Debridement, Antibiotics, and Implant Retention (DAIR) for the early prosthetic joint infection of total knee and hip arthroplasties: A Systematic Review

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What is already known?

- The incidence of PJI is estimated to be around 1-2% among all joint replacements. With the progressive increased number of joint replacement procedures performed worldwide, the number of PJI is expected to increase in the following years.
- Although in recent years steps have been made to provide pathways and guidance for individuals with a PJI, there remains a lack of evidence and therefore consensus across many facets of patient care. This may partly explain the variability of success rates in revision surgery for PJI across the literature.
- Treatment strategies included surgical irrigation, debridement, antibiotic therapy, and implant retention with or without polyethylene exchange (DAIR). Alternative options are represented by one-stage or two-stage revision surgery.

What are the new findings?

- DAIR is an overall successful treatment for early postoperative and acute hematogenous PJIs in hip and knee prostheses.
- There is still a lack of studies, in particular of RCTs, comparing DAIR with one-stage and two-stage revision protocols in the setting of early PJIs.

ABSTRACT

Purpose: Early Prosthetic Joint Infection (PJI) represents one of the most fearsome complications of joint replacement. No international consensus has been reached regarding the best approach for early prosthetic knee and hip infections. The aim of this updated systematic review is to assess whether DAIR is an effective choice of treatment in early postoperative and acute hematogenous PJI.

Methods: This systematic review was performed using the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. The diagnostic criteria defining a PJI, the most present pathogen and the days between the index procedure and the onset of the PJI were extracted from the selected articles. Additionally, mean follow-up, antibiotic regimen and success rate of the treatment were also reported.
Results: The articles included provided a cohort of 970 patients. Ten studies specified the joint of their cohort in PJIs regarding either hip prostheses or knee prostheses, resulting in 454 total knees and 460 total hips. The age of the patients ranged from 18 to 92 years. Success rates for the DAIR treatments in the following cohort ranged from 55.5% up to a maximum of 90% (mean value 71%).

Conclusion: Even though DAIR procedure is quite limited, it is still considered an effective option for patients developing an early post-operative or acute hematogenous PJI. However, there is a lack of studies, in particular of RCTs, comparing DAIR with one-stage and two-stage revision protocols in the setting of early PJIs, reflecting the necessity to conduct further high-quality studies to face the burden of early PJI.

Keywords: DAIR; knee; hip; Arthroplasty; early; infection

INTRODUCTION

Early periprosthetic joint infection (PJI) is a severe complication that can occur after joint replacement surgery [1, 2]. It is often associated with the need for multiple revision surgeries, recurring infections, prolonged courses of antibiotics, extended hospital stays, delayed aseptic loosening, and unfavourable functional outcomes [3-6]. The incidence of PJI is estimated to be around 1-2% among all joint replacements [7]. Furthermore, PJI has been found to contribute to 13% of revision hip arthroplasties and 23% of revision knee arthroplasties [8]. In fact, in cases where joint revision is necessary, this complication accounts for 39.6% of all surgical procedures [9-12].

With the progressive increased number of joint replacement procedures performed worldwide, the number of PJI is expected to increase in the following years [13, 14].

Infections associated with prosthetic joints can be categorized into three groups: early infections (occurring within three months after surgery), delayed infections (appearing between three and 24 months after surgery), and late infections (emerging more than 24 months after surgery). Early infections are typically characterized by sudden joint pain, swelling, redness, warmth at the site of the implant, and fever [15]. Another classification system, popularized by Tsukayama in the 1990s, divides prosthetic joint infections (PJIs) into four categories. This classification takes into account both the time elapsed since the operation and the presumed mode of infection: positive intraoperative cultures, early postoperative infections, hematogenous infections, and late chronic infections [16, 17]. Furthermore, McPherson
and colleagues proposed a staging system for PJIs that not only considers the type of infection but also factors in the host's condition [18, 19].

Different treatment strategies included surgical irrigation, debridement, antibiotic therapy, and implant retention with or without polyethylene exchange (DAIR). Debridement involves removal of the hematoma, fibrous membranes, sinus tracts, and devitalized bone and soft tissue.[15]

There are alternative options available such as one-stage or two-stage revision surgeries [2, 20-22]. Two-stage revision surgery has long been considered the ‘gold standard’. However, for patients with relatively healthy bone and soft tissue, no prior revision surgeries, or treatment involving effective antibiotics against biofilm-active microorganisms, the treatment of choice would be a one-stage exchange [23].

The options for complex and chronic PJIs are resection arthroplasty (RA) (without reimplantation), arthrodesis and amputation [24-27]. Non-surgical medical treatment such as antibiotic suppression therapy should be reserved for patients with comorbidities or contraindicated for surgery [7, 24]. However, the existing recommendations for treatment of the PJI have been refined further by new scientific evidence and clinical experiences [15, 28]. It is well known that one-stage revision surgery is usually used to compensate for the shortcomings of two-stage revision surgery in chronic PJI patients. There is no information on definitive indications for which one-stage revision surgery may be used as a primary surgical intervention instead of DAIR procedure in acute PJI patients [15, 28].

The DAIR treatment is less invasive, less technically demanding, has lower morbidity, shorter hospitalization, better bone stock preservation and lower economic burden; however, it is suitable for specific cases [27, 29, 30]. DAIR treatment indication is still debated among orthopaedic surgeons [29], as the rates of infection control range from 12% to 80%[29]. The decision to retain implants should be based on several factors: non-immunocompromised patients, low virulence microorganisms, and biofilm containment within a short period of time [24, 26, 27, 31, 32].

Two-stage revision has been the most successful alternative for PJI, with a 91% success rate for eradicating infection [25, 27]. However, revision surgeries are very challenging for both patients and surgeons. The patient will undergo multiple operations with more extended periods of reduced mobility. In addition, the surgeons will face significant challenges as difficulties in removing a cemented prosthesis, risk of bone loss and injuries to peri-prosthetic soft tissue [24, 27, 33].

One-stage revision surgery for PJI was introduced as a substitute for two-stage revision surgery on chronic PJI that has been reported to have equivalent infection-free success compared to two-stage revision, with lower mortality and morbidity, with less hospitalizations, shorter antibiotic treatment duration, and lower overall healthcare costs [25, 34,
However, if one-stage revision surgery is performed as a suboptimal treatment for patients with condition that is not suitable for DAIR procedure, it can be easily predicted that the outcome such as re-infection rate of one-stage revision surgery will be worse than DAIR procedure.

Given the aforementioned variables affecting the choice of treatment in the context on early prosthetic infections, the KLIC and the CRIME80 scoring systems have recently been developed with the goal of predicting DAIR failure after AP PJI and AH PJI, respectively [36].

The main goal of this systematic review is to assess the success rate, defined as implant retention with infection clearance, of DAIR in the context early postoperative and acute hematogenous PJI.

**MATERIALS AND METHODS**

*Study Selection*

The research question was formulated using a PIOS approach: Patient (P); Intervention (I); Outcome (O), and Study design (S).

This systematic review focused on patients with early PJI (P) (total hip or knee arthroplasty), treated by DAIR (I), in order to describe the recurrent infection rate (O). For this purpose, the following study designs were included (S): Non-Randomized Controlled Studies (NRCT) as Prognostic (PG), Prospective (PS), Retrospective (RS), Case-Series (CS), Case-Control (CC), Cohort (C) studies were included.

This systematic review aimed to describe the recurrence infection rate (O) in patients with early PJI (P) (total hip or knee arthroplasty), treated by DAIR (I) or one-stage revision (C). For this purpose, the following study designs were included (S): Randomized Control Trials (RCT) and Non-Randomized Controlled Studies (NRCT) as Prognostic (PG), Prospective (PS), Retrospective (RS), Case-Series (CS), Case-Control (CC), Cohort (C) studies were included.

**Inclusion and Exclusion Criteria**

As claimed by the Oxford Centre of Evidence-Based Medicine, Level I-IV articles were included in the analysis. Due to the semantic competencies of the authors, publications in English, French, Dutch, Spanish and Italian were included.

The aim of the current review was to analyse the outcomes of DAIR in context of either early postoperative or acute hematogenous infections. Several classifications have been proposed [15, 17, 19]. In order to include all the data coherently to the aim of the current study, only data regarding type I-III PJI according to Tsukayama et al.[17], grade...
I-II PJIs according to McPherson et al [19], or PJIs defined as “Early” according to the classification proposed by Zimmerli et al.,[15] were included in this systematic review.

Additionally, due to the potential bias arising from the hospital-specific risk of post-operative infections, multicenter studies were not included in the review, nor were studies reporting outcomes following chronic PJIs. Studies were the treatment for early post-operative or acute hematogenous PJI was different than DAIR were not considered eligible for this review and diagnostic criteria applied by the single authors to define a PJI needed to be explicit within their methods section.

Literature analysis, case reports, animal studies, cadavers or in vitro examinations, biomechanical information, technical records, reports to redactors, and instructional courses were omitted. Publications with inadequate features of surgical procedure, follow-up, age of patients, clinical inspection, rate of re-infection and statistical analysis were not considered eligible for this systematic review.

Search

A systematic review was performed using the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines [37]. An exhaustive study of the Medline, CINAHL, Cochrane, Embase, Ovid, Web of Science and Google Scholar databases was performed using the following string: (((DAIR) OR (debridement)) OR (antibiotic)) OR (implant retention)) AND (infection)) AND (periprosthetic)) AND (hip)) AND (knee).

Additional studies were searched among reference lists of selected papers and systematic reviews. Three independent reviewers (S.D.S., B.B., and A.L.) separately conducted the study and articles published from the inception of the databases to September 2022 have been included. The search was performed from August to September 2022.

Data Collection Process

Initial screening has been performed on all the articles for relevance by title and abstract and taking the full-text publication if the abstract did not let the examiners appraise the specific inclusion and exclusion parameters. The three investigators (S.D.S., A.L., and B.B.) independently analyzed the abstract of each article and then achieved a close understanding of all publications and extracted reports to reduce selection bias and errors. To avoid bias, the chosen publications, the corresponding credentials list, and the publications precluded from the analysis were examined, evaluated, and argued by all the writers. In case of disagreement, the senior reviewer (U.G.L.) decided. The number of articles included or excluded was registered and reported in the PRISMA flowchart (Figure 1). Rules by Moher et al. were followed in designing the PRISMA chart [38].
The trial’s design, conduct and reporting of results were performed in conformity to Good Clinical Practice guidelines reported in the World Medical Association (WMA) Declaration of Helsinki.

Figure 1. Study selection process and screening according to the PRISMA flow chart.

Data Items

General study characteristics extracted were: primary author, year of publication, country, type of study, level of evidence sample size, population demographics, sample size, gender, and mean age (Table 1). The diagnostic criteria defining a PJI, the most present pathogen and the days between the index procedure and the onset of the PJI are summarized in Table 2. Additionally, mean follow-up, antibiotic regimen and success rate of the treatment are reported in Table 3.

Study risk of bias assessment

The Risk of Bias in Non-Randomized Studies of Interventions (ROBINS-I) tool from Cochrane and the Joanna Briggs Institute Critical Appraisal Tool for Case Series were used to assess the quality of each research [39, 40]. Two reviewers (B.B., A.L.) independently assessed the papers and, if there was a dispute, a third reviewer (S.D.S) was consulted.

Statistical Analysis

Categorical data were summarized as frequencies and percentages. Continuous data were summarized as mean values, with standard deviations (SD) or range (i.e., minimum and maximum values). A meta-analysis was not performed at the end of the review due to the heterogeneity of the data of the selected articles.

RESULTS

Search Results

The literature search identified 695 total studies. No additional studies were found in the grey literature, and no unpublished studies were retrieved. Duplicated article removal resulted in the exclusion of 177 papers. Of the remaining 518 articles, 405 were removed as incompatible with the main aim of this review after the title and abstract evaluation. 113 full-text articles were then screened, leading to the elimination of 101 studies. In the latter exclusion process, the discarded articles were: articles reporting data from chronic or late-hematogenous PJIs (n=45), multicentre studies
(n=14), articles not specifying the type of PJI (n=17). Additionally, systematic reviews (n=14) and articles with no retrievable full text (n=11) were discarded.

At the end of the selection process, a total of 12 articles were considered eligible for this study. The PRISMA flowchart of the literature search is reported in Figure 1.

**Quality of Evidence**

The ROBINS-I tool for Non-Randomized Controlled Trials (NRCT) and the Joanna Briggs Institute Critical Appraisal Tool for Case Series were used to assess the methodological quality of each article [39, 40]. No Randomized Controlled Trials (RCT) were included in the review. Retrospective Case Controls (RCCs) were identified as low risk of bias [41, 42] or moderate risk of bias [32]. Retrospective Case Series (RCSs) were overall of good quality [36, 43-50].

The risk of bias assessments for RCTs, NRCTs, and CSs is reported in Figures 2 and 3.

**Figure 2.** The risk of bias assessments for NRCTs studies

**Figure 3.** The risk of bias assessments for Case Series studies

**Study characteristics**

The current review was comprised of 12 studies, of which three were RCCs [32, 41, 42] and nine were RCS [36, 43-50]. The 12 studies included (Table 1) were brought out from 2010 to 2022. Seven of the considered studies were carried out in the USA [32, 36, 41, 44, 46, 47, 49], with the remaining being located in Brasil [48], China [43], Germany [45], Netherlands [50] and Portugal [42]. Multicentre studies were considered ineligible due to the lack of homogeneity.

The articles included provided a cohort of 970 patients. Ten studies specified the joint of their cohort in PJIs regarding either hip prostheses or knee prostheses [36, 41, 43-50], resulting in 454 total knees and 460 total hips. The age of the patients ranged from 18 to 92 years.
The Musculoskeletal Infection Society (MSIS), the International Classification of Diseases, Ninth Revision codes (ICD-9-CM) and International Consensus Meeting Diagnostic Criteria (ICMDC) were applied for definition of PJIs in four [41, 45, 46, 48], one [47] and three [36, 49, 50] articles, respectively. The remaining studies defined PJIs with specific criteria reported in Table 2.

The most common pathogen species involved was the Staphylococcus spp. In particular, Staphylococcus Aureus was the most prevalent pathogen, present in nine out of 12 included studies [32, 36, 43-46, 48-50].

After the prophylactic administration, the antibiotic regimen was mainly culture-specific, leading to high heterogeneity among the cohort. The intravenous regimen had a minimum duration of two weeks.

Ten studies reported the mean follow-up regarding their cohorts [32, 36, 41-45, 47-49], resulting in a mean follow-up for the current review of 35.1 months. The remaining two articles had a minimum follow-up of 12 [46] and 24 [50] months each.

**Success Rate**

The average rate of success for the DAIR treatments in the following cohort was 71%. Treatment success was defined according to Masri et al. [51], Martinez-Pastor et al. [52] and Zimmerli et al. [15], who stated that a patient could be judged infection-free at follow-up if he or she was free of clinical signs for infection (fever, local pain, redness, warmth, sinus tract infection), and had a CRP level less than 10 mg/l.

Additionally treatment failure was defined according to Byren et al. and Masri et al. if surgery was required as a result of exacerbation or if a new infection appeared after a symptom-free phase within the follow-up period [45] [53].

Success rates below 60% were reported by Chalmers et al. [36] and by Klement et al.[46] with 58.4% and 55.5%, respectively. Highest rates were found by Estes et al. [44] and by Barros et al.[42] reaching 90% and 89.5%, respectively.

**Table 1, Population and Demographics**

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Country</th>
<th>Type of study</th>
<th>LOE</th>
<th>Sample size</th>
<th>Gender</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barros et al.; 2021</td>
<td>Portugal</td>
<td>RCC</td>
<td>III</td>
<td>38</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>
Chalmers et al.; 2021  USA  RCS  IV  122  70  52  67  55  65 ± 11.6
Chang et al.; 2017  China  RCS  IV  5  3  2  NR  NR
Estes et al.; 2010  USA  RCS  IV  20  16  4  NR  67 (28-91)
Fink et al.; 2017  Germany  RCS  IV  67  44  23  37  30  67.8 (30.0 – 80.0)
Klement et al.; 2019  USA  RCS  IV  189  80  109  NR  64.3 ± 12
Manrique et al.; 2019  USA  RCS  IV  176  58  118  91  85  62.2 (18-92)
Riesgo et al.; 2017  USA  RCC  III  74  36  38  47  26  61 (31-92)
Rudelli et al.; 2021  Brasil  RCS  IV  56  25  31  22  44  67
Tirumala et al.; 2021  USA  RCS  IV  149  90  59  76  73  66.4 ± 10.3
Van Kleunen et al.; 2010  USA  RCC  III  18  NR  NR  7  11  55.3 (40-90)
Veerman et al.; 2022  Netherlands  RCS  IV  56  32  24  NR  NR

LOE, Level Of Evidence; M, Male; F, Female; RCC, Retrospective Case Control; RCS, Retrospective Case Series; NR, Non-Reported

Table 2, Infection characteristics

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Diagnostic criteria</th>
<th>Most Present organism</th>
<th>Index-PJI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Type</td>
</tr>
<tr>
<td>Barros et al. 2021</td>
<td>At least one positive deep (subfascial) sample collected intra-operatively either synovial fluid or</td>
<td>CoNS, S. Aureus E.Coli</td>
<td>21 (32.), 18 (28.1), 7 (10.9)</td>
</tr>
<tr>
<td>Study</td>
<td>Definition</td>
<td>Organism</td>
<td>Count</td>
</tr>
<tr>
<td>---------------------</td>
<td>---------------------------------------------------------------------------</td>
<td>----------</td>
<td>-------</td>
</tr>
<tr>
<td>Chalmers et al.; 2021</td>
<td>ICMDC</td>
<td>MSSA</td>
<td>34 (28)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CNSA</td>
<td>25 (21)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MRSA</td>
<td>15 (12)</td>
</tr>
<tr>
<td>Chang et al.; 2017</td>
<td>At least two positive samples of the same microorganism identified or matched to blood, joint synovial fluid, or tissue culture</td>
<td>MRSA</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CoNS</td>
<td>1</td>
</tr>
<tr>
<td>Estes et al.; 2010</td>
<td>At least 2 or more positive cultures for the same organism with the same antibiotic sensitivity profile or Any patient meeting 2 or more of the diagnostic criteria explicited in the study</td>
<td>MSSA</td>
<td>4 (20)</td>
</tr>
<tr>
<td>Fink et al.; 2017</td>
<td>MSIS</td>
<td>S. aureus</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MSSE</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P. acnes</td>
<td>4</td>
</tr>
<tr>
<td>Klement et al. 2019</td>
<td>MSIS</td>
<td>S. aureus</td>
<td>110</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MRSA</td>
<td>56</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CoNSA</td>
<td>54</td>
</tr>
<tr>
<td>Riesgo et al.; 2017</td>
<td>MSIS</td>
<td>MSSE</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MSSA</td>
<td>6</td>
</tr>
</tbody>
</table>
Rudelli et al. 2021  MSIS  MRSA  11 24
Tirumala et al. 2021  ICMDC  S.aureus, Streptococcus sp.
Van Kleunen et al.; 2010 Purulent wound drainage, pain, fever, wound erythema, and elevated markers for infection
Veerman et al.; 2022  ICMDC  S. aureus  9 30

MSSA, Methicillin Sensitive Staphylococcus Aureus; MSSE, Methicillin Sensitive Staphylococcus Epidermidis; MRSE, Methicillin Resistant Staphylococcus Epidermidis; P. Acnes, Propionibacterium acnes; ICMDC, International Consensus Meeting Diagnostic Criteria; ICD-9-CM, International Classification of Diseases, Ninth Revision codes; S.Aureus, Staphylococcus Aureus; sp species; CNSA, Coagulase-negative Staphylococcus Aureus.

Table 3, Outcomes

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Antibiotic Regimen (IV)</th>
<th>Mean follow-up (mo)</th>
<th>Success rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barros et al.; 2021</td>
<td>Vancomycin, Piperacillin, Tazobactam</td>
<td>42.1 (24-66)</td>
<td>89.5</td>
</tr>
<tr>
<td>Chalmers et al.; 2021</td>
<td>NR</td>
<td>6</td>
<td>24</td>
</tr>
<tr>
<td>Chang et al.; 2017</td>
<td>Daptomycin</td>
<td>* 4</td>
<td>27</td>
</tr>
<tr>
<td>Estes et al.; 2010</td>
<td>Rifampicin combination therapy</td>
<td>6</td>
<td>3.5 (1.2-7.5)</td>
</tr>
</tbody>
</table>
### DISCUSSION

Although in recent years steps have been made to provide pathways and guidance for individuals with a PJI, there remains a lack of evidence and therefore consensus across many facets of patient care. This may partly explain the variability of success rates in revision surgery for PJI across the literature [13, 54, 55].

<table>
<thead>
<tr>
<th>Reference</th>
<th>Antibiotics</th>
<th>Follow-up (MO)</th>
<th>Success Rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fink et al; 2017</td>
<td>Vancomycin, Rifampicin</td>
<td>2</td>
<td>41.8 (24-132)</td>
</tr>
<tr>
<td>Klement et al.; 2019</td>
<td>NR</td>
<td>NR</td>
<td>* 12</td>
</tr>
<tr>
<td>Manrique et al.; 2019</td>
<td>NR</td>
<td>NR</td>
<td>70.3 (12.72-207)</td>
</tr>
<tr>
<td>Riesgo et al.; 2017</td>
<td>Vancomycin Povidone-iodine</td>
<td>* 6</td>
<td>34.9 ± 7.8 (12.9-66.4)</td>
</tr>
<tr>
<td>Rudelli et al.; 2021</td>
<td>Teicoplatin, Amikacin</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Tirumala et al.; 2021</td>
<td>Amoxicillin + Clavulanate, Amoxicillin + Clindamycin, Levofloxacin, Doxycycline, Vancomycin + Cefepine</td>
<td>* 6</td>
<td>72 (45-125)</td>
</tr>
<tr>
<td>Van Kleunen et al.; 2010</td>
<td>Cefazolin, Vancomycin</td>
<td>6</td>
<td>31 (13-57)</td>
</tr>
<tr>
<td>Veerman et al.; 2022</td>
<td>Cefazolin</td>
<td>NR</td>
<td>* 24</td>
</tr>
</tbody>
</table>

* *, minimum; IV, intravenous, MO, month
The main finding of this study is that DAIR is an overall successful treatment for early postoperative and acute hematogenous PJIs in hip and knee prostheses, confirming the current trends in the literature.

In the current review, treatment success rates ranged from 55.5% to 90%, with an average rate of 71%. This results are in line with the current literature [56] [57]. However, some of the available reviews did not include protocols using rifampin-based combination therapy, which offers benefit in PJIs caused by Staphylococcus species [58, 59], so they may not have ideally evaluated the outcome of DAIR [18].

One of the strengths of this systematic review relies on the fact that it considers only early post-operative and acute hematogenous PJIs, restricting the timing from the index procedure to the post-infection treatment, as well as conferring homogeneity to the study cohort. To the authors’ knowledge, no other reviews have analysed the role of DAIR excluding late and chronic PJIs.

In terms of prognostic factors, the timing of intervention is important. A short duration of symptoms and a small index procedure-to-DAIR timeframe are commonly considered the best prognostic factor in terms of eradication of infection, implant preservation and good functional outcomes [18, 60].

Also, to optimise the DAIR procedure, accurate patient history and preoperative workup, including the evaluation of patient comorbidities, must be performed. For example, obesity was considered a significant risk factor of PJI after the first hip and knee arthroplasty in different analyses [61, 62], but a clear correlation with failures after the DAIR procedure was not found [45, 63, 64].

The duration of antibiotic therapy and the specific pathogen responsible for the prosthetic joint infection (PJI) are crucial considerations in the context of the DAIR procedure. Typically, intravenous antibiotics for a period of 2 to 6 weeks following a DAIR procedure is administered [29, 58, 65-68]. However, according to recent guidelines by the Infectious Diseases Society of America (IDSA), a duration of 4 to 6 weeks of intravenous therapy is also recommended for PJIs caused by organisms other than staphylococci or in cases where Rifampin combination therapy cannot be utilized [69]. Furthermore, several studies have provided support for the implementation of long-term antibiotic suppression therapy for a minimum of 6 months after the DAIR procedure to enhance treatment outcomes [64, 70, 71].

The most common bacteria responsible for most PJIs are Staphylococcus aureus, Propionibacterium acnes, Staphylococcus epidermidis and coagulase-negative Staphylococcus [72], as confirmed by this review and by the study of Motififard and colleagues [73]. In this context, given the frequency with which staphylococci cause early-onset and late hematogenous PJIs, there has been significant work to try to define the optimal management of staphylococcal PJI treated with a DAIR procedure [18]. The combination of rifampicin plus levofloxacin highlights good results for acute
Staphylococcal infections [71, 74]. However, the necessary duration of therapy in some patients with PJI may need to be very long to continue the benefit [22].

When considering alternatives to DAIR, a 2-stage exchange technique is typically regarded as the "gold standard" for the management of late and chronic PJI. The success rate of hip arthroplasty surgery is almost 90%, according to long-term statistics. [75]. For knee arthroplasty infections treated with a two-stage arthroplasty exchange, the reported success rate ranges from 72% to 95% [33, 76-81]. However, it's important to note that this approach is typically reserved for patients with prolonged symptom duration and the presence of mature biofilms. [23], thus being more applicable to chronic PJIs.

In contrast to the two-stage revision protocol, an alternative approach known as the one-stage revision has been suggested, offering several advantages. These benefits include shorter hospital stays, avoidance of a second procedure along with its associated complications, enhanced post-operative mobility and pain management, as well as cost reduction [82]. However, it is important to note that the one-stage revision protocol is typically recommended for patients who have relatively intact or minimally compromised bone and soft tissue. Additionally, it is generally suitable for individuals who have not undergone previous revision surgeries or have not received treatment with biofilm-active antibiotics. In such cases, the one-stage exchange method is considered the preferred treatment option. [23].

In a meta-analysis encompassing 375 patients who underwent one-stage arthroplasty exchanges, the findings revealed a reinfection rate of 13%, indicating an 87% freedom from reinfection [83].

However, it is crucial to remember the primary objective behind arthroplasty, which is to alleviate pain and restore full functionality. The implant's fixation is designed to be dependable and long-lasting, minimizing the risks of fractures and damage to the surrounding soft tissues. Considering the dual objective of treating the infection while preserving optimal function, it is important to contemplate the option of retaining the implant. By doing so, the aim remains to achieve the best possible outcome in terms of both infection management and functional recovery [84].

Additionally, in contrast to DAIR, one-stage and two stage protocols appear to bear the disadvantages of increased costs, higher skills requirements and worse postoperative joint functions [14, 85-88] and they are more indicated in contexts of late and chronic infections, potentially after failed DAIR [89].

**Strengths**

The strengths of this study lie in the consistency of the cohort. Only early postoperative and acute hematogenous infections were included, given the fact that late and chronic PJI are associated with different outcomes and treatment strategies.
In addition, to improve the quality of the current review, all the included articles were subjectively evaluated by the Cochrane risk of Bias tools [40] and by the critical appraisal tool by the Joanna Briggs Institute [39] in order to determine their potential risk of bias: no articles were judged as having a critical risk of bias.

Furthermore, multicentre studies were excluded from this systematic review, in order to avoid potential bias due to treatments carried out in different settings and protocols.

**Limitations**

This study has some limitations. In some studies, data on the rate of re-infection, revision rate, microorganisms involved in infection, the protocol of antibiotics therapy are not reported or adequately explicated. In addition, the surgical procedure, duration, and type of antibiotics therapy are not consistent throughout the cohort, both due to the lack of a standardized protocol and to the different underlying pathogens causing the PJI, yielding severe bias in the reported outcomes.

At the same time, the higher rates of success reported in the current study may have occurred due to the small sample size of some included studies [43] and, additionally, the present results are not stratified between hips and knee infections.

The diagnostic criteria to define a PJI and the antibiotic regimen applied in each study are also not constant throughout the whole cohort and the inclusion of revision arthroplasties as index procedures may induce bias towards more unfavorable results. Also, another limitation of this study lies in the choice to exclude multi center studies, which, on one hand, aimed at avoiding diagnostic and treatment factors biased solely on the location, while on the other, majorly decreased the cohort of this study.

Additionally, the heterogeneous length of follow-up may generate some inconsistency within the outcomes, given also the fact that one study presents a mean follow-up of less than 12 months [48]. Furthermore, studies involving procedures from the late 90’ to the early 2000 may involve a greater risk of treatment failure due to the lack of update in the treatment that was performed at the time.

Finally, as observational studies constituted the main source for the analysis, selection bias and confounding due to diverse expectations in RTSA patients should be taken into consideration.

**Conclusions**

In conclusion, even though DAIR procedure is quite limited, it is still considered an effective option for patients developing an early post-operative or acute hematogenous PJI. However, there is a lack of studies, in particular of
RCTs, comparing DAIR with one-stage and two-stage revision protocols in the setting of early PJI, reflecting the necessity to conduct further high-quality studies to face the burden of early PJI.

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10.1007/s11999-014-3721-8


Figure 1. The PRISMA flowchart of literature search

Figure 2. The risk of bias assessments for NRCTs studies

Figure 3. The risk of bias assessments for Case Series studies

Table 1. Population and Demographics

Table 2. Infection characteristics

Table 3. Outcomes
Records identified from: Databases (n = 624) Registers (n = 71)

Records removed before screening:
- Duplicate records removed (n = 102)
- Records marked as ineligible by automation tools (n = 21)
- Records removed for other reasons (n = 54)

Records screened (n = 518)

Records excluded (n = 405):
- Treatment different from DAIR (n = 302)
- Not English (n = 16)
- Not related to knee/hip prosthesis (n = 26)

Reports sought for retrieval (n = 113)

Reports not retrieved (n = 0)

Reports assessed for eligibility (n = 113)

Reports excluded (n = 101):
- Systematic reviews (n = 14)
- Multicentre Studies (n = 14)
- Chronic/late PJs (n = 45)
- No PJI definition (n = 17)
- No Full-text available (n = 11)

Studies included in review (n = 12)

Reports of included studies (n = 12)
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<th>D2</th>
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Domains:
- D1: Bias due to confounding.
- D2: Bias due to selection of participants.
- D3: Bias in classification of interventions.
- D4: Bias due to deviations from intended interventions.
- D5: Bias due to missing data.
- D6: Bias in measurement of outcomes.
- D7: Bias in selection of the reported result.

Judgement:
- Moderate
- Low
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- **Y** Yes
- **N** No
- **U** Unclear

Journal Pre-proof
Declaration of interests

☐ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☒ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Umile Giuseppe Longo reports a relationship with Journal of ISAKOS that includes: board membership.