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Northern Infection Network Joint A; Wouthuyzen-Bakker, Marjan; Lowik, Claudia A. M.; Ploegmakers, Joris J. W.; Knobben, Bas A. S.; Dijkstra, Baukje; de Vries, Astrid J.; Mithoe, Glen; Kampinga, Greetje; Zijlstra, Wierd P.

Published in:
Journal of Arthroplasty

DOI:
10.1016/j.arth.2020.02.043

The Journal of Arthroplasty 35 (2020) 2204–2209

Contents lists available at ScienceDirect

The Journal of Arthroplasty

journal homepage: www.arthroplastyjournal.org

Complications - Infection

A Second Surgical Debridement for Acute Periprosthetic Joint Infections Should Not Be Discarded

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ARTICLE INFO

Article history:
Received 13 November 2019
Received in revised form
13 February 2020
Accepted 20 February 2020
Available online 26 February 2020

Keywords:
periprosthetic joint infection
second DAIR
acute
failure
treatment

ABSTRACT

Background: In acute periprosthetic joint infections (PJIs), a second surgical debridement (debridement, antibiotics, and implant retention [DAIR]) is generally not recommended after a failed first one. We identified the failure rate of a second DAIR and aimed to identify patients in whom an additional debridement might still be beneficial.

Methods: Patients with acute PJI of the hip or knee and treated with DAIR between 2006 and 2016 were retrospectively evaluated. A second DAIR was routinely performed provided that the soft tissue was intact. Failure of a second DAIR was described as (1) the need for additional surgical intervention to achieve infection control, (2) the need for antibiotic suppressive therapy due to persistent clinical and/or biochemical signs of infection, or (3) PJI related death.

Results: From the 455 cases treated with DAIR, 144 cases underwent a second debridement (34.6%). Thirty-seven cases failed (37/144, 25.7%). The implant needed to be removed in 23 cases (23/144, 16%). Positive cultures during the second DAIR (odds ratio 3.16, 95% confidence interval 1.29-7.74) and chronic renal insufficiency (odds ratio 13.6, 95% confidence interval 2.03-91.33) were independent predictors for failure in the multivariate analysis. No difference in failure was observed between persistent infection with the same microorganism and reinfection with a new microorganism (failure rate 31.6% vs 34.6%, $P = .83$).

Conclusion: A second DAIR had a low failure rate in our cohort of patients and the implant could be retained in the majority of them. Therefore, a second DAIR should not be discarded in acute PJIs.

The first-line treatment for acute periprosthetic joint infection (PJI) is surgical debridement, antibiotics, and implant retention (DAIR) [1]. The reported efficacy of DAIR varies between 30%-80%, depending on host-related factors, the duration of symptoms before debridement, the microorganism(s) causing the infection, and its susceptibility to antibiotics and surgical factors [2–6]. It is controversial whether an additional surgical debridement is useful in clinically failed cases. During the last International Consensus Meeting held in Philadelphia in 2018, it was stated that "after one failed DAIR procedure, strong consideration should be given to removal of components" [7]. Eight-five percent of the participating international experts agreed with this statement, indicating a strong consensus. The stated recommendation was primarily based on the observation that in many studies a second DAIR is an independent predictor for failure in multivariate analyses [8] and on 2 retrospective studies that described a 50% failure rate of a second debridement [9,10]. Although one can argue that, for this reason, an

No author associated with this paper has disclosed any potential or pertinent conflicts which may be perceived to have impending conflict with this work. For full disclosure statements refer to https://doi.org/10.1016/j.arth.2020.02.043.

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https://doi.org/10.1016/j.arth.2020.02.043
0883-5403/

additional debridement should be avoided, the prosthesis can still be retained in around half of these patients, which is extremely beneficial given the consequences of removal of the implant. In addition, some experts propose that an additional debridement is only justified when the first DAIR was not properly performed (ie, without exchange of mobile components) or when the second DAIR can be performed within a short time interval after the first. It also should be taken into consideration that a new infection with another microorganism might be introduced during the first DAIR, which makes the second DAIR—theoretically—the "first one" for the additional identified microorganism(s) and might therefore still be beneficial.

In this multicenter retrospective cohort study, we determined the efficacy of a second surgical debridement in patients with an acute PJI and aimed to identify which patients might still benefit from an additional DAIR. We hypothesized that treatment success of a second debridement would be higher: (1) if mobile components were not exchanged during the first debridement, (2) when performed within a short time interval after the first, and (3) if the need for a second debridement was due to a reinfection with another microorganism than due to persistence of the initial infection.

Materials and Methods

Study Design

Patients with an acute PJI of the hip or knee treated with DAIR in 2 general hospitals (Martini Hospital and Medical Center Leeuwarden) and 1 university hospital (University Medical Center Groningen) in the Netherlands were retrospectively evaluated. The inclusion period was between January 2006 and December 2016. PJI was diagnosed in retrospect according to the criteria defined by the Musculoskeletal Infection Society [11]. An acute PJI was defined as an acute onset of symptoms and signs of PJI existing for no longer than 3 weeks before DAIR was performed. Early acute PJI was defined as a PJI that developed within 90 days after joint arthroplasty, and a late acute PJI as those that developed after 90 days. Patients who received the second DAIR more than 3 months after the first DAIR, patients with a follow-up of less than 1 year, and patients who underwent arthroscopic debridement were excluded from the analysis.

DAIR Procedure

The DAIR procedure involved a median arthrotomy in knee arthroplasties and posterolateral arthrotomy in total hip arthroplasties. Surgical debridement was performed by removing debris and necrosis including synovectomy if indicated, followed by irrigation of the joint with 3-6 L of irrigation fluid. The modular components were optionally exchanged by new ones. Empirical broad-spectrum intravenous antibiotic treatment was started after obtaining a minimum of 5 intraoperative cultures of deep tissue and synovial fluid. Intravenous antibiotic treatment was adjusted according to the culture results and continued for at least 2 weeks before switching to an oral regimen, which was continued for an additional 10 weeks. In case of staphylococcal PJI, rifampin was added to the antibiotic regimen as soon as the wound was dry. Provided that the soft tissue is intact, it is routine practice in the participating hospitals to perform a second surgical debridement if the patient shows clinical signs of failure of the first DAIR without directly escalating to extraction of the prosthesis. A second DAIR was considered with the following clinical scenarios: persistent or recurrent wound leakage, redness of the wound suspected for infection, fever, and/or persistent elevated inflammatory markers without any alternative explanation.

Definition of Failure

Failure was described as (1) the need for an additional surgical intervention to achieve infection control (ie, a third debridement or removal of the prosthesis), (2) the need for antibiotic suppressive therapy due to persistent clinical and/or biochemical signs of infection, or (3) PJI related death. A persistent infection was defined as isolation of the same microorganism with identical antibiogram during the second DAIR as the one cultured during the first DAIR. A reinfection was defined as isolation of a new microorganism during the second DAIR.

Statistical Analysis

A chi-squared test (or a Fisher's exact test when appropriate) was used to analyze the difference between groups for categorical variables, and a Student's *t*-test (or Mann-Whitney *U*-test when data were not normally distributed) for continuous variables. Possible risk factors for failure were selected and analyzed using univariate analysis. Variables with a significance level of <0.1 were analyzed in a binary multivariate logistic regression model. All analyses were 2-tailed and *P*-values <.05 were considered as statistically significant. Data were presented as mean ± standard deviation when data were normally distributed or median ± interquartile range when data were not normally distributed. Statistical analysis was performed using SPSS, version 23.0 (SPSS Inc, Chicago, IL).

Results

Patient Characteristics and Failure Rate

A total of 455 cases were included in the analysis. Three of the 455 patients that underwent the first DAIR procedure were culture negative (0.7%). From the total cohort of 455 patients, 144 (31.6%) underwent a second debridement due to persistent clinical signs of infection, including 15 late acute and 129 early acute PJIs. Thirty-nine of the 121 knees (32%) and 105 of the 334 hips (31%) underwent a second DAIR procedure. The clinical need for a second DAIR was more often observed in patients with a serum C-reactive protein level of >115 mg/L at initial clinical presentation (45.1% [65/144] vs 34.4% [107/311], $P = .03$) and in *Staphylococcus aureus* PJI (54.9% [79/144] vs 42.8% [133/311], $P = .02$). In 58% of cases, the second DAIR was performed within 14 days after the first DAIR (84/144). Intraoperative cultures during the second DAIR were negative in 89 of 144 cases (62%), the same microorganism—as the one cultured during the first DAIR—was found in 19 cases (13.2%), a new microorganism was cultured in 26 cases (18.1%), and both in the remaining 10 cases (6.9%). Persistent infection at the time of the second DAIR was highest for PJI caused by enterococci (enterococci: 23.8%, Gram-negative rods: 16.0%, streptococci: 12.0%, and *S aureus*: 10.1%). From the 144 cases that underwent a second surgical debridement, 37 cases failed (25.7%). From the failures, additional surgical intervention to achieve infection control was needed in 26 cases: 11 cases underwent immediate implant removal and 15 patients received a third debridement. From the patients that underwent a third debridement, the implant finally needed to be removed in 12 of them (80%). Thus, from the 144 cases that underwent a second DAIR, the implant needed to be removed in 23 cases, which is 16% of the total cohort. None of the patients that failed after a second DAIR procedure and underwent subsequent exchange arthroplasty was in need of amputation during follow-up. One of the patients who failed a third DAIR procedure did undergo amputation. Patients with a late acute PJI had a higher failure rate of a second DAIR compared to early acute PJI, but this difference was not statistically significant (40% [6/15] vs 24% [31/129], $P = .18$).

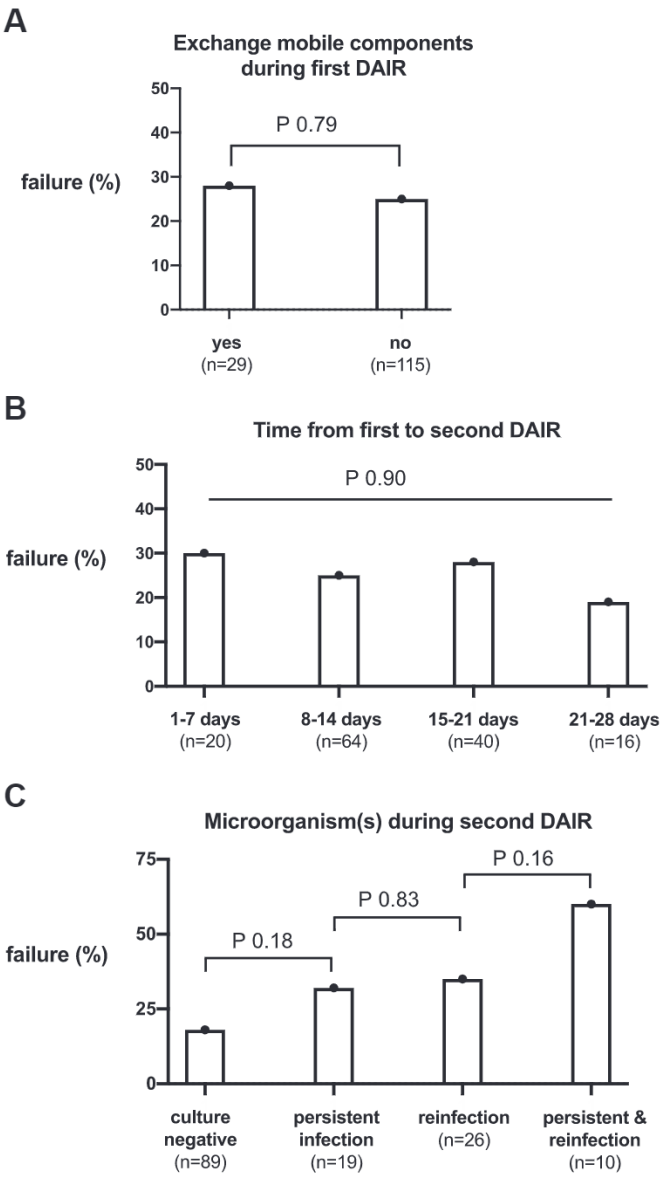

Fig. 1. Failure of the second DAIR in relation to the exchange of mobile component during the first DAIR (A), the time interval between the first and second DAIR (B), and the microorganisms cultured during the second DAIR (C). Persistent infection: the same microorganism was cultured during the second DAIR as the one cultured during the first DAIR. Reinfection: a new microorganism was cultured during the second DAIR as the one cultured during the first DAIR. DAIR, debridement, antibiotics, and implant retention.

Risk Factor Failure Second Surgical Debridement

We did not find a higher success rate of the second DAIR in patients in whom the mobile component was not exchanged during the first DAIR, nor in patients who underwent the second DAIR within a short time interval (ie, within 14 days) after the first one (Fig. 1A and 1B). We did observe a higher failure rate in patients who had positive cultures during the second DAIR compared to those with negative cultures (failure rate 38.2% vs 18.0% respectively, $P = .007$) (Fig. 1C). However, in those with positive cultures, no difference in failure was observed between persistent infection with the same microorganism and reinfection with a new microorganism (failure rate 31.6% vs 34.6% respectively, $P = .83$). The highest failure rate was observed in those who had both persistent infection and reinfection (60%), but only a limited number of cases fell into this subcategory (n = 10).

To identify risk factors for failure of the second DAIR, we performed a univariate and multivariate analysis. We included several variables in the univariate analysis on medical history, characteristics of the infected implant, clinical presentation, microorganisms cultured during the first and second DAIR, and surgical techniques (Table 1). Although enterococcal PJI was more often associated with persistence of positive cultures during the second DAIR, failure of the second DAIR was not associated with the microorganism causing the infection, nor with characteristics of the infected implant, timing of the second DAIR, or the initial clinical presentation. In addition, no difference in failure rate was observed for hips and knees (failure rate of 25.7% vs 25.6% respectively, $P = .99$).

Positive cultures during the second DAIR (odds ratio [OR] 3.16, 95% confidence interval [CI] 1.29-7.74) and chronic renal insufficiency (OR 13.6, 95% CI 2.03-91.33) were the only independent predictors for failure of the second DAIR. Surprisingly, a BMI >30 kg/m^2 was an independent predictor for treatment success (OR 0.26, 95% CI 0.09-0.72). Therefore, we subanalyzed patients with a BMI ≤30 and >30 kg/m^2 (Table 2), and found that patients with a BMI >30 kg/m^2 were younger, were less often diagnosed with rheumatoid arthritis, had lower inflammatory parameters during the initial clinical presentation, and had a significantly lower rate of persistent infection during the second debridement.

Discussion

In this multicenter cohort study, we demonstrated a high success rate of a second DAIR in patients who had clinical failure of the first DAIR, and the implant could be retained in 84% of cases. Our data indicate that—in contrast to the International Consensus Meeting recommendation—a second DAIR should not be discarded in the treatment of acute PJIs provided that the soft tissue is intact after the first DAIR procedure. Due to the low number of culture negative PJIs in the initial cohort, we are not able to conclude about the success rate of a second DAIR procedure in this particular patient category.

Unlike what we hypothesized, we did not find a higher success rate of a second DAIR in patients in whom the mobile component were not exchanged during the first DAIR, nor in the patients who underwent the second DAIR within a short time interval after the first one. We did find a higher failure rate in cases with positive cultures during the second DAIR, but no difference was found between those who had persistent infection and those who had reinfection with a new microorganism. In addition, failure of the second DAIR was not related to the type and location of the prosthesis, the initial clinical presentation, or the microorganism(s) causing the PJI. Chronic renal insufficiency, BMI ≤30 kg/m^2, and positive cultures during the second DAIR were the only independent predictors for failure in the multivariate analysis. As the latter is unknown prior to surgery, only the presence of renal insufficiency and a BMI ≤30 kg/m^2 can aid in the decision-making process to choose for an additional debridement or not. Our finding that obese patients had a higher success rate compared to nonobese patients was unexpected and in contrast to previous findings, as obesity has been described as risk factor for failure in revision arthroplasties, in particular in 2-stage revisions [12–14]. Furthermore, in a previous study, we did not find any difference in failure rate of DAIR between obese and nonobese patients [15]. Selection bias should be considered as potential explanation of our finding. In primary hip arthroplasty for example, a higher rate of wound leakage is described in obese patients [16], which could have prompted the surgeon to perform the second DAIR at a lower threshold compared to nonobese. However, the rate of culture

Table 1
Clinical Characteristics of Patients With a Failed or Successful Second DAIR.

	Nonfailures Second DAIR (n = 107), %	Failures Second DAIR (n = 37), %	*P*-Value	OR MV Analysis (95% CI)	*P*-Value
Baseline characteristics					
Gender: male	43.9	51.4	.44		
Age >80 y	33.6	45.9	.18		
BMI >30 kg/m^2	46.9	26.5	.04[a]	0.29 (0.11-0.78)	**.01**
Smoking	15.2	22.6	.35		
Medical history					
Ischemic heart disease	21.5	32.4	.18		
Heart failure	11.2	21.6	.12		
Diabetes mellitus	20.6	24.3	.63		
COPD	24.3	29.7	.52		
Chronic renal insufficiency	1.9	13.5	.01[a]	13.6 (2.03-91.33)	**.007**
Rheumatoid arthritis	6.5	16.2	.09[a]	1.09 (0.27-4.34)	.91
Medication					
Immunosuppressive drugs	14.0	18.9	.48		
Acenocoumarol	27.1	32.4	.54		
Infected implant					
Primary prosthesis	15.9	21.6	.43		
Cemented prosthesis	86.0	89.2	.62		
Knee	27.1	27.0	.99		
Initial clinical presentation					
Duration of symptoms >10 d	34.6	29.7	.59		
Temperature >38.5°C	22.4	21.6	.92		
CRP >115 mg/L	42.1	54.1	.21		
Leukocytes >15 cells/μL	27.1	32.4	.54		
Bacteremia[b]	9.3	13.5	.48		
Late acute PJI	8.4	16.2	.19		
Microorganism during first DAIR					
Staphylococcus aureus	54.2	56.8	.79		
Streptococci	18.7	13.5	.48		
Gram-negative rods	17.8	16.2	.83		
Enterococci	14.0	16.2	.74		
Polymicrobial	40.2	37.8	.80		
Microorganism during second DAIR					
Culture positive[c]	31.8	56.8	.008[a]	3.16 (1.29-7.74)	**.01**
Persistent infection[d]	12.1	16.2	.53		
Reinfection[d]	15.9	24.3	.25		
Persistent and reinfection[d]	3.7	16.2	.02		
Surgical techniques DAIR					
Exchange of mobile components first DAIR	19.6	21.6	.79		
Exchange of mobile components second DAIR	26.2	29.7	.68		
>14 d between first and second DAIR	42.1	40.5	.87		
>21 d between first and second DAIR	10.8	15.0	.53		
>30 d between arthroplasty and second DAIR[e]	53.1	38.7	.16		
>60 d between arthroplasty and second DAIR[e]	6.1	6.5	.95		

Bold values indicate a statistical significance of $P < .05$.
BMI, body mass index; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; DAIR, debridement, antibiotics, and implant retention; OR, odds ratio; MV, multivariate; CI, confidence interval; PJI, periprosthetic joint infection.
[a] Variables with a *P*-value <.1 were included in the MV binary logistic regression analysis.
[b] Patients in whom no blood cultures were obtained were considered as blood culture negative cases.
[c] Intraoperative cultures during the second DAIR were positive.
[d] The microorganism cultured during the second DAIR was the same (persistent) or different (reinfection) as the one cultured during the first DAIR.
[e] Only described for early acute PJIs.

positivity during the second DAIR was similar between obese and nonobese patients, suggesting a similar risk group for failure. The fact that obese patients that underwent a second DAIR were younger, were less often diagnosed with rheumatoid arthritis, had lower inflammatory parameters during the initial clinical presentation, and had a significantly lower rate of persistent infection could be a potential explanation for the better outcome. For this reason, obesity should probably be interpreted as surrogate marker for the better outcome observed in this patient category, and not as protective factor per se.

We observed a lower failure rate of a second DAIR compared to other studies. Lizaur-Utrilla et al [17] compared the outcome of DAIR of the knee with 2-stage exchange arthroplasty. From the 39 patients that underwent DAIR, 24 failed and received a second debridement. All of these 24 cases failed, and the patients either underwent arthrodesis or implant removal. It is unclear why the failure rate of the second DAIR in this cohort was so high. In our study, we did not find a higher failure rate in knees, but in other studies knees had a higher failure rate of the second DAIR compared to hip [9,18]. A possible explanation could be that Lizaur-Utrilla et al include patients with a fistula, suggesting a bad quality of soft tissue and chronicity of the infection. We only included patients in whom the soft tissue was intact after the first DAIR and patients who underwent the second DAIR within 3 months after the first. It is reasonable to assume that performing a DAIR after this time period greatly reduces the success rate. In the study performed by Triantafyllopoulos et al [9], 19 of 141 patients (13.4%) underwent a second DAIR, and the infection was controlled with retention of the implant in 10 cases (52.6%). Due to the relatively low numbers of cases that underwent a second DAIR, no risk factors for failure of the second debridement could be described. However, a higher failure rate was observed in those who underwent the second DAIR more than 20 days after the first one and in those with a late acute PJI. Our cohort entailed only a few patients with late acute PJIs, which makes

Table 2
Clinical Characteristics of Obese (BMI >30 kg/m^2) vs Nonobese Patients (BMI ≤30 kg/m^2).

	BMI ≤30 (n = 76), %	BMI >30 (n = 54), %	*P*-Value
Baseline characteristics			
Gender: male	46.1	57.4	.20
Age >80 y	48.7	22.2	**.002**
Smoking	13.6	19.6	.39
Medical history			
Ischemic heart disease	25.0	27.8	.72
Heart failure	14.5	14.8	.96
Diabetes mellitus	21.1	25.9	.52
COPD	23.7	31.5	.32
Chronic renal insufficiency	3.9	7.4	.39
Rheumatoid arthritis	13.2	3.7	.07
Medication			
Immunosuppressive drugs	17.1	11.1	.34
Acenocoumarol	32.9	24.1	.28
Infected implant			
Primary prosthesis	80.3	88.9	.19
Cemented prosthesis	82.9	92.6	.12
Knee	23.7	37.0	.10
Initial clinical presentation			
Duration of symptoms >10 d	26.3	38.9	.13
Temperature >38.5°C	26.3	20.4	.43
CRP >115 mg/L	50.0	37.0	.14
Leukocytes >15 cells/μL	36.8	20.4	**.04**
Bacteremia[a]	14.5	5.6	.12
Late acute PJI	13.2	5.6	.15
Microorganism during first DAIR			
Staphylococcus aureus	56.6	48.1	.34
Streptococci	18.4	20.4	.78
Gram-negative rods	14.5	22.2	.25
Enterococci	10.5	20.4	.12
Polymicrobial	35.5	50.0	.10
Microorganism during second DAIR			
Culture positive[b]	35.5	42.6	.41
Persistent infection[c]	17.1	5.6	**.048**
Reinfection[c]	13.2	25.9	.06
Persistent and reinfection[c]	5.3	11.1	.22
Surgical techniques DAIR			
Exchange of mobile components first DAIR	17.1	22.2	.47
Exchange of mobile components second DAIR	21.1	33.3	.12
>14 d between first and second DAIR	43.4	46.3	.75
>21 d between first and second DAIR	18.4	14.8	.59
>30 d between arthroplasty and second DAIR[d]	57.6	47.1	.26
>60 d between arthroplasty and second DAIR[d]	6.1	5.9	.97

Bold values indicate a statistical significance of $P < .05$.
BMI, body mass index; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; DAIR, debridement, antibiotics, and implant retention; PJI, periprosthetic joint infection.
[a] Patients in whom no blood cultures were obtained were considered as blood culture negative cases.
[b] Intraoperative cultures during the second DAIR were positive.
[c] The microorganism cultured during the second DAIR was the same (persistent) or new (reinfection) as the one cultured during the first DAIR.
[d] Only described for early acute PJIs.

it difficult to draw conclusions about this particular patient group. We did observe a higher failure rate of a second debridement in late acute PJIs, but this difference was not statistically significant. Previous studies have demonstrated that the failure rate of DAIR is higher for late acute compared to early acute PJIs when caused by staphylococci. For this reason, a second DAIR probably should be avoided in this subcategory of patients [4,19].

Our study has some limitations. A first potential limitation of our study is the relatively large amount of patients that had negative cultures during the second DAIR (62%), suggesting that the DAIR was performed in a patient group with a low risk of persistent infection. In the study of Triantafyllopoulos et al [9], all 19 patients that underwent the second DAIR had positive cultures. On the other hand, we had strict criteria for clinical failure of the first DAIR, and the percentage of patients that underwent a second DAIR (34.6%) is in agreement with the failure rate of DAIR in literature [2–6]. Other studies reporting the outcome of a second DAIR procedure did not report the culture results of the second debridement [10,17–20]. A second limitation is that we were not able to collect detailed data on clinical characteristics closely to the second DAIR, but only at initial presentation (ie, prior to performing the first). Finally, we did not compare the outcome of a second DAIR procedure to immediate exchange arthroplasty. Some surgeons prefer immediate exchange arthroplasty because of soft tissue concerns if the second DAIR also fails. There have been reports in literature that the outcome of exchange arthroplasty is worse when performed after a failed DAIR procedure, but these data are controversial [21–25]. In our cohort, none of the patients that failed a second DAIR procedure and underwent subsequent exchange arthroplasty were in need for amputation. Moreover, although there may be a selection bias, the outcome of a second DAIR in our study appeared to be similar or even better than a 2-stage exchange procedure after a failed DAIR procedure [21,24,25], thereby favoring a second DAIR over a more rigorous 2-stage exchange procedure.

To our knowledge, our study is the largest analysis so far evaluating the outcome of a routinely performed second DAIR procedure in a clinically failed first one, provided that the soft tissue remained intact after the first DAIR. Our data indicate that a second DAIR procedure should not be discarded in acute PJIs. Patients who have positive cultures during the second DAIR have a higher risk of subsequent failure, but the implant can still be retained in the vast majority with a minimal follow-up period of 1 year.

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