotic tissue as well as removal of all implants. Biopsies were sent from a minimum of five sites within the debrided joint, including from bone and synovium, for histological and microbiological analysis. Cement spacers were made using casting moulds provided by Zimmer Biomet (Zimmer Biomet, Warsaw IN, USA). The cement spacers were made using 80 g Palacos R+G (Haraeus, Hanau, Germany) containing 1 g gentamycin with 3 g vancomycin and 3 g cefuroxime added. The cement was then allowed to harden in the moulds and implanted into the dead space as an articulating spacer.

Post-operatively patients were placed on six weeks of antibiotics, with intravenous vancomycin and oral rifampicin being the first-line empiric agents. After culture and sensitivity were obtained, antibiotics were tailored to the cultured organism and where possible oral agents were given (cloxacillin or linezolid with rifampicin) and the patients were discharged to continue their six-week course as outpatients. Following the six weeks of antibiotics, a minimum period of two weeks was allowed before repeat blood investigations were done, including white cell count, C-reactive protein, erythrocyte sedimentation rate and ferritin-iron ratio. If these were suppressed after the antibiotic-free period, the second stage was planned.

The second stage consisted of removal of the cement spacers and a repeat debridement of the joint and bone ends. In cases where the eradication was clinically questionable, an alpha-defensin test was planned to be done; if positive, a repeat first stage would be performed, and where negative, we would proceed with the second stage. Multiple biopsies were again taken at the time of reimplantation, and reimplantation with revision implants was performed based on the bone defects encountered for each case, an example of which can be seen in *Figure 1*. This was done despite evidence indicating that reimplantation cultures often did not correlate with poorer outcomes.^{5,14} Following the second stage operation, patients were treated for another six weeks with antibiotics based on the original first stage culture results and tailored if needed based on the repeat culture results.

The success of this systematic intervention was based on the Delphi-based international multidisciplinary consensus criteria for the resolution on PJI published in 2013.¹⁰ Here, success was defined as: 1) no clinical failure (healed wound without fistula or draining sinus and pain-free joint, and no recurrence by the same organism; 2) no subsequent surgical intervention after reimplantation for infection; 3) no death caused by a condition linked to PJI.

Results

We reviewed a total of 2 125 entries for all arthroplasty procedures performed between January 2013 and April 2019, with 1 912 entries for primary arthroplasty procedures done. Of the primary arthroplasty procedures done, total hip arthroplasty accounted for 1 041 entries and total knee arthroplasty accounted for 871 entries. From these entries, 19 patients were identified to have undergone two-stage revisions for chronic PJI, with eight hips and 11 knees in that cohort. There were no patients documented to have required

Table 1: Classification of PJI based on clinical presentation¹²

	Type 1	Type 2	Type 3	Type 4
Timing	Positive intra-operative culture	Early post-operative infection (A: superficial, B: deep)	Acute haematogenous infection	Late chronic infection
Definition	>2 positive intra-operative cultures	Infection within 30 days of surgery	Haematogenous seeding in well-functioning prosthesis	Chronic infection present >30 days

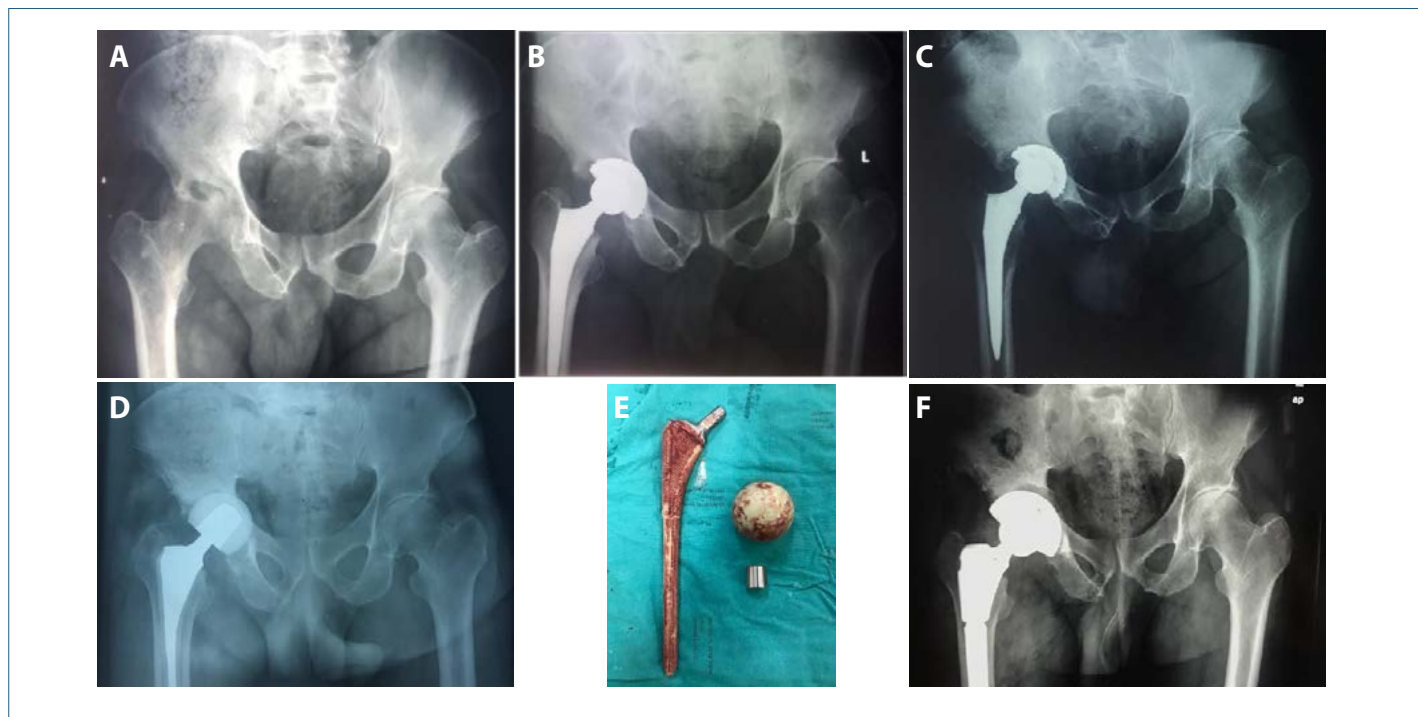


Figure 1. Case representing a two-stage hip revision. A: initial pre-operative radiograph showing right hip avascular necrosis; B: post primary total hip arthroplasty; C: proximal femur and acetabular lucency when presenting with draining sinus; D: first stage debridement with articulating cement spacer, with spacer removed at second stage (E); F: final implants following second stage reimplantation

a repeat first stage for questionable clearance and reimplantation. This correlates to an overall chronic infection rate of 0.99% (0.76% for hips and 1.26% for knees) as defined by Tsukayama.¹² With regard to these findings, it should be kept in mind that our institution is a referral centre and some revisions were done for primary joints done at other hospitals. Similarly, we operate on patients from a large demographic area and some complications may not have returned to our institution but rather been managed elsewhere.

Of note there were also a total of 79 patients identified who were managed for acute post-operative periprosthetic joint infections (Tsukayama type 2). Of these, 51 were hips and 28 were knees. This correlated to an acute infection rate of 4.13% (4.9% for hips, 3.2% for knees). These patients were managed with debridement and implant retention (DAIR) with exchange of modular components, followed by six weeks of targeted antibiotics based on intra-operative culture specimens. There were no patients noted to

have presented with acute haematogenous infection (Tsukayama type 3). Of the patients identified with acute infection, none progressed to two-stage revision following initial surgical management.

From the identified 19 patients with Tsukayama type 4 infection, 12 were found to have documented follow-up data which allowed them to be assessed according to the aforementioned Delphi-based international multidisciplinary consensus definition of success (five hips, seven knees). The remaining patients had insufficient data on record or had not followed up again at our institution for assessment and were thus excluded from the study. The outcomes relating to treatment success were captured and tabulated (Table II). All patients undergoing revision were classified as type B hosts according to McPherson *et al.*^{15,16} who modified the Cierny-Mader classification for osteomyelitis (Table III) to include specific local and systemic factors (Table IV).

Table II: Patient details and outcomes

Patient	Joint involved	Time between revision stages (months)	Time since reimplantation (months)	Wound healed	Pain	Subsequent surgeries
1	Hip	24	36	Yes, no sinus	Improved	No
2	Hip	5	4	Yes, no sinus	Improved	No
3	Knee	5	6	Yes, no sinus	Improved	No
4	Knee	4	6	Yes, no sinus	Improved	No
5	Knee	29	29	Yes, no sinus	None	No
6	Hip	3	34	Yes, no sinus	None	No
7	Knee	10	17	Yes, no sinus	Improved	No
8	Hip	6	24	Yes, no sinus	Improved	No
9	Knee	6	28	Yes, no sinus	None	No
10	Hip	RIP	RIP	RIP	RIP	RIP
11	Knee	5	20	Yes, no sinus	Improved	No
12	Knee	7	78	Yes, no sinus	None	Knee fusion

Table III: Host classification by McPherson¹⁶

	Description
Type A	Uncompromised, normal host
Type B	Compromised host with one or two local and/or systemic factors
Type C	Significant compromise with more than two compromising factors or one of the following <ul style="list-style-type: none"> • Neutrophils <1 000 • CD4 count <100 • Intravenous drug user • Other chronic active infection • Haematological malignancy

Table IV: Local and systemic compromising factors as described by McPherson¹⁶

Systemic factors	Local factors
Age >80 years	Active infection >3–4 months
Diabetes	Synovial cutaneous fistula
Immunosuppressive medication	Soft tissue loss from prior trauma
Systemic inflammatory disease (RA, SLE)	Vascular insufficiency (arterial or venous)
Malignancy	Prior peri-articular fracture (crush)
Hepatic insufficiency (cirrhosis)	Multiple previous incisions (skin bridge)
Chronic indwelling catheter	Prior local irradiation to wound area
Renal failure requiring dialysis	Subcutaneous abscess >8 cm ³
Pulmonary insufficiency	
Alcoholism	
Chronic malnutrition	
Current nicotine use	
Systemic immune compromise	

RA: rheumatoid arthritis; SLE: systemic lupus erythematosus

From the 12 patients with completed data there were four males and eight females, with a mean age at follow-up of 61.66 years (range 51–75, median 61). The mean follow-up time for the cohort was 25.6 months (range 4–78, median 24), with the mean time between the first and second stages being 9.45 months (range 3–29, median 6). One patient was found to have demised following the first stage of the revision process as a result of severe sepsis secondary to systemic *Pseudomonas aeruginosa*. A second patient had recurrence of sepsis two years after the second stage, and subsequently underwent a knee fusion. All remaining patients (10/12, 83.3%) had complete wound healing with no erythema

or recurrence of sinus tract formation. Four patients reported no residual joint pain, with seven reporting some residual pain but an improvement compared to before the revisions.

Discussion

The diagnosis and management of PJI remains controversial with no definitive diagnostic tests¹⁷ or clear universally accepted management protocol or definition of treatment success. The diagnosis is based on a combination of clinical examination findings and laboratory results.¹⁷ The Musculoskeletal Infection Society (MSIS) together with the Infectious Disease Society of America (IDSA) previously developed criteria aimed at standardising the definition and diagnosis of PJI in 2011.¹³ These criteria were the recently revised into a scoring system¹⁷ to add weighting to different aspects of the criteria and possibly improve diagnostic accuracy.

The management of PJI is as contentious as the diagnosis, with multiple proposed treatment algorithms used in the literature. The literature becomes more confusing as there have been multiple definitions of treatment success or treatment failure, thus making the comparison of reported success rates difficult (*Table V*).⁵ Because of these diverse criteria for success, we used the Delphi-based international multidisciplinary consensus definition.¹⁰ Two-stage revision remains the gold standard for chronic PJI,² but success has also been reported for one-stage revision performed under strict conditions.^{18,19}

Within the realms of two-stage revision there remains controversy regarding the preferred protocol.^{5,20,21} Our unit followed a similar protocol as described by Sukeik *et al.*² as far as possible, with some alteration to these steps based on the constraints of an overburdened public health system with long waiting lists and occasional drug availability constraints. This led to our patients having an extended spacer retention time averaging 9.45 months (range 3–29 months, median 6 months). Fu *et al.*²² found the optimal timing of reimplantation to be between 12 and 16 weeks, but had a mean spacer retention time of 24 weeks in their success group²² whereas our time to reimplantation translates to approximately 110 weeks. Despite these challenges our short-term results remain promising with 83.3% of reviewed patients showing good wound healing and improvement in pain and function without subsequent surgery.

Other authors have proposed some variation to the described two-stage approach. Chung *et al.* recently described a protocol of two-stage debridement but with retention of implants.²³ They

Table V: Reported success rates following two-stage revision for PJI (adapted from Akgün *et al.*⁵)

Study (individually referenced in above article by Akgün <i>et al.</i>)	Number of patients	Definition of failure	Rate of infection eradication (%)
Chen <i>et al.</i>	155 hips	Repeated operation Long-term antibiotics	91.7
Oussedik <i>et al.</i>	39 hips	Recurrent infection	96
Tan <i>et al.</i>	186 knees 81 hips	Delphi-based definition	76
Lange <i>et al.</i>	82 hips	Kamme <i>et al.</i>	85.4
Triantafyllopoulos <i>et al.</i>	239 knees 261 hips	Wound healing problems Elevated ESR/CRP Long-term suppression	91.2
Fink <i>et al.</i>	36 hips	Clinical signs of infection CRP more than 10 mg/dl Osteolysis	100
Berend <i>et al.</i>	186 hips	Further surgery for infection	83
Ibrahim <i>et al.</i>	125 hips	Recurrence of infection	
Leung <i>et al.</i>	50 hips	Recurrence of infection	79

reported an overall success rate of 86.7% (93.8% in primary and 77.1% in revision arthroplasty) after an average follow-up of 41.8 months (12–171). In their protocol the modular components were removed, scrubbed and sterilised in the autoclave or antimicrobial soak then reinserted with antibiotic-impregnated cement beads. These beads were removed at repeat debridement five days later.²³

Other aspects of controversy affecting our methodology involve the relevance of a positive alpha-defensin test at the reimplantation stage. Our protocol was to repeat the first stage procedure in the presence of a positive result. This practice is costly and time consuming for the unit and the patient. Samuel *et al.*²⁴ found that at one year a positive alpha-defensin at reimplantation correlated poorly with the presence of persistent infection and recommended against its routine use in patients with cement spacers.²⁴ This finding is postulated to be a result of a possible inflammatory reaction to the cement spacer leading to higher false positive results.²⁵ Frozen section has been shown to correlate well with infection being present at time of reimplantation,²² but this was not part of our protocol as the service has been unavailable in the past, with staffing and resource constraints being cited as barriers to the service availability.

Complication rates for two-stage revisions are varied, with Ibrahim *et al.*²⁶ noting a high mortality rate (15%) in their study cohort, although there was no comparison group, whereas our cohort had a single sepsis-related mortality documented (8.3%). Higher rates of subsequent dislocation have also been reported,²⁷ with a 9% dislocation rate compared to the quoted 0.5%–5.3% dislocation rate in primary arthroplasty depending on the approach used.²⁸ Our cohort reported no such complications in the patients we were able to review. The possibility remains, however, that some unreviewed patients may have demised or dislocated since reimplantation but this was not ascertained.

Limitations of our study are the small numbers of patients undergoing revision reviewed and the short follow-up of the cohort relating to the recent nature of the digital database. The electronic database was also not completed for all patients, resulting in the exclusion of seven patients which, in a small cohort, could prove to be significant.

Conclusion

A high short-term infection cure rate was achieved using a standardised two-stage revision protocol despite institution-related alterations regarding time to reimplantation. Further follow-up is required to ascertain the medium- and long-term success of this management protocol, and the time to reimplantation should be shortened to be more in line with larger published studies.

Ethics statement

Prior to commencement of the study, ethical approval was obtained from the following ethical review board: HREC (Wits) clearance certificate M170415 (obtained 29/05/2017, annual update 27/02/2019). The authors declare that this submission is in accordance with the principles laid down by the Responsible Research Publication Position Statements as developed at the 2nd World Conference on Research Integrity in Singapore, 2010.

All procedures 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.

Declaration

The authors declare authorship of this article and that they have followed sound scientific research practice. This research is original and does not transgress plagiarism policies.

Author contributions

JdP contributed to the conception and design of the work; the acquisition, analysis, and interpretation of data for the work; drafting the work; final approval of the version

to be submitted to the journal and ongoing input regarding corrections and editing. RG conceptualised the work and contributed to design and interpretation of the work. Further contributions include critical revision and expression of intellectual content, as well as final approval of the version submitted to the journal. VS contributed to design of the work, analysis and interpretation of the data as well as revision and final approval. NF contributed to the collection of the data as well as approval of the final version. CF conceptualised the work and contributed to design and interpretation of the work. Further contributions include critical revision and expression of intellectual content, as well as final approval of the version submitted to the journal.


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