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RESEARCH

Chronic infections of knee megaprostheses: are "Off-Label" DAIR-Plus or partial two-stage exchange viable options?

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Abstract

Introduction Two-stage revision for chronic periprosthetic joint infections (PJI) of knee megaprostheses is complex and often results in significant bone loss. DAIR-Plus and other partial exchange procedures, involving debridement with partial prosthesis removal but retaining stems, are typically used for acute PJI but may benefit select chronic cases. This study aimed to: (i) assess DAIR-Plus and partial two-stage exchange outcomes in chronic megaprosthesis infections; and (ii) identify prognostic factors to guide their use versus full component removal.

Materials and methods Twenty-three patients underwent DAIR-Plus or partial two-stage exchange (PTSE) procedures for chronic knee megaprosthetic PJI between 2000 and 2022. Nineteen patients, were included. Targeted antibiotics were administered based on Infectious Disease Specialist recommendations. Infection eradication was evaluated using clinical and serologic parameters.

Results Nineteen patients (mean age 53.4 years) underwent 13 DAIR-Plus and 7 PTSE. PJI-free survival was 57.9% at 1 year, 47.4% at 2 and 5 years, and 42% beyond 5 years. Among failures, 6 had persistent infection and 5 relapsed (mean time to relapse: 13.75 months). Four additional patients achieved infection control after further two-stage revisions; 7 remained uncontrolled, leading to 6 amputations and 1 chronic suppressive treatment. Outcomes did not differ significantly by age, gender, host status, oncological history, radiotherapy, or surgical approach. *Staphylococcus spp.* caused 63% of infections and were associated with significantly lower PJI-free survival at final follow-up (25% vs. 62% for other organisms, $p = 0.048$).

Conclusions DAIR-Plus provided lasting infection control in selected chronic PJI cases, with nearly half remaining infection-free long term with notable advantages such as bone stock preservation and faster recovery. Partial two-stage exchange does not appear to offer additional advantages over DAIR-Plus. Outcomes were not influenced by clinical factors, but *Staphylococcus spp.* infections showed significantly lower success.

Keywords Periprosthetic joint infections · Knee megaprostheses · DAIR · DAIR-Plus · Partial exchange

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Introduction

Periprosthetic joint infections (PJI) in megaprostheses are more common and challenging than in conventional total joint arthroplasties (TJA), with infection rates ranging from 15 to 40% [1]. Surgical treatment often requires complex procedures with high re-infection rates, potentially leading to amputation in some cases [2, 3]. The high infection risk is due to factors like large implant surface area, extensive soft tissue damage, blood loss, and long surgery times. Additionally, patients may have compromised health [4, 5]. Oncology patients often face immunosuppression from chemotherapy and increased wound complications from radiotherapy [4, 5]. Non-oncological patients typically have a history of multiple failed surgeries, further raising the risk of infection [3]. Both groups also face higher risks due to poor nutrition and an elevated Charlson Comorbidity Index [6, 7].

Acute PJIs [8], which occur within 6 weeks of surgery or within 7 weeks of new symptoms according to the recent International Consensus Meeting of Istanbul 2025, are treated in conventional TJA with DAIR (Debridement, Antibiotics, Irrigation, and Implant Retention), with a success rate of over 70% [9, 10]. In chronic PJI, implant removal through one- or two-stage surgery is the gold standard [11–13]. For acute megaprostheses PJI, the success rate of DAIR drops to 30–35% [14] due to limited exposure and inadequate debridement. DAIR-Plus, which includes removing mobile components while retaining the stems, has shown fair results [15–17]. DAIR-Plus in chronic cases may avoid the need for complete implant removal and extensive procedures, reducing risks like bone loss, extensor apparatus damage, and complex reconstructions. A non-stem-removal approach can be an attractive option especially for knee megaprostheses PJI [18], due to the unique challenges of the anatomical site as the limited soft tissue coverage and the need to manage the extensor mechanism [19]. In addition, when significant bone loss occurs following difficult stem removal, reconstruction can be particularly challenging, with a high risk of further complications. For the same reason some advocate a partial two-stage exchange (PTSE), with removal of modular components, retaining of the stems and positioning of a cement spacer [6, 14].

Several articles discuss DAIR-Plus and other partial exchange revision variations in megaprostheses PJIs, but they often lack clarity regarding their definition, technical aspects, timing of PJI, and outcomes based on timing, implant site, and prognostic factors. The limited data affects the reliability of results. It remains unclear whether those treatment strategies are viable for chronic cases, which patients would benefit from them, and whether their use in megaprostheses should be expanded or reduced.

This study aimed to reduce bias by focusing on knee megaprostheses with similar patient characteristics and treatment principles. It specifically examined chronic PJIs of knee megaprostheses and provided a clear definition of the surgical technique. The study's objectives were answer these questions: (i) what are the results of DAIR-Plus and partial two-stage exchange in chronic knee megaprostheses PJIs? (ii) What prognostic factors can guide surgeons in determining which cases are suitable for DAIR-Plus or PTSE and which require more invasive procedures?

Materials and methods

Twenty-three patients underwent DAIR-Plus or partial two-stage exchange procedures for chronic knee megaprosthetic infections at our institution between 2000 and 2022. Four cases were excluded due to patient death from disease progression before completing two years of follow-up after PJI treatment, leaving 19 patients in the study. Inclusion criteria: (i) Distal femur or proximal tibia resection and reconstruction with a megaprosthesis (including total femur reconstructions); (ii) Periprosthetic infection diagnosed according to ICM 2018 [20], one major criterion positive or score $\geq$ 6. In patients who underwent surgery before 2018 diagnosis of PJI was retrospectively confirmed; (iii) Surgical treatment with stem retention (DAIR-Plus or partial two-stage exchange); (iv) DAIR-Plus procedure as first treatment or second treatment after previous standard DAIR; (v) antibiotic treatment according to protocol (see below); (vi) minimum 2 years of follow-up (FU).

Exclusion criteria: (i) acute PJI, less than 6 weeks from the index procedure or less than 7 days from symptoms development [8]; (ii) infection prior to the implantation of the megaprosthesis; (iii) incomplete data; (iv) follow-up after surgery less than two years, unless infection recurrence after DAIR-Plus before two years.

The DAIR-Plus procedure was reserved for select cases, primarily based on preoperative imaging showing well-fixed stems, where implant removal would risk significant bone loss and compromise future reconstruction. This approach was generally, but not exclusively, applied when the microorganism and its antibiotic resistance were identified preoperatively. Patient preference also played a role, as some patients refused multiple or more invasive surgeries upon infection diagnosis. In some cases, the decision to perform DAIR-Plus instead of a one-stage or two-stage revision was made during surgery, following unsuccessful attempts to remove the stems without opening a cortical window on the diaphysis. The choice between DAIR-Plus and PTSE depended mainly on the presence of a sinus tract or poor soft tissue conditions, which made adequate coverage difficult.

All patients underwent joint aspiration prior to the procedure to confirm diagnosis of PJI and to isolate the microorganism responsible. During surgery at least five samples were taken to confirm the diagnosis and to repeat cultures. Infection was considered healed when clinical signs of PJI were absent (rubor, calor, swelling, leakage) and blood tests (CRP, ESR) were negative at a minimum follow-up of two years. Amputations and chronic suppressive antibiotic therapy (SAT) were considered failures of PJI treatment.

We collected demographic data, patients' history of implant revision prior to PJI, microorganisms responsible for the infection, surgical treatment of PJI, PJI-free survival at 1, 2, 5 and >5 years following DAIR-Plus and PTSE, subsequent treatments following failure, PJI-free survival after additional procedures and final infection control status.

We compared the outcomes of DAIR-Plus and PTSE in terms of PJI resolution at the selected timepoints based on age, gender, host status according to McPherson [21], oncological history, history of radiotherapy (RT), whether DAIR-Plus or PTSE were performed. Patient consent was collected pre-operatively after they were informed of the procedure following the principles of the Declaration of Helsinki. The study was conducted with approval from our local Ethics' Committee (19710_OSS).

All statistical analyses were performed using SPSS software version 21 (SPSS Inc., Chicago, IL, USA). The Kolmogorov-Smirnov test was used to check the normal distribution of the continuous variables and thus the t-test was used for unpaired and paired continuous variables, and the chi-square test of Fisher exact test were applied for categorical variables. Statistical significance was set at $p<0.05$.

Surgical technique

DAIR-Plus one stage

Definition: DAIR-Plus one-stage involves removing the mobile components of the megaprosthesis while retaining the stem and other components, followed by immediate reconstruction with a new body of the megaprosthesis. In distal femur megaprostheses, the femoral component is exchanged while retaining the femoral stem and tibial component. For proximal tibia replacement, the tibial stem and femoral component are retained.

Technique: The patient is positioned supine, and the leg is fully draped, including the hip. A longitudinal incision is made over the distal thigh, knee and proximal tibia, on the previous scar (usually anterolateral with a lateral parapatellar approach, sometimes anteromedial with a medial parapatellar approach, according to initial pathology). The approach must allow for accurate debridement and implant removal while protecting the quadriceps. The distal exposure may be extended along the tibial crest. Before removing the mobile components, microbiological culture samples are collected. Thorough debridement of infected and necrotic tissue is performed, followed by removal of the insert, disassembly of the implant, and removal of the megaprosthesis body (distal femur or proximal tibia). The stability of the retained components and stem is tested and confirmed, with additional culture samples taken from the stem-implant interface. After completing debridement, the field is rinsed with at least 3 L of betadine-diluted solution and saline. Trial components are then tested for length, axis, and stability, followed by placement of the definitive implant. The wound is closed in layers with a watertight closure of the capsule. A vacuum-generating drape can be applied in case of poor soft tissue conditions. Post-surgery, the patient begins rehabilitation immediately to restore full range of motion and weight-bearing (Fig. 1).

Partial two-stage exchange

Definition: In these cases, a cement spacer is positioned in static mode after removal of the mobile components, followed by reimplantation in 6–12 weeks.

Technique: Positioning, surgical exposure, debridement, and irrigation are performed as in the DAIR-Plus one-stage procedure. After changing gloves, drapes and surgical instruments, preparation of the cement spacer begins. Three to four batches of antibiotic-loaded cement are mixed and molded, then positioned during the late setting phase (7–8 min after preparation) around the femoral stem taper and in the gap left by the femoral component. Wound closure follows, with closed incision VAC therapy if full skin closure is at risk. Post-surgery, a brace is applied in full extension, allowing toe-touch weight bearing. Reimplantation is performed 6–12 weeks later, after clinical and lab tests confirm infection resolution, in consultation with an Infectious Disease Specialist. No antibiotic holiday is taken. At reimplantation, the spacer is removed, additional debridement is performed, and irrigation is repeated. Reconstruction is completed as in the DAIR-Plus one-stage method (Fig. 2).

Antibiotics therapy

All cases were discussed with an Infectious Diseases Specialist before and during treatment. If a microorganism was isolated from preoperative joint aspiration, targeted therapy was initiated based on intraoperative culture results. If no bacteria were identified before surgery, empiric therapy with vancomycin and piperacillin-tazobactam was started until re-evaluation with intraoperative cultures. In the early years of the series, gentamycin was used instead of piperacillin-tazobactam. The minimum therapy duration was 6

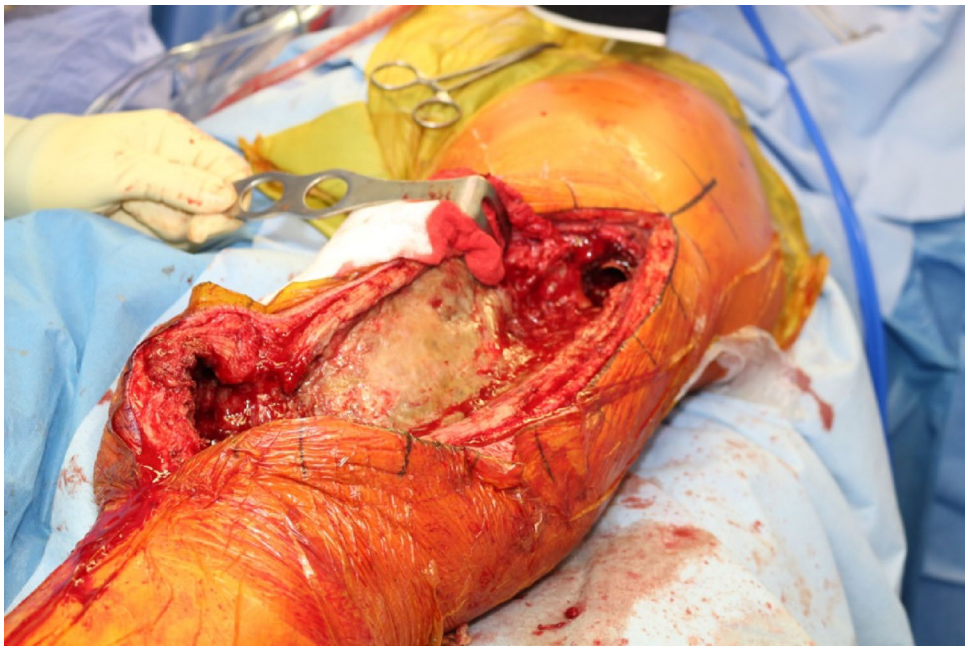

Fig. 1 Result of extensive debridement following removal of the femoral component with retention of the stem

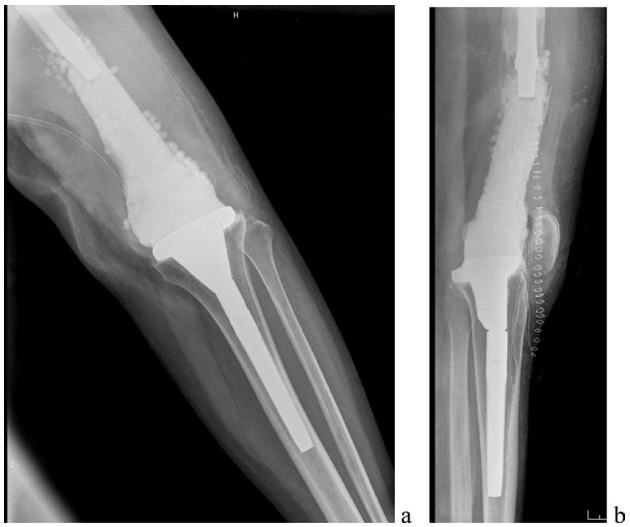

Fig. 2 **a–b** Partial two-stage exchange with use of Calcium-Phosphate beads loaded with antibiotics. X-rays antero-posterior and lateral views

weeks, with a switch to oral antibiotics when feasible, based on antibiogram results. After reimplantation in PTSE, the antibiotic protocol was adjusted according to new tissue sample analysis.

For culture-negative PJI, the treatment included 2 weeks of intravenous vancomycin and piperacillin-tazobactam (or gentamycin), followed by at least 4 weeks of oral therapy. The oral regimen consisted of rifampicin and levofloxacin, or a sulfonamide combined with doxycycline.

Amputation

The decision to proceed with amputation was made in the following situations:

(i) persistent PJI after a two-stage exchange with repeated spacer exchanges; (ii) recurrent PJI after a two-stage exchange when joint reconstruction was no longer feasible; (iii) the patient's decision not to undergo any further surgical procedures.

Results

Nineteen patients were included in the study, 12 females – 7 males, average age 53.4 years (18–87); 12 oncological and 7 non-oncological. The DAIR-Plus was performed in 13 cases and partial two-stage exchange in 7, One patient underwent both a DAIR-Plus one-stage and a PTSE procedure for persistent PJI (Tables 1 and 2). The average time from the last surgery before PJI was 56.8 months (1.6–272.7). Mean follow-up (FU) was 6.9 years (range 2–18, σ 3.88). Among PJI-free patients, mean FU was 7.5 years; specifically, 8.75 years (range 3–18) in those treated successfully with DAIR-Plus/PTSE. PJI-free survival after DAIR-Plus/PTSE was 57.9% (11/19) at 1 year, 47.4% (9/19) at 2 and 5 years, and 42% (8/19) beyond 5 years. Among failures, 6 cases showed persistent infection and 5 had relapses. The average time to relapse was 23 months (range 7–60), but excluding one late relapse (after 5 years, likely a new infection), the adjusted mean relapse time was 13.75 months. All patients, except one, underwent additional surgical procedures due to persistence or recurrence of PJI. Four additional patients (21%)

Table 1 Demographic data

Number of cases	19	4 excluded
Sex	12 F 7 M	
Age	53.4	range 18–87
Oncological	12	
Non-oncological	7	
Host status (McPherson)	5 A 13 B 1 C	
Implant	15 Distal Femur Megaprosthesis 4 Proximal Tibia Megaprosthesis	9 Cemented stems 7 Uncemented stems 3 Hybrid
Average time from last surgery to PJI (months)	56.8	range 1.6–272.7.6.7
Mean Follow-up	6.9 years (2–18)	
Radiotherapy	4 yes 15 no	
Microorganism	Culture Negative 4 Polymicrobial 1 *St. aureus* 5 *St. epidermidis* 4 *St. haemolyticus* 2 *St. cromogenes* 1 *Enterobacter cloacae* 1 *Streptococcus oralis* 1	

Table 2 Treatment details and outcomes

PJI-free overall	12 yes (63%) 7 no (37%)	6 amputations (31.6%) 1 SAT
PJI-free survival rate following DAIR-Plus and PTSE	11/19 (57.9%) 1y FU 47.4% 2y FU 47.4% 5y FU 42% >5y FU	
DAIR-Plus/PTSE outcomes	13 (68.4%) DAIR-Plus 7 (28.6%) Partial two-stage exchange*	6/13 (46%) PJI-free > 5y FU 2/7 (28.6%) PJI-free > 5y FU
Patients PJI-free following failed DAIR-Plus/PTSE	4/11 (36.4%)	1 two-stage exchange 3 two-stage exchange with multiple spacer exchanges
Mean FU PJI-free patients following a failed DAIR-Plus/PTSE	6.2 y (4–8)	

* One patient underwent both a DAIR-Plus one-stage and a Partial two-stage exchange procedure for persistent PJI. After 6 months, the patient experienced a recurrence of PJI and subsequently underwent a complete two-stage exchange with multiple spacer exchanges, resulting in final resolution of the infection (PJI-free at 8 years follow-up)

PTSE Partial two-stage exchange

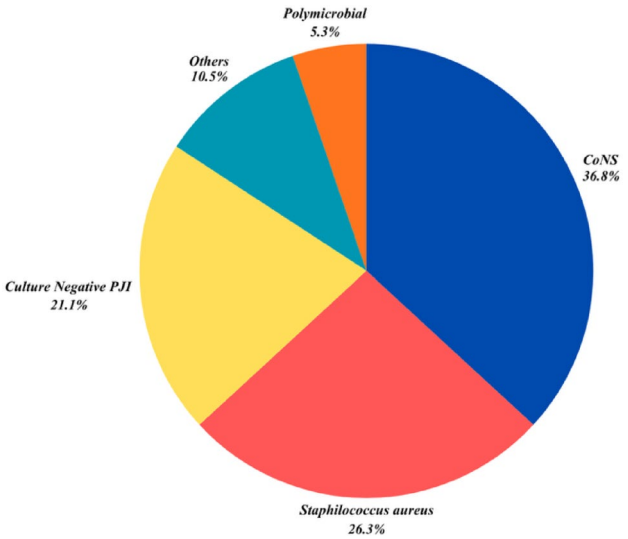

Fig. 3 Microorganisms profile. CoNS: *Coagulase-negative staphylococci*. Others: *Streptococcus oralis*, *Enterobacter cloacae*. Polymicrobial: *Vancomycin-resistant Enterococcus faecium*, *Corynebacterium striatum and Psychrobacter phenylpyruvicus*

achieved infection control through further two-stage revisions, often requiring multiple spacer exchanges (mean 5.75 procedures per patient, range 3–9), with a mean FU of 6.5 years (range 4–8). Infection control could not be achieved in 7 patients, resulting in 6 amputations (32%) and 1 case managed with chronic suppressive antibiotic therapy. Patients who underwent amputation had a mean of 4.66 surgical procedures for PJI (range, 2–6), and the time from the the DAIR-Plus or PTSE procedures to the amputation was 3.8 years (range, 2–6 years).

No significant differences in DAIR-Plus outcomes were observed based on clinical or demographic factors. Mean age was similar between the PJI-free and failure groups (52.2 vs. 54.3 years, $p=0.43$). Gender showed no association with outcome (57.1% PJI-free in males vs. 33% in females, $p=0.43$), nor did host status (40% PJI-free in type A vs. 42.8% in B/C, $p=0.91$). Oncological history (41.7% vs. 42.3%, $p=0.95$) and prior radiotherapy (25% vs. 46.7%, $p=0.43$) were also not associated with success. Similarly, no significant difference was found between DAIR-Plus (46.1%) and PTSE (28.6%) procedures ($p=0.44$).

The microbiological profile is shown in Fig. 3. The majority of PJIs ($n=12$; 63%) were caused by *Staphylococcus* spp. PJI control was achieved in 58% of patients with staphylococcal infections, compared to 71% for other microorganisms ($p=0.32$) (Table 3). Of the 7 treatment failures (71.4%), 5 were associated with *Staphylococcus* spp. 62% of cases caused by culture-negative or other microorganisms were PJI-free at final FU, while only 25% of staphylococcal PJIs were PJI free at last FU after DAIR-Plus. This difference was statistically significant ($p=0.048$).

Table 3 Treatment outcomes based on microorganism profile

Microorganism	Nr.	Treatment	Outcomes
Coagulase-negative staphylococci (CoNS)	7	7 DAIR-Plus 1 PTSE*	2/7 (28,6%) PJI-free 3/7 (71%) PJI-free with following treatments 2 failures (amputation)
Staphylococcus aureus	5	2 DAIR-Plus 3 PTSE	1 PJI-free, 1 failure (amputation) 3/3 failed, 1 PJI-free following two-stage exchange, 2 amputations
Culture Negative PJI	4	3 DAIR-Plus 1 PTSE	2/3 PJI-free; 1/3 amputation (host C) PTSE failed, PJI control with SAT
Polymicrobial	1	PTSE	PJI-free
Others	2	1 DAIR-Plus 1 PTSE	2/2 PJI-free

* One patient underwent both a DAIR-Plus one-stage and a Partial two-stage exchange procedure for persistent PJI. After 6 months, the patient experienced a recurrence of PJI and subsequently underwent a complete two-stage exchange with multiple spacer exchanges, resulting in final resolution of the infection (PJI-free at 8 years follow-up)

SAT Suppressive Antibiotics Therapy; *PTSE* partial two-stage exchange

Others: *Streptococcus oralis* and *Enterobacter cloacae*

Discussion

The Birmingham Orthopaedic Oncology Meeting (BOOM) in January 2024 established two-stage exchange as the gold standard for managing PJI in the context of megaprostheses. However, some groups have argued that the morbidity associated with the removal of well-fixed stems may not be warranted in the context of two-stage revisions [22]. Recent literature has classified all procedures involving stem retention under the term DAIR, whereas DAIR-Plus encompasses more extensive interventions, including the removal of the megaprosthesis body [23]. At our institution, the standard approach to chronic PJI in knee megaprostheses involves a two-stage procedure with complete prosthesis exchange, with DAIR-Plus reserved for selected cases. Cases treated with partial two-stage exchange are even more selectively chosen. This option is occasionally reserved for patients in whom complete implant removal would be excessively aggressive, but whose local skin conditions place them at risk of wound-closure failure if treated with a one-stage procedure. This treatment preference accounts for the relatively limited sample size in our study. Recent studies similarly report a limited number of DAIR-Plus procedures, often encompassing multiple anatomical sites and both acute and chronic PJIs. Additionally, certain studies fail to clearly delineate whether the intervention constituted a true one- or two-stage revision or if it adhered to DAIR-Plus criteria [2, 6, 23–25].

In our series, DAIR-Plus and PTSE achieved a 57.9% PJI eradication rate at one year, comparable to results seen with DAIR in acute PJIs in conventional TJA. However, this effectiveness diminished over time, with eradication rates dropping to 47.6% at five years and just 42% at long-term follow-up. The difference between DAIR-Plus and PTSE was not significant ($p = 0.44$), though the healing rate was 46.1% for DAIR-Plus vs. 28,6% PTSE. While PJI healing rate following DAIR-Plus in our series was lower than the 60–70% reported for two-stage procedures [23], it was comparable to the 40–50% success rate of one-stage procedures [2, 6, 26] and superior to DAIR without component exchange (20–30%) [14, 27]. The PJI eradication rate following PTSE procedures is more comparable to outcomes observed with standard DAIR than to those achieved with complete two-stage exchanges. Although the difference in healing rates between DAIR-Plus and PTSE was not statistically significant—likely due to the limited number of cases included—our results suggest that a one-stage procedure may be preferable, and that partial two-stage exchange does not substantially increase the likelihood of success. When complete implant removal is not feasible because of the risk of major bone loss, or when the patient declines a full revision, immediate reimplantation of definitive components may be more appropriate than the placement of a temporary cement spacer. These numbers should also be interpreted in light of the characteristics of the patient population included in the study: 63% had oncologic diseases and 74% were McPherson host grade B or C. Four patients (17.4%) were excluded from the analysis because they died before reaching two years of follow-up. Life expectancy should therefore be considered in the decision-making process. In patients with poor prognosis, DAIR-Plus achieved PJI control in 57.6% of cases at one year and 47.6% at five years. Although this approach carries a high risk of recurrence, it offers a significantly less invasive treatment with immediate functional recovery in terms of range of motion and weight-bearing. From this perspective, a thorough discussion with the patient and their support network is essential. Furthermore, partial two-stage exchange should be reserved for highly selected cases, as it does not appear to improve the likelihood of success and is associated with limited functional recovery during the interval before reimplantation.

The average DAIR-Plus success rate in the literature is 54% (range 39–68%), but comparisons are challenging due to mixed acute and chronic PJI cases. Asokan [28] reported a 64.3% success rate for DAIR-Plus in a group of non-oncological patients, showing 100% success in acute cases (4 patients) but only 50% (5 out of 10 patients) in chronic cases. Sukhonthamarn [3] reported a 68% DAIR-Plus success rate but only four chronic PJI were included in his series. González [29] found that 2- and 5-year re-infection

rates were comparable for DAIR-Plus and two-stage procedures, but did not distinguish success rates by infection timing.

The need for further treatment in up to 50% of patients raises an important question: can prior DAIR-Plus impact the success of a subsequent two-stage exchange? If two-stage procedures are most effective as a first-line treatment, delaying them with a DAIR-Plus could hinder PJI eradication potentially reducing the benefits of less invasive methods. This is especially concerning with megaprostheses, where healing outcomes after one- and two-stage exchanges are already suboptimal. While conventional TJA has a PJI healing rate of 80–90% [30], the rate for megaprostheses is only 60–70% at best [31].

Azmangarhi reported reduced efficacy of two-stage revision following other procedures [14], while Asokan [28] demonstrated a high success rate for two-stage exchange after failed DAIR-Plus. Gundavda [24] conducted two-stage revision after DAIR and DAIR-Plus in 21 patients, successfully controlling PJI in 20, though 11 required spacer exchanges or additional procedures for complete healing. A systematic review [32] on DAIR's impact on subsequent two-stage procedures in conventional total joint PJI found no significant increase in two-stage failure, but couldn't rule it out.

In our series the overall infection resolution rate was 63%, consistent with published results. However, considering re-infection following DAIR-Plus (11 cases), only 36% became infection-free following other treatments. Our data cannot determine if this low success rate is due to the prior DAIR-Plus procedure or patient characteristics independent of treatment. Larger studies with comparison groups are needed to address this issue.

Prognostic factors

Our analysis of patient-related prognostic factors for DAIR-Plus success did not reveal clear detrimental factors. Women showed a trend of lower success rates, but oncological versus non-oncological disease had no impact on outcomes. This may be because, while oncological patients have negative prognostic factors like radiotherapy and chemotherapy, non-oncological patients receiving megaprostheses often have a history of multiple failed surgeries, increasing the risk of infection and soft tissue compromise.

Few studies report patients-related prognostic factors for DAIR-Plus success. Azamgarhi found a HR 4.441 for re-infection with severe soft tissue damage [14]. Gonzalez indicated BMI and CKD as negative prognostic factors [29]. In a large case series, cementless fixation was considered a good prognostic factor against re-infection [26]. While implanting a megaprosthesis after prior PJI is a significant risk factor for re-infection [14], we excluded such cases from our series.

Despite the limited number of patients, we demonstrated that the responsible pathogen is could be a prognostic factor for treatment failure. In our series, staphylococcal PJIs, regardless of the antibiotic resistance profile or species involved, had the worst outcomes, with 5 out of 7 failures occurring in staphylococcal infections. The success rate of our treatments in these cases was only 25%. This is concerning, as staphylococcal PJIs are the most common type of infection [6, 24]. A microorganism-centered approach may be crucial in decision-making, but more data are necessary to confirm our results.

Limitations

The retrospective nature of our study limited our ability to obtain complete data on antibiotic resistance profiles and perioperative antibiotic therapy details. Additionally, the small sample size may affect the strength and validity of our findings. The limited indication for DAIR-Plus procedures in the already small population of patients receiving megaprostheses makes it difficult to gather large patient series. Multicenter studies are needed to collect more robust data.

Another limitation is the lack of a comparison group with patients undergoing one- or two-stage complete revisions. While we compared our results to existing literature, this limitation remains and readers should be aware of it.

Despite these limitations, our study has notable strengths. By focusing on megaprostheses around the knee and using specific inclusion criteria, we ensured a well-defined and homogeneous patient population, enhancing the reliability of our findings. Furthermore, we provided a clear definition of DAIR-Plus and partial two-stage exchange, including detailed descriptions of the surgical technique and clinical indications. To our knowledge, this is the only study in the literature to include such a specific patient group, enabling a focused analysis of treatment outcomes in this context.

Conclusion

The DAIR-plus can be considered for selected patients with knee megaprosthetic PJI, even in cases of chronic infection. While it can yield acceptable short- and mid-term outcomes, it is associated with a substantial risk of recurrence at long-term follow-up. Nevertheless, when successful, this approach offers important advantages, such as preservation of bone stock and reduced recovery time. Partial two-stage exchange does not appear to improve outcomes; therefore, when complete implant removal is not feasible or is refused by the patient, efforts should be made to proceed with a

single-stage treatment. DAIR-Plus Patient-related prognostic factors are not yet well defined. Infections caused by *Staphylococcus spp* appeared to be more difficult to eradicate using the DAIR-Plus approach, which may prompt surgeons to consider a more invasive approach. However, more robust data are needed to confirm this hypothesis.

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Author contributions DS conceptualization, data analysis, methodology, writing original draft preparationMI supervision, formal analysisMC, FC Data Curation, InvestigationEN ResourcesDAC supervision, writing review & editingGS conceptualization, methodology, data curation, writing review & editing.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Conflict of interest The authors declare no competing interests.

References

1. Morii T, Morioka H, Ueda T, Araki N, Hashimoto N, Kawai A et al (2013) Deep infection in tumor endoprosthesis around the knee: a multi-institutional study by the Japanese musculoskeletal oncology group. BMC Musculoskelet Disord 14:51. https://doi.org/10.1186/1471-2474-14-51
2. Gonzalez MR, Pretell-Mazzini J, Lozano-Calderon SA (2024) Risk Factors and Management of Prosthetic Joint Infections in Megaprostheses—A Review of the Literature. Antibiotics. https://doi.org/10.3390/antibiotics13010025
3. Sukhonthamarn K, Tan TL, Strony J, Brown S, Nazarian D, Parvizi J (2021) The Fate of Periprosthetic Joint Infection Following Megaprosthesis Reconstruction. JBJS Open Access. https://doi.org/10.2106/JBJS.OA.21.00003
4. Pilge H, Gradl G, von Eisenhart-Rothe R, Gollwitzer H (2012) Incidence and outcome after infection of megaprostheses. HIP Int 22:83–90. https://doi.org/10.5301/HIP.2012.9576
5. Biau D, Faure F, Katsahian S, Jeanrot C, Tomeno B, Anract P (2006) Survival of total knee replacement with a megaprosthesis after bone tumor resection. J Bone Joint Surg 88:1285–1293. https://doi.org/10.2106/JBJS.E.00553
6. Nucci N, Gazendam A, Gouveia K, Ghert M, Wilson D (2020) Management of infected extremity endoprostheses: a systematic review. Eur J Orthop Surg Traumatol 30:1139–1149. https://doi.org/10.1007/s00590-020-02699-y
7. Holm CE, Bardram C, Riecke AF, Horstmann P, Petersen MM (2018) Implant and limb survival after resection of primary bone tumors of the lower extremities and reconstruction with megaprostheses fifty patients followed for a mean of forteen years. Int Orthop 42:1175–1181. https://doi.org/10.1007/s00264-018-3861-7
8. Cashman J, McCarroll P, Choong P, Neuwirth A, Carvalho PI, Budhiparama N et al (2025) International consensus meeting ICM Istanbul 2025. HK 48: what patients are candidates for Debridement, implant retention, and antibiotic administration. DAIR)?, Instanbul
9. Chen AF, Romanò CL, Drago L, Parvizi J (2016) Infection after joint arthroplasty. In: Kates SL, Borens O (eds) Principles of orthopedic infection management, 1st edn. Thieme, Davose, pp 189–212
10. Hulleman CWJ, de Windt TS, Veerman K, Goosen JHM, Wagenaar F-CBM, van Hellemondt GG (2023) Debridement, antibiotics and implant retention: a systematic review of strategies for treatment of early infections after revision total knee arthroplasty. J Clin Med 12:5026. https://doi.org/10.3390/jcm12155026
11. Razii N, Clutton JM, Kakar R, Morgan-Jones R (2021) Single-stage revision for the infected total knee arthroplasty. Bone Joint Open 2:305–313
12. Bloch B (2020) How i do it — Second stage revision total knee arthroplasty. Knee 27:2007–2012. https://doi.org/10.1016/j.knee.2020.08.012
13. Theil C, Bockholt S, Gosheger G, Dieckmann R, Schwarze J, Schulze M et al (2024) Surgical management of periprosthetic joint infections in hip and knee megaprostheses. Medicina. https://doi.org/10.3390/medicina60040583
14. Azamgarhi T, Warren S, Aston W, Pollock R, Gerrand C (2023) Risk factors for recurrent infection in the surgical treatment of infected massive endoprostheses implanted for musculoskeletal tumours. J Orthop Surg Res. https://doi.org/10.1186/s13018-022-03446-1
15. Flint MN, Griffin AM, Bell RS, Wunder JS, Ferguson PC (2007) Two-stage revision of infected uncemented lower extremity tumor endoprostheses. J Arthroplasty 22:859–865. https://doi.org/10.1016/j.arth.2006.11.003
16. Osmon DR, Berbari EF, Berendt AR, Lew D, Zimmerli W, Steckelberg JM et al (2013) Diagnosis and management of prosthetic joint infection: clinical practice guidelines by the infectious diseases society of Americaa. Clin Infect Dis 56:e1–25. https://doi.org/10.1093/cid/cis803
17. Theil C, Schneider KN, Gosheger G, Schmidt-Braekling T, Ackmann T, Dieckmann R et al (2022) Revision TKA with a distal femoral replacement is at high risk of reinfection after two-stage exchange for periprosthetic knee joint infection. Knee Surg Sports Traumatol Arthrosc 30:899–906. https://doi.org/10.1007/s00167-021-06474-2
18. Khakzad T, Karczewski D, Thielscher L, Reiter K, Wittenberg S, Paksoy A et al (2022) Prosthetic joint infection in mega-arthroplasty following shoulder, hip and knee malignancy—a prospective follow-up study. Life. https://doi.org/10.3390/life12122134
19. Schmolders J, Koob S, Schepers P, Pennekamp PH, Gravius S, Wirtz DC et al (2017) Lower limb reconstruction in tumor patients using modular silver-coated megaprostheses with regard to perimegaprosthetic joint infection: a case series, including 100

patients and review of the literature. Arch Orthop Trauma Surg 137:149–153. https://doi.org/10.1007/s00402-016-2584-8
20. Parvizi J, Tan TL, Goswami K, Higuera C, Della Valle C, Chen AF et al (2018) The 2018 definition of periprosthetic hip and knee infection: an Evidence-Based and validated criteria. J Arthroplasty 33:1309–1314e2. https://doi.org/10.1016/j.arth.2018.02.078
21. Coughlan A, Taylor F (2020) Classifications in brief: the McPherson classification of periprosthetic infection. Clin Orthop Relat Res 478:903–908. https://doi.org/10.1097/CORR.0000000000001133
22. Jeys LM, Thorkildsen J, Kurisunkal V, Puri A, Ruggieri P, Houdek MT et al (2024) Controversies in orthopaedic oncology. Bone Joint J 106-B:425–9. https://doi.org/10.1302/0301-620X.106B5.BJJ-2023-1381
23. Sigmund IK, Gamper J, Weber C, Holinka J, Panotopoulos J, Funovics PT et al (2018) Efficacy of different revision procedures for infected megaprostheses in musculoskeletal tumour surgery of the lower limb. PLoS One. https://doi.org/10.1371/journal.pone.0200304
24. Gundavda MK, Katariya A, Reddy R, Agarwal MG (2020) Fighting megaprosthetic infections: what are the chances of winning? Indian J Orthop 54:469–476. https://doi.org/10.1007/s43465-020-00080-z
25. Berger C, Parai C, Tillander J, Bergh P, Wennergren D, Brisby H (2023) High risk for persistent peri-prosthetic infection and amputation in mega-prosthesis reconstruction. J Clin Med. https://doi.org/10.3390/jcm12103575
26. Mavrogenis AF, Pala E, Angelini A, Calabro T, Romagnoli C, Romantini M et al (2015) Infected prostheses after lower-extremity bone tumor resection: clinical outcomes of 100 patients. Surg Infect Larchmt 16:267–75. https://doi.org/10.1089/sur.2014.085
27. Allison D, Huang E, Ahlmann E, Carney S, Wang L, Menendez L (2014) Peri-prosthetic infection in the orthopedic tumor patient. Reconstr Rev 4:13–17. https://doi.org/10.15438/rr.4.3.74
28. Asokan A, Ibrahim MS, Thompson JW, Haddad FS (2022) Debridement, antibiotics, and implant retention in non-oncological femoral megaprosthesis infections: minimum 5 year follow-up. J Exp Orthop. https://doi.org/10.1186/s40634-022-00469-9
29. Gonzalez MR, Acosta JI, Clunk MJ, Bedi ADS, Karczewski D, Newman ET et al (2024) Debridement, antibiotics, and implant retention (DAIR) plus offers similar periprosthetic joint infection treatment success rates to two-stage revision in oncologic megaprosthesis. J Arthroplasty 39:1820–7. https://doi.org/10.1016/j.arth.2024.01.021
30. Zhao Y, Fan S, Wang Z, Yan X, Luo H (2024) Systematic review and meta-analysis of single-stage vs two-stage revision for periprosthetic joint infection: a call for a prospective randomized trial. BMC Musculoskelet Disord. https://doi.org/10.1186/s12891-024-07229-z
31. Grimer RJ, Belthur M, Chandrasekar C, Carter SR, Tillman RM (2002) Two-stage revision for infected endoprostheses used in tumor surgery. Clin Orthop Relat Res 395:193–203. https://doi.org/10.1097/00003086-200202000-00022
32. Tan L, Yang J, Yang Z (2022) Impact of prior failed irrigation and debridement on outcomes of subsequent two-stage revision arthroplasty: a systematic review and meta-analysis. Eur Rev Med Pharmacol Sci 26:9125–9203