



Does Early Debridement, Antibiotic Therapy and Implant Retention (DAIR) have a Role in Managing Periprosthetic Joint Infection of the Knee in Indian Scenario: A Retrospective Analysis of Outcomes

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Abstract

Purpose To report outcomes of Debridement, Antibiotic therapy and Implant Retention (DAIR) for periprosthetic knee joint infections (PJI) in the Indian population and to study factors influencing outcomes.

Methods This was a Retrospective study of 80 cases of acute PJI after total knee arthroplasty who were treated by DAIR, within 2 weeks of onset of infection. A standardised institutional management protocol was applied to all cases. Patients were followed up for a minimum 1 year. Outcomes of DAIR were classified as successful or unsuccessful based on resolution or persistence of infection, and subsequent requirement of revision surgery. Influence of factors, like comorbidities, culture status and microbiological characteristics of causative organism, on outcomes was assessed.

Results Overall 55 patients (68.75%) had successful eradication of infection after DAIR. 27 (33.7%) patients were culture negative and 53 (66.2%) patients grew organisms on culture. There was no statistically significant difference in outcomes ($p=0.082$) between culture-positive cases (69.8% success rate) and (66.7% success rate) in culture negative cases. Furthermore, no difference in outcomes was observed in culture-positive patients between those who grew Gram-positive organisms versus Gram-negative organisms ($p=0.398$) Similarly, patient comorbidities did not significantly alter the outcomes after DAIR ($p=0.732$).

Conclusion Our study demonstrates that early DAIR within 2 weeks of onset of infection using a standard protocol during surgery and postoperatively can result in good outcomes. Patient comorbidities, culture status (positive versus negative), Gram staining characteristics of organisms and the identity of pathogenic bacteria did not influence outcomes of DAIR for acute PJI.

Keywords Infection · Periprosthetic infection · DAIR · Culture · Outcomes · Arthroplasty

Introduction

Periprosthetic Joint Infection (PJI) is a dreaded complication with a reported prevalence of 1.5–2% after TKA [1]. PJI leads to considerable morbidity because of pain, multiple surgeries and considerable economic burden, even leading to loss of livelihood [2].

There are various techniques described for the treatment of PJI after TKA, such as debridement with or polyethylene exchange, single-stage or two-stage revision arthroplasty, long-term antibiotic suppression and arthrodesis. Among them, Debridement Antibiotic therapy and Implant Retention (DAIR) is a commonly performed procedure, previously reported to have poor outcomes [3, 4]. But with improved surgical techniques, better antibiotic regimens and involvement of multidisciplinary team of surgeons and infectious

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disease specialists, DAIR has shown to have improved results in the management of acute PJI after TKA [5, 6].

Most of the published literature on DAIR is from the western population and none published from the Indian subcontinent. This is important, because the microbial flora causing infections in India may be different from the Caucasian population and the antibiotic resistance pattern may also be different due to the indiscriminate use of antibiotics in humans and animals in India [7, 8].

The aim of this study is to assess the outcomes of DAIR for periprosthetic infection after TKA in Indian patients, by assessing success rates after DAIR. Objectives of this study are to.

- a. Study effect of patient/ host comorbidities on outcomes of DAIR for PJI
- b. Identify the common organisms causing PJI in the Indian population and evaluate the influence of microbiological factors (culture status, identified organism and Gram-staining characteristics) on outcomes after DAIR

Materials and Methods

This study was a retrospective study of patients undergoing Debridement, Antibiotic therapy and Implant Retention (DAIR) for periprosthetic knee joint infections. The study was conducted at a single tertiary care centre. Patients who underwent early DAIR for PJI of the knee (defined as surgery within 2 weeks of onset of infection or symptom duration less than 2 weeks) at our institute between January 2012 and January 2018 were evaluated. The study was approved by the Institute Ethics Committee (Approval Number- SS/2017/IEC157).

Eligibility criteria for inclusion in the study are- patients of any age and of both genders, with a diagnosis of periprosthetic joint infection of the knee who underwent DAIR surgery for “Early PJI” (Defined as a diagnosed infection less than 1-month from the index TKA surgery) or for an “Acute hematogenous PJI” (defined as a late infection, more than 1 month since index surgery, with symptom duration less than 2 weeks). These definitions are based on the guidelines of the Musculoskeletal Infections Society (MSIS) [9] and the Tsukayama [10] Classification of PJI. A minimum of 1-year follow-up was necessary for inclusion. Cases with primary or index surgery performed at our institute, as well as referral cases were included in this study. Exclusion criteria are loss to follow-up, incomplete case records, patients who underwent prior simple debridement or incision & drainage (I & D) or any other revision surgery of the implanted joint. A total of 80 patients were identified and met the eligibility criteria for inclusion in the study.

Patient demographic details such as age, sex, side operated, time from index surgery to onset of infection were recorded. Inflammatory markers Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP) and the WBC counts were used in the diagnosis. Variables hypothesized to influence outcomes like comorbidities (such as diabetes mellitus, hypertension, hypothyroidism, hypo-albuminaemia), culture status, Gram-staining characteristics, organism isolated, early versus late infections were analysed. Outcomes were classified as “Successful” (defined as clinical eradication of infection, with return to function) and “Unsuccessful” (defined as persistence of infection with elevated inflammatory markers and local signs of infection warranting further treatment, with 2-stage revision or repeat debridement).

Institutional Protocol for Debridement, Antibiotic Therapy and Implant Retention

All the patients of PJI were diagnosed and operated by a single surgeon, using a standardised surgical technique and antibiotic protocol developed in coordination with our Infectious Diseases (ID) specialist. Clinical signs of infection included acute inflammatory signs of joint effusion, erythema, local warmth and presence of active discharging sinuses communicating with the joint. All patients underwent pre-operative aspiration of the knee, with samples sent for culture-sensitivity, synovial fluid cytology and microbiological staining. DAIR involved removal of polyethylene insert, extensive synovectomy, thorough lavage of the joint using 12 l of normal saline, Betadine solution, Chlorhexidine solution and bacitracin solution. Intra-operatively, tissue was collected from a minimum of three different sites and sent for culture-sensitivity. A new polyethylene insert was implanted at the end of procedure.

Postoperatively, all patients were started on empirical broad-spectrum antibiotics in consultation with an infectious disease specialist, which was then tailored depending on the antibiotic sensitivity of organisms identified from the tissue sent. Patients were given intravenous antibiotics for 2 weeks followed by oral administration of the same for a *minimum period* of 4 weeks. Cessation of antibiotics was done based on the resolution of symptoms and trends of inflammatory markers. Culture negative cases were continued on empirical intravenous broad-spectrum antibiotics for 6 weeks upon the recommendation of infectious disease specialist. All patients in the postoperative period were evaluated by a speciality trained Orthopaedic surgeon and data recorded in the hospital PJI database for a minimum period of 1 year.

Patients were serially monitored clinically for signs of improvement and with inflammatory markers. Serial plain radiographs were obtained every 3-months to look for radiolucencies consistent with implant loosening. In three patients with indeterminate diagnosis of recurrence, a three phase

Gallium-67 nuclear bone-scan was used to diagnose infection. All details of subsequent revision procedures, including re-infecting organism were recorded in all the cases of revision surgery.

Statistical Analysis

A univariate analysis with medians for continuous variables and proportions for categorical variables was performed to determine factors influencing outcomes after a poly-exchange surgery for periprosthetic joint infection after total knee arthroplasty. Medians were evaluated for statistical significance using the Chi-square test. The analysis was unadjusted for age or gender. With confidence intervals of 95%, a p value less than 0.05 was considered statistically significant. Non-parametric variables were assessed using the Fisher exact test. Significance of comorbidities was assessed with sub-group analysis using Analysis of Variance (ANOVA) in influencing outcomes. All datapoints were collated and analysed in Excel datasheet (Microsoft, Excel™ 2016).

Results

Eighty patients met the eligibility criteria and were included in the study. There were 35(43.8%) Males and 45(56.2%) females in this study population. The average age was 63.5 years.

The primary outcome studied was the outcome of DAIR surgery. A total of 55 (68.75%) patients had documented successful outcomes with clinical resolution of infection. 25 (31.25%) had “unsuccessful” outcomes and these patients required further revision surgery for their PJI. Mean time interval between index surgery and the onset of symptoms of infection was found to be 7.29 months (\pm 11.83 months). Baseline information of the study subjects are summarised in Table 1.

A total of 56 (70%) patients in the study population had at least one comorbid condition and 24 (30%) patients did not have any comorbid condition. Of the 24 patients without any comorbid conditions, 19 (79.2%) patients were treated successfully, in comparison to unsuccessful outcomes in 5 patients (20.8%). If any single or combination of comorbidities was considered, 36 patients (64.3%) were treated successfully and 20 (35.7%) patients had treatment failure. Differences in outcomes were not significantly influenced by presence or absence of comorbidities ($p=0.732$). Comorbidities in the study population are summarised in Table 2.

The antibiogram of culture-positive cases is summarised in Table 3. Of the 80 cases, 27 (33.7%) cases were culture negative and 53 (66.2%) cases were culture positive. Among

Table 1 Baseline Information of the study population

Demographic variable	Value
Total Study Population Size	$N=80$
Gender	
Males, n (%)	35 (43.75%)
Females, n (%)	45 (56.25%)
Average age (years)	63.5 years
Mean Body Mass Index (kg/m^2)	28.6 (\pm 6.2)
Mean interval between Index surgery and Onset of infection	7.29 months (\pm 11.83 months)
Outcomes of DAIR	
Successful, n (%)	55, 68.75%
Unsuccessful, n (%)	25, 31.25%
Culture characteristics	
Culture positive, n (%)	53 (66.2%)
Culture negative, n (%)	27 (33.7%)

N Number

Table 2 Comorbidities in the study population

Patients with comorbidities	n (%)
Diabetes (DM) only	9 (11.3%)
Hypertension (HTN) only	19 (23.8%)
Diabetes and Hypertension	18 (22.5%)
Multiple (DM, HTN with CAD/CKD, Hypothyroidism)	7 (8.8%)
Rheumatoid Arthritis	3 (3.8%)
No comorbidities	24 (30%)
Total	80 (100%)

CAD Coronary Artery Disease, CKD Chronic Kidney Disease, n Number

the culture-positive cases, 37 patients (69.8%) had successful outcomes when compared with 18 patients (66.7%) success in culture negative cases. Culture status of the patients undergoing DAIR did not significantly affect outcomes of surgery for PJI ($p=0.082$).

Gram-staining characteristics of organisms were evaluated to study the influence of Gram-staining properties on outcomes after surgery for periprosthetic joint infection. Calculated as a *percentage of total number of infections* ($n=80$), 31 (38.8%) infections were due to Gram-positive organisms (GPC) and 25 (31.3%) were due to Gram-negative (GNC) organisms, showing equal preponderance of both types of organisms. There was no statistical difference in outcomes based on the Gram-staining properties of the organisms ($p=0.398$). The influence of culture-status and Gram-staining characteristics on outcomes is summarised in Table 4.

The *most common organism* isolated overall and within the GPC group was *Staphylococcus aureus* ($n=20$), out of

Table 3 Antibiogram of PJI cases included in the study

Organism	n (%)
Gram-positive organisms	30 (36.1%)
Methicillin-Sensitive <i>Staphylococcus aureus</i> (MSSA)	19 (22.8%)
Methicillin-Resistant <i>Staphylococcus aureus</i> (MRSA)	4 (4.8%)
Methicillin-Sensitive <i>Staphylococcus epidermidis</i>	2 (2.4%)
<i>Streptococcus pyogenes</i>	2 (2.4%)
<i>Streptococcus mutans</i>	1 (1.2%)
<i>Enterococcus faecalis</i>	4 (4.8%)
Gram-negative organisms	26 (31.3%)
<i>E. Coli</i>	9 (10.8%)
<i>Klebsiella pneumoniae</i>	6 (7.2%)
<i>Pseudomonas aeruginosa</i>	3 (3.61%)
<i>Enterobacter cloacae</i>	4 (4.8%)
<i>Acinetobacter</i> species	3 (3.61%)
<i>Serratia marcescens</i>	1 (1.2%)
Acid-Fast Bacteria	1 (1.2%)
Mycobacterium tuberculosis	
n = Number-Negative cases	29 (35%)

which 4 (20%) were MRSA. In the GNB group, *E. Coli* was the commonest organism isolated ($n = 9$).

Of the 25 patients with treatment failures, 22/25 (88%) of cases underwent 2-stage revision arthroplasty. Of these 21/22 (95.4%) went on to have successful outcomes with eradication of infection at most recent follow-up, with one case requiring re-debridement 3-months after the second-stage of the 2-stage revision procedure. Three patients underwent single-stage revision arthroplasty, 2 of which were managed successfully.

Infections were classified as early or peri-operative (onset of symptoms less than 1-month after index surgery) and late acute hematogenous infections (onset more than 1-month after index surgery, with symptom duration less than 2 weeks). In this study, there were 25 (31.3%) early infections and 55 (68.7%) late infections. 19 (76%) of “early” infections and 36 (65.5%) of “late” infections

had successful outcomes. The outcomes were comparable and there was no statistically significant difference in outcomes ($p = 0.890$) between the two groups (early versus late).

Discussion

Periprosthetic Joint Infection (PJI) after total knee arthroplasty is a perplexing problem that causes considerable concern to both patients and operating surgeons. Periprosthetic infections are on the rise with increasing number of total knee replacements being performed in India and abroad. The treatment for PJI after TKA often causes considerable burden on both finances and health of the patient, which has significant ramifications in a country like India, where access to healthcare and affordability of patients is severely constrained [11]. It is not difficult to comprehend that this procedure is popular in India due to several advantages. First, the cost of the procedure is cheaper comparable to a single-stage or two-stage revision arthroplasties. Second, two-stage revisions can lead to considerable joint pain and reduced mobility in the interim period leading to restriction of daily activities and thereby livelihood. Third, revision arthroplasty leads to considerable bone loss, soft tissue degradation and can lead to periprosthetic fractures, especially in elderly patients with osteoporosis, during the surgery leading to suboptimal outcomes.

This study shows that DAIR can result in successful outcomes if performed meticulously irrespective of comorbid conditions and the causative organisms.

The influence of the time interval between onset of infection after index surgery and its influence on success rate of DAIR is debatable. Our study shows that the time interval between onset of infection and the index surgery does not significantly influence the outcome of DAIR as all patients reported good outcomes irrespective of the interval. This is similar to the results reported by Bene et al. [12] who concluded that the timing of onset of infection after index

Table 4 Influence of microbiological factors on outcomes after DAIR

Microbiological factors	Outcomes		p value
	Successful (n, %)	Unsuccessful (n, %)	
Culture status of infection (Total $N = 80$), (n, %)			
Culture positive (53, 66.2%)	37/53 (69.8%)	16/53 (30.2%)	0.082
Culture negative (27, 33.7%)	18/27 (66.7%)	9/27 (33.3%)	
Staining Characteristics ^a			
Gram positive (31, 38.8%)	22/31 (71%)	9 (29%)	0.398
Gram negative (25, 31.3%)	15/25 (60%)	10 (40%)	

^aTotally bacteria were identified by microscopy and Gram staining in 56 infections, but organisms cultured were 53. Three cases remained culture negative

surgery does not reduce the likelihood of success rate following DAIR for PJI. Several studies have reported good results when patients are treated early (< 15 days) with DAIR following onset of infection to eradicate the formation of biofilm. Kuiper et al. [13] recommended that patients should be operated within 1 week of onset of symptoms with a meticulous surgical technique using gentamicin sponges to obtain successful outcomes. Similarly, a prospective multicentre study published by Cobo et al. [14] reported better success rates in patients who underwent early surgery following onset of infection when compared to patients who underwent surgery late. In this study we performed DAIR within 2 weeks of the onset of the symptoms of infection, with successful outcomes in majority of the patients. Early detection of infection and treatment may be associated with improved outcomes.

Several studies previously published have shown poor outcomes after DAIR for PJI with a reported failure rate of as high as 70% [4, 15]. However, most of these studies were conducted when precise guidelines for diagnosis and management for PJI have not been introduced. Moreover, these studies included both hips and knees and the surgical technique was not uniform. However, recent studies have reported good outcomes after DAIR when surgeons followed the guidelines laid down for diagnosis and management of PJI along with a uniform surgical technique [7, 12]. Our study, with a success rate of 67.5%, shows that good results can be obtained with DAIR. A standardised surgical approach, meticulous removal of infected material and implementation of antibiotic protocols in conjunction with an infectious diseases' specialist may contribute to improved outcomes.

Influence of Patient Comorbidities on Outcomes of DAIR

The presence of medical comorbidities such as diabetes, obesity, hypothyroidism has shown to result in suboptimal functional outcomes and predispose to increased complications following TKA [16, 17]. Our assessment of the influence of comorbidities on the success rate after DAIR in our study group did not reveal any significant differences between patients with comorbidities and those who did not have any comorbidity. These results are similar to those reported by Buller et al. [5], Narayanan et al. [7] who reported no difference in the success rate of patients based on their body mass index (BMI), Diabetes, ASA grading and presence of inflammatory arthritis. However, other studies have reported suboptimal outcomes in patients with atrial fibrillation, chronic obstructive pulmonary disease (COPD), diabetes and, therefore, have recommended two-stage revision arthroplasty in this subset of patients [12]. We believe

our analysis is limited by the small sample size and thereby precludes us from arriving at any definite conclusions.

Influence of Microbiological Factors on Outcomes

The percentage of patients infected with culture-negative organisms in our study group is 33.7%, which is high compared to previous studies [4, 5, 7]. One probable reason for the higher rate of culture-negative cases is that some of these patients were referred from other centres and were already started on antibiotics [18]. Previous studies have shown that infection with Methicillin-Resistant Staphylococcus Aureus (MRSA) is an independent risk factor contributing to failure after DAIR [19]. Similarly, culture-negative infections are difficult to manage due to lack of specific antibiotics. However, we did not find any significant differences in the success rate among patients based on the organism isolated or culture-sensitivity. This is similar to the findings of Fehring et al. [4] and Narayanan et al. [7] who reported no difference in outcomes based on the organism identified.

This study has certain limitations. The retrospective nature of the study results in a heterogenous population group with a limited sample size and a relatively short follow-up (1 year). The second limitation of this study is that we have included only patients who underwent early debridement within 2 weeks following onset of infection and did not include the results of patients who underwent “delayed DAIR” (which was performed in cases with symptom duration more than 2 weeks). The third limitation was the antibiotic duration was not uniform among all the patients as it was given as per the discretion of infectious disease specialist and patient symptoms. However, the strength of this study is that a uniform standardised surgical technique of DAIR was performed at a single centre and by a single surgeon thereby ensuring that surgical technique-dependant factors did not influence the outcomes assessed. Another strength of the study is the complete follow-up of all patients who met the eligibility criteria. There was no loss to follow-up, with details available on subsequent revision procedures for patients who unfortunately had persistent infections after DAIR.

Conclusion

Early-DAIR for periprosthetic joint infections of the knee in the Indian population is associated with good outcomes and successful eradication of infection in a majority of cases. Host factors like patient comorbidities did not influence outcomes after DAIR. Microbiological characteristics of the PJI like early versus late infections, culture status, Gram-staining properties of organisms and antibiotic resistance patterns of common pathogens (like MRSA) did not

significantly influence outcomes of DAIR. DAIR is a very promising strategy to deal with early and late hematogenous infections after TKA in the Indian scenario. Treatment failures still occur, and are distressing both for the patient and the surgeon, and these persistent infections need to be studied in detail to improve outcomes in the future.

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Compliance with Ethical Standards

Conflicts of Interest The authors have no conflicts of interest to declare.

Ethical Approval This study was approved by the Institute Ethics Committee.

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