

## High Cure Rate for Acute Streptococcal Prosthetic Joint Infections Treated With Debridement, Antimicrobials, and Implant Retention in a Specialized Tertiary Care Center

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Streptococcal prosthetic joint infections (PJIs) treated with debridement, exchange of removable parts, antibiotics, and implant retention within 3 weeks from symptom onset had an implant survival rate of 97.9% and an implant survival rate without suppressive antimicrobials of 80.9%. Treatment centralization for acute streptococcal PJIs to specialized centers makes excellent cure rates possible.

**Keywords.** arthroplasty; bone and joint infection; DAIR; rifampin.

A not-so-good prognosis for streptococcal prosthetic joint infections (PJIs) treated with debridement, antibiotics, and implant retention (DAIR) has been reported by a large international multicenter study, with a failure rate of 42% [1]. This high failure rate might be because the removable parts were only exchanged in 53% of the cases, and the DAIR was not limited to acute cases (ie,  $\leq 3$  weeks from symptom onset). The treatment practices also varied greatly between the 52 participating hospitals, with a mean of 9 PJIs treated per hospital. However, better outcomes for streptococcal PJIs treated with DAIR have also been reported [2, 3].

Finding high failure rates following DAIRs in streptococcal PJIs is alarming, especially when an unsuccessful DAIR might be a risk factor for failure following 2-stage exchange [4–6]. However, DAIR is a very attractive treatment option because, when successful, it is tolerated even by elderly and morbid patients, requires a shorter hospital stay, allows faster recovery, and has a lower treatment cost [7].

Our aim in this study was to examine the success rate for DAIR-treated streptococcal PJIs in a specialized tertiary care center when the patient selection, surgical technique, and

antimicrobials used were appropriate. This was used to verify whether a recommendation for centralizing acute PJI treatment to specialized centers was justifiable.

### METHODS

A retrospective analysis of consecutive DAIR-treated streptococcal PJIs in a single specialized tertiary care center (Helsinki University Hospital, Peijas Hospital) between 1 January 2008 and 15 April 2017 was performed for 54 cases. In this joint replacement unit, nearly 3000 hip or knee arthroplasties are performed annually, with demanding PJI treatment centralized from the district. The strictly obeyed inclusion criteria were removable parts were exchanged, DAIR was performed within 3 weeks of symptom onset, and DAIR was the first surgical procedure for PJI treatment.

Seven patients were excluded: 4 because the removable parts were not exchanged (eg, monoblock tibial component), 2 for a DAIR delay  $>3$  weeks, and 1 because the DAIR was not the first operation. The outcomes of these excluded patients were 3 patients were with long-term suppressive antimicrobial, 1 patient died because of heart insufficiency 1 month after DAIR, the hip prosthesis was removed from 1 patient because of repeated hip dislocations, and 2 patients were cured and no suppressive antimicrobials were used.

There were 13 patients in this study who were earlier included in the multicenter study of Lora-Tamayo et al [1]. According to the Infectious Diseases Society of America, a PJI was defined as the presence of a sinus tract communicating with the prosthesis, acute inflammation upon histological examination, purulence surrounding the prosthesis, and/or  $\geq 2$  evaluable samples yielding the same organism [8]. Enterococci or obligate anaerobes such as peptostreptococci were not included.

The following data were retrieved from the medical records: age at DAIR, sex, infected joint, comorbidities, immunosuppressive agent use, penicillin allergy, infection type (postoperative or hematogenous, defined as an acute PJI after an uneventful postoperative course and after confirmed or suspected bacteremia), microbiological findings, C-reactive protein (CRP) value, surgical procedures performed, and antimicrobial agents used. The patients were followed from DAIR until prosthetic joint removal, death, or the chart review. At the time of discharge, each patient was reminded to contact the operating hospital if they had any infection relapse symptoms. With very uniform healthcare in the area, the general practitioners and paramedics know to refer a patient with a painful or infected prosthetic joint to the correct center. The follow-up of 1 monomicrobial streptococcal PJI ended with a new hematogenous infection caused by a different bacterium,

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*Staphylococcus lugdunensis*, later in the follow-up after an uneventful antimicrobial-free period.

Mean values and standard deviations (SDs) were calculated for the normally distributed continuous variables, whereas median values and interquartile ranges (IQRs) were calculated to portray the nonnormally distributed data. Pearson  $\chi^2$  and Fisher exact tests were used as univariate analyses for the categorical variables, and the Mann-Whitney *U* test was used for the continuous variables. Multivariate tests were performed, but they were underpowered (data not shown).

## RESULTS

In our center, 47 acute streptococcal PJIs were treated with DAIRs, including removable part exchanges, between 1 January 2008 and 15 April 2017. Of the infected joints, 26 (55.3%) were hips and 21 (44.7%) were knees. There were more hematogenous origin PJIs [29/47 (61.7%)] than postoperative [18/47 (38.3%)]. The blood cultures were positive in 19.1% of the cases. The mean age of the patients was 66.4 years (SD, 12.3; range, 21–92), 40.4% were males, 10.6% had rheumatoid arthritis, and 8.5% were taking immunosuppressive medications. One patient (2.1%) had chronic renal failure (baseline creatinine >150 mg/L). The CRP mean (highest value before DAIR) was 272 mg/L (SD, 121.7; range, 8–521).

DAIR was performed a median of 5 days after symptom onset (IQR, 3–8) and a median of 3 days (IQR, 2–5) after admission. Orthopedic surgeons specialized in arthroplasty performed all DAIRs.

In 91.5% of the cases, a streptococcus was the only pathogen (8.5% were polymicrobial infections). The causative streptococci were group A streptococci (*n* = 2), *Streptococcus agalactiae* (*n* = 11), group G streptococci (16), *Streptococcus anginosus* group (*n* = 5), *Streptococcus salivarius* (*n* = 1), other viridans streptococci (*n* = 10), and *Streptococcus pneumoniae* (*n* = 2). All the streptococci were sensitive to penicillin, except the 2 *S. pneumoniae*. The minimal inhibitory concentration (MIC) for penicillin was 1 mg/L. In the polymicrobial infections, the other microorganisms included 3 *Staphylococcus epidermidis*, 2 *Staphylococcus hemolyticus*, and 1 other coagulase-negative staphylococcus. All the polymicrobial PJIs were postoperative infections with discharging wounds. Among the postoperative PJIs, the median time interval from symptom onset to DAIR was significantly longer among polymicrobial PJIs compared to monomicrobial (10.5 vs 3.5 days; *P* = .005).

All the antimicrobial treatments were planned and followed up by an infectious disease specialist, and all the patients received intravenous  $\beta$ -lactams for a median of 28 days (range, 14–38). The total antimicrobial treatment median time was 90 days. The most common oral antimicrobials used were amoxicillin, clindamycin, and cephalexin. Rifampin was used for more than 21 days in 5 cases (10.6%), either for a polymicrobial infection that included staphylococcus (4 cases) or for *S. pneumoniae* with a penicillin MIC of 1 mg/L.

After the median follow-up time of 2.9 years (IQR, 1.5–4.9), 97.9% of the original prostheses were retained (95% confidence interval [CI], 88.9%–99.6%), and 80.9% of the patients had the original prosthetic joint without antimicrobial treatment (95% CI, 67.5%–89.6%). None of the patients died because of the infection. One (2.1%) prosthesis was removed because of a persistent infection, and a 2-stage exchange was performed. No relapses emerged after discontinuing the antimicrobial treatment.

At the chart review, a long-term suppressive antimicrobial was in use in 8 (17.0%) patients. Suppressing antimicrobial use was reduced during the study period, with 28.6% and 7.7% of the patients treated between 2008 and 2013 and between 2014 and 2017, respectively (*P* = .115). No suppressive antimicrobials were indicated by clinical signs of an active infection. The suppressive antimicrobial indications were an unwillingness to risk relapse due to several comorbidities or a tumor megaprosthesis.

In the univariate analyses, the statistically significant risk factors for either implant removal or long-term suppressive antimicrobial treatment were a hematogenous origin (*P* = .009; odds ratio, 1.45; 95% CI, 1.14%–1.85%), higher American Society of Anesthesiologists class (*P* = .023), and age (*P* = .047).

## DISCUSSION

The implant survival rate in DAIR-treated acute streptococcal PJIs was high when they were performed in a specialized center within 3 weeks from symptom onset, the removable parts were exchanged, and optimal antimicrobials were used under the guidance of an infectious disease specialist. In the monomicrobial infections, rifampin was not needed.

When compared to a large international multicenter study of DAIR-treated streptococcal PJIs [1], the current study achieved clearly higher implant and antimicrobial-free implant survival rates. The exchange of removable parts has been shown to improve survival [1, 9]. In our specialized center, a wide variety of removable parts are available. All the patients are operated by orthopedic surgeons specialized in arthroplasty, and the surgeons always perform a meticulous open debridement of the infected joint. The patients who did not meet the strict inclusion criteria had clearly poorer outcomes. When performed according to a strict protocol, DAIR has exhibited better outcomes in previous studies [2, 10]. In our study, median time from onset of symptoms to DAIR was short at 5 days, and from admission to DAIR it was 3 days. This rapid access to treatment may explain in part the successive outcomes [10].

In the professional treatment of PJIs, the multidisciplinary team includes an infectious disease specialist, microbiology laboratory, and orthopedic surgeons. In our cases, all antimicrobial treatments were planned by infectious disease specialist, and the majority of the PJIs were treated with  $\beta$ -lactams. Rifampin was not needed to cure the monomicrobial streptococcal PJIs. This is in line with most previous publications [11, 12], except the multicenter study in which rifampin was a predictor of success [1].

In that study, the rifampin usage varied widely between the centers, and it could be associated with some other differences in the surgical or medical treatment protocols, for example, a higher biofilm burden because the removable parts were not exchanged.

Especially in the early years of DAIR use in our center, long-term suppressive antimicrobials were used occasionally with vulnerable patients. After the first DAIR results were evaluated in our unit, the proportion of long-term suppressive antimicrobials was reduced in 2013, and no infection relapses have emerged to date. However, the 17% proportion of patients on suppressive antimicrobials was a limitation of our study.

International multicenter studies are excellent for collecting a large number of rare disease cases and performing very valuable risk factor analyses. However, according to our study, centralizing the DAIR gives excellent results. Thus, we recommend that acute PJI treatment only be performed in high-volume centers with specialized orthopedic surgeons, and infectious disease specialists who have an interest in PJI treatment, and with a wide variety of prosthesis components available.

## Note

**Potential conflicts of interest.** All authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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