19 patients underwent multiple DAIR procedures [3]. Of the 19 patients who underwent multiple (two or three) DAIR procedures, 10 (52.6%) achieved implant retention with infection control. Of the 122 patients who underwent a single DAIR, 78 (63.9%) achieved implant retention with infection control. All failures underwent prosthesis removal and two-stage reimplantation. The difference in failure rate between those who underwent multiple DAIR and those who underwent a single DAIR was not statistically significant. This study was limited by several factors. The authors included both primary and revision surgeries, as well as a heterogenous mixture of acute postoperative PJI and late-hematogenous PJI. The manuscript also had no clear protocol for which patients underwent repeat DAIR or a different procedure. Furthermore, there was no protocol for patients to undergo additional DAIR or any notation of the timing. Patients who underwent a second DAIR greater than 20 days after the first DAIR had 97.4% lower odds of achieving success compared to patients undergoing the second procedure less than 20 days after the first [3].

A multicenter retrospective analysis by Urish et al. demonstrated 109 out of 216 patients who underwent DAIR after TKA required an additional procedure [4]. Of the 109 failures, 59 underwent repeat DAIR. Ultimately, of the patients who failed initial DAIR, only 28.4% had DAIR as their final procedure; thus, subsequent irrigation and debridement had a failure rate of over 70%.

Another retrospective study compared 64 patients who underwent DAIR (n = 39) versus two-stage revision (n = 25) within three months of primary TKA. Of the 39 patients who underwent DAIR, there were 24 failures (61.5%) and all 24 underwent repeat DAIR [5]. All 24 DAIR procedures failed to control the infection [5]. The DAIR patients underwent on average 3.2 additional surgical procedures (range 1-6) to control the infection whereas the two-stage exchange patients underwent a mean of 2.2 surgical procedures (range 2-4). A further study by Vilchez et al. of 53 THA and TKA patients with PJI treated with DAIR, demonstrated that the need for a secondary DAIR was predictive of failure [6].

The literature demonstrates a second DAIR procedure has, at best, equivalent success as an initial DAIR procedure. In order to avoid additional surgical procedures, resection arthroplasty should be considered after an initial DAIR procedure.

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QUESTION 12: What is the optimal length of antibiotic treatment following debridement, antibiotics and implant retention (DAIR) for acute periprosthetic joint infections (PJIs)?

RECOMMENDATION: The optimal length of antibiotic treatment following DAIR remains relatively unknown as there is considerable heterogeneity regarding the length, dose and administration of treatment. A minimum of six weeks of antibiotic therapy seems to be sufficient in most cases of PJIs managed by DAIR-provided surgical treatment.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 91%, Disagree: 8%, Abstain: 1% (Super Majority, Strong Consensus)

RATIONALE

Acute PJIs may be treated by DAIR [1,2]. In this setting, antimicrobial therapy is administered at high doses during the postoperative period. The median success rate for DAIR for management of acute PJI varies from 34.8 - 100% [3–23]. However, none of the published reports directly compare the outcome of DAIR in relation to the length of antibiotic treatment.

In addition, the details of antibiotic treatment such as the route of administration, dose and the duration of therapy, appear to be missing. Two studies, though not providing the route of antimicrobial treatment, stated that patients undergoing DAIR in the cohort received at least six weeks and a median of seven weeks (range, 3 to 39 weeks) of antimicrobial treatment [9,10]. Majority of the studies reporting the outcome of DAIR [3,5,7,13–18] used an antibiotic treatment regimen based up the algorithm proposed by Zimmerli et al. [1]. The latter consists of 7 to 14 days of intravenous antibiotics, followed by 3 to 6 months of oral antibiotics with activity against bacteria in biofilm (e.g., ciprofloxacin, adjunct therapy with rifampin).

Four studies report that intravenous antibiotic was used in their cohort, with or without adjunctive oral antibiotics during the course of treatment for a median duration of six weeks [8,12,19,24]. A single study discloses that the patients received oral antibiotics only after the DAIR procedure, with a duration of six weeks to lifelong treatment [2]. The remaining 11 studies used a combination of intravenous, followed by oral antibiotic therapy. In these studies, the median duration of intravenous antibiotic therapy was 6 weeks and among the seven studies which reported the duration of oral antibiotics, the median was 16 weeks (range 9 weeks to lifelong).

TABLE 1.Comparative studies addressing the length of antimicrobial therapy in the setting of PJI managed by DAIR

Ref	Design	N	Etiology	Antimicrobials	Observations
26	Observational, retrospective, one center	112	Various	6 weeks of β-lactams/ glycopeptides, followed by oral tratment	Length of therapy did not predict the likelihood of failure
35	Observational, retrospective, comparative, non-randomized, one center	60	Various (mostly Staphylococci)	Common use of rifampin and ciprofloxacin	A 6-week treatment was non-inferior than a 12-week treatment
36	Observational, retrospective, comparative, pre-post design, one center	50	Various (mostly Staphylococci)	Common use of rifampin and fluoroquinolones	An 8-week treatment was non-inferior than long standard treatments (3-6 months)
37	Obervational, retrospective, comparative,non-randomized, multicenter	87	Various (mostly Staphylococci)	Rifampin-based combinations	Same outcomes for 6-week and 12-week treatments
38	Multicenter Randomised Clinical Trial	63	Staphylococci	Levofloxacin + Rifampin	ITT analysis: 8-week treatment was non-inferior than 3-6 months. PP analysis : a trend towards non-inferiority was observed.

All studies included hip and knee prostheses. N, number of patients included (referring to those managed by debridement, antibiotics and implant retention); ITT, intention-to-treat; PP, per-protocol.

There appears to be a wide variation in the length of treatment, route of administration and the type of antimicrobial therapy that is selected for patients undergoing DAIR. The heterogeneity in the literature and the clinical practice may arise as a result of the fact that there are no reliable clinical or biological parameters that allows clinicians to assess the response to treatment and hence determine the optimal length of antimicrobial therapy [25]. There is a weak signal in the literature to suggest that after a "critical" period of antimicrobial therapy, no further improvement in outcome is encountered by extending the antimicrobial treatment. In fact, some investigators have stated that the length of antimicrobial therapy does not influence the outcome of treatment of PJI patients by DAIR [26]. To the contrary some investigators believe that prolonged antimicrobial therapy is more likely to lead to masking of the infection and a delay in identifying treatment failure [26,27].

There is little literature regarding the optimal route of administration of antimicrobial therapy. Majority of treating clinicians would recommend that patients undergoing DAIR should receive intravenous antimicrobials, at least initially. One observational non-randomized comparative study, concludes that the only factor associated with failure was the selection of oral antibiotics and not the duration of treatment [4]. The majority of studies that advocate the use of a six- to eight-week course of antibiotic therapy, state that intravenous antibiotics for two weeks followed by four to six weeks of oral antibiotics is optimal [27–34].

There are three observational non-randomized comparative studies showing no differences in success of DAIR when long or short course of antimicrobials were used (Table 1). In a study by Bernard et al., that included a cohort of 60 patients managed by DAIR, the success rate among patients treated for six weeks of antimicrobials was not lower than those treated for 12 weeks [35]. In 2012, Puhto et al. published a pre-post comparison of 50 patients with PJI treated for 8 weeks vs. 72 patients who received either 3 (hips) or 6 (knees) months of treatment, showing similar success rates (63 vs.67% in the intention-to-treat analysis, and 89 vs.87% in the per-protocol analysis) [36]. More recently, Chaussade et al. analyzed 87 episodes of PJI managed by DAIR, with similar success rates when patients were treated for 6 or 12 weeks [37]. All three studies included knee and hip cases, all type of organisms with a predominance of Staphylococci and varying antibiotic regimen.

One randomized multicenter study compared an 8-week course of levofloxacin plus rifampin vs.a long course, three of oral therapy for hip PJI and six months of therapy for knee PJI in the setting of Staphylococcal PJI managed by DAIR [38]. Although the number of patients included was low, the non-inferiority hypothesis of the 8-week course was proven in the intention-to-treat analysis (success rate of 73 vs. 58% for the short course and long course groups, respectively; n = 66), and a trend towards non-inferiority was observed in the per-protocol analysis (cure rate of 92 and 95%; n = 44) [38]. The results of the DATIPO study, an ongoing French multicenter randomized clinical trial comparing 6 weeks vs. 12 weeks of antimicrobial therapy for patients with PJI undergoing surgical management, including DAIR, is eagerly awaited.

While the results of high level studies are awaited and based on the evaluation of the available literature, it appears that six to eight weeks of antimicrobial therapy is the ongoing standard for patients undergoing DAIR. There is less evidence regarding the optimal route of administration, with majority of the studies advocating the initial treatment should include intravenous route. The type of antimicrobials is also based on the organisms isolated with studies proposing that antibiotics targeting biofilm, such as rifampin, should also be part of the treatment algorithm.

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QUESTION 13: What is the most effective combination of antibiotics in the treatment of acute periprosthetic joint infections (PJIs) caused by methicillin-resistant *Staphylococcus aureus* (MRSA) that has undergone surgical management with debridement, antibiotics and implant retention (DAIR)?

RECOMMENDATION: We recommend a combination of a parenteral antibiotic plus oral rifampin for one to six weeks, followed by rifampin and a companion highly bioavailable oral drug for additional three months, depending on the susceptibility profile of MRSA, patient tolerability and side effect profile.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 88%, Disagree: 10%, Abstain: 2% (Super Majority, Strong Consensus)