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Exchange of Modular Components Improves Success of Debridement, Antibiotics, and Implant Retention

An Observational Study of 575 Patients with Infection After Primary Total Hip Arthroplasty

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Background: Debridement, antibiotics, and implant retention (DAIR) is a surgical treatment for periprosthetic joint infection (PJI). DAIR is a desirable treatment option from an economic and patient perspective, if successful. The aim of this observational study was to compare the rates of success, defined as no additional reoperations due to PJI, between DAIR with exchange of modular components and DAIR without exchange in patients who had first-time PJI after primary total hip arthroplasty (THA).

Methods: Patients with PJI at the site of a primary THA who were treated with DAIR in Sweden between January 1, 2009, and December 31, 2016, were identified in the Swedish Hip Arthroplasty Register. Supplementary questionnaires were sent to orthopaedic departments for additional variables of interest related to PJI. The primary end point was another reoperation due to PJI within 2 years after the first-time DAIR. DAIR with exchange was compared with DAIR without exchange using Kaplan-Meier survival analysis and Cox regression analysis.

Results: A total of 575 patients treated with DAIR for a first-time PJI at the site of a primary THA were analyzed; 364 underwent component exchange and 211 did not. The exchange of components was associated with a lower rate of reoperations due to PJI after DAIR (28.0%) compared with non-exchange (44.1%). The Kaplan-Meier implant survival estimate for exchange was 71.4% (95% confidence interval [CI] = 66.9% to 76.3%) compared with 55.5% (95% CI = 49.1% to 62.7%) for non-exchange. With the analysis adjusted for confounders, DAIR with exchange was associated with a significantly decreased risk of another reoperation due to PJI compared with non-exchange (hazard ratio [HR] = 0.51 [95% CI = 0.38 to 0.68]).

Conclusions: In patients with a first-time PJI at the site of a primary THA, DAIR with exchange of modular components was superior to non-exchange DAIR. Surgeons should strive to exchange components when they perform DAIR, but there is a need to further identify how DAIR best should be practiced and which patients benefit from it.

Level of Evidence: Therapeutic Level III. See Instructions for Authors for a complete description of levels of evidence.

Periprosthetic joint infection (PJI) is a serious complication and is the most common cause of early reoperations after total hip arthroplasty (THA)[1]. Treatment of these PJIs requires multiple considerations such as the type of infection and the patient's status and preferences[2]. The definitions of successful debridement, antibiotics, and implant retention (DAIR) vary, and reported success rates have ranged from 37% to 87%[3-10]. Numerous factors influence the success, such as timing of surgery, type of bacterial growth, choice of antimicrobial therapy, and individual patient and surgical factors[4,5,10-12]. As implant preservation is desirable from a patient and economic perspective, it is important to identify correct indications and how the procedure should be best performed[12-14].

With regard to surgical factors, the exchange of modular components is associated with a higher success rate than non-exchange[4,8,11,12]. Although the exchange of components has become more common[7], both methods are still used and current evidence is based on case series, mainly with small study

Disclosure: This research was funded by regional research grants (ALFGBG-719961) and the Doktor Felix Neubergh Foundation. On the **Disclosure of Potential Conflicts of Interest** forms, *which are provided with the online version of the article*, one or more of the authors checked "yes" to indicate that the author had a relevant financial relationship in the biomedical arena outside the submitted work (http://links.lww.com/JBJSOA/A230).

samples and in cohorts mixing primary and revision THAs. Using the Swedish Hip Arthroplasty Register (SHAR) and data from case records, we aimed to evaluate the success rate of DAIR in a relatively large cohort of patients with first-time PJI and to determine if the exchange of components is a means of improving outcome in patients treated with DAIR.

Materials and Methods

Study Design and Setting

DAIR operations due to PJI after primary THA conducted in Sweden between January 1, 2009, and December 31, 2016, were identified using SHAR. The SHAR is a nationwide register for hip arthroplasty in which all orthopaedic departments in Sweden participate. The SHAR collects baseline information on hip arthroplasty including reoperations and implant revisions. In the SHAR, revisions are defined as procedures involving an exchange, extraction, or addition of implant components. Reoperations are defined as all types of open surgical procedures related to the prosthesis. In validation studies, the SHAR was found, on average, to be 92% complete with regard to revisions (year 2017) and 67% complete with regard to reoperations due to PJI (based on data from 2005 to 2008)[1,15]. After cross-matching with the Swedish Drug Register, missing cases were added, probably resulting in a completeness of >95% for 2005 to 2008. Thereafter, completeness with regard to revisions has ranged from 91% to 94.7% for 2009 to 2016[1].

The SHAR contains information on age, sex, primary diagnosis, surgical details, and implant-specific details. However, it does not contain sufficient information for comprehensive infection research[16]. Therefore, supplementary questionnaires on DAIR operations performed between January 1, 2009, and December 31, 2016, were sent to every orthopaedic department in Sweden. The questionnaires included variables related to the infection on a patient level (see Appendix, Supplementary Table 1) and were completed between September 2018 and November 2019. The questionnaire data were merged with SHAR data on additional reoperations and revisions in February 2020. Follow-up was set at 2 years for each patient.

Patients with a first-time PJI after primary THA due to any diagnosis were included. PJI was defined according to the major criteria described by the Musculoskeletal Infection Society (MSIS), modified to include patients with intraoperative purulence[17]. The questionnaire data were used for diagnosis. Patients who did not meet the criteria or were treated with delayed wound closure after DAIR (secondary suturing) were excluded, as were patients with sepsis, bilateral PJI, known endocarditis, or terminal cancer (Fig. 1).

The study was approved by the Regional Ethical Review Board in Gothenburg, Sweden (DNR 804-17 with amendments T053-18 and 2019-00957).

Variables

Exposure

The exposure of interest was whether modular components (femoral head and/or liner) were exchanged during the DAIR procedure (exchange) or not (non-exchange).

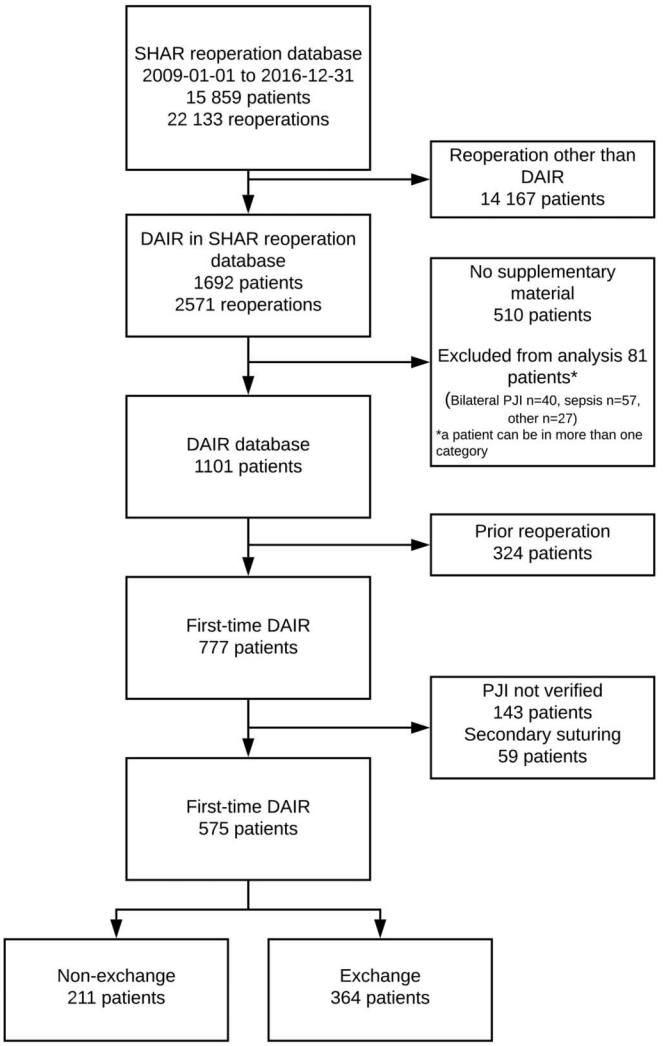

Fig. 1

Flow diagram of study inclusion.

Outcomes

Any additional reoperation due to PJI during the follow-up period of 2 years after the first DAIR procedure constituted the primary outcome. Revision of bone-anchored implant components—i.e. the femoral stem and/or the acetabular cup—due to PJI was the secondary outcome.

Symptom onset was defined as the first time that the patient contacted the health-care system with suspected PJI. If a patient presented with symptoms immediately postoperatively (persistent wound leakage), symptom onset was considered the day of surgery. When symptom onset was reported only in terms of months, the longest symptom duration was chosen (beginning on the first day of the given month).

Infections were considered polymicrobial if there was growth of >1 species in intraoperative culture samples (additional microbes observed did not need to be present in >2 culture results). Coagulase-negative staphylococci (CoNS) were grouped together as they were not always determined to

the species level. *Staphylococcus lugdunensis* and *S. aureus* were grouped together for analysis because they have similar virulence[18].

The duration of antimicrobial treatment was predefined in the questionnaires as <4 weeks, 4 to 12 weeks, and >12 weeks. Cessation of antimicrobial treatment was either the date of treatment failure (i.e., the date of a new reoperation) or the date at which antimicrobial treatment was stopped. If patients underwent a reoperation <4 weeks after DAIR, antibiotic treatment was set as <4 weeks. Antimicrobial treatment given at discharge from the hospital was registered as oral treatment. Patients who underwent another reoperation before discharge were registered as not having had oral treatment because of the short treatment period. Any change in antimicrobial therapy after discharge was noted.

Statistical Analysis

Kaplan-Meier survival analysis was performed with exchange of modular components as the independent factor and time to a new reoperation due to PJI after DAIR as the end point. Patients were censored at death or at 2 years after DAIR, whichever came first. Revision of bone-anchored components subsequent to DAIR was analyzed in the same way.

Cox regression analysis was conducted to compare the risk of a new reoperation due to PJI between patients treated with exchange DAIR and those treated with non-exchange DAIR. Furthermore, a Cox regression analysis was used to compare the risk of revision of bone-anchored components subsequent to exchange and non-exchange DAIR. Potential confounders were included in the model (Table III). Plots of Schoenfeld residuals were visually inspected to check the proportional hazard assumption. American Society of Anesthesiologists (ASA) Physical Status classifications were not available for the entire cohort, but a sensitivity analysis using the same model was performed for reoperations due to PJI for all cases with complete data. Due to the diversity of antimicrobial treatment and difficulties in identifying categories, this factor was not included in the regression models. Hazard ratios (HRs) are presented with 95% confidence intervals (CIs).

In a subgroup (n = 151), collected data contained information on suppressive antimicrobials and clinical symptoms of additional infection. The findings in this subgroup are presented descriptively in an attempt to describe infection resolution, defined as no additional reoperation, no suppressive antimicrobial treatment, and no clinical symptoms of infection.

Data were analyzed using R software (version 3.6.1; R Foundation for Statistical Computing).

Results

Study Population

A review of the SHAR reoperation database identified 2,571 DAIR procedures in 1,692 patients. Supplementary questionnaires were collected for 1,182 patients (69.9%), and the remaining 510 (30.1%) were excluded because of a lack of supplementary data. A total of 575 patients met the study inclusion criteria (Fig. 1). There were 364 in the exchange group and 211 in the non-exchange group.

TABLE III Multivariable Analysis of Reoperations Due to PJI within 2 Years After DAIR*

	HR	95% CI†
DAIR procedure		
Non-exchange	1	
Exchange	0.51	**0.38-0.68**
Primary diagnosis		
Osteoarthritis	1	
Trauma	1.09	0.74-1.61
Other	1.29	0.82-2.01
Sex		
Male	1	
Female	0.81	0.60-1.11
Age	1.00	0.98-1.01
Time from primary THA to symptoms		
≤30 days	1	
>30 days	1.01	0.72-1.41
Time from symptoms to DAIR		
≤7 days	1	
>7 days	0.74	0.52-1.06
Bacterial growth		
S. aureus/S. lugdunensis	1	
Polymicrobial	0.70	0.48-1.02
CoNS	0.53	**0.31-0.92**
Streptococci	0.85	0.54-1.34
Other	1.00	0.61-1.62
Negative‡	0.85	0.30-2.38
Fixation		
Uncemented	1	
Any component cemented	0.93	0.60-1.46

*Model adjusted for primary diagnosis, sex, age, time from primary THA to symptoms, time from symptoms to DAIR, bacterial growth, and method of fixation. †Significant values are in bold. ‡Presence of sinus tract or intraoperative purulence.

The demographic characteristics were similar for the patients in the exchange and non-exchange groups (Table I). Although not significant, the greatest difference between the groups was the time of symptom onset, with 73.4% in the exchange group having symptoms within 30 days compared with 66.8% in the non-exchange group. Overall, the most common bacterial growth was polymicrobial (31.3%) and monomicrobial growth of *S. aureus* or *S. lugdunensis* (28.7%). In the exchange group, the head was exchanged in 297 cases (81.6%) and both the head and the liner, in 67 (18.4%) (see Appendix, Supplementary Table 2).

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TABLE I Demographic Data for the Study Group*

	Study Cohort (N = 575)	Non-Exchange (N = 211)	Exchange (N = 364)
Age* *(yr)*	69.9 (11.2)	69.5 (12.2)	70.2 (10.7)
Sex *(no. [%])*			
Female	278 (48.3)	96 (45.5)	182 (50.0)
Male	297 (51.7)	115 (54.5)	182 (50.0)
ASA class *(no. [%])*			
1	63 (11.0)	24 (11.4)	39 (10.7)
2	278 (48.3)	98 (46.4)	180 (49.5)
3	179 (31.1)	60 (28.4)	119 (32.7)
4	5 (0.9)	4 (1.9)	1 (0.3)
Missing	50 (8.7)	25 (11.8)	25 (6.9)
Body mass index* *(kg/m^2)*	28.8 (5.4)	29.2 (5.6)	28.5 (5.2)
Primary diagnosis *(no. [%])*			
Primary osteoarthritis	403 (70.1)	146 (69.2)	257 (70.6)
Trauma-related	129 (22.4)	44 (20.9)	85 (23.4)
Other	38 (6.6)	17 (8.1)	21 (5.8)
Inflammatory joint disease	10	5	5
Osteonecrosis	15	8	7
Tumor	2	1	1
Missing	5 (0.9)	4 (1.9)	1 (0.3)
Fixation *(no. [%])*			
At least 1 component cemented	485 (84.3)	178 (84.4)	307 (84.3)
Uncemented	87 (15.1)	30 (14.2)	57 (15.7)
Missing	3 (0.5)	3 (1.4)	0 (0.0)
Time from primary THA to symptoms			
Median (interquartile range) *(days)*	17 (11-37)	18.5 (12-43)	17 (11-33.5)
No. (%) of patients			
≤30 days	408 (71.0)	141 (66.8)	267 (73.4)
>30 days	162 (28.2)	67 (31.8)	95 (26.1)
Missing	5 (0.9)	3 (1.4)	2 (0.5)
Time from symptoms to DAIR			
Median (interquartile range) *(days)*	3 (1-8)	3 (1-8)	4 (1-4)
No. (%) of patients			
≤7 days	409 (71.1)	150 (71.1)	259 (71.2)
>7 days	161 (28.0)	58 (27.5)	103 (28.3)
Missing	5 (0.9)	3 (1.4)	2 (0.5)
Bacteria *(no. [%])*			
Polymicrobial growth	180 (31.3)	66 (31.3)	114 (31.3)
S. aureus/S. lugdunensis	165 (28.7)	56 (26.5)	109 (29.9)
Streptococci	79 (13.7)	30 (14.2)	49 (13.5)
CoNS	77 (13.4)	31 (14.7)	46 (12.6)
Other	62 (10.8)	21 (10.0)	41 (11.3)
Negative†	12 (2.1)	7 (3.3)	5 (1.4)

*The values are given as the mean (standard deviation). †Presence of sinus tract or intraoperative purulence.

Reoperations Due to PJI

Somewhat unexpectedly, the only reason for additional surgery within 2 years was PJI. Of all 575 patients, 195 (33.9%) underwent additional surgery. Of the patients with additional surgery, 111 (19.3%) underwent >1 reoperation (Table II). During the follow-up period, 12.8% (27) of the patients in the

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TABLE II Outcomes and Types of Reoperations

	Non-Exchange (N = 211)	Exchange (N = 364)
Reoperation due to PJI *(no. [%])*	93 (44.1)	102 (28.0)
No. of reoperations* after DAIR *(no. [%])*		
0	118 (55.9)	262 (72.0)
1	36 (17.1)	48 (13.2)
2	25 (11.8)	23 (6.3)
≥3	32 (15.2)	31 (8.5)
Revision of bone-anchored components due to PJI *(no. [%])*	43 (20.4)	49 (13.5)
Complete extraction	34	39
Exchange of cup/liner + stem	5	7
Exchange of cup/liner	3	2
Exchange of stem ± head	0	1
Partial extraction	1	0
Death by 2-year follow-up *(no. [%])*	27 (12.8)	39 (10.7)

*Due to infection, at 2-year follow-up.

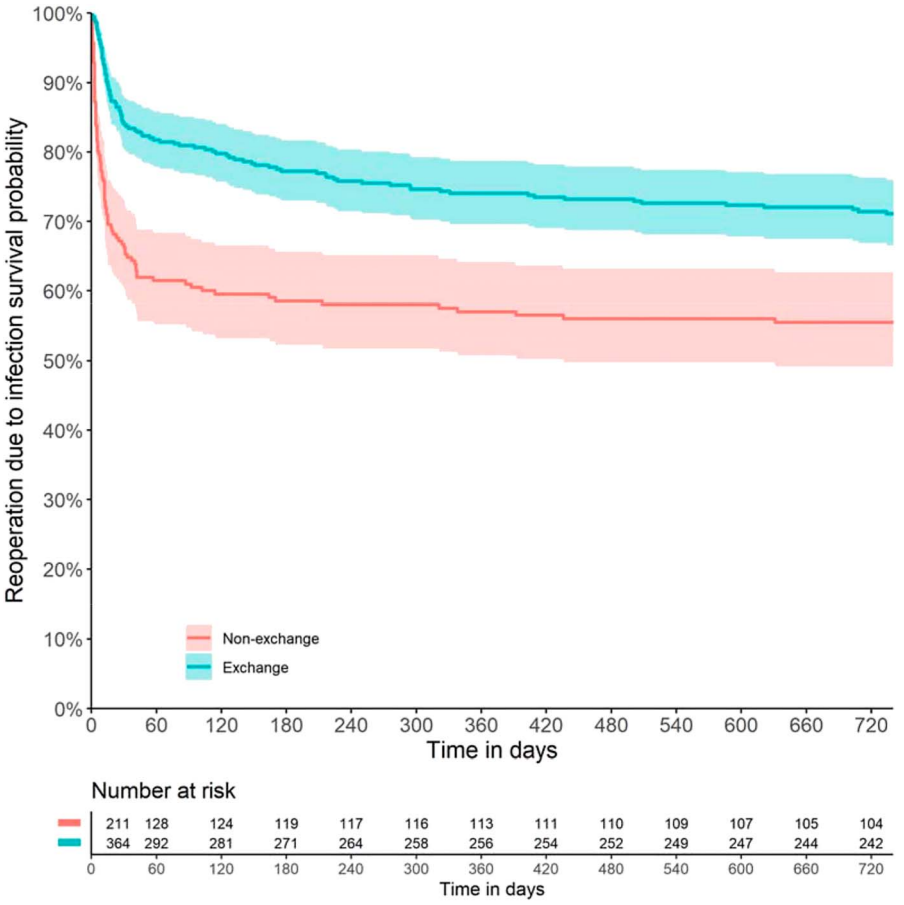

Fig. 2

Survival analysis, using Kaplan-Meier estimates, with reoperations due to infection within 2 years after DAIR (with and without the exchange of modular components) as the end point. The shaded areas represent the 95% CIs.

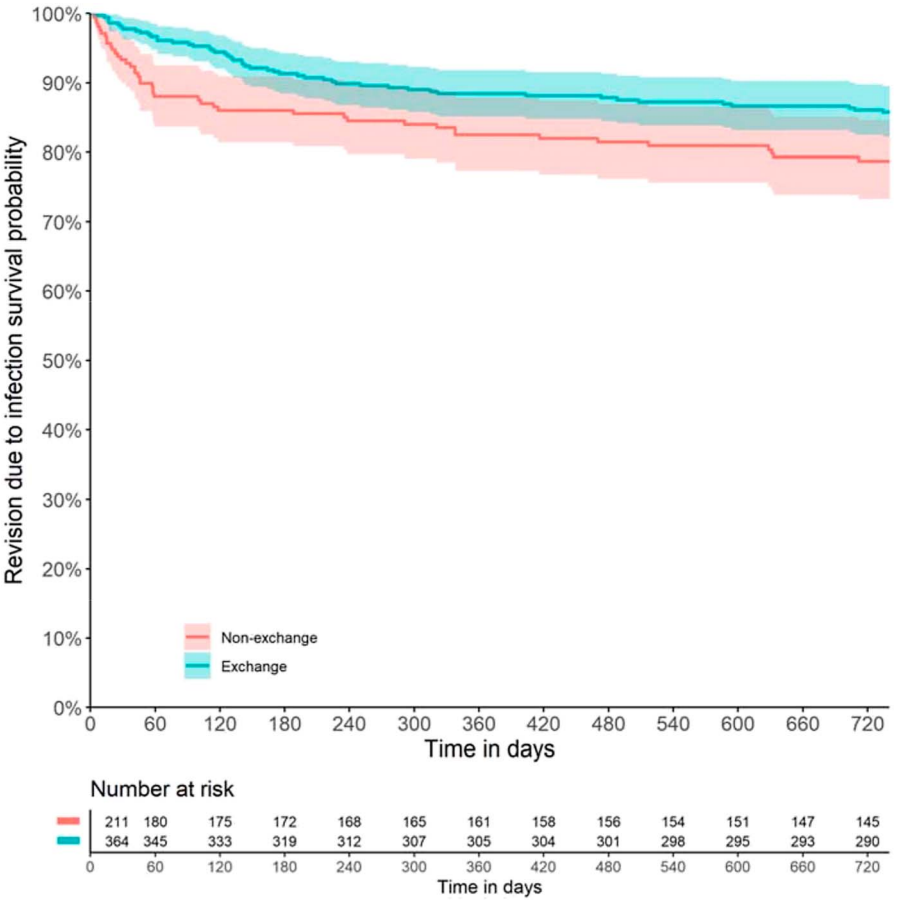

Fig. 3

Survival analysis, using Kaplan-Meier estimates, with revision of bone-anchored components due to infection within 2 years after DAIR (with and without exchange of modular components) as the end point. The shaded areas represent the 95% CIs.

non-exchange group and 8.0% (39) in the exchange group died.

Analysis of DAIR with Exchange Compared with Non-Exchange

Overall, the exchange of components was associated with a lower rate of reoperations (28.0%) compared with non-exchange (44.1%) (Table II). This difference was reflected in the Kaplan-Meier implant survival estimate for exchange (71.4% [95% CI = 66.9% to 76.3%]) compared with non-exchange (55.5% [95% CI = 49.1% to 62.7%]) (Fig. 2).

In the unadjusted analysis, DAIR with exchange resulted in a 48% reduction in the risk of additional surgery compared with non-exchange (HR = 0.52 [95% CI = 0.39 to 0.68]). After adjustment for confounders, the corresponding HR was 0.51 (95% CI = 0.38 to 0.68), indicating only minor confounding effects (Table III).

In the multivariable analysis, patients infected with *S. aureus* or *S. lugdunensis* had a higher risk of another reoperation compared with those with CoNS infection (Table III). The primary diagnosis, age, sex, time to symptom onset,

TABLE IV Analysis of the Subgroup of Patients in Whom Infection Resolution Was Determined

	Non-Exchange (N = 59)	Exchange (N = 92)
Infection resolution *(no. [%])*	26 (44.1)	57 (62.0)
Recurrent infection *(no. [%])*	33 (55.9)	35 (38.0)
Reoperation *(no.)*	30	34
Lifelong antibiotics *(no.)*	1	0
Persistent infection *(no.)*	2	0
Suspected infection *(no.)*	0	1

TABLE V Distribution of Patients in Non-Exchange and Exchange Groups in Relation to Antimicrobial Treatment*

	Non-Exchange (N = 211)	Exchange (N = 364)
AB prior to DAIR *(no. [%])*		
Yes	84 (39.8)	140 (38.5)
No	118 (55.9)	215 (59.1)
Missing	9 (4.3)	9 (2.5)
Postoperative oral AB type *(no. [%])*		
RIF and any other AB	71 (33.6)	188 (51.6)
RIF and CIP/LEVO	39	93
RIF and CLI	19	47
RIF and FA	9	31
RIF and other	4	17
Other	85 (40.3)	138 (37.9)
No oral AB/missing†	55 (26.1)	38 (10.4)
Duration of postoperative AB *(no. [%])*		
<4 wk‡	70 (33.2)	54 (14.8)
4-12 wk	54 (25.6)	145 (39.8)
>12 wk	83 (39.3)	164 (45.1)
Missing	4 (1.9)	1 (0.3)
Change of postoperative AB *(no. [%])*		
Yes	40 (19.0)	60 (16.5)
No	149 (70.6)	267 (73.4)
Missing	22 (10.4)	37 (10.2)

*AB = antibiotic agents, RIF = rifampicin, CIP = ciprofloxacin, LEVO = levofloxacin, CLI = clindamycin, and FA = fusidic acid. †Includes both patients with missing data and patients who had a reoperation subsequent to the DAIR but prior to discharge. ‡Includes patients who had a reoperation within 4 weeks after the initial DAIR.

symptom duration, and type of fixation were not found to be associated with an increased risk of another reoperation. In a sensitivity analysis of the 525 patients for whom the ASA classification was included in the registry, the risk reduction for DAIR with exchange remained stable (HR = 0.48 [95% CI = 0.35 to 0.65]) (see Appendix, Supplementary Table 3).

Analysis of Revision of Bone-Anchored Components Due to Infection

Revision of bone-anchored components was performed in 92 (47.2%) of the 195 patients who required additional surgery subsequent to DAIR (Table II). DAIR with exchange corresponded to better implant survival (86.1% [95% CI = 82.5% to 89.8%]) compared with non-exchange (78.8% [95% CI = 73.3% to 84.6%]) (Fig. 3).

The unadjusted analysis showed a lower risk of revision of bone-anchored components after DAIR with exchange (HR = 0.61 [95% CI = 0.41 to 0.92]), but the adjusted analysis showed no significant difference between the 2 DAIR methods (HR = 0.69 [95% CI = 0.45 to 1.05]) (see Appendix, Supplementary Table 4). The risk of revision of bone-anchored components was greater in patients who underwent DAIR >30 days after their initial procedure (see Appendix, Supplementary Table 4).

PJI Resolution in Subgroup of Patients with Additional Information

In the subgroup of patients (n = 151) with additional information on infection status, 83 (55.0%) had resolution of the PJI and 68 (45.0%) did not. Of the 68 patients in whom the PJI did not resolve after the DAIR, 64 underwent a reoperation due to the PJI, meaning that 4 cases (5.8%) were not captured using reoperation as a marker of recurrent PJI (Table IV). Patients who underwent DAIR with exchange had a higher percentage of PJI resolution (62.0%) compared with those treated with non-exchange DAIR (44.1%).

Antimicrobial Treatment

Of the 575 patients in the cohort, 224 (39.0%) had received antimicrobial treatment within 2 weeks prior to the DAIR procedure (Table V). Biofilm-active antimicrobial therapy (polytherapy with rifampicin) was more common after DAIR with exchange.

Discussion

In this study of patients with PJI after primary THA, DAIR with exchange of components was more successful than non-exchange DAIR. The success rates, although evaluated using a reoperation as the end point, lie within the range of previously reported rates[3-8]. There is existing evidence that an exchange improves success rates[4,8,11,13], but it should be noted

that the results were based mainly on smaller study samples. Our study adds to evidence that surgeons should strive to include component exchange when they perform DAIR. In theory, the rationale for an exchange may be the presence of biofilm on implant components. Bacterial biofilm is recognized as a challenge in the treatment of PJI, but to our knowledge there is limited research correlating it with clinical outcome.

Multiple DAIR procedures may be a means to improve outcome[13]. Redefining our definition of a successful DAIR to include success after multiple consecutive DAIR procedures would improve the results of this study. For example, if we had evaluated success after 2 consecutive DAIR procedures, the overall success rate would have been higher (Table II). However, we evaluated the success rate after 1 DAIR in accordance with the strong consensus for considering resection arthroplasty after 1 failed DAIR[11].

The secondary outcome of this study was revision of bone-anchored components due to PJI, as this is a resource-demanding procedure with considerable impact on the patient's quality of life. No significant difference in this outcome was observed between the exchange and non-exchange groups. Surgeon preference and other factors influencing the choice of revision subsequent to a single DAIR are unknown, and our result should be interpreted with consideration of this uncertainty.

Patients infected with *S. aureus* or *S. lugdunensis* had a higher risk of having a reoperation than those with a CoNS infection. CoNS infections were associated with treatment failure in a previous study[10], but they have also been reported be associated with outcomes equal to those of *S. aureus* PJI[3]. We did not have access to resistance profiles of causative microbes, and our finding is difficult to explain. The type of causative microbe did not affect the risk of revision of bone-anchored components, which may be due to the cohort size (type-II statistical error). In a meta-analysis, an age of >70 years was associated with better infection control by DAIR[19]. An explanation may be that elderly patients are less likely to be subjected to additional surgery because of their age, which may also be true for our cohort as age, despite its associated comorbidities, was not identified as a significant risk factor.

DAIR within 7 days after symptom onset has been associated with better outcomes[5,10,11]; however, there is also research favoring DAIR within 21 days after symptoms[19]. Symptom duration was not identified as a risk factor in our study with a cutoff of either 7 or 21 days, which conflicts somewhat with the previous results. No difference in outcomes, other than in the rate of revisions of bone-anchored components, was found in association with the time from the primary procedure to symptoms (≤30 or >30 days). It is difficult to establish cutoffs for symptom duration and time to symptom onset[11], and this factor remains ambiguous[5,11,20,21]. The general theory for the importance of timing is the establishment of biofilms. However, the effect of biofilms needs to be further evaluated.

There are limitations of the current study. The end point was a reoperation and not infection resolution. However, our subanalysis showed that 94% of patients with recurrent infection were captured using reoperations as the end point. Reoperations can therefore be regarded as a reasonable measure for studying recurrent infection.

Reoperations without exchange of modular components are at greatest risk for underreporting to the SHAR, with 40% being unrecorded according a validation study that Lindgren et al. conducted in 2014 on data from 2005 to 2008[15]. Although no recent validation study has been conducted on reoperations for PJI, the increased awareness of PJI[22] and initiatives such as PRISS (Prosthesis-Related Infections Shall be Stopped) in Sweden and the Second International Consensus Meeting (ICM) on Musculoskeletal Infection may improve SHAR registration[23,24]. However, the registration completeness may affect the study results, and there is a risk of selection bias. Our results should be interpreted in light of the risk that reoperations subsequent to a first-time DAIR may not have been captured in the SHAR.

Uriarte et al. reported a significantly higher failure rate when DAIR was performed by general orthopaedic surgeons compared with hip surgeons[25]. Experience was not considered in the current study. A factor that possibly contributes to the difference between the outcomes of the 2 DAIR methods is that non-exchange DAIR may be carried out by general orthopaedic surgeons, or residents, who do not specialize in hip arthroplasty surgery. Furthermore, the DAIR procedures in this study were not conducted in accordance with a standard protocol. At best, the participating clinics may have had a routine for the procedure, but this is unknown. However, the effect of adherence to standardized treatment protocols has not yet been evaluated[7].

To our knowledge, the current study is the largest on DAIR after primary THA. As DAIR fails in 13% to 63% of patients[3-10], additional efforts, such as evaluating the procedure in randomized trials, should be made to identify how DAIR should best be conducted and who benefits from it[3-7].

Conclusions

In patients with first-time PJI after primary THA, DAIR with exchange of modular components was superior to non-exchange DAIR. Our observations could be biased by selection of hip surgeons, who preferentially perform exchange of modular components, and by factors unknown to us. However, DAIR is a viable option for the treatment of early PJI and there is a need to further identify how it best should be conducted and which patients benefit from it.

Appendix

eA Supporting material provided by the authors is posted with the online version of this article as a data supplement at jbjs.org (http://links.lww.com/JBJSOA/A231). ■

Note: The authors thank Swedish hospitals for providing data to the SHAR as well as the local coordinators and doctors who provided us with the supplementary questionnaires. Furthermore, they thank Dr. Jonatan Tillander for his invaluable input on categorization of bacteria and antimicrobials.

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