



Review article

One- or two-stage exchange for periprosthetic shoulder infection: Systematic review and meta-analysis[☆]



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ABSTRACT

Introduction: One-stage exchange is the gold-standard for management of periprosthetic shoulder infection. The present review compares efficacy between 1- and 2-stage exchange in this indication.

Material and methods: We performed a systematic literature review and meta-analysis following the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses" (PRISMA) criteria. The literature search used the Medline, Embase and Central data-bases. The studies included assessed 1- and 2-stage exchange in periprosthetic shoulder infection. The main outcome was reinfection rate, and the secondary outcome postoperative complications rate.

Results: Twenty-one studies, for 501 patients, were included: 5 assessing 1-stage exchange, 11 2-stage, and 5 both. Mean follow-up was 4.3 years (range, 2–6.1 years). Mean reinfection rates ranged between 0 and 50% in 1-stage exchange and between 0 and 36.8% in 2-stage exchange. The combined rate was 7% (95% CI, 3.8–12.5%) in 1-stage and 21.3% (95% CI, 16–27.9%) in 2-stage exchange. Mean complications rates ranged between 0 and 50% in 1-stage exchange and between 5.7% and 73% in 2-stage exchange. The combined rate was 17% (95% CI, 11.9–23.9%) in 1-stage and 32.8% (95% CI, 25.8–40.6%) in 2-stage exchange.

Discussion: To our knowledge, the present meta-analysis is the first to assess results in 1- and 2-stage exchange for chronic periprosthetic shoulder infection.

Conclusion: One-stage exchange seemed to provide better results, with less reinfection and fewer complications than 2-stage exchange.

Level of evidence: I, meta-analysis.

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1. Introduction

Prosthetic infection is a severe complication in joint replacement surgery. The increasing number of shoulder replacements inevitably leads to an increase in periprosthetic shoulder infection, directly impacting morbidity and health-care costs. Infection is the main cause of revision surgery in the first 2 years following shoulder replacement [1].

The rate of postoperative periprosthetic shoulder infection is 0.98%, and higher in case of revision surgery and arthroplasty for trauma. The main bacterium involved is *Cutibacterium acnes* [2–10].

Treatment strategies are inspired by those in total knee or hip prosthetic infection, and comprise: long-course suppressive antibiotic therapy [11,12], synovectomy without implant exchange [13–16], resection arthroplasty [13,17–22], arthrodesis [23], and 1- or 2-stage implant exchange [24–29]. Isolated suppressive antibiotic therapy or synovectomy show high failure rates in chronic infection. Resection arthroplasty has better results in terms of recurrence but poorer functional results [13,17,30].

Two-stage exchange is often considered the gold-standard, but involves multiple surgery, greater number and duration of hospital stays, and functional impairment [31,32].

One-stage exchange consists in extensive synovectomy associated to removal of all implants and any cement, with reimplantation in the same step. This requires a single admission and single anesthesia, with lower cost and better functional results [33]. Superiority over 2-stage exchange, however, is unproven. To our knowledge, no randomized controlled trials have compared 1- versus 2-stage exchange in periprosthetic shoulder infection.

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Several observational studies compared reinfection rates, involving different bacteria and/or recurrence, in 1- versus 2-stage exchange, with conflicting results.

We performed what is, to our knowledge, the first systematic review and meta-analysis comparing reinfection after 1- and 2-stage exchange in periprosthetic shoulder infection.

The objective was to compare efficacy between 1- and 2-stage exchange to manage chronic periprosthetic shoulder infection. The main study hypothesis was that reinfection and complications rates are the same on both strategies.

2. Materiel and methods

The systematic literature review and meta-analysis were conducted according to “Preferred Reporting Items for Systematic Reviews and Meta-Analyses” (PRISMA) guidelines [34].

2.1. Search strategy

The literature search was conducted in 3 data-bases: MEDLINE via PubMed, the Cochrane Central Register of Controlled Trials (CENTRAL 2018, number 10), and EMBASE. Search-terms concerned surgery (“shoulder”, “arthroplasty”, “prosthesis”, “one-stage”, “two-stage”), and complications (“sepsis”, “infection”). A specific search algorithm was drawn up for each data-base; the reference lists of retrieved articles and previous systematic reviews were examined. Ongoing trials were identified on the ClinicalTrials.gov website. The search was closed on October 15 2018.

2.2. Selection of studies

Studies were included that assessed results in 1- or 2-stage exchange for periprosthetic shoulder infection, in whatever language. No systematic reviews or expert opinions were included. Relevant studies were selected by 2 authors (FA and BM), working independently and resolving differences by consensus. Excluded studies and reasons for exclusion were listed.

2.3. Study quality assessment

Study quality was assessed on “Methodological Index for Non-Randomized Studies” (MINORS) score [35], taking account of:

stated aim, consecutive inclusion, prospective data collection, unbiased evaluation of endpoint, follow-up appropriate to endpoint (2 years for sepsis), <5% loss to follow-up, prospective calculation of study size, adequate control group, baseline equivalence of groups, and adequate statistical analysis.

Two authors (FA and BM) performed this assessment, with systematic discussion of divergences.

2.4. Data extraction

Data were extracted on a standardized form by 2 authors (FA and BM), working independently. Data comprised: publication date, journal, country, patient demographics (age, gender), implant type, follow-up after revision, type of procedure (1-stage, 2-stage), microbiology (germs) and clinical data (reinfection, complications other than reinfection, functional score), and sample size.

The main endpoint was reinfection at 2 years post-revision (number of reinfected patients as a proportion of all patients). The secondary endpoint was complications (number of complications as a proportion of all patients) rate.

2.5. Statistical analysis

Data were analyzed on R software (R Core Team 2014). Reinfection and complications rates were assessed with 95% confidence intervals (95% CI). Statistical heterogeneity was assessed on the I^2 statistic as: 25–49%, low heterogeneity; 50–74%, moderate heterogeneity; >75%, high heterogeneity. Relative risk with 95% CI was computed using a fixed effects model when heterogeneity was low and a random effects model otherwise. Funnel plots were constructed to assess publication bias.

3. Results

3.1. Study identification and selection

The initial search identified 1,118 eligible studies. After elimination of duplicates, the predefined inclusion/exclusion criteria were applied, selecting 21 studies, for 501 patients and 503 shoulders. [7,13,29,31,36–52] (Fig. 1: flowchart).

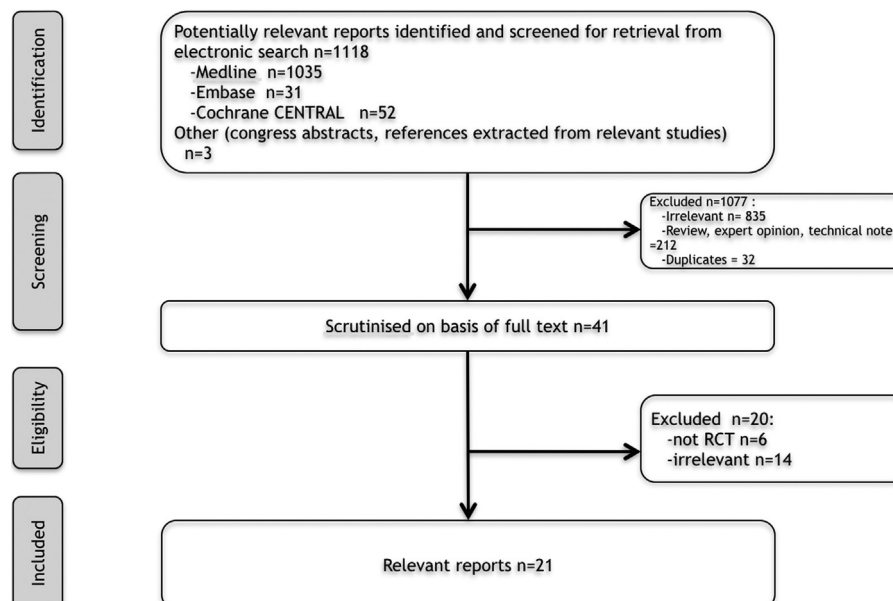


Fig. 1. Flow chart.

3.2. Study characteristics and quality

There were no randomized controlled or comparative studies. Ten studies assessed 1-stage ($n=170$) [13,29,38,40,42–44,46,50,51] and 16 2-stage exchange ($n=228$) [7,13,29,31,36,37,39–41,44,45,47–49,51,52]. Five reported results for both, and their data were split for analysis.

Studies were published between 2001 and 2018. Mean follow-up was 4.3 years (range, 2–6.1 years) (Tables 1 and 2).

Mean MINORS score was 12.2 (range, 9–14) (Table 3).

3.3. Characterization of infection

Five studies reported type of infection in 1-stage exchange and 11 in 2-stage exchange, all following Sperling's classification: 5 acute infections (<3 months postoperatively), 25 subacute (3 months to 1 year) and 29 late (>1 year) in 1-stage and respectively 12, 40 and 101 in 2-stage exchange [29].

3.4. Microbiology

Germs were reported in 8 of the 9 1-stage and 13 of the 16 2-stage studies. They comprised *C. acnes* in at least 71 cases of the 168 infections (42%) in the 1-stage group, and 32 of the 228 (14%) in the 2-stage group. Prevalences were, however, not precisely reported in all studies. Other isolates comprised coagulase-negative *Staphylococci* and *Staphylococcus aureus*.

3.5. Reinfection rates

Mean reinfection rates at a minimum 2 years' follow-up ranged between 0 and 50% in 1-stage and between 0 and 36.8% in 2-stage exchange.

Overall reinfection rate in 1-stage exchange was 7% (95% CI, 3.8–12.5%) (Fig. 2). I^2 was 0%: i.e., absence of heterogeneity. The funnel graph was symmetrical: i.e., absence of publication bias (Fig. 3).

In 2-stage exchange, the rate was 21.3% (95% CI, 16–27.9%) (Fig. 4). I^2 was 18.9%: i.e., low heterogeneity. The funnel graph was symmetrical: i.e., absence of publication bias (Fig. 5).

3.6. Complications rates

Mean complications rates were reported in 9 studies for 1-stage [13,29,38,40,42,43,46,50,51] and 13 for 2-stage exchange [7,13,31,37,39–41,44,47–49,51,52], and ranged between 0 and 50% and between 5.7% and 73.7%, respectively.

Complications comprised unexpected intra- and post-operative events requiring specific treatment. Eighty-four revision procedures were reported, for all causes beside reinfection. The most frequent complication was implant dislocation requiring conversion to reverse prosthesis or insert exchange. Others comprised hematoma, acromial non-union and periprosthetic fracture. Overall there were 85 revisions. It was not possible to analyze complications as specific to one or other strategy.

The combined complications rate in 1-stage exchange was 17% (95% CI, 11.9–23.9%) (Fig. 6). I^2 was 0%. The funnel graph was symmetrical (Fig. 7).

In 2-stage exchange, the rate was 32.8% (95% CI, 25.8–40.6%) (Fig. 8). I^2 was 65.8%. The funnel graph was asymmetrical: i.e., greater publication bias in small-sample studies (Fig. 9).

4. Discussion

Periprosthetic shoulder infection is a rare but severe complication. The present review reports results for 1- and 2-stage exchange. One-stage exchange led to less reinfection and fewer complications.

Given the expected rise in periprosthetic shoulder infection with increasing numbers of shoulder replacements, well-defined treatment strategies are needed.

To date, diagnostic and treatment strategies for periprosthetic shoulder infection are based on those for total knee and hip prostheses. The present results agree with previous reports on periprosthetic knee and hip infection. Two-stage exchange has been the reference attitude in periprosthetic infection [9,29,53–55]. However, lower-limb studies show that 1-stage exchange has a role to play, for medical, functional and economic reasons [32,56]. The present results, in favor of 1-stage exchange, confirm this trend.

The main complication was dislocation requiring surgical revision for polyethylene insert exchange. Other complications comprised hematoma and fracture. Given the small number of studies and the even smaller number reporting complications, it was not possible to analyze complications according to strategy.

The present review had certain limitations. In the absence of any randomized controlled trials, only retrospective and non-randomized studies could be included. Secondly, no pooled analysis of functional results could be made, as this was not systematically dealt with in the studies. One-stage exchange seemed to give better functional results, but it may be that these candidates were in better preoperative health. Further, ideally randomized controlled, studies are needed to assess functional results.

Perioperative antibiotic therapy was not taken into account, as studies did not systematically report type of bacterium, antibiogram, antibiotics administered and duration of administration.

C. acnes, methicillin-resistant *S. aureus* and coagulase-negative staphylococci were the most frequent isolates. [29,57–66] We also included negative culture results, on the hypothesis that the cultures had not been kept long enough to reveal slow-growing strains such as *C. acnes*. In case of recurrence of infection after 1- or 2-stage exchange, isolates were not always reported, making it impossible to distinguish new infection from reinfection by the same bacterium.

Several systematic reviews have collated results for 1- and 2-step exchange in periprosthetic shoulder infection [18,67], but this is the first meta-analysis on the subject, to our knowledge.

Bonneville reported that 1-stage exchange was feasible if the bacterium was identified preoperatively; otherwise, 2-stage exchange was recommended in active patients, with resection arthroplasty as treatment of choice for patients with low functional demand [1]. George and Nelson, in a systematic review of 1- and 2-step exchange in periprosthetic shoulder infection, reported reinfection rates of respectively 9.2% and 6.2% [68,69]. Garrigues, Torrens et al., in the International Consensus Meeting on Musculoskeletal Infection, considered indications for 1- and 2-step exchange to be difficult to specify; analysis showed superiority of 1-stage exchange in subacute periprosthetic shoulder infection [70].

We were not able to perform subgroup analysis between acute and subacute versus chronic infection, for lack of data. Most studies used Sperling's 3-stage classification (acute, subacute, late), which cannot be superimposed on the Tsukayama classification classically used to distinguish acute (<1 month) from chronic (>1 month) infection in guiding treatment [29,71]. Studies also failed to specify whether strategy differed in late infection or in case of comorbidity. Although demographic data were sparse, the 1- and 2-stage groups were comparable.

Table 1
Description of studies assessing 1-stage exchange.

Reference	Number of infected shoulders	Mean follow-up (years)	Microbiology	Classification of infection according to Sperling	Implant type	Active anterior elevation (°) (pre to post)	External rotation (pre to post)	Functional assessment	Reinfection rate (%)	Complications rate (%)
Beekman et al.	11	2	<i>C. acnes</i> : n = 6, polymicrobial n = 2 <i>S. aureus</i> : n = 1, CNS n = 3	Acute: n = 3 Subacute: n = 7 Chronic: n = 1	RSA: n = 11			Constant 45 to 55	9.1	28
Coste et al.	3		CNS <i>S. albus</i> , <i>C. acnes</i>	Subacute: n = 1 Chronic: n = 1				Constant 35 to 66	0	0
Cuff et al.	10	3.58	<i>S. aureus</i> : n = 2, none: n = 4, CNS: n = 1, <i>C. albicans</i> : n = 1 <i>E. faecalis</i> : n = 1		HA: n = 10			ASES 36 to 62.6	0	30
Hsu et al.	27	3.8	<i>C. acnes</i> : n = 27	Chronic: n = 27	HA: n = 12, TSA: n = 9			SST 3.2 to 7.8	0	11
Ince et al.	16	5.8	<i>C. acnes</i> : n = 2, <i>S. capitis</i> : n = 2, CNS, <i>M. tuberculosis</i>		TSA: n = 15, RSA: n = 1			Constant 33.6	0	18.75
Jacquot et al.	5	NR			RSA: n = 5				0	Nr
Klatte et al.	35	4.7	CNS: n = 13, <i>C. acnes</i> : n = 12	Acute: n = 4 Subacute: n = 15 Chronic: n = 16	HA: n = 23, TSA: n = 5, RSA: n = 6			Constant 51.1	6	14.2
Sevelde et al.	14	5.8	<i>C. acnes</i> : n = 8, CNS: n = 3, polymicrobial: n = 3		HA: n = 11, RSA n = 3			Constant 27 to 65	7	7
Stone et al.	45	3.8	<i>C. acnes</i> : n = 16, CNS: n = 17, <i>S. aureus</i> : n = 10			23 to 32°	57 to 113°	ASES 33.6 to 60	4	16
Sperling et al.	2	2	CNS, <i>Acinetobacter calcoaceticus</i> , <i>Corynebacterium</i>	Subacute: n = 2	HA: n = 2	Up to 180°	Up to 30°	SST 1.8 to 5	50	50

NR: not reported; CNS: coagulase-negative staphylococcus; *C. acnes*: *Cutibacterium acnes*; *M. Tuberculosis*: *Mycobacterium tuberculosis*; *S. aureus*: *Staphylococcus aureus*; *S. capitis*: *Staphylococcus capitis*; *C. albicans*: *Candida albicans*, *E. faecalis*: *Enterococcus faecalis*. HA: hemiarthroplasty; TSA: total shoulder arthroplasty; RSA reverse I shoulder arthroplasty.

Table 2
Description of studies assessing 2-stage exchange.

Reference	Number of infected shoulders	Mean follow-up (years)	Microbiology	Classification of infection according to Sperling	Implant type	Active anterior elevation (°) (pre to post)	External rotation (pre to post)	Functional assessment	Reinfection rate (%)	Complications rate (%)
Achermann et al.	7	3.8	MRSA, <i>E. coli</i> , <i>Corynebacterium bovis</i> , <i>S. aureus</i> , <i>Streptococcus dysgalactiae</i>	Acute: n = 1 Subacute: n = 2 Chronic: n = 4					85.70	Nr
Assenmacher et al.	35	4.1	<i>C. acnes</i> (n = 13), CNS (n = 12), MRSA (n = 2), <i>Pseudomonas</i> sp (n = 2), <i>Bacillus</i> sp (n = 1), polymicrobial (n = 1), no growth (n = 4)	Acute: n = 1 Subacute: n = 6 Chronic: n = 28	HA: n = 10, TSA: n = 24, RSA: n = 1	64 to 118	14 to 41		85	5.7
Buchalter et al.	19	5.3	<i>C. acnes</i> (n = 8), <i>E. faecalis</i> n = 1, Polymicrobial: n = 6, CNS: n = 1, <i>Corynebacterium</i> : n = 1	Acute: n = 1 Subacute: n = 7 Chronic: n = 10	HA: n = 4	58 to 119	14 to 19		79	16
Coste et al.	10	2.6	Nr	Acute: n = 1 Subacute: n = 2 Chronic: n = 7	TSA: n = 13 RSA: n = 2 TSA, HA		11 to 14	Constant 15 to 35	60	10
Cuff et al.	12	3.6	<i>E. cloacae</i> , CNS, <i>C. acnes</i> , <i>S. aureus</i>		HA	43 to 79	10 to 25	ASES 28 to 48	100	58.3
Ghiselings et al.	3	4.7	<i>C. acnes</i> : n = 1, CNS: n = 1	Acute: n = 1 Subacute: n = 2 Chronic: n = 10	RSA			Constant 22.7 post operative	100	33
Ortmaier et al.	12	6.1	<i>Corynebacterium</i> : n = 1, <i>C. acnes</i> : n = 4, CNS: n = 1, polymicrobial: n = 6	Subacute: n = 2 Chronic: n = 10	RSA	To 80		Constant up to 52.2 post operative	75%	41.7
Jacquot et al.	14	3	<i>C. acnes</i> , CNS		RSA			Constant 39 to 44	64	36
Jerosh et al.	8	Nr	Nr	Chronic: n = 8	HA			Constant to 48 post operative	100	Nr
Lee et al.	12	3.4	Nr			81.7	40.4	Constant 32.9 to 66.8	100	16.7
Sabesan et al.	17	3.8	<i>Staphylococci</i> spp: n = 7, <i>C. acnes</i> : n = 5	Acute: n = 2 Subacute: n = 8 Chronic: n = 7	RSA, TSA, HA	123	26		94	35
Romano et al.	17	3.8	MRSA, CNS, <i>C. acnes</i> , polymicrobial		RSA, HA	55	12	Constant 26 to 38	100	15.9
Sperling et al.	3	2	CNS, <i>S. aureus</i> , <i>C. acnes</i>	Chronic: n = 3	TSA		up to 30		100	Nr
Stone et al.	19	3.8	<i>S. aureus</i> , CNS, <i>C. acnes</i> : n = 7, polymicrobial: n = 6		RSA, TSA HA	45 to 127	11 to 39		79	11
Strickland et al.	19	2.9	<i>C. acnes</i> , CNS, no growth n = 4, <i>S. aureus</i> : n = 3, <i>Enterococcus</i> : n = 1	Acute: n = 3 Subacute: n = 7, chronic: n = 9	TSA, HA	42 to 89	30 to 43		63.2	73.7
Torrens et al.	21	Nr	CNS: n = 4, <i>C. acnes</i> : n = 8, polymicrobial: n = 3, no bacteria = 9	Acute: n = 2, subacute: n = 4 Chronic: n = 15	HA, RSA	46.1 to 78.2		Constant 16.3 to 34.1	85.8	42.8

NR: not reported; CNS: coagulase-negative *staphylococcus*; *C. acnes*: *Cutibacterium acnes*; *S. aureus*: *Staphylococcus aureus*; *S. capitis*: *Staphylococcus capitis*; MRSA: methicillin-resistant: *staphylococcus aureus*; sp: species. HA: hemiarthroplasty; TSA: total shoulder arthroplasty; RSA: reverse shoulder arthroplasty.

Table 3
Quality analysis of studies on MINORS criteria.

Authors	Criteria												Total
	A stated aim of the study	Inclusion of consecutive patients	Prospective collection of data	Endpoint appropriate to the aim of the study	Unbiased evaluation of endpoint	Follow-up period appropriate to the major endpoint	Loss to follow-up less than 5%	Prospective calculation of the study size	An adequate control group	Contemporary group	Baseline equivalence of groups	Adequate statistical analysis	
Achermann et al.	1	0	0	1	2	2	1	0	n/a	n/a	n/a	2	9
Assemacher et al.	2	0	0	2	2	2	0	0	n/a	n/a	n/a	2	10
Beekman et al.	1	2	0	1	2	2	0	0	n/a	n/a	n/a	2	10
Buchalter et al.	2	0	0	2	2	2	2	0	n/a	n/a	n/a	2	12
Coste et al.	1	2	0	2	2	2	1	0	n/a	n/a	n/a	2	12
Cuff et al.	1	2	0	2	2	2	1	0	n/a	n/a	n/a	2	12
Ghiselings et al.	2	0	0	2	2	2	0	0	n/a	n/a	n/a	2	10
Hsu et al.	2	2	0	2	2	2	2	0	n/a	n/a	n/a	2	14
Ince et al.	2	2	0	2	2	2	2	0	n/a	n/a	n/a	2	14
Jacquot et al.	1	0	1	1	2	2	0	0	n/a	n/a	n/a	2	11
Jerosh et al.	1	0	0	2	2	2	0	0	n/a	n/a	n/a	2	9
Klatte et al.	1	2	0	1	2	2	1	0	n/a	n/a	n/a	2	11
Lee et al.	2	2	0	2	2	2	1	0	n/a	n/a	n/a	2	13
Ortmaier et al.	1	2	0	2	2	2	2	0	n/a	n/a	n/a	2	13
Romano et al.	1	2	1	2	2	2	1	0	n/a	n/a	n/a	2	13
Sabesan et al.	2	2	0	2	2	2	0	0	n/a	n/a	n/a	2	12
Sevelde et al.	2	2	1	2	2	2	0	0	n/a	n/a	n/a	2	13
Stone et al.	2	2	0	2	2	2	0	0	n/a	n/a	n/a	2	12
Sperling et al.	2	2	0	2	2	2	1	0	n/a	n/a	n/a	2	13
Strickland et al.	2	2	0	2	2	2	1	0	n/a	n/a	n/a	2	11
Torrens et al.	2	0	0	2	2	2	0	0	n/a	n/a	n/a	2	12

n/a: not applicable. 0: not reported; 1: reported but inadequate; 2: reported and adequate.

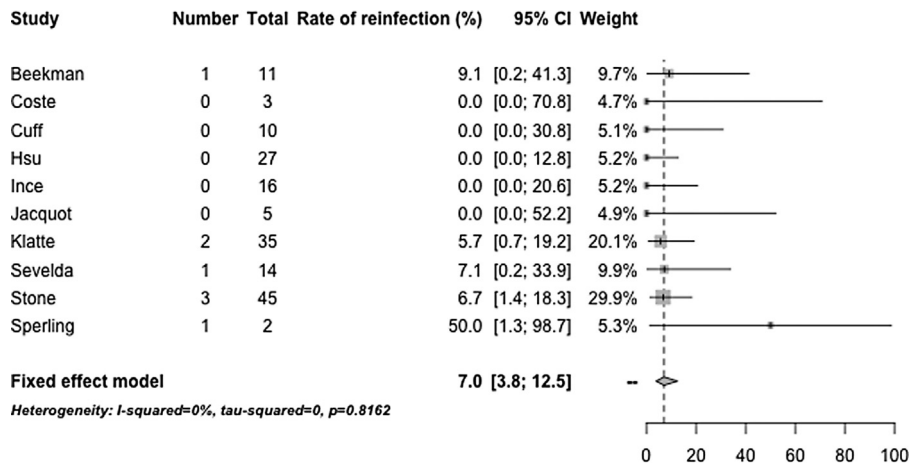


Fig. 2. Forrest plot: rate of reinfection one-stage exchange.

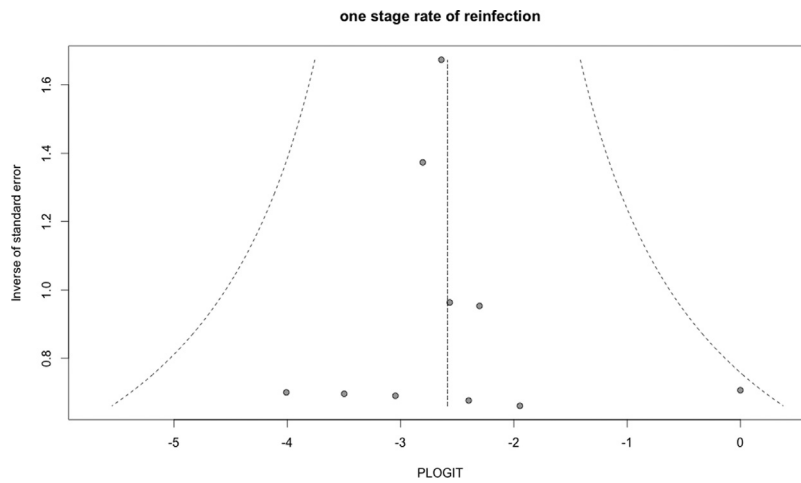


Fig. 3. Funnel plot: rate of reinfection one-stage exchange.

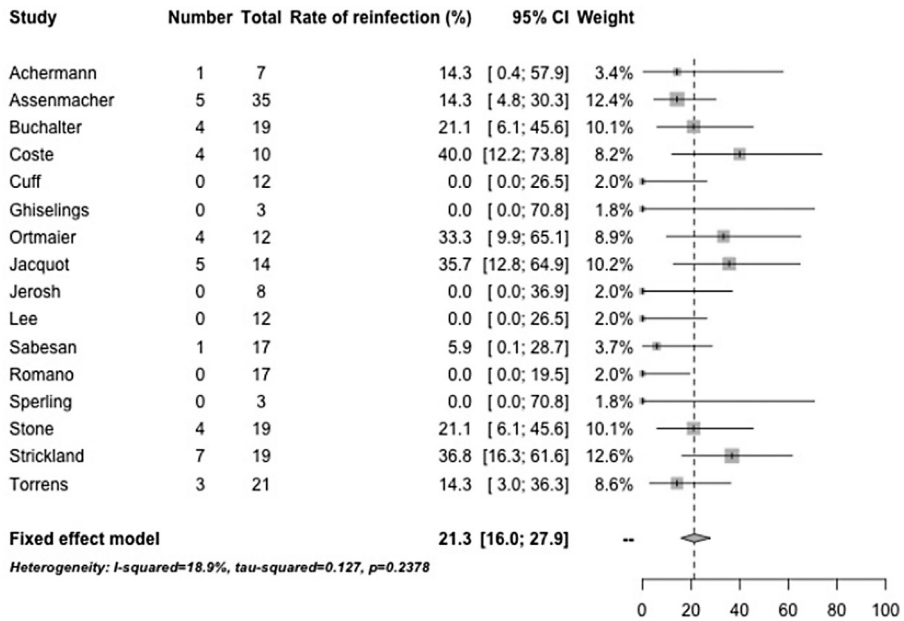


Fig. 4. Forrest plot: rate of reinfection two-stage exchange.

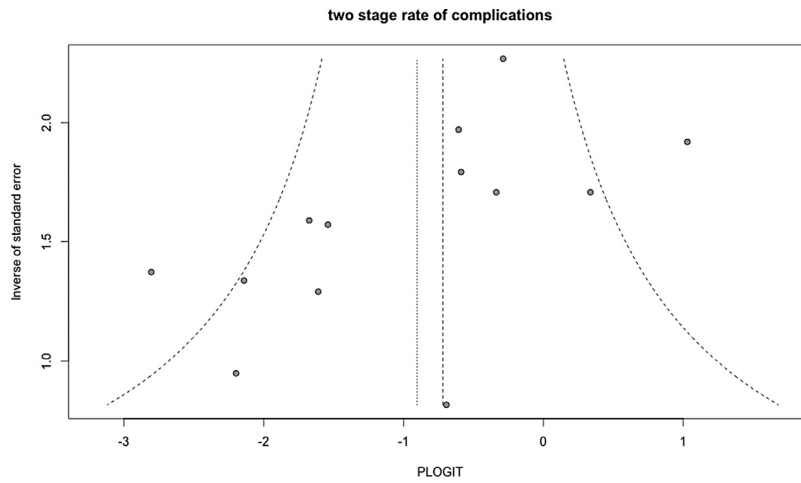


Fig. 5. Funnel plot: rate of reinfection two-stage exchange.

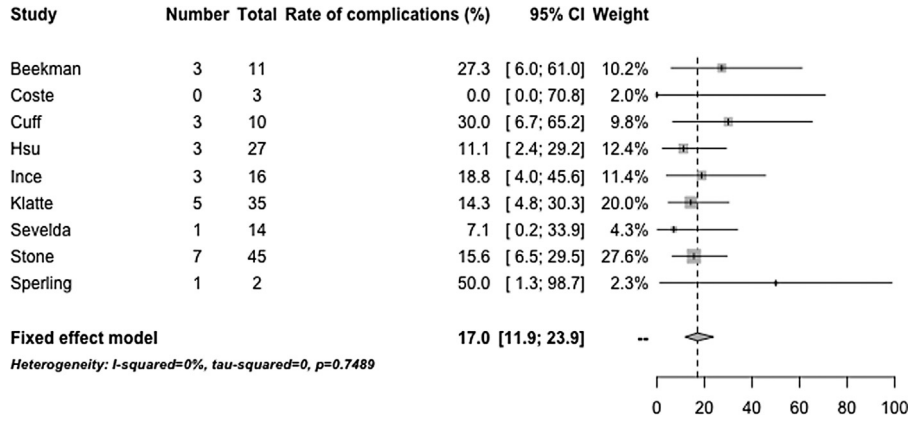


Fig. 6. Forrest plot: rate of complications one-stage exchange.

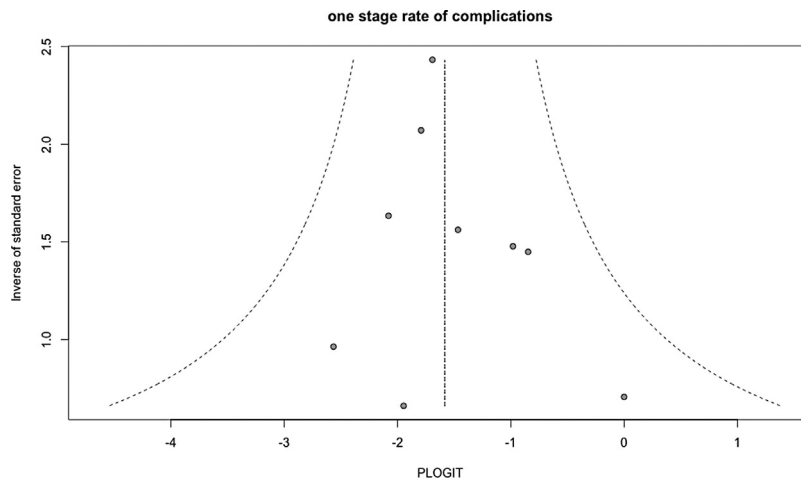


Fig. 7. Funnel plot: rate of complications one-stage exchange.

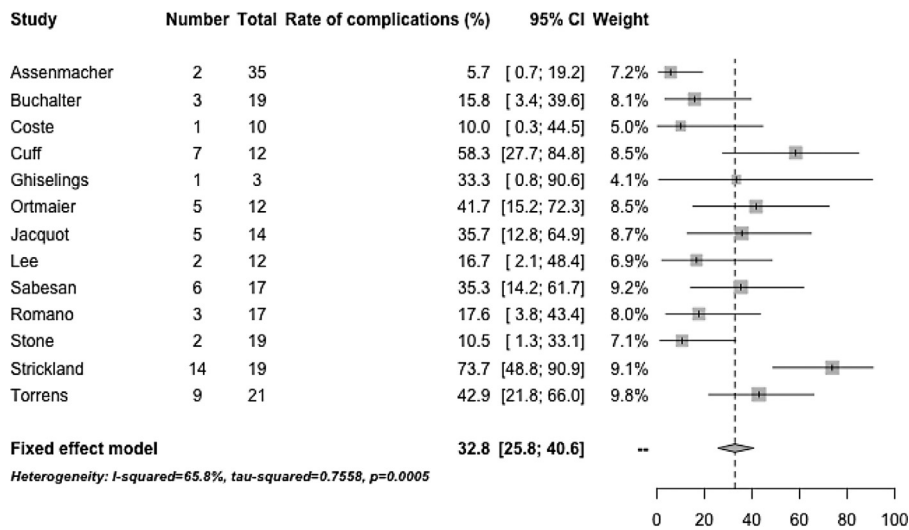


Fig. 8. Forrest plot: rate of complications two-stage exchange.

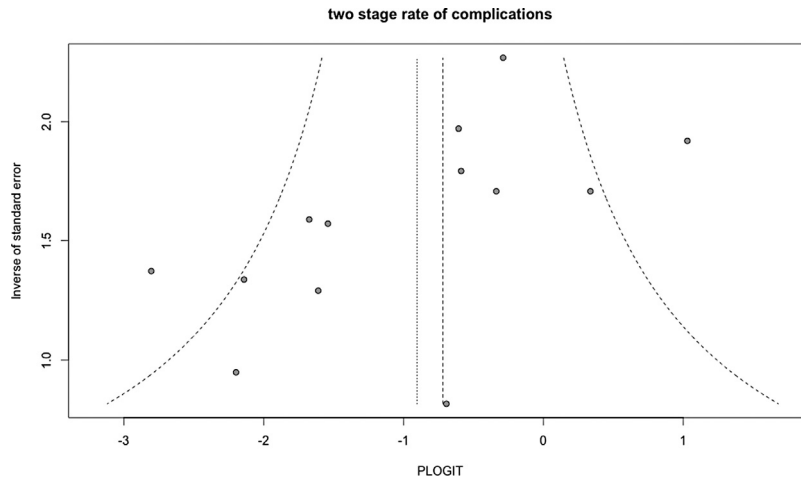


Fig. 9. Funnel plot: rate of complications two-stage exchange.

5. Conclusion

In periprosthetic shoulder infection, 1-stage exchange gives better results than 2-stage exchange, with 3-fold less reinfection (7% [95% CI, 3.8–12.5%] versus 21.3% [95% CI, 16–27.9%]) and almost 2-fold fewer complications (17% [95% CI, 11.9–23.9%] versus 32/8% [95% CI, 25.8–40.6%]). Functional benefit, however, remains undetermined, and further studies are needed.

Disclosure of interest

The authors declare that they have no competing interest.

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Contribution

Florence Aim wrote the manuscript.
 Blandine Marion contributed to article selection and data extraction.
 Younes Kerroumi read the manuscript and helped with statistics.

Vanina Meyssonier checked the microbiological data.
 Simon Marmor corrected the manuscript.

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