scrubbed in an effort to remove biofilm [11,13]. Various antibiotic solutions can be used intraoperatively, including dilute betadine and Dakin’s solution. Culture-driven systemic antibiotics are also important for successful treatment and co-treatment with rifampin should be utilized in Staphylococcal PJIs [6]. Prolonged or chronic antibiotic suppression may also be necessary. The use of local antibiotics in addition to the administration of systemic antibiotic agents is an area of consideration. Modular components and the exposed metal of megaprostheses can be covered with antibiotic eluting cement, though there is no clinical evidence comparing the efficacy of such methods versus more simple modular exchange.

The most important factors contributing to treatment failure are longer duration of symptoms, a longer time after initial arthroplasty, the need for multiple debridements, the retention of exchangeable components and PJI caused by MRSA [6,11,12]. One- or two-stage revision should be performed if DAIR fails [11,13].

In general, DAIR is a treatment option for acute PJI with a megaprosthetic with varying levels of success in selected and non-complicated patients. The heterogeneity inherent in these cases makes comparisons difficult and there is always some degree of individualization in choice of treatment.

REFERENCES


QUESTION 9: What factors are associated with the successful treatment of acute periprosthetic joint infection (PJI) using debridement, antibiotics and implant retention (DAIR)?

RECOMMENDATION: The following factors have been shown to be associated with treatment success in acute PJIs treated with DAIR:

- Exchanging the modular components during debridement
- Performing a debridement within at least seven days, but preferably as soon as possible, after the onset of symptoms
- Adding rifampin to the antibiotic regimen, particularly when combined with a fluoroquinolone, in cases of susceptible staphylococci
- Treatment with fluoroquinolones in cases of susceptible gram-negative bacilli

The following factors have been shown to be associated with treatment failure in acute PJIs treated with DAIR:

- Host related factors: rheumatoid arthritis, old age, male sex, chronic renal failure, liver cirrhosis and chronic obstructive pulmonary disease
- Prosthesis indication: fracture as indication for the prosthesis, cemented prostheses and revised prostheses
- Clinical presentation representing the severity of the infection: a high C-reactive protein (CRP), a high bacterial inoculum and the presence of bacteremia
- Causative microorganisms: S. aureus and Enterococci

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 92%, Disagree: 5%, Abstain: 3% (Super Majority, Strong Consensus)

RATIONALE

The success of DAIR depends on multiple host- and implant-related factors, clinical presentation, intraoperative variables, causative microorganism(s) and their antibiotic sensitivities and the antibiotic regimen. It is of note, that the described factors related to treatment outcome in some studies, are not always confirmed by others.

Most factors associated with success of DAIR are demonstrated in retrospective studies, entailing a high risk of selection bias, especially for those factors involving certain treatment strategies. Therefore, prospective validation is critical for most of the described variables and differences between cohorts should be taken into consid-
eration in interpreting risk factors. In addition, the success of DAIR depends on the definition of treatment failure and the total duration of follow-up, which also differed amongst the selected studies.

Factors that are consistently shown in the literature to increase the chance of treatment success are:

**Exchange of Modular Components**

The bacterial load detected on polyethylene is higher compared to metal components of prostheses, presumably due to its rough surface that favors the adherence of bacteria [1]. Therefore, exchanging the modular components will reduce the amount of biofilm present on foreign material. Moreover, removing the modular components during DAIR (i.e., femoral head and/or polyethylene component) provides better access to the joint capsule for radical debridement. Tsang et al. reviewed all cohort studies published between 1977 and 2015 on the outcome of DAIR in hip PJI. The success rate of DAIR in studies where all patients underwent modular component exchange was 73.9% (471/637 patients; 95% confidence interval (CI), 70 to 77) compared to 60.7% (245/404 patients; 95% CI, 56 to 65) in patients in whom modular components were retained (p < 0.0001) [2]. In addition, Grammatopoulos et al. demonstrated in a cohort of 82 acute hip PJsIs a treatment success of 93.3% when modular components were exchanged versus 75.7% when modular component were retained (p = 0.02) [3]. Smaller studies confirm the same in acute PJsIs of the knee [4,5]. The beneficial effect of modular exchange was also demonstrated as independent predictors of treatment success in large multi-center cohort studies evaluating the outcome of DAIR in hip and knee PJsIs caused by methicillin-resistant S.aureus (n = 345, hazard ratio (HR) 0.65, p < 0.026) [6], streptococci (n = 462, HR 0.66, p < 0.01) [7], and solely late acute PJsIs (n = 340, odds ratio (OR) 0.35, p = 0.02).

**Performing DAIR within at Least Seven Days after the Onset of Symptoms**

Several studies demonstrated that the duration of symptoms are significantly shorter in patients who were successfully treated with DAIR compared to patients in whom treatment failed [8-13]. In most studies, the most prominent difference between success and failure is observed using a symptom duration of one week as optimal cut-off [3,10,11,14,15]. Urish et al. demonstrated a treatment success rate of 52.2% in 216 knee PJsIs when DAIR was performed within one week after the onset of symptoms. Additional multivariate analysis in this study showed that the chance of failure increased when DAIR was postponed to two weeks after onset of symptoms (HR 1.68), and further increased after four weeks of symptoms (HR 2.34) [14]. Grammatopoulos et al. demonstrated a treatment success rate of 90.7% in 82 hip PJsIs when DAIR was performed within one week after the onset of symptoms versus 75.0% when DAIR was performed after one week (p = 0.05) [3]. As the maximum days of symptom duration was not well described in all studies and chronic PJIs are indeed included in some [3,10,12,14], the beneficial effect of debridement within one week may be overestimated in these studies for solely acute PJIs. However, a study performed in 110 patients who had a maximum of 32 days of symptoms indicates the same conclusion [8,9]. These authors demonstrated that for each additional day of postponing DAIR, the odds of implant retention decreased by 15% and 7.5% for hip and knee PJIs, respectively. In the same study, multivariate analysis showed that performing a DAIR within five days was an independent predictor for treatment success, with an OR of around 0.05 for both hips and knees (95% CI 0.01 to 0.24). These data support the concept that a DAIR should be performed within one week to increase the chance of treatment success, but should preferably be performed as soon as possible.

**The Addition of Rifampin in Staphylococci PJI**

In the randomized controlled trial performed by Zimmerli et al. in 1998, 24 patients with an infected orthopaedic implant caused by staphylococci and treated with surgical debridement were randomized to antimicrobial treatment with combination ciprofloxacin/ rifampin or with ciprofloxacin monotherapy. Adding rifampin to the antibiotic regimen improved treatment success from 98 - 100% (p = 0.02) [16]. Although relatively small in sample size, this study served as the foundation of adding rifampin to the antibiotic regimen in staphylococcal PJI. Thereafter, the benefit of rifampin was primarily demonstrated in observational studies [6,17-19]. In a prospective study including 86 monomicrobial staphylococcal knee PJsIs treated with open debridement, rifampin-based regimens had a 40% higher treatment success compared to other regimens (p = 0.01) [17]. Moreover, the addition of rifampin has shown to be a strong independent predictor for treatment success in multivariate analyses [6,20]. The greatest beneficial effect of rifampin has been shown when combined with a fluoroquinolone, which can be explained by the effectivity of fluoroquinolones against biofilm and by drug-interactions of rifampin with several other antibiotics but not with levofloxacin, the most frequently used fluoroquinolone. In a retrospective study of gram-positive infections treated with DAIR, Tornero et al. demonstrated that rifampin combined with linezolid, co-trimoxazole or clindamycin (which are known to have a drug-interaction with rifampin) was associated with a lower failure rate (27.8%) compared to a combination of rifampin with levofloxacin, ciprofloxacin or amoxicillin (8.3%) (p = 0.026) [19]. The greater benefit of the fluoroquinolone-rifampin combination therapy compared to other antibiotic regimens was also illustrated by Puhto et al. in a study of 113 patients with acute PJI: compared to rifampin-ciprofloxacin, the HR for treatment failure was significantly increased in the rifampin-other antibiotics group (HR 6.0, 95% CI 1.5 to 28.8, p = 0.014), and even higher in patients treated without rifampin (HR 14.4, 95% CI 3.1 to 66.9, p < 0.01) [20]. In addition, Senneville et al., observed the same in 41 patients with acute S. aureus PJI treated with DAIR: treatment success was 93.8% in the fluoroquinolone-rifampin group, 66.7% in the rifampin-other antibiotics group and 57.2% in regimens without rifampin (p = 0.11) [21]. Altogether, these data indicate that adding rifampin to the antibiotic regimen, particularly when combined with a fluoroquinolone, is associated with an increased chance of treatment success in acute PJI treated with DAIR.

**The Use of Fluoroquinolones in Gram-negative PJI**

The protective effect of antibiotic treatment with a fluoroquinolone is demonstrated in two prospective and one retrospective observational study [19,22,23]. In a prospective cohort of 22 patients with early PJI caused by gram-negative organisms, the use of fluoroquinolones was associated with a lower failure rate (7.1%) compared to other antibiotic regimens (37.5%) (p = 0.04) [19]. In addition, in a cohort study of 47 cases, treatment with a fluoroquinolone in susceptible gram-negative bacilli was associated with a better outcome (p = 0.0009) and was an independent predictor of treatment success (OR, 9.09; 95% CI, 1.96 to 50; p<0.005) [23]. Finally, a large retrospective, multicenter study on gram-negative PJI was performed in 16 Spanish hospitals in which DAIR was performed in 72% of the cases (174/242 cases) [22]. The overall success rate of DAIR was 68%, which increased to 79% in gram-negative PJIs treated with ciprofloxacin. In agreement with the previous study, ciprofloxacin treatment exhibited an independent protective effect in the multivariate analysis (HR 0.23; 95% CI, 0.13 to 0.40; p < 0.001). In all of these studies, no propensity score matching was performed to correct for possible selection bias. In addition, it should be noted that in most of the performed studies, oral therapy with fluoroquinolones was compared with oral beta-
lactam antibiotics. Questioning the superiority of fluoroquinolones, Grossi et al. demonstrated that treatment with high dose intravenous beta-lactam antibiotics (alone or with the addition of another antimicrobial agent) was not inferior to treatment with fluoroquinolones [24]. Although this study had a relatively small sample size (n = 76) and included both DAIRs and staged revision surgeries, it does provide some evidence for the possibility that alternative intravenous antibiotic regimens and/or combination therapy may be as effective as treatment with fluoroquinolones. More studies are required to confirm this finding.

Factors that are consistently shown in the literature to decrease the chance of treatment success are:

**Host-related Factors**

The importance of host factors in the outcome of patients with a PJI was highlighted by McPherson et al., who described the first grading of the medical and immune status of the host to predict outcome [25]. However, this grading system was not validated in large cohorts of patients who underwent DAIR. For patients managed with DAIR, three large cohort studies in streptococci, staphylococci and late acute PJI identified patients with rheumatoid arthritis (RA) as an important risk factor for failure [6,7]. This high risk for failure in RA patients has been demonstrated in smaller studies as well [10,26,27]. The most pronounced risk was observed for late acute PJIs, demonstrating a failure rate of 74% in patients with RA versus 43% in patients without (p < 0.001), and was shown to be an independent predictor for failure in the multivariate analysis, with an OR of 5.1 (95% CI 1.1–24.3, p = 0.04). Age has been independently associated with worse outcome in a recent large cohort of late acute PJIs, showing that patients older than 80 years old had a significantly higher risk of failure (OR 2.6). In addition, a clear correlation between treatment failure and age has also been described in a large cohort of early PJIs [28]. Male sex [28], chronic renal failure [7,22,29] and liver cirrhosis [29,30] were also identified as independent predictors of failure in patients treated with DAIR. Patients with chronic obstructive pulmonary disease (COPD) showed an increased risk for failure in late acute PJIs only. In this study, COPD was not a significant predictor for failure in the multivariate analysis (OR 2.9, 95% CI 0.99–8.68, p < 0.05).

**Prosthesis Indication**

Despite the fact that fracture and revision arthroplasties have a higher predisposition for infection [31–34], these arthroplasties have been associated with a higher risk for treatment failure in acute PJIs as well. Fracture as an indication for the prosthesis has been shown to be associated with DAIR failure in three studies of early acute PJIs [28,29,35] and in one study of late acute PJIs as well. With an average failure rate that is 20–30% higher compared to osteoarthritis, fracture as an indication for prosthesis has shown to be an independent predictor for treatment failure in two studies [29]. The same holds true for revision arthroplasty compared to infected primary arthroplasty, with a failure rate that is 12–22% higher [29,36], and even higher in knees [4]. Revision arthroplasty has been shown to be an independent predictor for failure in early acute PJI [29,36]. Only one study demonstrated an increased risk for failure in cemented prostheses, with an OR of 8.7 in the multivariate analysis [29].

**Clinical Presentation**

Several factors considered as surrogate parameters for the severity of the infection have been associated with treatment failure: a high CRP at clinical presentation [6,23,28,29,37], the amount/percentage of positive intraoperative cultures representing the bacterial inoculum [28,29] and bacteremia/sepsis [7,28,29,38]. In most of these studies, these factors are closely correlated to one another. In case of CRP value, an average cut-off value of >115 mg/L has been associated with an increased failure rate, depending on the type of infection (late acute or early acute). Notably, late acute/hematogenous infections appear to be associated with worse outcomes compared to early acute/post-surgical infections, especially when the infection is caused by S. aureus [6,15,20,37–41].

**Causative Microorganism**

It has been demonstrated in several studies that an infection caused by S. aureus is associated with an increased risk of failure [28,36,42,43]. In a large retrospective cohort of 386 early acute PJIs performed by Löwik et al., the percentage of failure was 17% higher when the infection was caused by S. aureus compared to other microorganisms (47.5% vs.30.2%, p < 0.001). S. aureus infection was also a prominent risk factor for failure in late acute PJIs, illustrated by an OR of 3.52 for S. aureus in the multivariate analysis. Methicillin-resistant S. aureus (MRSA) infection was associated with an increased risk for failure in a study performed by Cobo et al., but this was not demonstrated as an independent variable in the multivariate analysis [40]. Indeed, Lora-Tamayo et al. clearly demonstrated that MRSA infections have similar failure rates as methicillin-susceptible S. aureus, although the time to failure differs [6]. Next to S. aureus, overall, poor outcomes have been described for enterococcal PJIs [43–46]. The largest analysis on enterococcal PJI have been performed by Tornor et al., who reported a failure rate of 53% in 94 patients treated with DAIR [45]. Subanalysis demonstrated that infection caused by E. faecium have a worse outcome than those caused by E. faecalis (72% vs. 42% failure, p < 0.04). Indeed, two studies identified the presence of enterococci as an independent risk factor for failure in acute PJI treated with DAIR [43].

Ultimately, a clinical risk score including the most potent factors associated with treatment failure and treatment success should be developed to predict the individual chance of treatment success. One of the main objectives of risk scores would be to identify patients with high failure rate using DAIR. To be of most clinical use, these scores should preferably include preoperative variables only. So far, two articles described a risk score for failure in early acute PJIs (KLC-score, Fig. 1A) [29] and late acute PJIs (CRIMEBo-score, Fig. 1B) treated with DAIR. These risk scores can aid in the clinical decision making to choose an alternative surgical approach and/or to intensify the antimicrobial regimen.

**REFERENCES**

TABLE 1. Literature review of factors associated with successful treatment of acute PJI using debridement, antibiotics, and implant retention

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>N</th>
<th>PJI</th>
<th>Variables</th>
<th>Failure Rate</th>
<th>Univariate (OR or HR)</th>
<th>Multivariate (OR or (a)HR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tsang, 2017 [2]</td>
<td>1296</td>
<td>Early &amp; late</td>
<td>Symptoms ≤7 d vs. &gt;7 d Exchange of modular components (yes vs. no)</td>
<td>28% vs. 48%, p = 0.0001</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Grammatopoulos, 2017 [3]</td>
<td>82</td>
<td>Early &amp; late</td>
<td>Symptoms ≤7 d vs. &gt;7 d Interval since arthroplasty ≤6 w vs. &gt;6 w Exchange of modular components (yes vs. no)</td>
<td>9% vs. 25%, p = 0.05</td>
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<td>-</td>
</tr>
<tr>
<td>Zhang, 2017 [4]</td>
<td>34</td>
<td>Early &amp; late</td>
<td>Exchange of modular components (yes vs. no)</td>
<td>39% vs. 100%, p = 0.008</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Choi, 2011 [5]</td>
<td>32</td>
<td>Early &amp; late</td>
<td>Exchange of modular components (yes vs. no)</td>
<td>47% vs. 100%, p = 0.001</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Lora-Tamayo, 2013 [6]</td>
<td>345</td>
<td>Early &amp; late</td>
<td>Immunesuppression Immunosuppression (yes vs. no)</td>
<td>71% vs. 43%, p = 0.006</td>
<td>2.31</td>
<td>2.23</td>
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<td></td>
<td></td>
<td></td>
<td>Bacteremia (yes vs. no)</td>
<td>65% vs. 41%, p = 0.001</td>
<td>2.29</td>
<td>1.81</td>
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<td></td>
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<td></td>
<td>Polymicrobial (yes vs. no)</td>
<td>65% vs. 41%, p = 0.005</td>
<td>1.76</td>
<td>1.77</td>
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<td></td>
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<td></td>
<td>CRP</td>
<td>41% vs. 56%, p = 0.004</td>
<td>1.29</td>
<td>1.22</td>
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<td></td>
<td></td>
<td></td>
<td>Exchange of modular components (yes vs. no)</td>
<td>71% vs. 41%, p = 0.003</td>
<td>0.56</td>
<td>0.65</td>
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<td>Need of ≥2 debridements (yes vs. no)</td>
<td>NP, p = 0.008</td>
<td>1.98</td>
<td>1.63</td>
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<td></td>
<td></td>
<td></td>
<td>Levofloxacin + rifampin</td>
<td>NP, p = 0.02</td>
<td>0.50</td>
<td>0.42</td>
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<td></td>
<td>Vancomycin + rifampin</td>
<td>NP, p = 0.02</td>
<td>0.34</td>
<td>0.29</td>
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<tr>
<td>Lora-Tamayo, 2017 [7]</td>
<td>462</td>
<td>Early &amp; late</td>
<td>Chronic renal failure (yes vs. no)</td>
<td>54.5% vs. 40.8%, p = 0.05</td>
<td>1.58</td>
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<td></td>
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<td>Rheumatoid arthritis (yes vs. no)</td>
<td>64.9% vs. 40.0%, p &lt; 0.01</td>
<td>2.23</td>
<td>2.36</td>
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<td></td>
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<td></td>
<td>Immunosuppression (yes vs. no)</td>
<td>60.4% vs. 39.9%, p &lt; 0.01</td>
<td>1.86</td>
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<td>Revision (yes vs. no)</td>
<td>53.6% vs. 38.3%, p &lt; 0.01</td>
<td>1.60</td>
<td>1.37</td>
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<td></td>
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<td>Late post-surgical infection (yes vs. no)</td>
<td>62.9% vs. 38.2%, p &lt; 0.01</td>
<td>1.41</td>
<td>2.20</td>
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<td>Bacteremia (yes vs. no)</td>
<td>47.7% vs. 37.9%, p = 0.02</td>
<td>1.44</td>
<td>1.69</td>
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<td>Exchange of modular components (yes vs. no)</td>
<td>33.0% vs. 51.6%, p &lt; 0.01</td>
<td>0.59</td>
<td>0.60</td>
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<tr>
<td>Wouthuyzen-Bakker, 2018 [8]</td>
<td>340</td>
<td>Late</td>
<td>Gender, male vs. female Age &gt; 80 y vs. ≤ 80 y old</td>
<td>49.1% vs. 40.6%, p = 0.11</td>
<td>2.02</td>
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<td></td>
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<td>COPD (yes vs. no)</td>
<td>54.8% vs. 42.3%, p = 0.06</td>
<td>2.60</td>
<td>2.90</td>
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<td></td>
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<td>Active malignancy (yes vs. no)</td>
<td>55.9% vs. 43.8%, p = 0.18</td>
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<td>5.13</td>
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<td></td>
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<td>RA (yes vs. no)</td>
<td>51.7% vs. 44.4%, p = 0.04</td>
<td>-</td>
<td>5.39</td>
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<td></td>
<td>Immunesuppression</td>
<td>74.1% vs. 42.5%, p = 0.001</td>
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<td>2.00</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Immunosuppression</td>
<td>61.5% vs. 42.9%, p = 0.03</td>
<td>-</td>
<td>3.52</td>
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<tr>
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<td></td>
<td>Fracture (yes vs. no)</td>
<td>70.6% vs. 41.9%, p = 0.02</td>
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<td>0.35</td>
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<td>Revision (yes vs. no)</td>
<td>54.2% vs. 41.7%, p = 0.04</td>
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<td></td>
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<td>CRP &gt; 150 vs. ≤ 150 mg/L</td>
<td>47.9% vs. 41.7%, p = 0.06</td>
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<td>Bacteremia (yes vs. no)</td>
<td>56% vs. 39.8%, p = 0.005</td>
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<td>S. aureus (yes vs. no)</td>
<td>53.9% vs. 38.7%, p = 0.005</td>
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<td></td>
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<td>Exchange of modular components (yes vs. no)</td>
<td>36.4% vs. 52.4%, p = 0.004</td>
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<tr>
<td>Urish, 2017 [14]</td>
<td>206</td>
<td>Early &amp; late</td>
<td>Symptoms ≤7 d vs. &gt;7 d S. aureus vs. other</td>
<td>NP, p = 0.004</td>
<td>1.77</td>
<td>1.68</td>
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<td>Koh, 2015 [15]</td>
<td>52</td>
<td>Early &amp; late</td>
<td>Early vs. late PJI</td>
<td>18.7% vs. 47.3%, p = 0.04</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Author, Year</td>
<td>N</td>
<td>PJI</td>
<td>Variables</td>
<td>Failure Rate</td>
<td>Univariate (OR or HR)</td>
<td>Multivariate (OR or (a)HR)</td>
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<tr>
<td>Triantafillopoulos, 2015 [9]</td>
<td>78</td>
<td>NP</td>
<td>Thyroid disease Duration of symptoms MR-staphylococci</td>
<td>68.7%, p = 0.03 p = 0.0001 57%, p = 0.004</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Kuiper, 2013 [10]</td>
<td>91</td>
<td>Early &amp; late</td>
<td>RA (yes vs. no) Symptoms ≤7 d vs. &gt;7 d Early vs. late PJ</td>
<td>70% vs. 30%, p = 0.03 26.6% vs. 48.4%, p = 0.02 31% vs. 71.4%, p = 0.04 NP, p = 0.001 69% vs. 28%, p = 0.009</td>
<td>-</td>
<td>1.2-8.4' 1.1-366' 2.2-98' 1.8-309'</td>
</tr>
<tr>
<td>Marculescu, 2006 [11]</td>
<td>99</td>
<td>Early &amp; late</td>
<td>Sinus tract Symptoms &gt;8d</td>
<td>61%, p = 0.002 p = 0.04</td>
<td>2.85</td>
<td>1.79</td>
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<tr>
<td>Buller, 2012 [12]</td>
<td>309</td>
<td>Early &amp; late</td>
<td>Symptoms &lt;21 d vs. ≥21 d ESR Pre-previous infection in the same joint (yes vs. no) Resistant-GP vs. others</td>
<td>NP, p = 0.001 p = 0.02 55% vs. 44%, p = 0.009</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Hsieh, 2009 [13]</td>
<td>154</td>
<td>Early &amp; late</td>
<td>GN vs. GP</td>
<td>73% vs. 53%, p = 0.002</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Tornero, 2016 [16]</td>
<td>143</td>
<td>Early</td>
<td>Suboptimal vs. optimal (rifampin for GP and FQ for GN) antibiotic treatment</td>
<td>31% vs. 8%, p = 0.004</td>
<td>-</td>
<td>4.92</td>
</tr>
<tr>
<td>Puhto, 2015 [20]</td>
<td>113</td>
<td>Early &amp; late</td>
<td>Early vs. late PJ Leukocytes &gt; vs. ≤ 10x10⁹/l Ineffective empirical antibiotics vs. effective Rifampin+ciprofloxac in vs. Rifampin+other vs. other</td>
<td>30.8% vs. 54.3%, p = 0.002 50% vs. 24.6%, p &lt; 0.01 60% vs. 33%, p &lt; 0.006 10% vs. 40% vs. 70%, p &lt; 0.01</td>
<td>-</td>
<td>R+C vs. R+O: 6 R+C vs. O: 14</td>
</tr>
<tr>
<td>Holmberg, 2015 [17]</td>
<td>145</td>
<td>Early &amp; late</td>
<td>Revision (yes vs. no) Rifampin vs. no rifampin</td>
<td>63% vs. 23%, p = 0.02 19% vs. 59%, p = 0.01</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Vilchez, 2011 [38]</td>
<td>65</td>
<td>Early &amp; late</td>
<td>Early vs. late PJ Need of ≥2 debridements</td>
<td>24.5% vs. 58.7%, p = 0.02 NP, p = 0.001</td>
<td>2.57</td>
<td>4.61</td>
</tr>
<tr>
<td>El Helou, 2010 [18]</td>
<td>91</td>
<td>Early &amp; late</td>
<td>Rifampin vs. no rifampin</td>
<td>4% vs. 40%, p = 0.03</td>
<td>-</td>
<td>0.11</td>
</tr>
<tr>
<td>Zimmerl, 1998 [16]</td>
<td>18</td>
<td>Early</td>
<td>Rifampin+cipro floxac in vs. cipro floxac in</td>
<td>100% vs. 58%, p = 0.02</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Senneville, 2011 [21]</td>
<td>41</td>
<td>Early &amp; late</td>
<td>Rifampin+FQ vs. other</td>
<td>6% vs. 32%, p = 0.001</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Martinez-Pastor, 2009 [23]</td>
<td>47</td>
<td>Early &amp; late</td>
<td>FQ vs. no FQ for GN PJI CRP &gt; vs. ≤ 15 mg/dL</td>
<td>7% vs. 52%, p = 0.005 50% vs. 17%, p = 0.04</td>
<td>-</td>
<td>9.09 3.57</td>
</tr>
<tr>
<td>Tornero, 2015 [29]</td>
<td>222</td>
<td>Early</td>
<td>Chronic renal failure (yes vs. no) Liver cirrhosis (yes vs. no) Femoral neck fracture / revision surgery vs. primary Cemented prosthesis (yes vs. no) CRP &gt; vs. ≤1.5 mg/dL</td>
<td>60% vs. 20%, p &lt; 0.001 48% vs. 21%, , p = 0.004 35% vs. 38% vs. 16%, p = 0.003 25% vs. 19%, p = 0.39 56% vs. 16%, p &lt; 0.001</td>
<td>-</td>
<td>5.92 4.46 4.39 / 4.34 8.71 12.3</td>
</tr>
<tr>
<td>Rodriguez-Pardo, 2014 [22]</td>
<td>174</td>
<td>Early &amp; late</td>
<td>Ciprofloxac in (yes vs. no) Chronic renal failure</td>
<td>21% vs. 60%, p &lt; 0.001 NP, p &lt; 0.02</td>
<td>-</td>
<td>0.23 2.56</td>
</tr>
<tr>
<td>Grossi, 2016 [24]</td>
<td>35</td>
<td>Early &amp; late</td>
<td>Ciprofloxac in (yes vs. no)</td>
<td>21% vs. 28%, p = 0.65</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Author, Year</td>
<td>N</td>
<td>PJ</td>
<td>Variables</td>
<td>Failure Rate</td>
<td>Univariate (OR or HR)</td>
<td>Multivariate (OR or (a)HR)</td>
</tr>
<tr>
<td>-------------------</td>
<td>-----</td>
<td>-----</td>
<td>---------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------------</td>
<td>-----------------------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td>Löwik, 2018 [28]</td>
<td>386</td>
<td>Early</td>
<td>CRP &gt;115 vs. ≤115 mg/L; Gender, male vs. female; Left-sided prosthesis (yes vs. no); Sepsis (yes vs. no); Ischaemic heart disease (yes vs. no); Fracture (yes vs. no); Gentamicin impregnated beads or sponges (yes vs. no); S. aureus (yes vs. no)</td>
<td>55.2% vs. 30.3%, p &lt; 0.001; 46.6% vs. 33.2%, p = 0.08; 46.7% vs. 31.1%, p = 0.002; 52.1% vs. 35.1%, p = 0.007; 50.6% vs. 35.3%, p = 0.013; 52.8% vs. 33.3%, p = 0.047; 43.0% vs. 23.7%, p = 0.001</td>
<td>50.2% vs. 36.6%, p = 0.022</td>
<td>-</td>
</tr>
<tr>
<td>Hsieh, 2013 [26]</td>
<td>154</td>
<td>Early &amp; late</td>
<td>RA (yes vs. no)</td>
<td>78% vs. 48%, p = 0.002</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Son, 2017 [27]</td>
<td>25</td>
<td>Early &amp; late</td>
<td>RA (yes vs. no)</td>
<td>50% vs. 5%, p = 0.04</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Tornero, 2014 [30]</td>
<td>160</td>
<td>Early</td>
<td>Liver cirrhosis (yes vs. no) CRP &gt; vs. ≤12 mg/dL GN not treated with a FQ vs. treated with a FQ_</td>
<td>67% vs. 29%, p &lt; 0.001; 47% vs. 29%, p = 0.04; 57% vs. 31.5%, p = 0.005</td>
<td>-</td>
<td>12.4; 1.06; 6.5</td>
</tr>
<tr>
<td>Bergkvist, 2016 [35]</td>
<td>35</td>
<td>Early</td>
<td>Hip fracture (yes vs. no)</td>
<td>64% vs. 19%, p = 0.01</td>
<td>-</td>
<td>8.3</td>
</tr>
<tr>
<td>Byren, 2009 [36]</td>
<td>112</td>
<td>Early &amp; late</td>
<td>Arthroscopy vs. open S. aureus vs. others Revision vs. primary</td>
<td>53% vs. 12%, p = 0.008; 30% vs. 24%, p = 0.05; 34.6% vs. 12.8%, p = 0.008</td>
<td>5.4; 2.6; 2.6</td>
<td>4.2; 2.9; 3.1</td>
</tr>
<tr>
<td>Vilchez, 2011 [37]</td>
<td>53</td>
<td>Early</td>
<td>CRP &gt; vs. ≤ 22 mg/dL. Need of 2nd debridement (yes vs. no)</td>
<td>54.5% vs. 16.6%, p = 0.01; 75% vs. 18.4%, p = 0.006</td>
<td>-</td>
<td>20.4; 9.8</td>
</tr>
<tr>
<td>Rodriguez, 2010 [39]</td>
<td>50</td>
<td>Late</td>
<td>S. aureus GN</td>
<td>62.5%, p = 0.01; 0%, p = 0.01</td>
<td>3.08; 0.46</td>
<td>5.3; 0.6</td>
</tr>
<tr>
<td>Cobo, 2011 [40]</td>
<td>139</td>
<td>Early</td>
<td>MRSA (yes vs. no)</td>
<td>66.6% vs. 39.6%, p = 0.05</td>
<td>-</td>
<td>None</td>
</tr>
<tr>
<td>Tande, 2016 [41]</td>
<td>43</td>
<td>Late</td>
<td>S. aureus</td>
<td>66.6% vs. 39.6%, p = 0.05</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Letouvet, 2016 [42]</td>
<td>60</td>
<td>Early &amp; Late</td>
<td>Number of prior surgeries S. aureus (yes vs. no) Antibiotic treatment &lt; 3 months</td>
<td>p = 0.03; 50% vs. 22%, p = 0.02; 46% vs. 23.5%, p = 0.01</td>
<td>2.7; 3.4</td>
<td>6.3; 9.4; 20</td>
</tr>
<tr>
<td>Soriano, 2006 [43]</td>
<td>47</td>
<td>Early</td>
<td>Enterococcus spp or MRSA vs. others</td>
<td>87.5% vs. 9%, p = 0.003</td>
<td>-</td>
<td>17.6</td>
</tr>
<tr>
<td>Kheir, 2017 [44]</td>
<td>87</td>
<td>Early &amp; Late</td>
<td>VSE VRE Polymicrobial with enterococci</td>
<td>35%; 50%; 56%</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Tornero, 2014 [45]</td>
<td>203</td>
<td>Early &amp; Late</td>
<td>VSE VRE</td>
<td>41.8% vs. 72%</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Duijf, 2015 [46]</td>
<td>44</td>
<td>Early</td>
<td>Enterococcus sp</td>
<td>34%</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

CRP, C-reactive protein; PJL, periprosthetic joint infection; NP, information not provided; MR, methicillin-resistant; ESR, erythrocyte-sedimentation rate; CNS, coagulase-negative staphylococci; GP, gram-positive cocci; GN, gram-negative bacilli; FQ, fluoroquinolone; VSE, vancomycin-susceptible enterococci; VRE, vancomycin-resistant enterococci; RA, rheumatoid arthritis.
1 Confidence interval 95%.
2 Sub-group analysis of patients with a post-surgical PJL due to methicillin-susceptible S. aureus (MSSA).
3 Sub-group analysis of patients with a post-surgical PJL due to methicillin-resistant S. aureus (MRSA).
4 Sub-group analysis of patients with a post-surgical PJL due to staphylococci.
5 Randomized, placebo-controlled, double-blind trial.
6 Including patients treated with DAIR and prosthesis exchange.
7 Only depicted when p-value < 0.05.
8 Only depicting the results associated with overall failure.


QUESTION 10: Does performing a debridement, antibiotics and implant retention (DAIR) affect the outcome of a subsequent two-stage exchange arthroplasty?

RECOMMENDATION: Unknown. Based on the available evidence, it is not known if prior DAIR adversely affects the outcome of a subsequent two-stage exchange arthroplasty.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 93%, Disagree: 6%, Abstain: 1% (Super Majority, Strong Consensus)

RATIONALE:
There are several surgical treatment options for periprosthetic joint infection (PJI), including irrigation and debridement (I&D) with modular component exchange and one- or two-stage exchange arthroplasty, with the ultimate choice depending on a number of variables, including chronicity of infection, organism and antibiotic sensitivity patterns, host factors and experience of surgeon. I&D with implant retention has been an attractive strategy in select circumstances as it is less morbid for the patient and less costly to the healthcare system overall. However, the failure rate of I&D is not insignificant, averaging 68% in the literature (61-82%). Following treatment failure of an I&D, the recommendation for subsequent treatment is often a two-stage exchange arthroplasty. The question remains whether the initial attempt at I&D adversely affects the outcome of the subsequent two-stage exchange arthroplasty.

Two earlier studies and one very recent study on this subject seemed to indicate that failure of an initial I&D and modular component exchange leads to a higher than expected failure rates of subsequent two-stage exchange arthroplasty. Sherrell et al. performed a multicenter retrospective review of periprosthetic knee infections treated with a two-stage procedure following an initial treatment.