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REVIEW ARTICLE

Aggressive Early Debridement in Treatment of Acute Periprosthetic Joint Infections After Hip and Knee Replacements

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Abstract:

Background:

Periprosthetic Joint Infection Remains a Dreaded Complication After Hip and Knee Replacement Surgery.

Treatment Options for Acute Postoperative and Acute Hematogenous Infections Include Arthroscopic or Open Debridement With Retention or Exchange of the Prostheses. This Review Article Aims to Summarize the Evidence for Management of Acute Postoperative And Acute Hematogenous Infections.

Methods:

A Systematic Literature Search Was Performed Using a Computer-based Search Engine Covering Medline (OvidSP), PubMed Database (U.S. National Library of Medicine, National Institutes of Health), Embase, Web of Science, Cochrane and Google Scholar for Relevant Articles.

Results:

Common Themes Around Treatment of Acute Postoperative and Acute Hematogenous Infections Discussed in this Review Include the Timing of Intervention, Description of the Optimal Procedure and How we Perform it at our Institution, the Role of Arthroscopic Debridement, Most Commonly Isolated Micro-organisms and Prognostic Factors for Infection Control.

Conclusion:

Success in Treating Acute Postoperative and Acute Hematogenous Infections Depends on Early Diagnosis and Aggressive Surgical Debridement Combined With Effective Antibiotic Therapy.

Keywords: Acute, Arthroplasty, Debridement, Hip, Irrigation, Knee, Periprosthetic joint infection.

INTRODUCTION

Despite all precautions taken in patient selection and patient optimization preoperatively, periprosthetic joint infection (PJI) after hip and knee replacements remains an important yet difficult complication to manage. While historical rates of early PJIs have been reported as high as 9.5% [1], nowadays the infection rates have declined to less than 2% [1, 2] after primary and up to 6% after revision surgery [3]. However, a recent study by Avram *et al.* [4] evaluating 30-day hospital readmission rates after joint arthroplasty showed that infections accounted for the majority of

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readmissions (23%).

Several systems for classification and staging of PJIs have been proposed [5]. However, the most widely accepted classification system was devised by Tsukayama *et al.* [6] and comprises four categories based on the clinical presentation as follows: (1) positive intraoperative cultures when at least two specimens obtained at the time of revision surgery are positive for the same organism on culture (2) early post-operative infection that occurs less than 1 month post-operatively (3) late chronic infection that develops with an insidious clinical onset one month or more from the primary operation and (4) acute hematogenous infection which is a result of hematogenous spread of an organism from a remote site to the affected joint where the prosthesis has been implanted. Patients found to have a positive intraoperative culture are usually managed with six weeks of intravenous antibiotics and no further operative intervention is needed [5, 6]. For late chronic PJI, two-stage exchange procedure is considered the gold standard treatment and is associated with good rates of infection control [1, 7 - 9]. In early post-operative and acute hematogenous infections, open or arthroscopic debridement with retention or exchange of the prostheses and antibiotic therapy has been conventionally the treatment of choice [10 - 13]. The potential advantages with such approaches in acute infection over a two-stage procedure would be avoiding the technical difficulty of the surgery involved, the morbidity and costs of prolonged immobilization of patients and possibly restoring the full function of the affected limb. The main aim of early aggressive debridement is to control the infection prior to biofilm formation, and hence the importance of intervening in a timely fashion [14].

This review article aims to summarize the evidence for management of acute postoperative and acute hematogenous infections after hip and knee replacements with emphasis on timing of intervention, description of the optimal procedure and how we perform it at our institution, the role of arthroscopic debridement, most commonly isolated micro-organisms and prognostic factors for infection control.

ACUTE INFECTION AND TIMING OF INTERVENTION

There is currently no consensus on the definition of acute infection and the optimal time for effective intervention [15, 16]. Tsukayama *et al.* [6] defined infections occurring within 4 weeks postoperatively as early infections. Toms [17] proposed a classification in which stage I infections occur within the first six weeks after the surgery. Zimmerli *et al.* [18] defined early infection as an infection that occurs within the first two months postoperatively, while Coventry [19] accepted a 3 months cut-off following the index operation.

On the other hand, acute hematogenous infection is usually associated with a documented or suspected antecedent bacteraemia and is characterized by acute onset of symptoms, involving a well-fixed prosthesis that has been functioning properly for months or years [5, 6]. The most frequent primary seeding site is skin and soft tissue infections [14]. However, other sources of infection may include the urinary, respiratory, and gastrointestinal tracts, as well as recent dental work [20].

Recent clinical practice guidelines by the Infectious Diseases Society of America [16] suggest performing an incision and drainage in patients diagnosed with a periprosthetic infection who have a stable prosthesis without a sinus tract and are within approximately 30 days of prosthesis implantation or less than 3 weeks of onset of infectious symptoms. Evidence from the literature varies in relation to the optimum time window of intervention with debridement, irrigation and prosthesis retention after the commencement of clinical symptoms and signs of infection [21, 22]. There is no dispute though, that rapid intervention is a primary prognostic factor because it may prevent the formation of biofilm by the infecting bacteria [23]. In fact, it has been reported that early biofilms are relatively unstable and so more susceptible to elimination by host defence systems and microbiological agents [24]. For example, Brandt *et al.* [25] showed that a higher probability of treatment failure was strongly associated with the initiation of debridement later than 2 days after onset of symptoms.

Aboltins *et al.* [26] highlighted that the short median duration of 7 days until the debridement, was a key to excellent outcomes. Similarly Crockarell *et al.* [27] suggested a 6 days cut-off from onset of symptoms for early intervention. Meehan *et al.* [28] reported worse infection control rates when the treatment was started after 4 days. Sukeik *et al.* [11] reported good infection eradication after total hip replacement (THR) when the intervention was commenced within 5 days (90% infection control vs. 77% for treatment within 6 weeks) and another case series by Peel *et al.* [29] showed better outcomes when treatment was instigated within 24h of symptoms onset.

HOW TO PERFORM THE IRRIGATION AND DEBRIDEMENT (I&D)

The best approach to the debridement procedure varies in different reports. However, it is important that the joint is opened *via* the pre-existing wound under aseptic conditions [30], and then a complete synovectomy is performed. The debridement should include an aggressive removal of all non-vital and infected periarticular tissues, the cement, wires, cables and non-absorbable sutures. The debridement should only be performed if the prosthesis is stable, so this should be confirmed carefully intra-operatively.

Several authors [6, 11, 26, 31 - 33] suggested exchanging the polyethylene liner or modular parts of the prosthesis, especially for total knee replacements (TKRs) to access the posterior capsule and perform an extensive debridement. In particular, a recent multi-centered study including hip and knee arthroplasties found that exchanging the modular component of the prosthesis reduced the risk of failure by 33% [31]. Additionally, the early removal of all modular components may prevent formation of the resistant biofilm and reduce the overall bacterial burden. All retained components should be scrubbed with bacterocidal solutions such as sodium hypochlorite (Dakin's solution) [2], or diluted betadine [11]. Copious irrigation with 6-9L using pulse lavage should be performed [2, 11, 32]. However some reports in trauma surgery have expressed concerns regarding the use of high pressure lavage as it may potentially spread the infection deeper [34, 35]. Once the debridement is completed, the operating team should completely change gloves, gowns and surgical setup, and the modular components are then exchanged [36, 37]. Kelm *et al.* also [38] showed good outcomes using the vacuum-assisted closure (V.A.C.) system after debridement in treatment of early PJI with eradication of infection in 26/28 cases at a mean follow-up of 36 months (range 12-87 months). At our institute, we perform an open aggressive debridement including a complete synovectomy, debridement of all aspects of the infected joint, irrigation with hydrogen peroxide, Betadine® solutions and pulsatile lavage using at least 9 litres and then exchanging all mobile components.

SINGLE VS. MULTIPLE PROCEDURES

There is no conclusive evidence or consensus as to whether a single surgical debridement is sufficient or whether multiple repeat procedures are necessary for optimal treatment. Mont *et al.* [37] in their series of 24 infected total knee arthroplasties performed 1-3 debridements and achieved an overall 83% infection control at 48 months (range 24-140 months) follow-up. In another series of 10 infected TKRs, Tsumura *et al.* [39] reported good results with repeated synovectomy, debridement, and continuous irrigation (7-29 days) with an overall 80% infection control. However, various studies in the literature [10, 40, 41] showed no extra advantage when patients were treated with repeat debridements. In fact, a recent study comparing patients receiving a single *vs.* multiple surgical debridements showed that the strategy of a single surgical debridement proved to be at least as effective in controlling the infection and retaining the hip implant as routinely performing multiple debridements, without compromising the clinical end result [42]. On the other hand, repeat cultures during the second or third debridement identified resistant bacteria even though the initial cultures showed growth of sensitive pathogens [42]. Another multi-centered study reported that out of the 83 knees that had undergone previous irrigation and debridement, 28 (34%) failed subsequent two-stage revision and required reoperation for persistent infection [43]. Similarly, Gardner *et al.* [44] reported that the success of two-stage revision due to infection in TKR may be affected after a failed open debridement associated with polyethylene liner exchange. At our institute, following failure of a first attempt, we perform a maximum of two further debridements before proceeding to any other surgical intervention, taking into consideration patients' comorbidities and risks for surgery and patients' preference for type of treatment. Our results show an overall 77% infection control rate at 5 years follow-up using this strategy [11].

HOW MANY SAMPLES?

The definitive diagnosis of PJI is made when the same organism is isolated from at least 2 intraoperative cultures of specimens taken during the debridement surgical procedure. At least 3 and preferably 5-6 periprosthetic intraoperative tissue samples, joint fluid sample and the explanted component itself should be sent to the microbiology lab for aerobic and anaerobic cultures [2, 15, 16, 45, 46]. The samples should be collected from areas that macroscopically appear infected based on the clinical suspicion of the surgeon; these should include superficial, deep and periprosthetic tissues [2]. The incubation period for cultures should be at least 7 days. However, reports published recently suggest prolonging incubation for 14 days as this increases the chances of identifying organisms that otherwise may remain culture negative [47, 48]. Implant sonication has also proven to be an accurate tool in isolating bacteria from the biofilm on the extracted implant even with patients who are receiving antibiotic treatment [15, 16, 49]. It is worth noting that

intraoperative cultures, although presumed to be the gold standard for identifying the infected organism, are possibly subject to false-positive and false negative results. In some cases despite the presence of clear signs for infection including gross purulence, cultures may still be negative [50]. Possible causes may be inappropriate collection of samples, short incubation duration and the use of antimicrobial therapy prior to samples collection [51]. Interestingly though, Ghanem *et al.* [52] demonstrated that the administration of preoperative antibiotics to patients with a positive preoperative joint aspirate did not interfere with the isolation of the infecting organism from intraoperative culture samples more than when antibiotics were stopped.

ROLE OF ARTHROSCOPY

Arthroscopic treatment is attractive as a less invasive procedure than open debridement. However, only few reports have been published demonstrating the role and outcomes of I&D with arthroscopy. The main limitation with an arthroscopic procedure is the difficulty to access all compartments and parts of the joint to perform a proper debridement, especially the posterior compartment in TKR, which is limited by the presence of the insert.

Flood and Kolarik [53] were the first in 1988 to report successful arthroscopic treatment in 2 patients with acutely infected TKRs. Waldman *et al.* [54] showed that only 6/16 patients (38%) presenting with acute infection within 7 days or less of a TKR retained their prosthesis at a mean follow-up of 64 months (range, 36-151 months). They concluded that an arthroscopic debridement should be reserved to selected cases such as the anticoagulated or medically unfit patients. Various reports have since been published on the role of arthroscopic debridement in TKRs. For example, Dixon *et al.* [55] and Chung *et al.* [56] reported that in 9 out of 15 patients (60%) and 10 out of 16 patients (62.5%) respectively, infection has been controlled. Furthermore Chung *et al.* [56] suggested the use of at least one arthroscopic posterior portal to get access to the posterior compartment in order to perform a more meticulous irrigation and debridement.

While knee arthroscopy has shown a possible role in managing periprosthetic infection, arthroscopy of the hip joint for infected hip arthroplasty is less well described with only 11 cases in the literature reported to have undergone an arthroscopy in the setting of PJI [57]. Hyman *et al.* [58] observed no recurrence of infection in 8 patients treated with arthroscopic irrigation and debridement of late acute periprosthetic infection and then a prolonged course of antibiotics at 70 months follow up. However, they suggested that effective treatment requires early diagnosis, prompt arthroscopic debridement, well-fixed components, a sensitive microorganism, and patient tolerance to and compliance with the antibiotic therapy. Similarly McCarthy *et al.* [59] reported successful treatment in 2 patients treated with arthroscopic lavage and debridement plus intravenous antibiotics. It is important though to note the technical complexity of hip arthroscopy in evaluation and treatment of infection due to the limitations of performing traction and the presence of intra-articular scar tissue and adhesions.

INFECTION CONTROL RATES

The literature indicates that infection control rates using an I&D strategy and prosthesis retention are lower compared to those reported after one or two-stage revision surgery [67]. However, I&D remains an attractive option for treating acute PJIs with an overall infection control rate ranging between 15-91% Table (1) and average infection control after a single procedure of 45.9% according to the review by Romano *et al.* [68] and 51.3% according to Chen *et al.* [69].

Romano *et al.* [68] highlighted that differences in patient selection and indications for surgery occur between centers treating infection, and hence standard protocols should be used to provide more homogenous results. Furthermore, differences in antibiotic regimes and duration of administration postoperatively may also influence infection control. The lack of standardized surgical techniques and the fact that not all studies exchanged modular components may also explain the variable results. Although changing the liner should theoretically reduce the total amount of bacteria in the joint and lead to better infection control rates, there are currently no randomized studies that demonstrated the superiority of one treatment over the other.

In a recent systematic review by Anagnostakos and Schmitt [22] which included 11 studies reporting on 292 cases of periprosthetic hip infections, five different treatment modalities including debridement, antibiotics, irrigation, and retention (DAIR) of the prosthesis have been identified. As expected, older studies showed lower infection control rates which the authors related to the advances in surgical techniques, introduction of vacuum assisted therapy and the use of pulsatile lavage. On the other hand, the study was inconclusive for favouring a treatment strategy over another due to the variability of antibiotics administered from four weeks up to one year postoperatively.

Among a cohort of 40 patients who underwent I&D and exchange of the modular components for acute hematogenous infections, Konigsberg *et al.* [63] reported a high rate of mortality with 25% of patients dying within two years of treatment. The authors concluded that acute hematogenous infection might be a marker of poor general health as almost half of the patients in this series had some critical medical co-morbidity that rendered them immunocompromised and may have predisposed them to developing infection.

Table 1. Studies reporting infection control rates after irrigation and debridement.

Author, year	Type of study	Joint	No. of implants	No. of eradicated infections	% of eradicated infections	Exchange of mobile part	Mean Follow-up (months)
Aboltins 2007 [32]	Retrospective	Hip/knee	20	18	90	Partly	32
Aboltins 2011 [26]	Prospective	Hip/knee	17	15	88.2	Yes	28
Ackermann 2014 [21]	Retrospective	Hip/knee	50	46	91.6	Partly	24
Azzam 2010 [40]	Retrospective	Hip/knee	104	46	44	29%	68
Betz 2014 [60]	Retrospective	Hip	38	7	18.4		
Bradbury 2009 [61]	Retrospective	Knee	19	3	15.85	Yes	43
Brandt 1997 [25]	Retrospective	Hip/knee	33	12	36.3	No	78
Crockarell 1998 [27]	Retrospective	Hip	19	4	21.1	No	75.6
Deirmengian 2003 [62]	Retrospective	Knee	31	11	35	No	48
Konigsberg 2014 [63]	Retrospective	Hip/knee	42	33	76	Yes	56
Koyonos 2011 [64]	Retrospective	Hip/knee	102	64	62.7	No	54
Kuiper 2013 [41]	Retrospective	Hip/knee	91	60	66	Partly	35
Lora-Tamayo 2013 [31]	Retrospective	Hip/knee	341	199	55	Yes	
Mont 1997 [37]	Prospective	Knee	24	20	83	Yes	48
Marculescu 2006 [66]	Retrospective	Hip/knee	91	56	56.5	Partly	24
Peel 2013 [29]	Retrospective	Hip/knee	112	94	83.9	Partly	33.5
Sukeik 2012 [11]	Retrospective	Hip	26	20	77	Yes	79
Tsukayama 1996 [6]	Prospective	Hip	41	35	68	Yes	82

Despite the wide use of I&D, it is still based on non-randomized retrospective studies and/or expert opinion. Large cohort studies or randomized controlled trials with high power, to define who the best candidates for this treatment option are and what the ideal procedure should be are still lacking.

PROGNOSTIC FACTORS FOR INFECTION CONTROL

Many studies have analyzed factors associated with success or failure of the I&D procedure. One of the most recognized factors associated with high failures is infection due to methicillin-resistant *Staphylococcus aureus* (MRSA) [69]. The poor prognosis and high risk of re-infection due to MRSA is linked to the limited availability of selective antibiotics and the potential insurgence of glycopeptide resistance in vancomycin-treated patients [60, 70]. Zürcher-Pfund *et al.* [71] treated 21 infected TKRs with a combination of debridement and antibiotics and followed them up for a mean of 7 years. They concluded that debridement and retention of prosthesis in infected TKRs is associated with high failure if MRSA is the infecting pathogen as opposed to streptococcal infections. One of the possible explanations is that MRSA is more virulent and hence adapts locally forming a biofilm with phenotypic resistance to many antibiotics [72]. Accordingly, the authors suggested that the decision for I&D with retention of the knee prosthesis should be dependent in the first instance on the nature of the infecting pathogen. Betz *et al.* [60] reported similar results in infected hip arthroplasties, with an average 21% failure rate of *Staphylococcus aureus* infections compared to no failure of streptococcal infections treated with DAIR. Interestingly, Lora-Tamayo *et al.* [31] reported that the treatment of MRSA PJIs was not less successful than methicillin-susceptible *Staphylococcus aureus* (MSSA) infections if rifampin-based antibiotic combinations were administered during the first 30 days after debridement to both groups.

While there are many studies describing the outcomes of PJI caused by MRSA, there are only few studies addressing the outcomes due to coagulase-negative staphylococci [73]. A recent study by Peel *et al.* [29] confirmed the clinical challenge in treating MRSA PJIs but reported excellent outcomes in eradicating coagulase-negative *Staphylococcus* infections treated with DAIR and a combination of rifampin and fusidic acid.

Similarly, Aboltins *et al.* [32] reported higher rates of infection control when patients were treated with oral antimicrobials, including fusidic acid and rifampicin together with the I&D procedure. In a randomized controlled trial, Zimmerli *et al.* [74] demonstrated that a combination of rifampin and ciprofloxacin for 3 to 6 months as an oral

antibiotic showed 100% infection control compared to 58% infection control when using ciprofloxacin alone. Morata *et al.* [13] reported recently that DAIR and linezolid with or without rifampicin is associated with a high remission rate and is an alternative treatment for infections due to fluoroquinolone and/or rifampicin-resistant staphylococci. Another important prognostic factor is the duration of symptoms prior to surgical intervention, *i.e.* better results are reported in patients with short duration of symptoms (< 4 weeks) presenting after the index procedure [15, 75]. Additionally, I&D should not be considered in patients with polymicrobial infection or in the presence of a sinus tract at the time of the debridement as this increases the risk of treatment failure (hazard ratio 2.84) [65, 76].

Other factors associated with failure are post-operative drainage for more than 2 weeks [77], a hinged prosthesis, loose components with radiologic evidence of osteitis and intra-articular purulence and retention of exchangeable components [76]. Comorbidities such as rheumatoid arthritis, diabetes mellitus, malignancy, use of immunosuppressive drugs and obesity have also been associated with increased risk of re-infection [22].

In particular, a body mass index (BMI) of more than 30 and having more than two co-morbidities has been shown to increase the risk of treatment failure [78].

CONCLUSION

The present review shows that irrigation and debridement, in combination with exchange of the modular components and optimal antibiotic therapy is effective in treating acute post-operative and acute hematogenous PJIs. However, patient selection is also imperative to avoid specific risk factors associated with high failure rates.

LIST OF ABBREVIATIONS

BMI	=	Body mass index
DAIR	=	Debridement antibiotics, irrigation, and retention
I&D	=	Irrigation and debridement
MRSA	=	Methicillin-resistant <i>Staphylococcus aureus</i>
MSSA	=	Methicillin-susceptible <i>Staphylococcus aureus</i>
PJI	=	Periprosthetic joint infection
TKR	=	Total knee replacement
V.A.C	=	Vacuum-assisted closure

CONFLICT OF INTEREST

Each author certifies that he or she, or a member of his or her immediate family, has no commercial interests that might pose a conflict of interest in connection with this work.

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