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QUESTION 5: What is the minimum necessary volume of irrigation solution to use in debridement, antibiotics and implant retention (DAIR) treatment of acute periprosthetic joint infection (PJI)?

RECOMMENDATION: We recommend that 6-9L of irrigation solution, including saline or antiseptic solution such as sterile dilute povidone-iodine, is used during DAIR treatment of acute PJI.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 90%, Disagree: 7%, Abstain: 3% (Super Majority, Strong Consensus)

RATIONALE

To date, there are no reported clinical studies relating to the optimal volume of irrigation required during DAIR treatment of PJI. However, variable outcomes have been reported with different institutions employing individual protocols for volumes of irrigation.

Few studies provide limited secondary data with regards to the ideal volume of irrigation to be used during total joint arthroplasty (TJA) in general and treatment of an infected joint in particular. In one such study, the authors were able to determine that four liters of sterile saline pulse lavage were sufficient to remove bone and polymethyl methacrylate (PMMA) debris exceeding 1µm in size from the joint during TJA. The authors extrapolated from their results that bacteria might effectively be removed with the same amount of irrigation given the similarity in size to the particulates assessed [1]. This model did not consider the effect of the developing bacterial biofilm on infected arthroplasty implants. DAIR has traditionally been thought to reduce the bacterial load and be effective in the acute period given that bacteria theoretically had not yet formed a glycocalyx biofilm. In another study, the authors used an in vitro model to determine the efficacy of biofilm removal from arthroplasty implants using high-pressure pulsatile lavage. Three liters of normal saline were used over an area measuring 1cm^2 recreating a prosthesis covered in *Staphylococcus aureus* biofilm. The authors concluded that pulse lavage is not able to sufficiently debride pre-existing biofilm. The volume of irrigation solution required was not investigated as a primary endpoint and the authors caution against extrapolating the results to clinical scenarios as their in vitro model potentially overestimated the amount of biofilm debrided by three liters of sterile saline pulse lavage [2]. More important than the volume of irrigation, researchers have found that the presence of staphylococcal infection, an elevated American Society of Anesthesiologists (ASA) score, or purulence were more likely to determine failure.

A comprehensive systematic review of the literature relating to open DAIR treatment of acute postoperative and hematogenous periprosthetic hip and/or knee joint infections, with or without modular component exchange, was performed. Databases searched include: PubMed, Embase, Cochrane Review and Google Scholar. Initial query generated 664 articles. Review articles and book chapters were excluded, while all references from such sources were screened for inclusion (spanning from 1990-2017). We included all Level I-IV studies that specified a certain volume of irrigation used per procedure and recorded the type of solution(s) used, mode of lavage administration, use of additive(s) and number of irrigation and debridements (I&Ds) performed. We included cases whereby some of the modular components may have been exchanged, but excluded those with dedicated planned staged exchanges. A total of 14 studies met the aforementioned criteria (Table 1) [3–16].

Typically, around 6 to 9L of solution were used during a single DAIR treatment, with 12 of the 14 studies utilizing up to 9L or more of irrigation solution. The evidence base for the specific irrigation volume is poorly defined within all studies, and recommendations for specific volumes in both primary and review articles reference consensus data obtained from previously published guidelines or individual protocols. [17–22] Therefore, this systematic review represents the body of evidence of actual irrigation volumes reportedly used in the literature.

No studies currently exist directly linking the necessary volume of irrigation to use in DAIR in acute PJI. Based on several retrospective studies, we extrapolate that the use of 6-9L of irrigation solution may be required when treating acute PJI. Prospective studies evaluating the volume of irrigation used as a study endpoint are required to better elucidate the optimal volume of irrigation in DAIR treatment of PJI.

TABLE 1. DAIR studies

Reference (Author, Year)	Study Design	n (acutePJIs)	Irrigation Solution	Additives	Volume Per Procedure (L)	Modular Revision	Infections Controlled
Mont et al (1997)	Prospective	24	NS	None	10	Yes	83%
Azzam et al (2010)	Retrospective	104	NS	Antibiotics	9	Some	44%
Estes et al (2010)	Retrospective	20	Castile soap solution	None	6 to 9	Yes	90%
Koyonos et al (2011)	Retrospective	102	NS	Antibiotics	9	No	35%
Royo et al (2013)	Retrospective	34	NS	Betadine/Peroxide	9	Some	74%
Kim et al (2014)	Retrospective	20	NS	Betadine	6 to 9	Yes	100%
Moojen et al (2014)	Retrospective	68	NS	None	3 to 6	Yes	21%
Koh et al (2015)	Retrospective	52	NS	None	9	Some	71%
Sousa et al (2016)	Prospective	23	NS	Chlorhexidine	7	Yes	85%
Tornero et al (2016)	Retrospective	143	Sterile Water	None	6 to 9	No	88%
Bryan et al (2017)	Retrospective	90	NS	None	6 to 9	Some	87%
Di Benedetto et al (2017)	Retrospective	20	NS	Betadine	6 to 9	Yes	80%
Duque et al (2017)	Retrospective	67	NS	Betadine/Dakin's/Bacitracin	12	Yes	69%
Narayanan et al (2017)	Retrospective	55	N/A	None	9	Yes	60%

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QUESTION 6: Is there a role for direct intra-articular antibiotic infusion following irrigation and debridement (I&D) for periprosthetic joint infection (PJI)?

RECOMMENDATION: The concept of achieving a minimum biofilm eradication concentration (MBEC) of antibiotics at the site of the infection is compelling. Despite the presence of retrospective studies reporting favorable outcome, because of heterogeneity in terms of adjunctive antibiotics, absence of a control group and small cohort size, the routine administration of intra-articular antibiotics in treatment of PJI is not justified. Prospective, randomized controlled trials (RCTs) are needed to support the routine use of intra-articular antibiotics as a stand-alone or adjunct treatment of PJI.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 92%, Disagree: 6%, Abstain: 2% (Super Majority, Strong Consensus)

RATIONALE

Current published evidence for intra-articular antibiotic infusion following irrigation and debridement for PJI is limited to small case series and retrospective cohort studies. The authors of all studies aimed to achieve higher concentrations of antibiotics at the site of the infection than is possible with systemic therapy. PJI is associated with the presence of biofilms and sessile bacteria that are encapsulated within a biofilm matrix are more difficult to eradicate than planktonic bacteria [1–7]. Biofilm is the single most important factor causing resistance of bacteria to antibiotics in the treatment of PJI. While modest antibiotic concentration can prevent biofilm formation, eliminating established biofilm is a different matter. Bacteria protected by biofilm requires concentrations that are orders of magnitude greater than the minimal inhibitory concentration for the planktonic forms of the same bacterium to eliminate resistant organisms that are protected by the glycocalyx.

A systematic review of the literature revealed that biofilm encapsulated bacteria requires MBEC of antibiotics that are several orders of magnitude (100-1000+) above the minimum inhibitory concentrations (MIC) sufficient to eradicate planktonic bacteria (Table 1). Currently, MBECs at the site of the joint infection are not achievable with traditional intravenous (IV) antibiotic therapy without systemic toxicity (Table 1). IV antibiotics generally do not achieve these levels of concentration in synovial fluid, but instead achieve levels around two to three times the MIC.