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 megaprosthesis 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

[1] Ercolano LB, Christensen T, McGough R, Weiss K. Treatment solutions are unclear for perimegaprosthetic infections. Clin Orthop Relat Res. 2013;471:3204–3213. doi:10.1007/s11999-013-2852-7.

[2] Hardes J, Gebert C, Schwappach A, Ahrens H, Streitburger A, Winkelmann W, et al. Characteristics and outcome of infections associated with tumor endoprostheses. Arch Orthop Trauma Surg. 2006;126:289–296. doi:10.1007/s00402-005-0009-1.

[3] Henderson ER, Groundland JS, Pala E, Dennis JA, Wooten R, Cheong D, et al. Failure mode classification for tumor endoprostheses: retrospective review of five institutions and a literature review. J Bone Joint Surg Am. 2011;93:418–429. doi:10.2106/JBJS.J.00834.

[4] Holzer G, Windhager R, Kotz R. One-stage revision surgery for infected megaprostheses. J Bone Joint Surg Br. 1997;79:31–35.

[5] Kapoor SK, Thiyam R. Management of infection following reconstruction in bone tumors. J Clin Orthop Relat Res Trauma. 2015;6:244–251. doi:10.1016/j.jcot.2015.04.005.

[6] Kuiper JW, Willink RT, Moojen DJF, van den Bekerom MP, Colen S. Treatment of acute periprosthetic infections with prosthesis retention: review of current concepts. World J Orthop. 2014;5:667–676. doi:10.5312/wjo.v5.i5.667.

[7] Rodríguez-Pardo D, Pigrau C, Lora-Tamayo J, Soriano A, del Toro MD, Cobo J, et al. Gram-negative prosthetic joint infection: outcome of a debridement, antibiotics and implant retention approach. A large multicentre study. Clin Microbiol Infect. 2014;20:O911-O919. doi:10.1111/1469-0691.12649.

[8] McDonald DJ, Fitzgerald RH, Ilstrup DM. Two-stage reconstruction of a total hip arthroplasty because of infection. J Bone Joint Surg Am. 1989;71:828–834.

[9] Eralp L, Ozger H, Kocaoglu M. Treatment strategies for infected megaprosthesis. Orthopaedic Proceedings. 2009;91-B:301–301. doi:10.1302/0301-620X.91BSUPP_II.0910301a.

[10] Hardes J, Ahrens H, Gosheger G, Nottrott M, Dieckmann R, Henrichs MP, et al. [Management of complications in megaprostheses]. Unfallchirurg. 2014;117:607–613. doi:10.1007/s00113-013-2477-z.

[11] Grammatopoulos G, Kendrick B, McNally M, Athanasou NA, Atkins B, McLardy-Smith P, et al. Outcome following debridement, antibiotics, and implant retention in hip periprosthetic joint infection - an 18-year experience. J Arthroplasty. 2017;32:2248–2255.

[12] Kuiper JWP, Vos SJC, Saouti R, Vergroesen DA, Graat HCA, Debets-Ossenkopp YJ, et al. Prosthetic joint-associated infections treated with DAIR (debridement, antibiotics, irrigation, and retention): analysis of risk factors and local antibiotic carriers in 91 patients. Acta Orthop. 2013;84:380–386. doi:10.3109/17453674.2013.823589.

[13] Kendoff D, Morgan-Jones R, Haddad FS, editors. Periprosthetic Joint Infections: Changing Paradigms. Springer International Publishing; 2016.

[14] Pilge H, Gradl G, von Eisenhart-Rothe R, Gollwitzer H. Incidence and outcome after infection of megaprostheses. Hip Int. 2012:S83-S90. doi:10.5301/HIP.2012.9576.

[15] Brandt CM, Duffy MC, Berbari EF, Hanssen AD, Steckelberg JM, Osmon DR. Staphylococcus aureus prosthetic joint infection treated with prosthesis removal and delayed reimplantation arthroplasty. Mayo Clin Proc. 1999;74:553–558. doi:10.4065/74.6.553.

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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 Enterococcoci

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 PJIs 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 PJIs 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 PJIs caused by methicillin-resistant and methicillin susceptible *S.aureus* ($n = 345$, hazard ratio (HR) 0.65, $p < 0.026$)) [6], streptococci ($n = 462$, HR 0.60, $p < 0.01$) [7] and solely late acute PJIs ($n = 340$, 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 53.2% in 216 knee PJIs 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) ($p = 0.002$) [14]. Grammatopoulos et al. demonstrated a treatment success rate of 90.7% in 82 hip PJIs 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 15.7% and 7.5% for hip and knee PJI, 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 58 - 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 staphylococci knee PJIs 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 higher failure rate (27.8%) compared to a combination of rifampicin 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 57.1% 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; p0.005) [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 been 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 Tornero 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 (KLIC-score, Fig. 1A) [29] and late acute PJIs (CRIME80-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

[1] Lass R, Giurea A, Kubista B, Hirschl AM, Graninger W, Presterl E, et al. Bacterial adherence to different components of total hip prosthesis in patients with prosthetic joint infection. Int Orthop. 2014;38:1597–602. doi:10.1007/s00264-014-2358-2.

[2] Tsang S-TJ, Ting J, Simpson AHRW, Gaston P. Outcomes following debridement, antibiotics and implant retention in the management of periprosthetic infections of the hip: a review of cohort studies. Bone Joint J. 2017;99-B:1458–66. doi:10.1302/0301-620X.99B11.BJJ-2017-0088.R1.

[3] Grammatopoulos G, Bolduc M-E, Atkins BL, Kendrick BJL, McLardy-Smith P, Murray DW, et al. Functional outcome of debridement, antibiotics and implant retention in periprosthetic joint infection involving the hip: a case-control study. Bone Joint J. 2017;99-B:614–22. doi:10.1302/0301-620X.99B5.BJJ-2016-0562.R2.

[4] Zhang C, Yan CH, Chan PK, Ng FY, Chiu KY. Polyethylene insert exchange is crucial in debridement for acute periprosthetic infections following total knee arthroplasty. J Knee Surg. 2017;30:36–41. doi:10.1055/s-0036-1579667.

[5] Choi H-R, von Knoch F, Zurakowski D, Nelson SB, Malchau H. Can implant retention be recommended for treatment of infected TKA? Clin Orthop Relat Res. 2011;469:961–969. doi:10.1007/s11999-010-1679-8.

[6] Lora-Tamayo J, Murillo O, Iribarren JA, Soriano A, Sánchez-Somolinos M, Baraia-Etxaburu JM, et al. A large multicenter study of methicillin-susceptible and methicillin-resistant Staphylococcus aureus prosthetic joint infections managed with implant retention. Clin Infect Dis. 2013;56:182–194. doi:10.1093/cid/cis746.

[7] Lora-Tamayo J, Senneville É, Ribera A, Bernard L, Dupon M, Zeller V, et al. The not-so-good prognosis of streptococcal periprosthetic joint infection

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

Author, Year	N	PJI	Variables	Failure Rate	Univariate (OR or HR)7	Multivariate (OR or (a)HR)7
Tsang, 2017 [2] Meta-analysis	1296	Early & late	Symptoms≤7 d vs. >7 d Exchange of modular components (yes vs. no)	28% vs. 48%, p = 0.0001 26% vs. 39%, p = 0.0001	-	-
Grammatopoulos, 2017 [3]	82	Early & late	Symptoms≤7 d vs. >7 d Interval since arthroplasty ≤6 w vs. >6 w Exchange of modular components (yes vs. no)	9% vs. 25%, p = 0.05 7.5% vs. 27.5%, p = 0.01 6.6% vs. 24.4%, p = 0.02	-	-
Zhang, 2017 [4]	34	Early & late	Exchange of modular components (yes vs. no)	39% vs. 100%, p = 0.008	-	-
Choi, 2011 [5]	32	Early & late	Exchange of modular components (yes vs. no)	47% vs. 100%, p = 0.001	-	-
Lora-Tamayo, 2013 [6]	345	Early & late	ImmunesuppresionImmunosuppression (yes vs. no) Bacteremia (yes vs. no) Polymicrobial (yes vs. no) CRP Exchange of modular components (yes vs. no) Need of ≥2 debridements (yes vs. no) [2]levofloxacin+rifampin [3]vancomycin+rifampin	71% vs. 43%, p = 0.006 65% vs. 41%, p = 0.001 59% vs. 41%, p = 0.005 NP, p = 0.001 41% vs. 56%, p = 0.004 71% vs. 41%, p = 0.003 NP, p = 0.008 NP, p = 0.02	2.31 2.29 1.76 1.29 0.56 1.98 0.50 0.34	2.23 1.81 1.77 1.22 0.65 1.63 0.42 0.29
Lora-Tamayo, 2017 [7][8]	462	Early & late	[8]Chronic renal failure (yes vs. no) [8]Rheumatoid arthritis (yes vs. no) [8]Immunesuppression (yes vs. no) [8]Revision (yes vs.no) [8]Late post-surgical infection (yes vs. no) [8]Bacteremia (yes vs. no) [8]Exchange of modular components (yes vs. no)	54.5% vs. 40.8%, p = 0.05 64.9% vs. 40.0%, p < 0.01 60.4% vs. 39.9%, p < 0.01 53.6% vs. 38.3%, p < 0.01 62.9% vs. 38.2%, p < 0.01 47.7% vs. 37.9%, p = 0.02 33.0% vs. 51.6% , p < 0.01	1.58 2.23 1.86 1.60 1.41 1.44 0.59	- 2.36 - 1.37 2.20 1.69 0.60
Wouthuyzen-Bakker, 2018 [8]	340	Late	Gender, male vs. female Age, > 80 y vs.≤ 80 y old COPD (yes vs. no) Active malignancy (yes vs. no) RA (yes vs. no) Immunesuppression Immunosuppression (yes vs. no) Fracture (yes vs. no) Revision (yes vs. no) CRP >150 vs. ≤150 mg/L Bacteremia (yes vs. no) S. aureus (yes vs. no) Exchange of modular components (yes vs. no)	49.1% vs. 40.6%,p = 0.11 54.8% vs. 42.3%, p = 0.06 55.9% vs. 43.8%, p = 0.18 51.7% vs. 44.4%, p = 0.04 74.1% vs. 42.5%, p = 0.001 61.5% vs. 42.9%, p = 0.03 70.6% vs. 41.9%, p = 0.02 54.2% vs. 41.7%, p = 0.04 47.9% vs. 41.7%, p = 0.06 56% vs. 39.8%, p = 0.005 53.9% vs. 38.7%, p = 0.005 36.4% vs. 52.4%, p = 0.004		2.02 2.60 2.90 - 5.13 - 5.39 - 2.00 - 3.52 0.35
Urish, 2017 [14]	206	Early & late	Symptoms ≤7 d vs. >7 d S. aureus vs. other	NP, p = 0.004 NP, p = 0.04	1.77 0.63	1.68 0.59
Koh, 2015 [15]	52	Early & late	Early vs. late PJI	18.7% vs. 47.3%, p = 0.04	-	-

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

Author, Year	N	PJI	Variables	Failure Rate	Univariate (OR or HR)7	Multivariate (OR or (a)HR)7
Triantafillopoulos, 2015 [9]	78	NP	Thyroid disease Duration of symptoms MR-staphylococci	68.7%, p = 0.03 p = 0.0001 57%, p = 0.004	-	-
Kuiper, 2013 [10]	91	Early & late	RA (yes vs. no) Symptoms ≤7 d vs. >7 d Early vs. late PJI ESR>60 mm/h CNS vs. others	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	-	1.2-84[1] 1-18[1] 1.1-366[1] 2.2-98[1] 1.8-309[1]
Marculescu, 2006 [11]	99	Early & late	Sinus tract Symptoms >8d	61%, p = 0.002 51%, p = 0.04	2.85 1.79	2.84 1.77
Buller, 2012 [12]	309	Early & late	Symptoms <21 d vs. ≥21 d ESR Previous infection in the same joint (yes vs. no) Resistant-GP vs. others	NP, p = 0.001 p = 0.02 55% vs. 44%, p = 0.009 65% vs. 44%, p = 0.005	-	-
Hsieh, 2009 [13]	154	Early & late	GN vs. GP	73% vs. 53%, p = 0.002	-	-
Tornero, 2016 [16]	143	Early	Suboptimal vs. optimal (rifampin for GP and FQ for GN) antibiotic treatment	31% vs. 8%, p = 0.004	-	4.92
Puhto, 2015 [20]	113	Early & late	Early vs. late PJI Leukocytes > vs. ≤ $10x10^9$/L Ineffective empirical antibiotics vs. effective [4]Rifampin+ciprofloxacin vs. Rifampin+other vs. other	30.8% vs. 54.3%, p = 0.002 50% vs. 24.6%, p < 0.01 60% vs. 33%, p < 0.006 10% vs. 40% vs. 70%, p < 0.01	- R+C vs. R+O: 6 R+C vs. O: 14	- 3.7 3.2 -
Holmberg, 2015 [17]	145	Early & late	Revision (yes vs. no) Rifampin vs. no rifampin	63% vs. 23%, p = 0.02 19% vs. 59%, p = 0.01	-	-
Vilchez, 2011 [38]	65	Early & late	Early vs. late PJI Need of ≥2 debridements	24.5% vs. 58.7%, p = 0.02 NP, p = 0.001		2.57 4.61
El Helou, 2010 [18]	91	Early & late	Rifampin vs. no rifampin	4% vs. 40%, p = 0.03	-	0.11
Zimmerli, 1998 [16][5]	18	Early	Rifampin+ciprofloxacin vs. ciprofloxacin	100% vs. 58%, p = 0.02	-	-
Senneville, 2011 [21]	41	Early & late	Rifampin+FQ vs. other	6% vs. 32%, p = 0.001	-	-
Martínez-Pastor, 2009 [23]	47	Early & late	FQ vs. no FQ for GN PJI CRP > vs. ≤ 15 mg/dL	7% vs. 52%, p = 0.005 50% vs. 17%, p = 0.04	-	9.09 3.57
Tornero, 2015 [29]	222	Early	Chronic renal failure (yes vs. no) Liver cirrhosis (yes vs. no) Femoral neck fracture / revision surgery vs. primary Cemented prosthesis (yes vs. no) CRP > vs. ≤11.5 mg/dL	60% vs. 20%, p < 0.001 48% vs. 21% , p = 0.004 35% / 38% vs. 16%, p = 0.003 25% vs. 19%, p = 0.39 56% vs. 16%, p < 0.001	-	5.92 4.46 4.39 / 4.34 8.71 12.3
Rodriguez-Pardo, 2014 [22]	174	Early & late	Ciprofloxacin (yes vs. no) Chronic renal failure	21% vs. 60%, p < 0.001 NP, p < 0.02	-	0.23 2.56
Grossi, 2016 [24]	35	Early & late	Ciprofloxacin (yes vs. no)	21% vs. 28%, p = 0.65	-	-

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

Author, Year	N	PJI	Variables	Failure Rate	Univariate (OR or HR)7	Multivariate (OR or (a)HR)7
Löwik, 2018 [28]	386	Early	CRP >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)	55.2% vs. 30.3%, p < 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 50.2% vs. 36.6%, p = 0.022		- 2.03 1.80 - 1.84 - NP NP
Hsieh, 2013 [26]	154	Early & late	RA (yes vs. no)	78% vs. 48%, p = 0.002	-	-
Son,2017 [27]	25	Early & late	RA (yes vs. no)	50% vs. 5%, p = 0.04	-	-
Tornero, 2014 [30]	160	Early	Liver cirrhosis (yes vs. no) CRP > vs. ≤12 mg/dL GN not treated with a FQ vs. treated with a FQ	67% vs. 29%, p < 0.001 47% vs. 29%, p = 0.04 57% vs. 31.5%, p = 0.005	-	12.4 1.06 6.5
Bergkvist, 2016 [35]	35	Early	Hip fracture (yes vs. no)	64% vs. 19%, p = 0.01	-	8.3
Byren, 2009 [36]	112	Early & late	Arthroscopy vs. open S. aureus vs. others Revision vs. primary	53% vs. 12%, p = 0.008 30% vs. 24%, p = 0.05 34.6% vs. 12.8%, p = 0.008	5.4 2.6 2.6	4.2 2.9 3.1
Vilchez, 2011 [37]	53	Early	CRP > vs. ≤ 22 mg/dL Need of 2nd debridement (yes vs. no)	54.5% vs. 16.6%, p = 0.01 75% vs. 18.4%, p = 0.006	-	20.4 9.8
Rodriguez, 2010 [39]	50	Late	S. aureus GN	62.5%, p = 0.01 0%, p = 0.01	3.08 0.46	5.3 0.6
Cobo, 2011 [40]	139	Early	MRSA (yes vs. no)	66.6% vs. 39.6%, p = 0.05	-	None
Tande, 2016 [41]	43	Late		66.6% vs. 39.6%, p = 0.05		
Letouvet, 2016 [42]	60	Early & Late	Number of prior surgeries S. aureus (yes vs. no) Antibiotic treatment < 3 months	p = 0.03 50% vs. 22%, p = 0.02 46% vs. 23.5%, p = 0.01	2.7 3.4	6.3 9.4 20
Soriano, 2006 [43]	47	Early	Enterococcus spp or MRSA vs. others	87.5% vs. 9%, p = 0.003	-	17.6
Kheir, 2017 [44][6]	87	Early & Late	VSE VRE Polymicrobial with enterococci	35% 50% 56%	-	-
Tornero, 2014 [45][6]	203	Early & Late	VSE VRE	41.8% 72%	-	-
Duijf, 2015 [46]	44	Early	Enterococcus sp	34%	-	-

CRP, C-reactive protein; PJI, 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 PJI due to methicillin-susceptible *S. aureus* (MSSA).

[3] Sub-group analysis of patients with a post-surgical PJI due to methicillin-resistant *S. aureus* (MRSA).

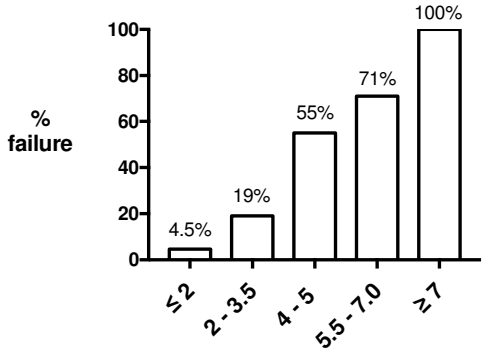
[4] Sub-group analysis of patients with a post-surgical PJI due to staphylococci.

[5] Randomized, placebo-controlled, double-blind trial.

[6] Including patients treated with DAIR and prosthesis exchange.

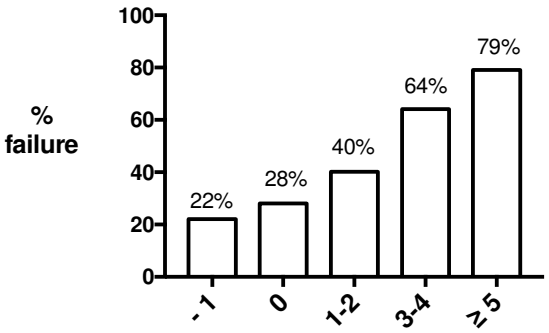
[7] Only depicted when p-value < 0.05.

[8] Only depicting the results associated with overall failure.



K	Chronic renal failure (Kidney)	**2**
L	Liver cirrhosis	**1.5**
I	Index surgery: indication prosthesis: fracture OR revision prothesis	**1.5**
C	Cemented prosthesis	**2**
	CRP > 115 mg/L	**2.5**

FIGURE 1A. KLIC preoperative risk score [19,28]



C	COPD	**2**
	CRP > 150 mg/L	**1**
R	Rheumatoid arthritis	**3**
I	Indication prosthesis: fracture	**3**
M	Male	**1**
E	Exchange of mobile components	**-1**
80	Age > 80 years	**2**

FIGURE 1B. CRIME80 preoperative risk score [19,28]

managed by implant retention: the results of a large multicenter study. Clin Infect Dis. 2017;64:1742–1752.
[8] Triantafyllopoulos GK, Poultsides LA, Sakellariou VI, Zhang W, Sculco PK, Ma Y, et al. Irrigation and debridement for periprosthetic infections of the hip and factors determining outcome. Int Orthop. 2015;39:1203–1209. doi:10.1007/s00264-015-2753-3.
[9] Triantafyllopoulos GK, Poultsides LA, Zhang W, Sculco PK, Ma Y, Sculco TP. Periprosthetic knee infections treated with irrigation and debridement: outcomes and preoperative predictive factors. J Arthroplasty. 2015;30:649–657. doi:10.1016/j.arth.2014.10.026.
[10] Kuiper JWP, Vos SJC, Saouti R, Vergroesen DA, Graat HCA, Debets-Ossenkopp YJ, et al. Prosthetic joint-associated infections treated with DAIR (debridement, antibiotics, irrigation, and retention): analysis of risk factors and local antibiotic carriers in 91 patients. Acta Orthop. 2013;84:380–386. doi:10.3109/17453674.2013.823589.
[11] Marculescu CE, Berbari EF, Hanssen AD, Steckelberg JM, Harmsen SW, Mandrekar JN, et al. Outcome of prosthetic joint infections treated with debridement and retention of components. Clin Infect Dis. 2006;42:471–478. doi:10.1086/499234.
[12] Buller LT, Sabry FY, Easton RW, Klika AK, Barsoum WK. The preoperative prediction of success following irrigation and debridement with polyethylene exchange for hip and knee prosthetic joint infections. J Arthroplasty. 2012;27:857-864.e1-4. doi:10.1016/j.arth.2012.01.003.
[13] Hsieh PH, Lee MS, Hsu KY, Chang YH, Shih HN, Ueng SW. Gram-negative prosthetic joint infections: risk factors and outcome of treatment. Clin Infect Dis. 2009;49:1036–1043. doi:10.1086/605593.
[14] Urish KL, Bullock AG, Kreger AM, Shah NB, Jeong K, Rothenberger SD, et al. A multicenter study of irrigation and debridement in total knee arthroplasty periprosthetic joint infection: treatment failure is high. J Arthroplasty. 2017.
[15] Koh IJ, Han SB, In Y, Oh KJ, Lee DH, Kim TK, et al. Open debridement and prosthesis retention is a viable treatment option for acute periprosthetic joint infection after total knee arthroplasty. Arch Orthop Trauma Surg. 2015;135:847–855. doi:10.1007/s00402-015-2237-3.
[16] Zimmerli W, Widmer AF, Blatter M, Frei R, Ochsner PE. Role of rifampin for treatment of orthopedic implant-related staphylococcal infections: a randomized controlled trial. Foreign-Body Infection (FBI) Study Group. JAMA. 1998;279:1537–1541.
[17] Holmberg A, Thórhallsdóttir VG, Robertsson O, W-Dahl A, Stefánsdóttir A. 75% success rate after open debridement, exchange of tibial insert, and antibiotics in knee prosthetic joint infections. Acta Orthop. 2015;86:457–462. doi:10.3109/17453674.2015.1026756.
[18] El Helou OC, Berbari EF, Lahr BD, Eckel-Passow JE, Razonable RR, Sia IG, et al. Efficacy and safety of rifampin containing regimen for staphylococcal prosthetic joint infections treated with debridement and retention. Eur J Clin Microbiol Infect Dis. 2010;29:961–967. doi:10.1007/s10096-010-0952-9.
[19] Tornero E, Morata L, Martínez-Pastor JC, Angulo S, Combalia A, Bori G, et al. Importance of selection and duration of antibiotic regimen in prosthetic

joint infections treated with debridement and implant retention. J Antimicrob Chemother. 2016;71:1395–1401. doi:10.1093/jac/dkv481.
[20] Puhto AP, Puhto T, Niinimäki T, Ohtonen P, Leppilahti J, Syrjälä H. Predictors of treatment outcome in prosthetic joint infections treated with prosthesis retention. Int Orthop. 2015;39:1785–1791. doi:10.1007/s00264-015-2819-2.
[21] Senneville E, Joulie D, Legout L, Valette M, Dezèque H, Beltrand E, et al. Outcome and predictors of treatment failure in total hip/knee prosthetic joint infections due to Staphylococcus aureus. Clin Infect Dis. 2011;53:334–340. doi:10.1093/cid/cir402.
[22] Rodríguez-Pardo D, Pigrau C, Lora-Tamayo J, Soriano A, del Toro MD, Cobo J, et al. Gram-negative prosthetic joint infection: outcome of a debridement, antibiotics and implant retention approach. A large multicentre study. Clin Microbiol Infect. 2014;20:O911-O919. doi:10.1111/1469-0691.12649.
[23] Martínez-Pastor JC, Muñoz-Mahamud E, Vilchez F, García-Ramiro S, Bori G, Sierra J, et al. Outcome of acute prosthetic joint infections due to gram-negative bacilli treated with open debridement and retention of the prosthesis. Antimicrob Agents Chemother. 2009;53:4772–4777. doi:10.1128/AAC.00188-09.
[24] Grossi O, Asseray N, Bourigault C, Corvec S, Valette M, Navas D, et al. Gram-negative prosthetic joint infections managed according to a multidisciplinary standardized approach: risk factors for failure and outcome with and without fluoroquinolones. J Antimicrob Chemother. 2016;71:2593–2597. doi:10.1093/jac/dkw202.
[25] McPherson EJ, Woodson C, Holtom P, Roidis N, Shufelt C, Patzakis M. Periprosthetic total hip infection: outcomes using a staging system. Clin Orthop Relat Res. 2002:8–15.
[26] Hsieh PH, Huang KC, Shih HN. Prosthetic joint infection in patients with rheumatoid arthritis: an outcome analysis compared with controls. PLoS ONE. 2013;8:e71666. doi:10.1371/journal.pone.0071666.
[27] Son WS, Shon OJ, Lee DC, Park SJ, Yang HS. Efficacy of open debridement and polyethylene exchange in strictly selected patients with infection after total knee arthroplasty. Knee Surg Relat Res. 2017;29:172–179.
[28] Löwik CAM, Jutte PC, Tornero E, Ploegmakers JJW, Knobben BAS, de Vries AJ, et al. Predicting failure in early acute prosthetic joint infection treated with debridement, antibiotics, and implant retention: external validation of the KLIC Score. J Arthroplasty. 2018
[29] Tornero E, Morata L, Martínez-Pastor JC, Bori G, Climent C, García-Velez DM, et al. KLIC-score for predicting early failure in prosthetic joint infections treated with debridement, implant retention and antibiotics. Clin Microbiol Infect. 2015;21:786.e9-786.e17. doi:10.1016/j.cmi.2015.04.012.
[30] Tornero E, Martínez-Pastor JC, Bori G, García-Ramiro S, Morata L, Bosch J, et al. Risk factors for failure in early prosthetic joint infection treated with debridement. Influence of etiology and antibiotic treatment. J Appl Biomater Funct Mater. 2014;12:129–134. doi:10.5301/jabfm.5000209.
[31] Guren E, Figved W, Frihagen F, Watne LO, Westberg M. Prosthetic joint infection-a devastating complication of hemiarthroplasty for hip fracture. Acta Orthop. 2017;88:383–389. doi:10.1080/17453674.2017.1301009.
[32] Kurtz SM, Lau E, Schmier J, Ong KL, Zhao K, Parvizi J. Infection burden for hip and knee arthroplasty in the United States. J Arthroplasty. 2008;23:984–991. doi:10.1016/j.arth.2007.10.017.
[33] Mortazavi SMJ, Molligan J, Austin MS, Purtill JJ, Hozack WJ, Parvizi J. Failure following revision total knee arthroplasty: infection is the major cause. Int Orthop. 2011;35:1157–1164. doi:10.1007/s00264-010-1134-1.
[34] Mortazavi SMJ, Schwartzenberger J, Austin MS, Purtill JJ, Parvizi J. Revision total knee arthroplasty infection: incidence and predictors. Clin Orthop Relat Res. 2010;468:2052–2059. doi:10.1007/s11999-010-1308-6.
[35] Bergkvist M, Mukka SS, Johansson L, Ahl TE, Sayed-Noor AS, Sköldenberg OG, et al. Debridement, antibiotics and implant retention in early periprosthetic joint infection. Hip Int. 2016;26:138–143. doi:10.5301/hipint.5000328.
[36] Byren I, Bejon P, Atkins BL, Angus B, Masters S, McLardy-Smith P, et al. One hundred and twelve infected arthroplasties treated with "DAIR" (debridement, antibiotics and implant retention): antibiotic duration and outcome. J Antimicrob Chemother. 2009;63:1264–1271. doi:10.1093/jac/dkp107.
[37] Vilchez F, Martínez-Pastor JC, García-Ramiro S, Bori G, Maculé F, Sierra J, et al. Outcome and predictors of treatment failure in early post-surgical prosthetic joint infections due to Staphylococcus aureus treated with debridement. Clin Microbiol Infect. 2011;17:439–444. doi:10.1111/j.1469-0691.2010.03244.x.
[38] Vilchez F, Martínez-Pastor JC, García-Ramiro S, Bori G, Tornero E, García E, et al. Efficacy of debridement in hematogenous and early post-surgical prosthetic joint infections. Int J Artif Organs. 2011;34:863–869. doi:10.5301/ijao.5000029.
[39] Rodríguez D, Pigrau C, Euba G, Cobo J, García-Lechuz J, Palomino J, et al. Acute hematogenous prosthetic joint infection: prospective evaluation of medical and surgical management. Clin Microbiol Infect. 2010;16:1789–1795. doi:10.1111/j.1469-0691.2010.03157.x.
[40] Cobo J, Miguel LGS, Euba G, Rodríguez D, García-Lechuz JM, Riera M, et al. Early prosthetic joint infection: outcomes with debridement and implant retention followed by antibiotic therapy. Clin Microbiol Infect. 2011;17:1632–1637. doi:10.1111/j.1469-0691.2010.03333.x.
[41] Tande AJ, Palraj BR, Osmon DR, Berbari EF, Baddour LM, Lohse CM, et al. Clinical presentation, risk factors, and outcomes of hematogenous prosthetic joint infection in patients with Staphylococcus aureus Bacteremia. Am J Med. 2016;129:221.e11-e20. doi:10.1016/j.amjmed.2015.09.006.
[42] Letouvet B, Arvieux C, Leroy H, Polard J-L, Chapplain JM, Common H, et al. Predictors of failure for prosthetic joint infections treated with debridement. Med Mal Infect. 2016;46:39–43. doi:10.1016/j.medmal.2015.11.007.
[43] Soriano A, García S, Bori G, Almela M, Gallart X, Macule F, et al. Treatment of acute post-surgical infection of joint arthroplasty. Clin Microbiol Infect. 2006;12:930–933. doi:10.1111/j.1469-0691.2006.01463.x.
[44] Kheir MM, Tan TL, Higuera C, George J, Della Valle CJ, Shen M, et al. Periprosthetic joint infections caused by Enterococci have poor outcomes. J Arthroplasty. 2017;32:933–947. doi:10.1016/j.arth.2016.09.017.
[45] Tornero E, Senneville E, Euba G, Petersdorf S, Rodriguez-Pardo D, Lakatos B, et al. Characteristics of prosthetic joint infections due to Enterococcus sp. and predictors of failure: a multi-national study. Clin Microbiol Infect. 2014;20:1219–1224. doi:10.1111/1469-0691.12721.
[46] Duijf SV, Vos FJ, Meis JF, Goosen JH. Debridement, antibiotics and implant retention in early postoperative infection with Enterococcus sp. Clin Microbiol Infect. 2015;21:e41-42. doi:10.1016/j.cmi.2015.01.006.

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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