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RESEARCH

Antibiotic-loaded calcium sulphate beads in in debridement, antibiotics, and implant retention (DAIR) for acute hip and knee periprosthetic joint infection: a retrospective comparative cohort study

Antonio Pirozzi[1] · Francesco Raspanti[2] · Niccolò Giabbani[2] · Matteo Piccica[3] · Letizia Attala[3] · Matteo Innocenti[1] · Marco Mugnaini[2] · Luigi Zanna[2]

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Abstract

Background The role of antibiotic-loaded calcium sulphate (CaS) beads as an adjunct to debridement, antibiotics, and implant retention (DAIR) for acute periprosthetic joint infection (PJI) remains controversial. This study compared outcomes between standard DAIR and DAPRI (DAIR plus antibiotic-loaded CaS beads).

Methods A retrospective single-center cohort study was conducted on 51 consecutive patients treated for acute hip or knee PJI between 2022 and 2025. Thirty-three patients underwent standard DAIR and 18 underwent DAPRI. The primary endpoint was septic failure, defined as recurrent infection requiring surgical intervention. The secondary endpoints were identification of clinical and surgical predictors of failure. Univariable logistic regression analysis was performed to evaluate factors associated with septic failure following implant-retention treatment for acute PJI.

Results Overall septic failure occurred in 13/51 patients (25.5%). Failure rates were 27.3% in the DAIR group and 22.2% in the DAPRI group, a difference that did not reach statistical significance ($p=0.750$). Recurrence with the same pathogen was less frequent after DAPRI (5.6% vs. 15.2%). In subgroup analyses, failure in acute hematogenous PJI was 25% with DAPRI versus 62% with DAIR ($p=0.099$), and in hip arthroplasty no failures occurred with DAPRI (0/7) versus 25% with DAIR (6/24; $p=0.293$). On univariable analysis, significant predictors of failure were acute hematogenous infection (OR 7.22; $p=0.008$), preoperative fistula (OR 5.66; $p=0.018$), and higher BMI (OR 1.15; $p=0.015$). Among aseptic complication we reported 2/31 (6.5%) cases of hip dislocation.

Conclusion DAPRI was not associated with a statistically significant reduction in septic failure compared with standard DAIR (27.3% vs. 22.2%; $p=0.750$) in this small, underpowered cohort. Exploratory subgroup analyses suggested a possible benefit in acute hematogenous PJI and hip arthroplasty, but these findings are hypothesis-generating and require confirmation in larger studies. Acute hematogenous infection, preoperative fistula, and higher BMI were significant univariable predictors of septic failure.

Keywords Periprosthetic joint infection · DAIR · DAPRI · Calcium sulphate beads · Acute infection · Hematogenous infection

Introduction

Periprosthetic joint infection (PJI) remains one of the most feared complications of modern joint arthroplasty, with an incidence that ranges from 0.5 to 2% after primary procedures and rises to 3–5% after aseptic revision arthroplasty [1–6]. It carries a five-year mortality that rivals many solid-organ malignancies, and its economic burden is projected to exceed $1.85 billion annually in the United States alone by 2030 [1, 2]. Despite advances in prophylaxis and surgical technique, PJI remains the leading indication for revision knee arthroplasty and the third most common

Extended author information available on the last page of the article

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cause of revision hip arthroplasty in national registries [7, 8]. For patients presenting with acute PJI, either as early postoperative infection or acute hematogenous infection, debridement, antibiotics, and implant retention (DAIR) is reported as the first-line surgical strategy, if the implant is stable and infection timing meets the criteria [9, 10]. DAIR aims to avoid the implant exchange and, when patient and organism selection criteria are met, achieves functional outcomes comparable to primary arthroplasty [11]. Despite these advantages, reported failure rates span an extraordinary range from 14% to 84%, reflecting the heterogeneity of patient populations, microbial virulence, and the adequacy of surgical debridement [12, 13]. A limitation of DAIR is the inability of systemically administered antibiotics to achieve bactericidal concentrations within biofilm on retained implant surfaces. Biofilm dramatically reduces antibiotic penetration, and even vigorous pulsatile lavage does not reliably eradicate it [14, 15]. To address this gap, absorbable calcium sulphate (CaS) beads loaded with antibiotics have been proposed as a local delivery adjunct to standard DAIR, a technique designated DAPRI (Debridement, Antibiotic Pearls, and Implant Retention) [16]. The most widely studied formulation, Stimulan® Rapid Cure (Biocomposites Ltd, Keele, UK), is mixed intraoperatively with vancomycin and an aminoglycoside, implanted into the debrided joint cavity, and fully resorbed over two to six weeks. In vitro elution studies demonstrate that released antibiotic concentrations consistently surpass the minimum inhibitory concentration (MIC) for the principal PJI pathogens throughout the entire resorption period, achieving local tissue levels orders of magnitude above those attainable by systemic therapy alone [17, 18]. Despite this compelling mechanistic rationale, the available clinical evidence comparing DAPRI with standard DAIR remains limited in scope and methodologically heterogeneous. Published comparative data have yielded inconsistent results, with reported failure rates ranging from 15% to 48% [16, 19, 20]. The majority of studies have failed to demonstrate a statistically significant overall advantage of local antibiotic delivery over standard DAIR, although subgroup analyses suggest a potential benefit in selected clinical presentations, such as acute hematogenous PJI. These findings, however, should be interpreted with caution given the considerable variability in patient populations, surgical protocols, and outcome definitions across the existing literature [20–23]. The aims of this study were: (1) to compare the rate of septic failure between DAPRI and standard DAIR in a consecutive single-center cohort of patients with acute PJI of the hip and knee; and (2) to identify clinical, microbiological, and surgical factors associated with treatment failure, with prespecified subgroup analyses by infection type, joint, and prior surgical history. Our hypothesis is that the addition of local antibiotic delivery might increase the success rate of patients with acute PJIs treated with DAIR.

Materials and methods

We conducted a single-center retrospective cohort study at a tertiary referral arthroplasty unit with a dedicated multidisciplinary PJI management program. Informed consent was obtained from all individual participants, and data were collected and stored in anonymous digital form in accordance with institutional ethical guidelines. All procedures performed in this study were in accordance with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Between June 2022 and May 2025, a total of 64 consecutive patients undergoing surgical treatment for acute PJI were screened from a prospectively maintained institutional database. Inclusion criteria were: confirmed PJI by 2018 International Consensus Meeting (ICM) major or composite minor criteria [24] acute presentation classified as either early postoperative (symptom onset within four weeks of index arthroplasty) or acute hematogenous (sudden symptom onset in a previously well-functioning prosthesis) [10, 25]; stable implant amenable to retention; and minimum 12 months of clinical follow-up. Exclusion criteria comprised: chronic PJI, prosthetic instability precluding implant retention, incomplete operative or outcome records and follow up less than 12 months. The following variables were extracted from the institutional database and verified against electronic medical records: age at time of intervention; gender; body mass index (BMI, kg/m²); Charlson Comorbidity Index (CCI); affected joint (hip, knee); infection type (early postoperative, acute hematogenous); preoperative C-reactive protein (CRP, mg/dL) and erythrocyte sedimentation rate (ESR, mm/h); presence of a preoperative cutaneous sinus tract; number of prior surgeries on the affected joint; history of prior aseptic and septic revision; time from diagnosis to surgery (days); follow-up duration (months).

Surgical technique

All procedures were performed by a senior arthroplasty surgeon using a standardized operative protocol common to both treatment arms. The choice between standard DAIR and DAPRI was not randomized; it reflected the operating surgeon's judgment together with antibiotic-loaded bead availability over the study period. As part of our perioperative protocols, patients routinely receive antibiotic prophylaxis with 2 gr of cefazolin intravenous. Formal arthrotomy with extensile exposure, radical synovectomy

and excision of all macroscopically infected and necrotic tissue were performed. At least five periprosthetic tissue samples for microbiological culture and histopathological analysis were collected. Vigorous mechanical debridement, mechanical disruption of the biofilm on retained surfaces by with an argon beam coagulator and the scrub of visible fixed component with 4% chlorhexadine gluconate-added brush were performed. Patients were also treated with further adjuncts such as a 3-minute intra-articular dilute povidone-iodine, 10% povidone-iodine, and/or hydrogen peroxide wash and then new modular components (femoral head and acetabular liner in hip arthroplasty; tibial polyethylene insert in knee arthroplasty) were implanted. In the DAPRI group, antibiotic-loaded CaS beads (Stimulan® Rapid Cure, Biocomposites Ltd, Keele, UK) were prepared intraoperatively following debridement and prior to wound closure (Fig. 1). Total bead volume (range 5–20 mL per patient) was adjusted at the surgeon's discretion based on joint size, extent of tissue contamination, and preoperative renal function. The antibiotic addiction was decided preoperatively according to the isolated microorganism under dedicated infectious disease specialist supervision. The Beads were distributed throughout the joint cavity, targeting the medial and lateral gutters and posterior recess in the knee, and the peritrochanteric tissue and acetabular fossa in the hip. In the DAIR group, no local antibiotic carrier was used.

Post-operative management

In both groups, all patients received empirical intravenous antibiotic therapy intraoperatively, when a preoperative microorganism was not isolated, immediately after samples collection, adjusted to targeted therapy based on culture and sensitivity results, and continued for a minimum of six weeks under the supervision of a dedicated infectious disease specialist [26]. All patients follow an identical, standard postoperative rehabilitation protocol, including weight-bearing as tolerated with crutches on the first postoperative day. Discharge from the hospital occurs when the patient achieves independence in activities of daily living. The first outpatient evaluation was scheduled approximately three weeks after surgery for laboratory testing, wound assessment, suture removal, review of definitive intraoperative cultures, and adjustment of antibiotic therapy when indicated. A second visit was performed at four to six weeks postoperatively and included clinical examination, radiographic assessment of implant positioning, and laboratory testing. Subsequent evaluations were conducted at approximately three, six, 12, 18, and 24 months after surgery. The procedure was considered successful when clinical presentation and serologic tests (ESR, CPR) normalize. The septic failure was defined as a composite of any of the following: reoperation for infection at the index joint; implant removal due to persistent or uncontrolled infection; the need for chronic suppressive antibiotic therapy beyond twelve months postoperatively; or infection-related mortality, according to Delphi-based consensus criteria [27]. Secondary outcomes included recurrence (re-isolation of a phenotypically identical organism on subsequent culture); reinfection (isolation of a phenotypically distinct organism), aseptic complication and prolonged wound drainage (persistent wound leakage beyond five days postoperatively). Intraoperative pathogens were categorized as: methicillin-sensitive Staphylococcus aureus (MSSA); methicillin-resistant S. aureus (MRSA); methicillin-resistant S. epidermidis (MRSE); coagulase-negative staphylococci (CoNS); Streptococcus spp.; Enterococcus spp.; Corynebacterium spp.; Gram-negative organisms; fungal; culture-negative; or other/polymicrobial. Antibiotic-resistant pathogens were defined as those demonstrating methicillin resistance, ESBL production, or carbapenem resistance.

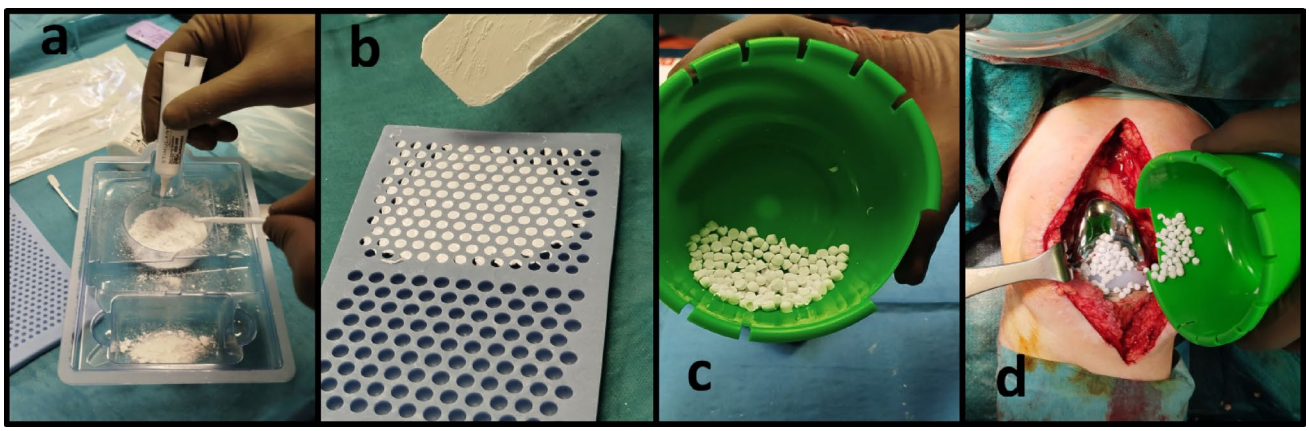

Fig. 1 Stimulan beads preparation **A** Adding the mixing solution from the tube into the bowl, **B** Paste application to fill every cavity of the sterile bead mat, **C** harden beads, **D** Placing the prepared beads into the surgical site

Statistical analysis

All analyses were performed in Python 3.11 (NumPy v1.26, pandas v2.1, SciPy v1.11). Continuous variables are reported as mean ± standard deviation (SD) and compared between groups using the two-sided Mann-Whitney U test, which does not assume normality and is appropriate for the skewed distributions and small sample sizes encountered in this cohort. Categorical variables are reported as count and percentage and compared using Fisher's exact test, preferred over the Pearson chi-square test whenever expected cell frequencies fell below five. Univariable logistic regression was performed to estimate odds ratios (OR) with 95% confidence intervals (CI) for each candidate predictor of septic failure; regression coefficients were obtained by maximum-likelihood estimation, with standard errors derived from the inverse Hessian matrix of the log-likelihood function at convergence, and *p*-values from the two-sided Wald test. Given the retrospective design, no a priori power calculation was performed; post-hoc power was therefore calculated for the primary comparison and the two pre-specified subgroups (acute hematogenous infection, hip arthroplasty) and is reported with the corresponding results. Multivariable logistic regression was not used as the primary analysis, owing to the limited number of failure events relative to candidate covariates; as an exploratory sensitivity analysis, a multivariable model was additionally fitted adjusting treatment modality for the two most imbalanced baseline variables (involved joint and Gram-negative pathogen).

Results

According to inclusion and exclusion criteria 51 patients constituted the final study cohort (Fig. 2). The final cohort comprised 33 patients in the DAIR group (64.7%) and 18 in the DAPRI group (35.3%), 31 total hip arthroplasties (THA) and 20 total knee arthroplasties (TKA). Patients' flow and baseline characteristics are reported in Table 1. The mean follow-up was 27 ± 12.1 months. The two groups were comparable across all baseline characteristics. The only statistically significant demographic difference was joint distribution: THA predominated in DAIR (73% vs. 39%; $p = 0.034$) while TKA was more frequent in DAPRI (61% vs. 27%; $p = 0.034$). In terms of microbiology, two significant differences in pathogen distribution were identified (Table 2). MSSA was the predominant causative organism in the DAPRI group (11/18, 61%) compared with the DAIR group (7/33, 21%; $p = 0.006$) and Gram-negative pathogens were identified exclusively in the DAIR group (7/33, 21% vs. 0/18, 0%; $p = 0.042$). MRSE showed a non-significant trend toward higher frequency in DAPRI (3/18, 17% vs. 1/33, 3%; $p = 0.120$). Culture-negative PJI occurred only in DAIR patients (5/33, 15% vs. 0/18; $p = 0.148$). The overall rate of septic failure was 13 of 51 patients (25.5%).

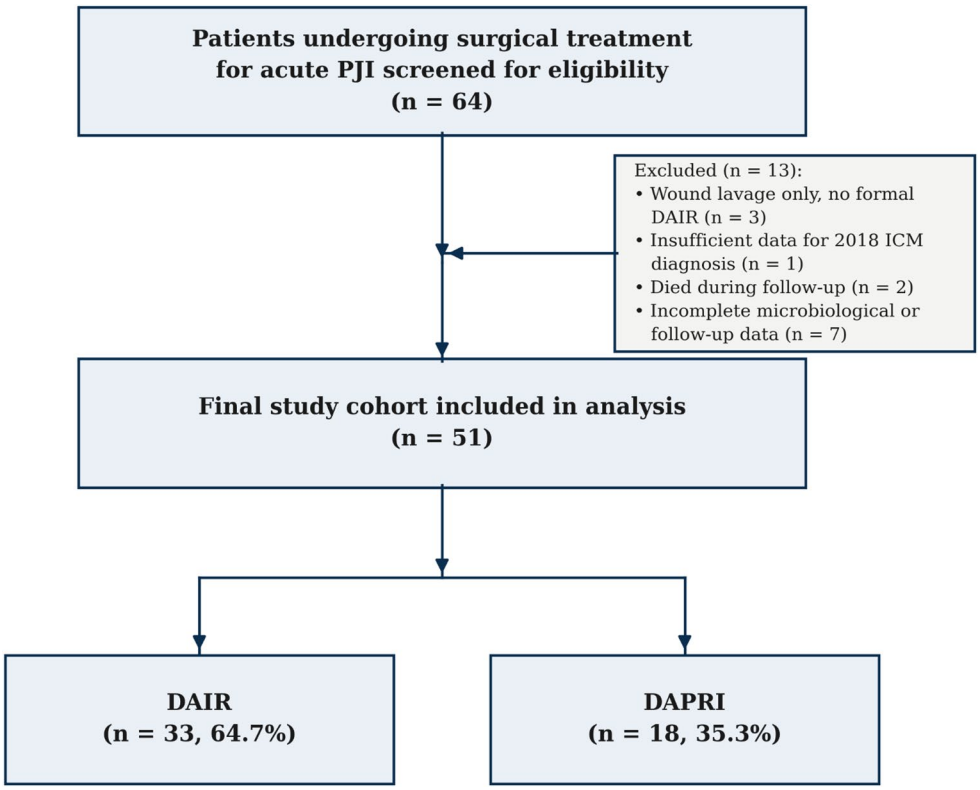

Fig. 2 Flow diagram of patient selection

Table 1 Baseline demographic and clinical characteristics of the study cohort ($n=51$)

Variable	DAIR ($n=33$)	DAPRI ($n=18$)	p-value
Age (years)	75.1 ± 9.7	75.4 ± 8.2	0.906
BMI (kg/m^2)	28.3 ± 6.6	29.4 ± 5.6	0.310
Charlson comorbidity index (CCI)	4.4 ± 1.6	4.2 ± 1.7	0.808
CRP at admission (mg/dl)	7.5 ± 7.0	10.2 ± 10.2	0.744
ESR at admission (mm/h)	54.8 ± 31.0	64.0 ± 11.3	0.411
Number of prior surgeries	1.6 ± 0.9	1.9 ± 1.2	0.386
Days from diagnosis to surgery	19.2 ± 11.3	14.1 ± 8.9	0.111
Male sex	15 (45%)	12 (67%)	0.240
Total hip arthroplasty	24 (73%)	7 (39%)	*0.034*
Total knee arthroplasty	9 (27%)	11 (61%)	*0.034*
Early postoperative PJI	20 (61%)	10 (56%)	0.726
Acute hematogenous PJI	13 (39%)	8 (44%)	0.726
Preoperative cutaneous fistula	9/33 (27%)	2/18 (11%)	0.288

BMI, Body mass index; CCI, Charlson Comorbidity Index; CRP, C-reactive protein; ESR, Erythrocyte sedimentation rate; PJI, Periprosthetic joint infection. Significant values $P<05$ are shown in italics

Table 2 Microbiological profile

Pathogen	DAIR n/33 (%)	DAPRI n/18 (%)	p-value
MSSA	7 (21%)	11 (61%)	*0.006*
Gram-negative organisms	7 (21%)	0 (0%)	*0.042*
MRSE	1 (3%)	3 (17%)	0.120
CoNS	3 (9%)	1 (6%)	1.000
MRSA	2 (6%)	0 (0%)	0.534
Enterococcus spp.	1 (3%)	1 (6%)	1.000
Corynebacterium spp.	3 (9%)	0 (0%)	0.544
Streptococcus spp.	0 (0%)	1 (6%)	0.353
Culture negative	5 (15%)	0 (0%)	0.148
Polymicrobial	4 (12%)	1 (6%)	0.645
Any resistant pathogen	5 (15%)	4 (22%)	0.703

MSSA, Methicillin-sensitive Staphylococcus aureus; MRSE, Methicillin-resistant Staphylococcus epidermidis; CoNS, Coagulase-negative staphylococci; MRSA, Methicillin-resistant S. aureus. Significant values $P<05$ are shown in italics

Table 3 Septic failure and post-operative wound drainage

Outcome	DAIR ($n=33$)	DAPRI ($n=18$)	p-value
Septic failure	9/33 (27.3%)	4/18 (22.2%)	0.750
Recurrence (same pathogen)	6/33 (18.2%)	1/18 (5.6%)	0.398
Reinfection (different pathogen)	4/33 (12.1%)	3/18 (16.7%)	0.686
Prolonged wound drainage (>5 days)	4/33 (12.1%)	2/18 (11.1%)	1.000

Significant values $P<05$ are shown in italics

Table 4 Septic failure by infection type—subgroup analysis

Infection type	DAIR failures	DAPRI failures	p-value
Early postoperative PJI	1/20 (5%)	2/10 (20%)	0.188
Acute hematogenous PJI	8/13 (62%)	2/8 (25%)	0.099

PJI, Periprosthetic joint infection. Significant values $P<05$ are shown in italics

Table 5 Septic failure according to the involved joints—subgroup analysis

Subgroup	DAIR failures	DAPRI failures	p-value
Hip arthroplasty	6/24 (25%)	0/7 (0%)	0.293
Knee arthroplasty	3/9 (33%)	4/11 (36%)	1.000
Both groups combined septic failure			
Hip arthroplasty ($n=31$ total)			6/31 (19.4%)
Knee arthroplasty ($n=20$ total)			7/20 (35.0%)

Significant values $P<05$ are shown in italics

Septic failure occurred in 9 out of 33 DAIR patients (27.3%) and 4 out of 18 DAPRI patients (22.2%) (Table 3). This difference did not reach statistical significance ($p=0.750$). Post-hoc power for this comparison was only 6.9% (1.143 patients per group would be needed for 80% power), so this result should be interpreted as inconclusive rather than as evidence of a treatment effect. Recurrence with the same pathogen was observed in the 6 of the DAIR group and in 1 DAPRI patient (6/33, 18.2% vs. 1/18, 5.6%; $p=0.398$), difference that did not reach statistical significance. No symptomatic hypercalcemia or radiographic heterotopic ossification were systematically documented in either group during the study period. Stratification by infection chronology revealed divergent trends (Table 4). In early postoperative PJI, DAPRI showed a numerically higher failure rate (2/8, 25%) than DAIR (1/20, 5%; $p=0.188$). In the acute hematogenous subgroup, DAIR failed in 8 of 13 patients (62%), compared to 2 of 8 DAPRI patients (25%; $p=0.099$). This absolute difference of 37% did not reach statistical significance and, given the small subgroup size and correspondingly low post-hoc power (39.1%), should be regarded as a hypothesis-generating exploratory observation rather than confirmatory evidence of benefit. The subgroup analysis according to joints was reported because the significant joint distribution imbalance between treatment groups ($p=0.034$) and the different failure rates after DAIR (Table 5). In hip arthroplasty, DAPRI was associated with 0% failure (0/7) compared to the 25% with DAIR (6/24; $p=0.293$), while in knee arthroplasty failure rates were similar between groups (DAIR 33% vs. DAPRI 36%; $p=1.000$). The overall lower failure rate in hip versus knee PJI (19% vs. 35%) is consistent with published data attributing worse knee outcomes to the larger synovial space and greater debridement complexity. Given the very small hip DAPRI subgroup ($n=7$), this observation should be regarded as exploratory and hypothesis-generating rather than evidence of a joint-specific

treatment benefit. The analysis of predictive factor of septic failure showed that treatment modality was not a statistically significant (DAPRI vs. DAIR: OR 0.76; 95% CI 0.20–2.94; $p=0.693$). On univariable analysis, three variables were significantly associated with higher failure odds: acute hematogenous infection type (OR 7.22; 95% CI 1.68–31.11; $p=0.008$), preoperative cutaneous fistula (OR 5.66; 95% CI 1.34–23.88; $p=0.018$), and BMI per unit increase (OR 1.15; 95% CI 1.03–1.29; $p=0.015$). Number of prior surgeries showed a borderline trend toward significance (OR 1.81; 95% CI 0.99–3.30; $p=0.052$). Age, CCI, joint, prior revision history, resistant pathogen, inflammatory markers, and time to surgery were not significant univariable predictors (Table 6). Among aseptic complication we reported 2/31 (6.5%) cases of hip dislocations, 1 treated surgically with constrained insert implantation and 1 with closed reduction. Post-hoc exploratory sensitivity analysis: after adjusting for the two variables with the largest baseline imbalance between groups (involved joint and Gram-negative pathogen), DAPRI remained associated with lower odds of septic failure relative to DAIR (adjusted OR 0.49, 95% CI 0.11–2.18; $p=0.352$), a point estimates similar to or somewhat stronger than the unadjusted comparison (OR 0.76). Knee joint (adjusted OR 2.48, 95% CI 0.60–10.35; $p=0.212$) and Gram-negative pathogen (adjusted OR 0.53, 95% CI 0.05–5.62; $p=0.599$) were not independently significant. This model had only 13 events across 3 covariates (events-per-variable = 4.3, below conventional thresholds), and Gram-negative pathogens occurred exclusively in the DAIR group, producing quasi-complete separation on that term and unstable variance estimation; these results should therefore be interpreted as hypothesis-generating only and not as a reliable adjusted effect estimate.

Table 6 Univariable logistic regression: candidate predictors of septic failure

Variable	OR	95% CI	*p*-value
DAPRI vs. DAIR (treatment modality)	0.76	0.20–2.94	0.693
Age (per year)	1.04	0.96–1.12	0.322
BMI (per kg/m^2 unit)	1.15	1.03–1.29	*0.015*
CCI (per point)	1.25	0.84–1.86	0.268
Acute hematogenous PJI (vs. early post-op)	7.22	1.68–31.11	*0.008*
Knee joint (vs. hip)	2.24	0.62–8.07	0.216
Prior septic revision	1.57	0.42–5.85	0.501
Prior aseptic revision	1.50	0.24–9.35	0.664
Number of prior surgeries	1.81	0.99–3.30	0.052
Resistant pathogen	0.81	0.14–4.48	0.804
Preoperative fistula	5.66	1.34–23.88	*0.018*
CRP at admission (mg/dL)	1.03	0.95–1.12	0.435
ESR at admission (mm/h)	1.00	0.95–1.04	0.846
Days from diagnosis to surgery	0.99	0.93–1.05	0.703

OR, odds ratio; CI, 95% confidence interval. Maximum-likelihood logistic regression. BMI, body mass index; Charlson Comorbidity Index, CCI; PJI, periprosthetic joint infection; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate. Significant values $P<05$ are shown in italics

Discussion

This retrospective cohort study compared DAIR and DAPRI in 51 consecutive patients with acute PJI treated at a single tertiary Center. The overall rate of septic failure was 25.5%. The comparison between DAIR (27.3%) and DAPRI (22.2%) did not reach statistical significance ($p = 0.750$), and we consider this lack of a demonstrable difference in septic failure to be the primary finding of the study [28]. Furthermore, we reported that in the whole cohort 3 variables were significant univariable predictors of significantly higher failure odds: acute hematogenous infection type (OR 7.22; 95% CI 1.68–31.11; $p = 0.008$), preoperative cutaneous fistula (OR 5.66; 95% CI 1.34–23.88; $p = 0.018$), and BMI per unit increase (OR 1.15; 95% CI 1.03–1.29; $p = 0.015$). In terms of addition of antibiotic-loaded CaS beads, our overall findings are consistent with the others comparative series. Tarity et al. [19] conducted the first comparative study restricted to the acute PJI setting, matching 20 DAPRI patients to 20 DAIR controls by CCI, and found no significant difference in 2-year failure (45% vs. 25%, $p = 0.21$) or 90-day early failure (5% vs. 5%, $p = 1.00$). In the largest series, Sigmund et al. [20] retrospectively analyzed 176 patients across a ten-year period at a high-volume Centre and similarly observed no overall benefit of CaS beads on reinfection or reoperation rates. However, a subgroup analysis of acute hematogenous PJI identified a significant reduction in reoperation with beads (25% vs. 61%; OR 0.2, 95% CI 0.1–0.8), comparable to our study. Smaller series by Flierl et al. [21], Reinisch et al. [22], and Indelli et al. [16] have reported failure rates ranging from 15% to 48% with DAPRI, without consistent evidence of superiority over standard DAIR [23, 28]. Our failure rates are lower than both of these series, 27.3% for DAIR and 22.2% for DAPRI, reflecting the strict acute-only inclusion and the standardized surgical protocol at our Centre. One of the exploratory findings warranting further investigation is the acute hematogenous subgroup analysis. In this subgroup, the DAIR failure rate reached 62%, among the highest reported in the literature for this infection type, and consistent with published data showing failure rates of 51–60% for hematogenous PJI treated with DAIR alone [20, 29]. In contrast, DAPRI achieved only 25% failure in the same subgroup ($p = 0.099$). While not statistically significant in isolation, this finding precisely mirrors the result reported by Sigmund et al. [20], who, with a larger hematogenous subgroup of 46 patients, found a statistically significant

reduction in reoperation rate (25% vs. 61%; OR 0.2, 95% CI 0.1–0.8) [20]. The similar direction and magnitude of effect across two independent institutions is noteworthy and supports acute hematogenous PJI as a subgroup warranting dedicated prospective investigation. The biological rationale for this differential effect is compelling. In hematogenous PJI, a remote bacteraemic source, most commonly endocarditis, pneumonia, or a genitourinary focus, continuously seeds the prosthetic interface with planktonic bacteria. Systemic antibiotics must achieve bactericidal tissue concentrations against an ongoing inoculum, often complicated by the hematogenous source itself. CaS beads provide sustained local concentrations exceeding the MIC for staphylococcal and streptococcal species throughout the two-to-six-week resorption period, precisely the window during which systemic antibiotic therapy is being optimized and the hematogenous source is being treated [17, 18]. This may also explain why hematogenous infections treated with DAPRI achieved failure rates approaching those of early postoperative PJI (25% vs. 20%), an observation replicated by Sigmund et al. and worthy of prospective investigation [20]. The joint-stratified subgroup analysis represents an original contribution of this study and provides a rationale for the hip-versus-knee comparison that reviewers may question. We considered this analysis not only clinically relevant, but methodologically necessary, given the significant joint distribution imbalance between groups (73% hip in DAIR vs. 39% in DAPRI; $p = 0.034$). Had we not performed this analysis, the possibility that the higher DAIR failure rate was partly attributable to the greater proportion of knee cases in DAPRI, which carry a higher overall failure risk [22], could not be assessed. In THA, DAPRI was associated with 0% failure (0/7) versus 25% with DAIR (6/24); however, this observation is based on only seven DAPRI patients with zero events (post-hoc power 21.8%) and must be regarded as hypothesis-generating rather than a demonstrated joint-specific effect. This is biologically plausible due to the contained anatomical space around the femoral neck and acetabular fossa may allow more uniform bead distribution and higher local antibiotic exposure than the multi-compartment knee joint. In knee arthroplasty, failure rates were comparable (33% vs. 36%), suggesting that CaS beads may not overcome the particular challenges of this joint, including the larger synovial volume requiring bead coverage, the polyethylene third-body wear concern raised by Tarity et al. [19], and the greater complexity of achieving complete synovectomy. Three factors emerged as significant univariable predictors of treatment failure. Acute hematogenous infection type carried the highest odds (OR 7.22), consistent with its biological complexity and the high failure rates reported across all series [12, 13, 20]. Preoperative cutaneous fistula (OR 5.66) represents established severe local infection with deep tissue involvement and the highest intra-articular biofilm burden, findings consistently reported as negative prognosticators for DAIR success in prior literature [12]. BMI (OR 1.15 per unit) likely captures the combined effects of impaired wound healing, reduced tissue perfusion at the infection site, and global immunosuppression associated with morbid obesity according to literature [30]. These three factors provide a practical framework for patient selection and preoperative counselling. This study addresses a highly relevant topic in contemporary PJI management and provides clinically relevant preliminary data on the use of antibiotic-loaded calcium sulphate beads during DAIR procedures. The standardized surgical protocol, the detailed description of the DAPRI technique, and the focus on acute PJI improve the consistency and reproducibility of the study. Another strength is the subgroup analysis, particularly in acute hematogenous infections, which offers valuable insights and generates important hypotheses for future prospective studies. Several limitations should be acknowledged. The retrospective, non-randomized, single-center design limits causal inference; treatment allocation reflected surgeon discretion and bead availability rather than a protocol-driven algorithm, introducing potential confounding by indication that cannot be excluded retrospectively. The small sample size ($n = 51$) yielded low post-hoc power for the primary comparison and both subgroup analyses, and at least six comparisons were performed without correction for multiple testing. Baseline imbalances in joint distribution and microbiology (Gram-negative infections occurring exclusively in the DAIR group) may have influenced outcomes; multivariable analysis was not used as the primary approach given the low events-per-variable ratio, and an exploratory sensitivity model adjusting for these imbalances, while not reversing the direction of the treatment comparison, remained imprecise. Adverse events potentially related to the calcium sulphate beads were not systematically screened for, and a formal cost-effectiveness analysis was beyond the scope of this study. Finally, although mean follow-up (27 ± 12.1 months) exceeded the commonly used 24-month benchmark for PJI outcome studies, individual follow-up as low as 12 months was possible, and late recurrences cannot be excluded. A minimum 1-year follow-up has, however, been shown to provide reliable outcome reporting in PJI cohorts, supporting the adequacy of our follow-up window [31].

Conclusion

In this retrospective cohort of acute PJI, DAPRI was not associated with a statistically significant reduction in septic failure compared with standard DAIR (22.2% vs. 27.3%;

$p=0.750$). Exploratory, hypothesis-generating subgroup analyses suggested a possible benefit of DAPRI in acute hematogenous infections (failure 25% vs. 62% with DAIR) and in hip arthroplasty (0% vs. 25%), but these small subgroups were small would benefit of confirmation with larger cohorts. Acute hematogenous infection (OR 7.22), preoperative fistula (OR 5.66), and elevated BMI (OR 1.15) were significant univariable predictors of failure. Routine use of DAPRI cannot be recommended on the basis of this study; rather, these findings justify a properly powered, ideally multicenter and prospective, comparative trial to determine whether local antibiotic delivery provides a genuine benefit over standard DAIR in acute PJI, particularly in the hematogenous and hip subgroups identified here.

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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.

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Authors and Affiliations

Antonio Pirozzi[1] · Francesco Raspanti[2] · Niccolò Giabbani[2] · Matteo Piccica[3] · Letizia Attala[3] · Matteo Innocenti[1] · Marco Mugnaini[2] · Luigi Zanna[2]

✉ Luigi Zanna
luigizanna90@gmail.com

Antonio Pirozzi
antonio.pirozzi@unifi.ti

Francesco Raspanti
francesco.raspanti@uslcentro.toscana.it

Niccolò Giabbani
niccolo.giabbani@uslcentro.toscana.it

Matteo Piccica
matteo.piccica@uslcentro.toscana.it

Letizia Attala
letizia.attala@uslcentro.toscana.it

Matteo Innocenti
matteo.innocenti@unifi.it

Marco Mugnaini
marco1.mugnaini@uslcentro.toscana.it

[1] Department of Orthopaedic, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy

[2] Department of Orthopaedic and Traumatology, Ospedale Santa Maria Annunziata, Florence, Italy

[3] Department of Infectious Diseases, Ospedale Santa Maria Annunziata, Florence, Italy