

Impact of prior failed irrigation and debridement on outcomes of subsequent two-stage revision arthroplasty: a systematic review and meta-analysis

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Abstract. – OBJECTIVE: This study aimed at examining if prior failed debridement, antibiotics, and implant retention (DAIR) for prosthetic joint infection have an impact on the success of subsequent two-stage revision arthroplasty (2SRA).

MATERIALS AND METHODS: Search was conducted on PubMed, Embase, and Google Scholar up to 14th April 2022 for studies comparing 2SRA with and without a history of DAIR.

RESULTS: Six retrospective studies were included. The success of 2SRA was defined as either absence of additional surgical intervention for infection or absence of antibiotic suppression or both. We noted no statistically significant difference in the odds of success between failed DAIR and no DAIR group, albeit with an inclination of reduced success with prior failed DAIR (OR 0.63 95% CI 0.33, 1.19 $I^2=66%$ $p=0.16$). Five studies reported adjusted outcomes. The meta-analysis demonstrated no statistically significant difference in the odds of success between failed DAIR and no DAIR groups (OR 0.57 95% CI 0.26, 1.26 $I^2=66%$ $p=0.17$). During sensitivity analysis, the removal of a single study changed the effect size indicating significantly lower success rates in failed DAIR group.

CONCLUSIONS: Our results indicate that patients undergoing 2SRA after failed DAIR may have a non-significant tendency of lower success rates as compared to patients directly undergoing 2SRA. However, current evidence is scarce and fraught with several limitations and there is a need for further research to delineate the impact of failed DAIR on the success of 2SRA.

Key Words:

Total joint arthroplasty, Knee, Hip, Infection.

Introduction

Total joint arthroplasty (TJA) is a routine elective surgical procedure performed worldwide. The number of primary and revision procedures has increased by a dramatic rate in the past decade¹. Indeed, a recent study² based on data from

the USA indicates that the number of TJA procedures is expected to increase by 85% in 2030.

Prosthetic joint infection (PJI) is a crippling complication noted in 1-2% of individuals undergoing TJA. It also accounts for approximately 15% of revision surgeries in such patients³. Despite a heightened interest in the prevention and treatment of PJI amongst the orthopedic community, there has been no reduction in the rate of this devastating complication for knee and hip joints^{4,5}. Recent models suggest that the rate of PJI will grow by 170% for knee and 176% for hip joint in the coming years². PJI and its subsequent management not only has a significant impact on the clinical outcomes and quality of life of the patient, but it confers a significant financial burden on the healthcare system as well^{4,5}. Since medical research is continuously striving towards optimum and cost-effective disease management, it is imperative to understand the success of different treatment options for the management of PJI.

Debridement, antibiotics, and implant retention (DAIR) is generally the preferred treatment option for PJI diagnosed in an early stage (within 4 weeks). The procedure involves open arthrotomy followed by irrigation and thorough debridement of the joint for all infected matter⁶. As implants are retained in this procedure, DAIR is low-cost, less invasive, and associated with reduced morbidity as compared to two-stage revision arthroplasty⁷. The success of DAIR has improved over the years with recent data suggesting favorable outcomes in >70% of patients with DAIR⁸. However, in case of treatment failure, two-stage revision arthroplasty (2SRA) remains the only definitive treatment option for managing PJI⁶.

Since DAIR is not 100% successful, a large number of patients undergo 2SRA with a prior history of DAIR and it is currently unclear if failed DAIR impacts the success of subsequent revision arthroplasty. In the past few years, researchers have tried to understand the role of prior failed DAIR on

outcomes of 2SRA but with conflicting results⁹⁻¹¹. While one study¹⁰ suggests that prior DAIR has no impact on overall success rates of 2SRA, other cautions surgeons and patients that failed DAIR would compromise the results of subsequent 2SRA⁹. Given such contrasting evidence, there is a need to systematically analyze data to present the best possible evidence to make informed clinical decisions. Thus, this review was planned to systematically search literature and pool data from individual studies to assess the impact of prior failed DAIR on outcomes of 2SRA.

Materials and Methods

Research Question

The research question of the study was: “Does prior failed DAIR impact the success rates of subsequent 2SRA?”. Reporting methodology of the PRISMA statement (Preferred Reporting Items for Systematic Reviews and Meta-analyses) was followed¹². The review was registered on PROSPERO (No. CRD42022325129).

Literature Search

Studies for the review were searched PubMed, Embase, and Google Scholar by two independent reviewers up to 14th April 2022. The researchers used the following term in different combinations: “arthroplasty”, “joint replacement”, “irrigation and debridement”, “debridement, antibiotics, and implant retention”, “prosthetic joint infection”, and “two-stage revision”. Further details of the search strategy can be found in **Supplementary Table I**. The search strategy was common for all databases. Due to the significantly high results in Google Scholar, only the initial 100 results were examined. This was considered to be the gray literature search while the remaining were primary databases. Duplicate search results were excluded, and the remaining unique studies were reviewed by titles/abstracts. Studies close to the review question were segregated and full text downloaded. The two reviewers independently read the articles for eventual inclusion. Any disagreements in selection were resolved by common consent. We further reviewed the bibliography of included studies for any other references.

Eligibility Criteria

The PICOS (Population, Intervention, Comparison, Outcome, Study type) inclusion criteria were: 1) all prospective/retrospective cohort and cross-sectional studies conducted on patients

undergoing 2-stage revision knee or hip joint arthroplasty for PJI (Population); 2) studies were to have an Intervention group with a history of failed DAIR before 2SRA (failed DAIR group) and a Comparative group of individuals directly undergoing 2SRA (No DAIR group); 3) studies were to assess the success of 2SRA (Outcomes). Criteria for success was not predefined and definition from the included studies were acceptable.

Exclusion criteria was: 1) studies not on patients undergoing revision arthroplasty; 2) studies failing to report required outcomes; 3) non-English language studies; 5) those with duplicate data. For duplicate studies, the one with the largest patient population was eligible.

Data Extraction and Quality Assessment

Two authors independently extracted data of the first author, study type, study location, joint studied, sample size, mean age, gender, number of diabetics, Carlson’s comorbidity index, the definition of success, type of follow-up, and study outcomes.

Risk of bias tool used for the review was the Newcastle-Ottawa scale (NOS)¹³. This was done independently by two researchers. NOS awarded stars for selection of study population, comparability, and outcomes, with the highest score of nine.

Statistical Analysis

RevMan, version 5.3 (Review Manager Web, The Cochrane collaboration, Copenhagen, Denmark) was the software selected for the analysis. We used a random-effects model for all outcomes. We pooled crude success rates using odds ratios (OR) with 95% confidence intervals (CI). We also used the multivariable-adjusted data on success rates for the meta-analysis. A sensitivity analysis was conducted for the primary outcome. A subgroup was performed based on the definition of success. Heterogeneity was judged by the I^2 statistic where 25-50% was low, 50-75% was medium, and >75% denoted substantial heterogeneity. We did not use funnel plots to assess publication bias as there were less than 10 studies in the analysis. $p \leq 0.05$ was considered statistically significant.

Results

1,373 unique articles were retrieved in the search (Figure 1). Of these, 12 studies were analyzed by the full texts. Finally, 6 articles met the inclusion criteria^{9-11,14-16}.

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Table I. Details of included studies.

Study	Location	Joint studied	Groups	Sample size	Mean Age (years)	Male gender (%)	BMI kg/m ²	DM (%)	CCI	Definition of success	Follow-up (years)	NOS score
Kavolus et al ⁹	USA	Hip	Failed DAIR No DAIR	49 65	57.6±13.8 63.2±13.2	46.9 53.8	NR	NR	NR	No additional surgery required due to infection after reimplantation	2	8
Lizaur-Utrilla et al ¹⁶	Spain	Knee	Failed DAIR No DAIR	43 49	73.3±6.2 72.5±7.5	34.9 22.4	32.6±7.4 31.7±7.1	37.2 30.6	2.7±1.6 2.2±1.2	No additional surgery required due to infection or antibiotic suppression after reimplantation	3	7
Kim et al ¹⁵	New Zealand	Knee	Failed DAIR No DAIR	75 63	64.5±9.6 67.3±10.3	61.3 58.7	34.2±9.3 30.8±7.3	24 27	3±1.9 3.3±1.9	Retention of components without antibiotics	2	8
Rajgopal et al ¹⁴	India	Knee	Failed DAIR No DAIR	88 96	69.5±NR 68.2±NR	48.9 36.5	28.8±NR 27.4±NR	34.1 20.8	NR	No additional surgery required due to infection or antibiotic suppression after reimplantation	2	8
Nodzo et al ¹¹	USA	Knee	Failed DAIR No DAIR	45 132	66.8±11.4 65.8±9.8	53.3 62.9	30.6±7.5 30.8±6.5	NR	3.1±1.9 3.5±2	No additional surgery required due to infection after reimplantation	4	8
Brimmo et al ¹⁰	USA	Knee	Failed DAIR No DAIR	57 693	68.1±10.4 66±11.1	58 47	NR	NR	NR	No additional surgery required due to infection after reimplantation	2	8

BMI, Body mass index; CCI, Carlson's comorbidity index; DAIR, debridement antibiotics and implant retention; DM, Diabetes Mellitus; NOS, Newcastle Ottawa Scale; NR, not reported.

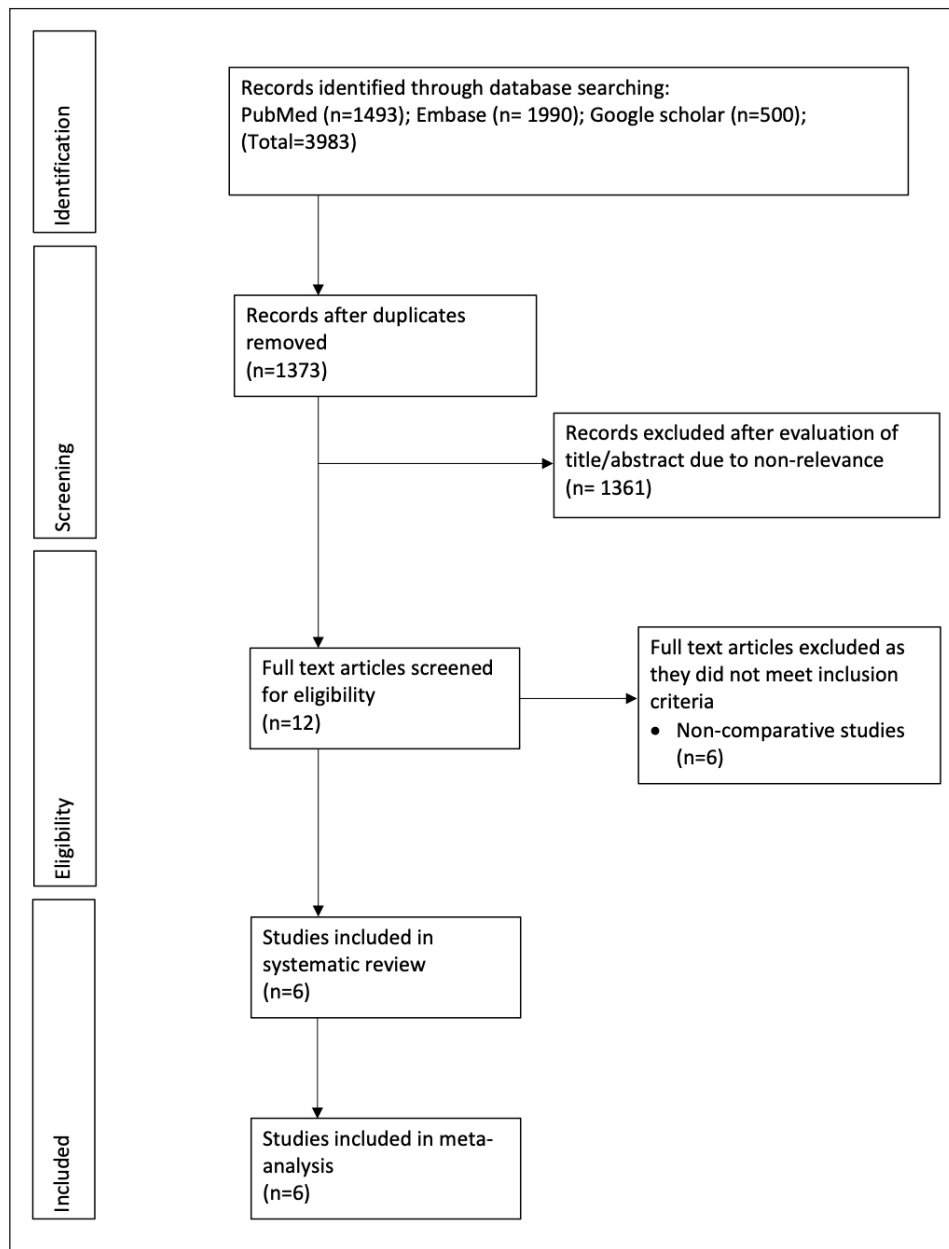


Figure 1. Study flow chart.

Three of the studies were conducted in the USA⁹⁻¹¹, while one each was conducted in India¹⁴, New Zealand¹⁵, and Spain¹⁶ (Table I). All were retrospective cohort studies. Only one study⁹ was conducted on patients undergoing hip arthroplasty, while the remaining were on knee joints. The sample size in the failed DAIR group varied from 43 to 75 patients, while those in the no DAIR group ranged from 49 to 693. The mean age of study population was above 55 years in all articles. There

were some variations in the definition of success in the included studies. It was defined as either absence of additional surgical intervention for infection or absence of antibiotic suppression or both. Antibiotic spacers were used by all studies after the first stage of revision arthroplasty and with the variable postoperative antibiotic protocol. The minimum follow-up amongst studies was 2 years from 2SRA. The NOS score was high for the included studies and ranged between 7-8.

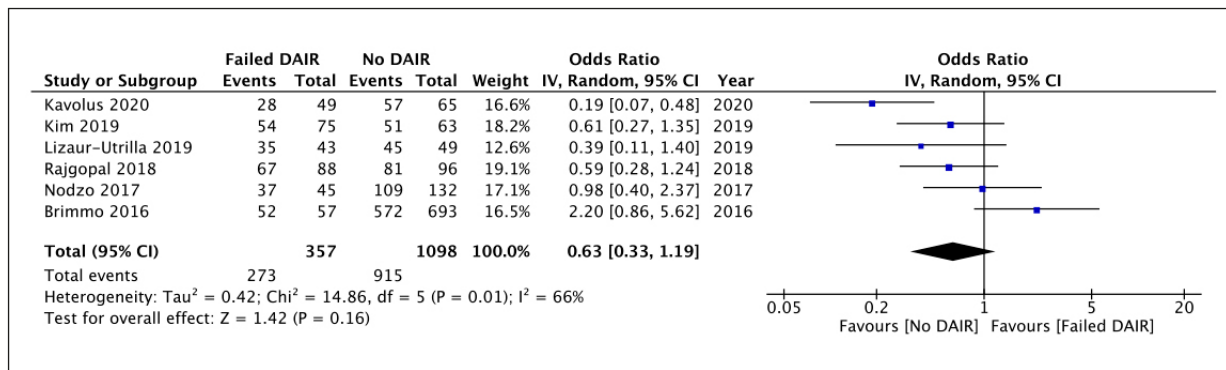


Figure 2. Meta-analysis of crude success rates between failed DAIR and no DAIR groups.

On combined analysis of all 6 studies, we noted no statistically significant difference in the odds of success between failed DAIR and no DAIR group, albeit with an inclination of reduced success with prior failed DAIR (OR 0.63 95% CI 0.33, 1.19 $I^2=66\%$ $p=0.16$) (Figure 2). On sensitivity analysis, the exclusion of the study of Brimmo et al¹⁰ changed the significance of the results with significantly reduced odds of success in the failed DAIR group (OR 0.50 95% CI 0.29, 0.85 $I^2=43\%$

$p=0.01$). Details of subgroup analysis depending upon the definition of success are presented in Table II. The power of the analysis was significantly reduced due to the fewer studies in each subgroup. Adjusted outcomes were reported by five of the six included studies. The meta-analysis demonstrated no statistically significant difference in the odds of success between failed DAIR and no DAIR groups DAIR (OR 0.57 95% CI 0.26, 1.26 $I^2=66\%$ $p=0.17$) (Figure 3). However,

Table II. Subgroup analysis of success of 2-stage revision joint arthroplasty based on definition of success.

Definition of success	Number of studies	Number of participants		Effect Size (Odds Ratios)
		Failed DAIR	No DAIR	
Crude success rates				
No additional surgery required due to infection after reimplantation	3	151	890	0.74 95% CI: 0.18, 2.99 $I^2=86\%$ $p=0.67$
No additional surgery required due to infection or antibiotic suppression after reimplantation	2	131	145	0.53 95% CI: 0.28, 1.01 $I^2=0\%$ $p=0.05$
Retention of components without antibiotics	1	75	63	0.61 95% CI: 0.27, 1.35 $I^2=-$ $p=0.22$
Adjusted success rates				
No additional surgery required due to infection after reimplantation	3	151	890	0.68 95% CI: 0.18, 2.58 $I^2=81\%$ $p=0.57$
No additional surgery required due to infection or antibiotic suppression after reimplantation	1	88	96	0.52 95% CI: 0.27, 1.00 $I^2=-$ $p=0.05$
Retention of components without antibiotics	1	75	63	0.25 95% CI: 0.03, 1.80 $I^2=-$ $p=0.17$

DAIR, debridement, antibiotics, and implant retention.

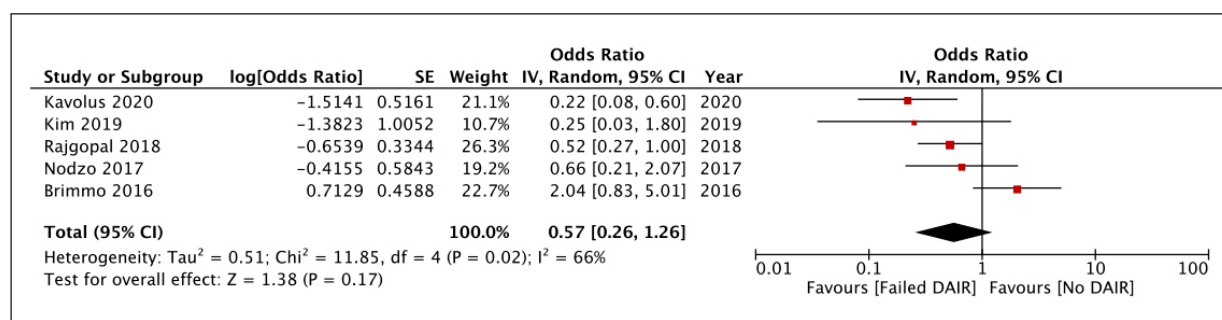


Figure 3. Meta-analysis of adjusted success rates between failed DAIR and no DAIR groups.

er, on sensitivity analysis, exclusion of the study of Brimmo et al¹⁰ again changed the significance of the results with significantly reduced odds of success in the failed DAIR group (OR 0.43 95% CI 0.26, 0.69 $I^2=0\%$ $p=0.0005$). Results subgroup analysis based on the definition of success is presented in Table II.

Discussion

2SRA is deemed to be the gold standard treatment for PJI. However, the time of infection, patient factors, type of microorganism, and availability of surgical skill are important considerations in choosing the most appropriate treatment plan. In this context, DAIR may be preferred owing to the lower morbidity and cost of the procedure¹⁷. However, does prior DAIR impact success rates of subsequent 2SRA? Our results indicate that although there is a tendency for higher failure rates of 2SRA in patients with failed DAIR, the difference is not statistically significant.

In our review, which included a pooled sample of 357 patients with failed DAIR, the success rates of 2SRA were noted to be 76.47%. On the contrary, the success rate in 1,098 patients directly undergoing 2SRA was 83.33%. These figures are more or less parallel to those reported in the literature. Single-arm studies like that of Sherrell et al⁷ have reported success rates of only 66% in a cohort of 84 patients undergoing 2SRA with prior failed DAIR. They defined success as no additional surgical intervention for infection and attributed the lower success rates to the additional time to recovery post DAIR. In another study, Gardner et al¹⁸ reviewed 44 cases of knee arthroplasty undergoing DAIR of which 25 patients (57%) failed and 19 patients underwent 2SRA. On final follow-up, only 11 (58%) of these revisions were deemed to

be successful. Cochran et al¹⁹, in a retrospective study of the Medicare database, evaluated success rates of 2,150 knee arthroplasty patients who underwent prior DAIR with liner exchange. After a follow-up of one year, 74.3% of cases were successful, but the success rate dropped to 60% after 6 years. In comparison, a recent study by Corona et al²⁰ has demonstrated a success rate of 80.6% in PJI patients undergoing 2SRA.

On comparing data with patients directly undergoing 2SRA, we noted that despite the lower success rates of failed DAIR group the difference was not statistically significant. On close analysis of the forest plot, it can be seen that a statistically significant difference in success rates between the two groups was noted only by Kavolus et al⁹, while the remaining studies noted no such difference. Also, on sensitivity analysis, exclusion of the study of Brimmo et al¹⁰ changed the significance of the results and indicated 50% lower odds of success in patients with prior DAIR on a pooled analysis of the remaining studies. One probable reason for this variation could be attributed to the eligibility criteria of Brimmo et al¹⁰. The authors excluded all patients who had DAIR two years before 2SRA and with a follow-up longer than four years. No such restriction was placed by the remaining studies.

The tendency of lower success rates of 2SRA with prior DAIR is difficult to explain as DAIR by itself is not deleterious. Pathophysiologically, there seems to be no harm in performing DAIR in acutely infected joints with appropriate indication. Kavolus et al⁹ have hypothesized that the time gap between initial DAIR and subsequent explantation may allow maturation of biofilm colonies, which enables the microorganisms to become more entrenched in the periprosthetic bone. Such deep-rooted infection may be difficult to eradicate with subsequent 2SRA leading to inferior outcomes. Secondly, the lower success with

failed DAIR may also be attributed to the baseline characteristics of these patients. Furthermore, due to the retrospective nature of the studies, there are obvious concerns regarding selection bias. Probably, patients without comorbidities who had PJI due to antibiotic-sensitive bacteria and received timely DAIR with successful outcomes were excluded from the analysis. Only those patients with comorbidities and resistant bacteria or those who did not receive appropriate DAIR may have been included in the failed DAIR group. Indeed, the literature suggests that the success of DAIR depends on several factors and is highly variable. Kunutsor et al²¹, in a meta-analysis of 99 observational studies, have reported the success of DAIR to be 61.4% ranging from a low of 11.1% to 100%. Such disparity was attributed to several differences in patient characteristics. Research has shown that polymicrobial infections and those caused by resistant organisms like *Staphylococcus Aureus* decrease the success rates of DAIR^{22,23}. A recent study has suggested that streptococcal PJI are also associated with worse outcomes after DAIR and *Streptococcus agalactiae* infection is an independent predictor of failure²⁴. In one study, Rajgopal et al¹⁴ noted higher failure rates in the failed DAIR group; however, on the exclusion of PJIs caused by resistant organisms, they found no difference in the success of 2SRA between failed and no DAIR groups. In addition to the type of microorganism, variables like patients' age, gender, comorbidities, symptoms duration, type and duration of antibiotic therapy can also impact outcomes of DAIR²⁵⁻²⁸.

In this context, it becomes important to analyze multivariable-adjusted success rates to provide a better delineation of outcomes in the two groups. In our second meta-analysis, we again noted no significant impact of prior DAIR on success rates of 2SRA on pooling adjusted outcomes from included studies. Also, as seen earlier, once the study of Brimmo et al¹⁰ was excluded, the results were again significantly in favor of direct 2SRA with prior DAIR reducing the success rates by 57%. However, owing to the small number of studies included in the review, the results may not allow for strong conclusions and there is a need for further research on this important subject.

Another important aspect to consider while interpreting the results is the variability in the definition of success for treatments of PJI. Tan et al²⁹, in a study of 703 PJI patients undergoing 2SRA have reported variable success rates ranging from 54.2% to 88.9% just based on different definitions

used. A standardized definition of success of surgical treatment of PJI has not evolved yet due to several factors like lack of reimplantation in some patients due to medical issues and difficulty in defining an adequate follow-up time²⁹. However, there is an urgent need to devise one single definition of success to ease comparison between different surgical procedures carried out at different centers worldwide for PJI. In this review, we noted three different definitions of success amongst the included studies. While we attempted to analyze the difference in outcomes using a subgroup analysis, the number of included studies in each subgroup was too scarce for definitive conclusions. All six studies were pooled in one analysis based on the optimism that the same definition was used in the failed DAIR and no DAIR groups in each study.

Limitations

The limitations of this review are quite a few. Other than the difference in definitions of success there were other variations between the included studies. One study was carried out on the hip joint while others were on the knee joint. The baseline patient characteristics, antibiotic regimen, microbiology of infection were variable in the included studies. Secondly, only six studies were available for analysis and all of them were retrospective in nature with a high tendency of selection bias. Thirdly, since the studies were conducted at variable periods and different centers worldwide there could have been differences in the treatment protocol along with variations in the surgical methodology. All these factors could have skewed the overall results. Fourthly, the period between DAIR and 2SRA was not reported by the included studies. At this point, it is unclear if this factor has an impact on treatment success. Lastly, the follow-up duration was also not congruent in the included studies.

Conclusions

Nevertheless, this review is the first to assess the role of prior DAIR on outcomes of subsequent 2SRA. Our review shows that patients undergoing 2SRA after failed DAIR may have a non-significant tendency of lower success rates as compared to patients directly undergoing 2SRA. However, current evidence is scarce and fraught with several limitations and there is a need for further research to delineate the impact of failed DAIR on the success of 2SRA.

Ethics Approval and Informed Consent

Not applicable.

Acknowledgments

Not applicable.

Data Availability

All data generated or analysed during this study are included in this published article.

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Authors' Contributions

LT and KY conceived and designed the analysis; Jie Y, Jian Y and ZY collected the data and performed the analysis; LT and KY wrote the paper.

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