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Timing of implant-removal in late acute periprosthetic joint infection. A multicenter observational study

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HIGH LIGHTS

- Patients with late acute PJI have a better outcome when treated with revision surgery instead of DAIR.
- Patients with late acute PJI can be selected for revision surgery according to the preoperative risk of DAIR failure defined by the CRIME80 score.
- The causative microorganism and its susceptibility to antibiotics should ideally be taken into account as well to decide for the best surgical approach.

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Timing of implant-removal in late acute periprosthetic joint infection. A multicenter observational study.

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ABSTRACT

Objectives: We evaluated the treatment outcome in late acute (LA) periprosthetic joint infections (PJI) treated with debridement and implant retention (DAIR) versus implant removal. *Methods:* In a large multicenter study, LA PJIs of the hip and knee were retrospectively evaluated. Failure was defined as: PJI related death, prosthesis removal or the need for suppressive antibiotic therapy. LA PJI was defined as acute symptoms <3 weeks in patients more than 3 months after the index surgery and with a history of normal joint function. *Results:* 445 patients were included, comprising 340 cases treated with DAIR and 105 cases treated with implant removal (19% one-stage revision (n=20), 74.3% two-stage revision (n=78) and 6.7% definitive implant removal (n=7). Overall failure in patients treated with DAIR was 45.0% (153/340) compared to 24.8% (26/105) for implant removal ($p<0.001$). Difference in failure rate remained after 1:1 propensity-score matching. A

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preoperative CRIME80-score ≥3 (OR 2.9), PJI caused by *S. aureus* (OR 1.8) and implant retention (OR 3.1) were independent predictors for failure in the multivariate analysis. *Conclusion:* DAIR is a viable surgical treatment for most patients with LA PJI, but implant removal should be considered in a subset of patients, especially in those with a CRIME80-score ≥3.

Keywords:

Periprosthetic joint infection, late acute, hematogenous, debridement, revision surgery, failure

INTRODUCTION

A periprosthetic joint infection (PJI) is a serious complication after joint arthroplasty and is accompanied by increased morbidity and mortality [1-2]. Clinical outcome is highly dependent on host related factors, clinical characteristics, the causative microorganism , and the applied antimicrobial therapy and surgical techniques [4, 10, 11]. Therefore, optimising treatment and composing tailored strategies are crucial to improve clinical outcome. We recently demonstrated that late acute PJIs have a relatively high failure rate when treated with surgical debridement and implant retention (DAIR) [21]. Failure seems to be most prominent when the infection is caused by *Staphylococcus aureus*, with reported failures of around 50%, which is higher than described for early acute / post-surgical PJIs [13, 17, 19-21]. Moreover, several preoperative variables, defined according to the CRIME80-score (i.e. **C**-reactive protein >150 mg/L, **C**hronic obstructive pulmonary disease, **R**heumatoid arthritis, fracture as

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Indication for the prosthesis, **M**ale gender, not **E**xchanging the mobile components during debridement and an age above **80** years), expose patients to a higher failure risk as well [21]. Despite the relatively high failure rate, a DAIR procedure is still recommended as the first line surgical approach for all acute PJIs if the implant is well fixed and if anti-biofilm antibiotics can be applied [15]. However, revision of the prosthetic implant might be a better treatment modality in a subset of patients with late acute infections [17]. For this reason, we compared the clinical outcome of patients with a late acute PJI treated with DAIR or immediate implant removal in a large multicenter observational cohort study and identified those patients who may benefit more from implant removal instead of DAIR. Propensity score matching was applied to correct for selection bias between both surgical techniques.

MATERIAL AND METHODS

Study design and inclusion criteria

We performed an international multicenter retrospective observational study in which data of all consecutive patients with a late acute PJI of the hip or knee between January 2005 and December 2015 were collected. If centers were not able to provide cases during the complete study period, a minimum of at least 10 consecutive cases was required to participate in the study. Late acute PJI was defined as patients with a history of normal joint function and who developed a sudden onset of symptoms and signs of a PJI, such as acute pain and/or swelling of the prosthetic joint. Patients with symptoms existing for longer than 3 weeks before surgical treatment was applied, patients who were within 3 months after the index arthroplasty, patients with a sinus tract and patients in whom antibiotic suppressive therapy

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was prescribed after surgery for other reasons than persistent signs of infection (e.g. because this was routine practice of the participating hospital and/or because the patient had severe comorbidity and was therefore, not eligible for future surgeries) were excluded from the analysis. PJI was defined according to the diagnostic criteria described by the Musculoskeletal Infection Society (MSIS) [16]. Multiple variables on patient characteristics, clinical presentation, microbiology results, surgical and antibiotic treatment and outcome were collected and analyzed. Patients treated with DAIR comprised the same cohort as described in our previous study [21]. Informed consent was retrieved when required by the ethics committee of the participating center.

Clinical outcome

Failure was defined as: i) the need for prosthesis removal due to persistent or recurrent signs of infection in the DAIR group or removal of the revised prosthesis in the removal group ii) the need for suppressive antibiotic therapy because of persistent clinical or biochemical signs of infection, iii) death due to the infection. The need for additional surgical debridement or spacer exchange in case of two-stage revisions were not considered as failure, but as part of the procedure. *Complete remission* was defined as a functional implant at the last follow-up, which was defined as the ability to walk without pain and the absence of clinical or biochemical signs of persistent infection.

Debridement and implant retention versus implant removal

The surgical techniques of the DAIR procedure, one-stage and two-stage revision surgery are extensively described in literature [3, 10]. In brief, in case of a DAIR procedure, visibly infected and necrotic tissue is excessively debrided, the wound is thoroughly irrigated using three to six liters of saline and mobile components are exchanged if possible. The same holds

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for a one-stage procedure, with the addition that the whole prosthesis is removed and exchanged for a new implant. Subsequent antimicrobial therapy is prescribed for a minimum of six weeks, but a duration of three months of antibiotics is most often applied for both procedures. During a two-stage procedure, the prosthesis is removed in the first stage and in most cases temporarily replaced by a cemented spacer loaded with antibiotics. Subsequent antimicrobial therapy is prescribed for a minimum of six weeks. In the second surgery, the new prosthesis is reimplanted during or after finishing antibiotic therapy for the initial infection. The applied antibiotic regimens in this study are depicted in Supplementary Table 1.

Statistical analysis

A Chi-square test (or a Fisher exact-test when appropriate) was used to analyze the difference between groups for categorical variables, and a student t-test (or Mann Witney U test when data was not normally distributed) for continuous variables. A Kaplan Meier survival curve with a cox-regression analysis was used to evaluate failure rate in time. To correct for bias between the DAIR group versus the implant removal group, a propensity score matching was performed. A propensity score was calculated using a logistic regression model in which the surgical strategy was used as the dependent variable, and variables that were significantly different between the implant retention group and the implant removal group as covariates. Matching was performed using a caliper of two decimals, and identical scores were randomized to perform the matching. Chi-square testing was performed to analyze the difference in outcome between both surgical approaches (implant retention versus implant removal). Univariate analysis using Pearson correlation was performed for determining risk factors for failure. Variables with a significance level of <0.2 were analyzed in a binary multivariate logistic regression model. The propensity score for DAIR was included in the

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model. For all analyses, p-values < 0.05 were considered as statistically significant. All analyses were two-tailed. Data were presented as mean ± Standard Deviation (SD) when data was normally distributed or median ± Inter Quartile Range (IQR) when data was not normally distributed. Statistical analysis was performed using SPSS, version 23.0 (SPSS Inc., Chicago, IL).

RESULTS

Patient characteristics implant retention versus implant removal

A total of 445 patients from 27 centers were included in the analysis. Table 1 shows the preoperative differences between patients with late acute PJI treated with DAIR and implant retention (n=340) versus patients in whom the implant was removed (n=105). In the implant removal group, one-stage revision was performed in 20 cases (19.0%), two-stage revision in 78 cases (74.3%), and definitive implant removal in 7 cases (6.7%) (Girdlestone for hips [n=5] and arthrodesis for knees [n=2]). Compared to implant removal, debridement with implant retention was performed more often in knee PJIs, cemented prostheses and in patients presenting with fever, a duration of symptoms for less than 10 days and with an identified source of infection. Factors associated with worse outcome in late acute PJIs, like *S. aureus* infections and preoperative risk factors predictive for failure according to the CRIME80-score (Table 2; including C-reactive protein and chronic obstructive pulmonary disease (C), rheumatoid arthritis (R), fracture as indication for the prosthesis (I), male gender (M), not exchanging the mobile components during DAIR (E), and age above 80 years (80) [21]) were similar between both groups.

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Clinical outcome implant retention versus implant removal

Table 1 shows the clinical characteristics and failure rate in the implant retention and implant removal group. The overall failure in patients treated with DAIR was 45.0% (153/340) versus 24.8% (26/105) in patients treated with implant removal ($p < 0.001$). There was no difference in failure rate between one-stage versus two-stage revision surgery: 25.0% (5/20) versus 24.4% (19/78), respectively (p 0.95). The higher failure rate in the implant retention group was dominated by the need for suppressive therapy because of persistent signs of infection and a relapse of infection during follow-up, while most of the failures in the implant removal group were due to a reinfection with another microorganism and PJI related death. The absolute number of PJI related death did not differ between both groups: 3.2% (11/340) for the implant retention group versus 4.8% (5/105) for the implant removal group, (p 0.52). The need for prosthesis removal as a primary endpoint for failure was the same in both groups. The higher failure rate in the implant retention group remained after propensity score matching for all significantly different variables between both groups as depicted in Table 1. We additionally performed a multivariate analysis including all variables with a P-value < 0.2 in the univariate analysis predictive for failure (i.e. the propensity score for DAIR, CRIME80-score ≥ 3, endocarditis, bacteremia, fever, < 1 year after the index surgery, use of immune suppressive drugs and *S. aureus* PJI). A preoperative CRIME80-score ≥ 3 (OR 2.9, 95% CI 1.7 – 4.9, $p < 0.001$), a PJI caused by *S. aureus* (OR 1.8, 95% CI 1.1 – 2.9, p 0.03) and implant retention (OR 3.1, 95% CI 1.7 – 5.8, $p < 0.001$) were the only significant independent predictors for failure. Although the exchange of mobile components during DAIR showed a significant decrease in failure rate from 52.4% (77/147) to 36.4% (64/176) (p 0.004), it remained significantly higher compared to implant removal (24.8% (26/105) p 0.04).

To assess whether the outcome of patients from centers with a high case load differed from the ones with a lower case load, we subdivided centers into 3 groups according to the number

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of cases they provided: i) less than 10 cases; ii) between 10 and 20 cases; iii) more than 20 cases. 5 centers provides less than 10 (18.5%), 10 centers between 10 and 20 (37.5%) and 12 center more than 20 cases (44%). Overall failure rates were 33.3% (12/36), 38.4% (38/99) and 41.6% (129/310), respectively (p 0.58). Failure rates of DAIR were 47.5% (10/21), 45.2% (28/62) and 44.7%(115/257), respectively (p 0.97).

Failure rates according to the preoperative CRIME80-score

Figure 1 shows the failure rate of patients treated with implant retention and implant removal according to the CRIME80-score [21], a scoring system that includes several host factors and that can be applied to decide which surgical treatment is preferred when the microorganism is not known prior to surgery. For cases treated with implant removal, the variable 'E' (Exchanging the mobile components) was not taken into account to calculate the score. Variables included in the score were complete in 395 out the 445 cases (88.8%). A high preoperative risk score for DAIR failure defined by a CRIME80-score ≥3, demonstrated a failure rate of 67.9% (53/78) in the DAIR group and a 16.7% failure rate (4/24) in the implant removal group ($p < 0.0001$). No significant difference in failure was observed with a CRIME80-score <3 (35.8% (78/218) versus 23.9% (16/67), respectively (p 0.07).

Failure rates according to the microorganism causing the infection and the possibility to exchange the mobile components

Figure 2 shows the failure rate in time between the different surgical strategies and causative microorganisms. The overall median follow-up of non-failures was 34 months (IQR 15 – 55) in the implant retention group versus 20 months (IQR 10 – 40) in the implant removal group (p 0.27). For PJI caused by microorganisms other than *S. aureus*, failure rate was 38.7% (77/199) in the implant retention group versus 23.7% (14/59) in the implant removal group (p

0.04). In the implant retention group, the exchange of mobile components during debridement showed a decrease in failure rate from 47.0% (39/83) to 29.6% (32/108) (p 0.01). When mobile components were exchanged, implant removal did not show any significant benefit in these cases (failure rate 29.6% (32/108) versus 23.7% (14/59), respectively, p 0.41). For PJI caused by *S. aureus*, failure rate was 53.9% (76/141) in the implant retention group versus 26.1% (12/46) in the implant removal group (p 0.001). The addition of rifampin in *S. aureus* PJI decreased failure rates from 65.2% (15/23) to 50.4% (57/113) (p 0.20). In patients with *S. aureus* PJI in whom the mobile components were exchanged had a failure rate of 47.1% (32/68) (p 0.02, compared to implant removal 26.1% (12/46)), and further decreased to 36.6% (15/41) when patients were subsequently treated with a fluoroquinolone in combination with rifampin. Within this group, failure rate was not statistically significantly different compared to implant removal (36.6% versus 26.1%, p 0.29). The difference between failure rates according to the surgical strategy was the same for hips and knees (Figure 2c en 2d).

Proposed surgical treatment algorithm

Based on our analyses, we propose a surgical treatment algorithm based on the CRIME80-score, the microorganism causing the infection and its susceptibility pattern (when available prior to surgery) to decide whether revision surgery instead of a DAIR procedure should be considered as first surgical treatment approach (Figure 3). According to this algorithm, a DAIR procedure is advised when the failure rate of DAIR is ≤ 50%, revision surgery should be considered if the failure rate of DAIR is > 50% - 65%, and revision surgery is advised when the failure rate of DAIR exceeds 65%. Because the microorganism causing the infection is mostly not known prior to surgery, we first subdivided patients according to their preoperative risk score for DAIR failure (Table 2). However, if the microorganism and its susceptibility to antibiotics are identified, a DAIR procedure maybe a viable treatment option

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in an additional subset of patients, especially in those infections caused by *S. aureus* in whom the mobile components can be exchanged and an antibiotic regimen of rifampin plus a fluoroquinolone can be administered (Figure 3).

Functional outcome in non-failures

Complete remission with a pain-free implant at the last point of follow-up was achieved in 85.9% of the non-failures. In the non-failure group, there was no difference in complete remission between the implant retention group and the implant removal group (Table 1). From the patients in the implant retention group who failed debridement and finally needed revision surgery (n=55), follow-up data was available in 41 cases (74.5%). During the last follow-up visit, 63.4% of these cases (26/41) had complete remission with a pain-free implant, while this was 84.3% (64/75) for patients in whom revision surgery was applied as a first surgical approach (p 0.007). There was no difference in functional outcome after revision surgery between cemented and uncemented prostheses (pain-free implant in 82.9% (29/35) versus 89.7% (26/29), respectively, p 0.44)).

DISCUSSION

Current international guidelines still recommend a DAIR procedure for all acute PJIs when the implant is well fixed and an antibiotic regimen potent against biofilm infection can be administered [15]. However, it is important to identify patients who have a high risk for DAIR failure prior to surgery in order to select the best surgical option. In line with this, using the same cohort of patients, we recently defined a preoperative risk score (CRIME80-score) to identify such high-risk patients for *late* acute PJIs [21]. Our current data suggests that patients with a CRIME80 score ≥ 3 (comprising 21% of the total cohort) will probably benefit more

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from revision surgery than from DAIR. DAIR was successful in only 35% of these patients, while treatment success increased to 83% when the implant was removed. These results were the same for hips and knees indicating that these joints can be approached the same. However, the causative microorganism and its susceptibility to antibiotics should preferably be taken into account as well, as this clearly affected treatment outcome in our analysis; *S. aureus* was an independent risk factor for failure in the multivariate analysis, but treatment success was higher when a rifampin based antibiotic regimen was administered.

To decide which percentual a priori chance of failure is acceptable to still recommend a DAIR procedure as a first surgical approach remains a matter of debate, and the advantages of a successful DAIR should be balanced against the consequences of failure. In our study we advised revision surgery if the apriori chance of DAIR failure exceeds more than 65%. It should be taken into account that revision surgery is more aggressive, especially when the implant is well fixed, and is associated with a higher economic burden and longer hospital stay [5,8]. Although several studies indicated that the success rate of revision surgery applied as salvage therapy after a failed DAIR is very low (ranging between 35 and 58%) [9, 12, 18], these low success rates have not been confirmed by others [6, 14]. In our analysis, around 35% of patients who received revision surgery after a failed DAIR procedure experienced pain at the site of the implant during the last outpatient clinic visit, while this was only 16% for those patients in whom revision surgery was performed as a first approach. These results suggest that functional outcome is worse when revision surgery is applied as salvage therapy, but previous studies evaluating several validated functional outcome scores do not support this finding [7, 12]. Our results do not indicate that applying revision surgery as first approach is not safe. Although not statistical different, in patients with a CRIME80-score ≥ 3, mortality rate was even higher when patients were treated with DAIR compared to implant removal (8.4% versus 4.2%).

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Our results should be interpreted in light of the following limitations. One of the limitations of our study was the retrospective study design with all the well-known limitations and risks for bias. Although we performed 1:1 propensity matching to control for bias, a randomized controlled trial remains the highest level of evidence in demonstrating the superiority of one treatment over another. In spite of the fact that we did not observe any differences in comorbidity and age between both treatment groups, we cannot completely rule out that a DAIR procedure was chosen based on the clinical judgment of the surgeon and therefore, by definition performed in a selected group of patients with a higher a priori chance to fail. Propensity score matching was only performed in a subset of patients that underwent DAIR (i.e. 24% of the total cohort), imposing the risk that the severely ill patients were excluded from the propensity analysis (i.e. high fever, shorter duration of symptoms), and a DAIR may still be the preferable treatment option in an acute setting for these patients despite a high CRIME80 score. In addition, we do not have data whether the implant was fixed or loosened during revision surgery and/or an osteotomy was necessary to remove the implant. In general, DAIRs are performed in fixed implants, and applying revision surgery in these cases, will lead to more bone destruction when removing the implant compared to loosened prostheses. Although we did not find any differences in functional outcome after revision surgery between cemented and uncemented protheses, the lack of this information subjects our study to selection bias as well, and propensity matching cannot fully correct for this. Finally, the outcome of DAIR is also determined by the antibiotic regimen that can be administered. *In vivo* animal models demonstrate the efficacy of rifampin combinations in orthopaedic implant related infections in cases with a low bacterial inoculum and young biofilm [22]. In particular the combination of rifampin with a fluoroquinolone has been proven to be a strong predictor of treatment success in patients with staphylococcal PJI [23]. When choosing the surgical strategy for late acute PJI, the causative microorganism and is susceptibility to antibiotics is

often not known, and thus, this factor for predicting the chance of treatment success cannot always be taken into account. All of these limitations should be taken into account when interpreting the results.

In conclusion, DAIR is a viable treatment option in most patients with late acute PJI, but outcome is significantly worse compared to implant removal. In patients with a high CRIME80-score (≥3) and in infections caused by *S. aureus* in particular in those in whom the mobile components cannot be exchanged and in whom a rifampin-based regimen cannot be administered, revision surgery should be considered.

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None

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LEGENDS FIGURES

Figure 1. Failure rate late acute PJI in patients with a high versus low CRIME80-score (depicted in Table 2) according to the surgical strategy.

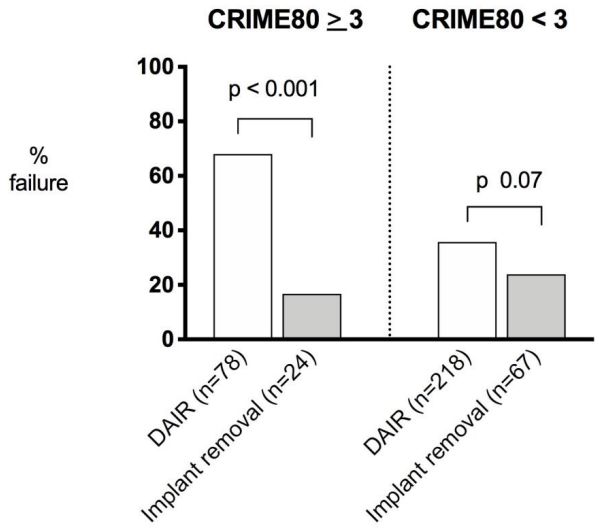

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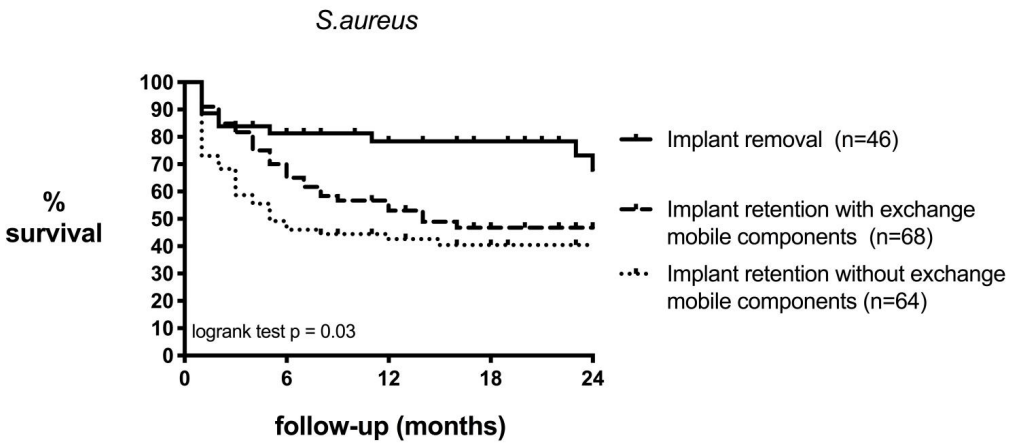
Figure 2. Outcome late acute PJI caused by *S. aureus* (A) and other microorganisms (B), knees (C) and hips (D) according to the surgical strategy. Survival is defined as treatment success, as described in the material and method section.



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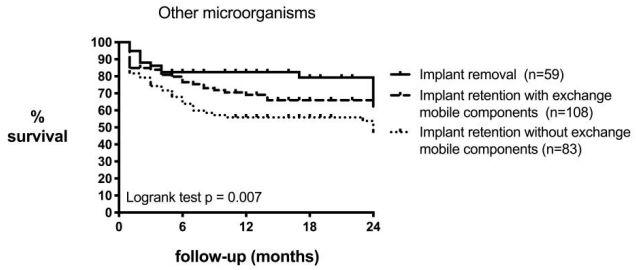
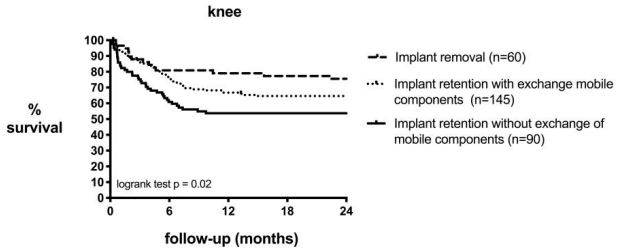

Other microorganisms
% survival
100
90
80
70
60
50
40
30
20
10
0
Logrank test p = 0.007
0
6
12
18
24
follow-up (months)
Implant removal (n=59)
Implant retention with exchange mobile components (n=108)
Implant retention without exchange mobile components (n=83)


knee
% survival
100
90
80
70
60
50
40
30
20
10
0
logrank test p = 0.02
0
6
12
18
24
follow-up (months)
Implant removal (n=60)
Implant retention with exchange mobile components (n=145)
Implant retention without exchange of mobile components (n=90)

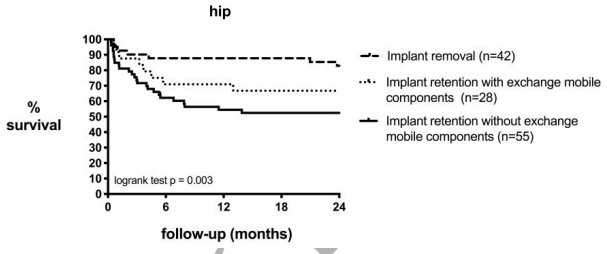

hip
% survival
100
90
80
70
60
50
40
30
20
10
0
logrank test p = 0.003
0
6
12
18
24
follow-up (months)
Implant removal (n=42)
Implant retention with exchange mobile components (n=28)
Implant retention without exchange mobile components (n=55)

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Figure 3. Surgical flow chart to determine if a DAIR procedure is feasible or if revision surgery should be considered as a first surgical approach. A DAIR procedure is advised in the Figure when the failure rate of DAIR is ≤ 50%, revision surgery should be considered if the failure rate of DAIR is > 50% - 65%, and revision surgery is advised when the failure rate of DAIR exceeds 65% in the studied subcategory.

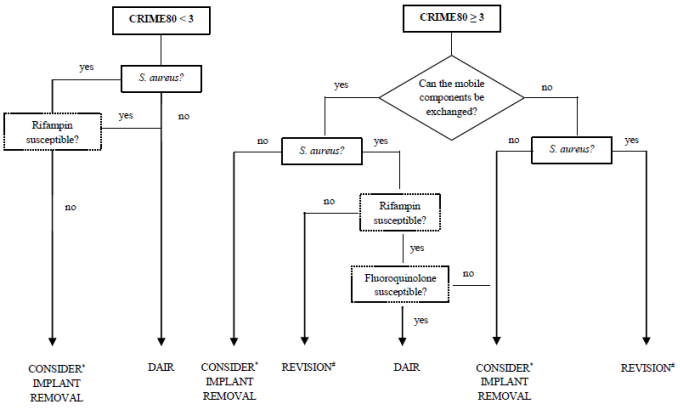

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Table 1. Patient characteristics late acute prosthetic joint infection (PJI) treated with surgical debridement and implant retention (DAIR) [n=340] versus implant removal [n=105 (1-stage revision (n=20), 2-stage revision (n=78) or definitive removal of the implant (n=7)]

	Total patient group			Propensity score matching 1:1		
	Implant retention (n=340)	Implant removal (n=105)	p-value	Implant retention (n=81)	Implant removal (n=81)	p-value
Baseline characteristics						
Gender, male	51.5% (175/340)	42.9% (45/105)	0.12	50.6% (41/81)	42.0% (34/81)	0.27
Age > 80 years*	21.5% (73/340)	20.0% (21/105)	0.75	19.8% (16/81)	22.2% (18/81)	0.70
BMI > 30	48.9% (110/225)	41.8% (28/67)	0.31	50.0% (25/50)	41.2% (21/51)	0.37
ASA classification ≥ III	48.6% (140/288)	44.4% (36/81)	0.51	47.1% (33/70)	42.6% (26/61)	0.60
Medical history						
Hypertension	59.6% (202/339)	61.9% (65/105)	0.67	64.2% (52/81)	61.7% (50/81)	0.67
Ischemic heart disease	12.1% (41/340)	8.6% (9/105)	0.32	8.6% (7/81)	7.4% (6/81)	0.77
Heart failure	9.1% (31/339)	6.7% (7/105)	0.43	2.5% (2/81)	3.7% (3/81)	0.65
Diabetes Mellitus	25.0% (85/340)	22.9% (24/105)	0.58	17.3% (14/81)	22.2% (18/81)	0.43
COPD*	10.0% (34/340)	14.3% (15/105)	0.22	4.9% (4/81)	13.6% (11/81)	0.06
Chronic renal insufficiency	7.6% (26/340)	11.4% (12/105)	0.23	6.2% (5/81)	6.2% (5/81)	1.0
Liver cirrhosis	3.2% (11/340)	6.7% (7/105)	0.12	6.2% (5/81)	3.7% (3/81)	0.47
Active malignancy	8.5% (29/340)	2.9% (3/105)	0.05	2.5% (2/81)	3.7% (3/81)	0.65
Rheumatoid arthritis*	7.9% (27/340)	5.7% (6/105)	0.45	8.6% (7/81)	7.4% (6/81)	0.77
Medication						
Oral anticoagulant	18.2% (61/336)	10.7% (11/103)	0.07	16.0% (13/81)	8.9% (7/79)	0.17

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Immune-suppressive drugs	11.5% (39/340)	7.6% (8/105)	0.26	11.1% (9/81)	9.9% (8/81)	0.80
Characteristics infected implant						
Knee	72.6% (247/340)	57.1% (60/105)	**0.003**	65.4% (53/81)	61.7% (50/81)	0.62
Indication prosthesis: fracture*	5.4% (17/313)	6.9% (7/101)	0.58	5.4% (4/81)	9.1% (7/81)	0.38
Revision prosthesis	28.4% (96/338)	32.4% (33/102)	0.44	30.9% (25/81)	31.6% (25/79)	0.92
Tumor prosthesis	4.3% (14/326)	4.9% (5/103)	0.81	3.9% (3/76)	3.8% (3/79)	0.96
Cemented stem	75.3% (186/247)	58.3% (49/84)	**0.003**	70.7% (41/58)	60.6% (40/66)	0.24
Age of the implant > 2 years	63.5% (216/340)	61.9% (65/281)	0.76	53.1% (43/81)	60.5% (49/81)	0.34
Clinical presentation						
Duration of symptoms > 10 days	20.9% (71/340)	30.5% (32/105)	**0.04**	22.2% (18/81)	18.4% (23/81)	0.37
Temperature > 38.5°C	21.3% (70/329)	5.9% (6/101)	**< 0.001**	16.9% (13/77)	6.5% (5/77)	0.05
Physical signs of inflammation	81.5% (264/324)	79.4% (81/102)	0.64	79.7% (59/74)	79.5% (62/78)	0.97
CRP > 150 mg/L*	60.4% (194/321)	53.2% (50/94)	0.21	60.0% (45/75)	59.2% (42/71)	0.92
Leucocytes > 17 cells/ µL	14.5% (46/317)	17.3% (18/104)	0.49	21.1% (16/76)	15.0% (12/80)	0.33
Bacteremia[1]	32.2% (109/339)	30.5% (32/105)	0.75	32.1% (26/81)	30.9% (25/81)	0.87

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Endocarditis	3.8% (13/340)	3.8% (4/105)	1.0	2.5% (2/81)	2.5% (2/81)	1.0
Source identified	45.9% (156/340)	33.7% (35/104)	**0.03**	37.0% (30/81)	38.8% (31/80)	0.82
Identified micro-organism						
Staphylococcus aureus	41.5% (141/340)	43.8% (46/105)	0.67	43.2% (35/81)	43.2% (35/81)	1.0
- Methicillin resistant	5.6% (19/340)	8.6% (9/105)	0.27	7.4% (6/81)	7.4% (6/81)	1.0
Enterococcus species	3.2% (11/340)	8.6% (9/105)	**0.02**	3.7% (3/81)	9.9% (8/81)	0.12
Streptococcus species	28.5% (97/340)	16.2% (17/105)	**0.01**	25.9% (21/81)	16.0% (13/81)	0.12
Gram negative rods	14.7% (50/340)	11.4% (12/105)	0.40	14.8% (12/81)	12.3% (10/81)	0.65
Outcome						
Overall failure	45.0% (153/340)	24.8% (26/105)	**< 0.001**	51.9% (42/81)	25.9% (21/81)	**0.001**
Failed cases						
- Need for implant removal	35.9% (55/153)	30.8% (8/26)	0.61	43.9% (18/42)	38.1% (8/21)	0.66
- Relapse of infection during FU	33.3% (51/153)	11.5% (3/26)	**0.03**	29.3% (12/42)	9.5% (2/21)	0.08
- Reinfection during FU	7.8% (12/153)	38.5% (10/26)	**< 0.001**	12.2% (5/42)	42.9% (9/21)	**0.006**
- Need for suppressive therapy	15.7% (24/153)	0% (0/26)	**0.03**	9.8% (4/42)	0.0% (0/21)	0.14
- Death due to PJI	7.2% (11/153)	19.2% (5/26)	0.05	4.9% (2/42)	9.5% (2/21)	0.48
Overall PJI related death	3.2% (11/340)	4.8% (5/105)	0.52	2.5% (2/81)	2.5% (2/81)	1.0
Complete	86.1% (155/180)	84.3% (64/75)	0.87	81.1% (30/37)	87.5% (49/56)	0.40

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remission in non-failures[2]						

[1]Patients in whom no bloodcultures were obtained were considered as bloodculture negative cases.

[2]Defined as: patients with a retained and pain-free implant at the last follow-up.

*Preoperative risk factors for failure in late acute PJI according to the CRIME80 score (6). BMI: Body Mass Index, ASA: American Society of Anesthesiologist, COPD: Chronic Obstructive Pulmonary Disease, CRP: C-Reactive Protein.

Table 2. CRIME80-score, pre-operative risk score for predicting DAIR failure in late acute periprosthetic joint infections.

CRIME80-score		
Variable	Description	Score
C	COPD	2
	CRP > 150 mg/L	1
R	Rheumatoid Arthritis	3
I	Index surgery (prosthesis indicated for a fracture)	3
M	Male gender	1
E	Exchange of mobile components	-1
80	Age > 80 years	2

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