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Outcome of single-stage versus two-stage exchange for revision knee arthroplasty for chronic periprosthetic infection

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- The gold standard for treating chronic periprosthetic joint infection is still considered to be double-stage exchange revision. The purpose of this review is to analyse the difference in terms of eradication rates and functional outcome after single- and double-stage prosthetic exchange for chronic periprosthetic joint infection around the knee.
- We reviewed full text articles written in English from 1992 to 2018 reporting the success rates and functional outcomes of either single-stage exchange or double-stage exchange for knee arthroplasty revision performed for chronic infection. In the case of double-stage exchange, particular attention was paid to the type of spacer: articulating or static.
- In all, 32 articles were analysed: 14 articles for single-stage including 687 patients and 18 articles for double-stage including 1086 patients. The average eradication rate was 87.1% for the one-stage procedure and 84.8% for the two-stage procedure. The functional outcomes were similar in both groups: the average Knee Society Knee Score was 80.0 in the single-stage exchange group and 77.8 in the double-stage exchange. The average range of motion was 91.4° in the single-stage exchange group and 97.8° in the double-stage exchange group.
- Single-stage exchange appears to be a viable alternative to two -stage exchange in cases of chronic periprosthetic joint infection around the knee, provided there are no contra-indications, producing similar results in terms of eradication rates and functional outcomes, and offering the advantage of a unique surgical procedure, lower morbidity and reduced costs.

Keywords: eradication rate; functional outcome; periprosthetic joint infection; single-stage exchange; total knee replacement; two-stage exchange

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Introduction

Prosthetic joint infection (PJI) remains one of the most serious complications of knee prosthesis implantation. Its incidence is reported as between 0.5% and 2.0% according to the risk factors.[1–4] It is the commonest reason for total knee arthroplasty (TKA) revision in the United States.[5] Of these revisions, 25% are due to infectious disease and the cost per case is 50,000 US dollars.[4–7] Today there are now two options for the treatment of delayed PJI around the knee: single- and two-stage revision arthroplasty.[8]

Two-stage revision is considered as the gold standard for revision in cases of PJI for knee arthroplasty. It was originally described by Insall et al in 1983[9] and secondly modified through the development of static spacers[10] and then articulating spacers in 2001.[11]

Single-stage exchange for periprosthetic joint infection is not a truly new technique: it was first described by Buchholz in the 1970s at the Endo Klinik in Hamburg and reported by Borden and Gearen[8] in 1987 and Göksan and Freeman[12] in 1992. The recent literature on the subject tends to suggest this as an alternative for revision in delayed infected knee arthroplasty. The main benefits are a single surgical procedure, a shorter period of antibiotic treatment and reduced costs.

The comparison of the two procedures ideally requires prospective, randomized, controlled trials but they are time-consuming and difficult to set up. The results of each case series are controversial, and the performance of single-stage compared to two-stage exchange remains unclear. In order to clarify this question, we performed a systematic review of the available literature comparing single- and double-stage exchange for delayed PJI around the knee, published between 1992 and 2018.

Materials and methods

A thorough systematic review of the literature was performed to identify articles reporting on one- or two-stage exchange in knee arthroplasty for periprosthetic joint infection. Articles written in English published from 1992 to 2018 were reviewed. The depth of details described in the materials and methods of each article varied markedly, making it impossible to perform a meta-analysis. Instead of this, a descriptive review of the results is presented. The international databases were searched and included: EMBASE; PubMed/Medline; Medline Daily Update; Medline In-Process and other non-indexed citations; Google Scholar; SCOPUS; CINAHL; Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews; NHS Health Technology Assessment.

The Mesh terms used for our research were based on the ones described by Jämsen et al for their own review:[13] "periprosthetic joint infection", "single-stage exchange", "two-stage exchange", "knee arthroplasty revision", "prosthesis-related infections", "direct exchange arthroplasty", "knee joint infection", "revision knee replacement".

The inclusion criteria were the following:

- Articles written fully or with an abstract in English
- Articles reporting infectious outcomes of either single-stage or double-stage exchange arthroplasty
- Articles reporting functional outcomes of either single-stage or double-stage exchange arthroplasty: range of motion or Knee Society Score (KSS), or Oxford Knee Score (OKS) or Hospital for Special Surgery Knee Score (HSS)
- Study design classifiable as: randomized controlled trial; comparative prospective study; prospective case series with no comparison group; comparative retrospective study; retrospective study with no control group
- The study population had to be 10 or more and cases with a minimum follow-up of six months (note that most studies use at least one year follow-up)
- The following information should have been reported: number of patients, type of treatment, and number of recurrent infections after treatment

Our principal aim was to compare the rate of recurrence of infection after one- and two-stage exchange and the second was to explore the differences in terms of functional outcomes. Knee Society Score (KSS), Oxford Knee Score and the Hospital for Special Surgery Knee Score (HSS) were used to measure the clinical outcomes in most studies. The pre- and post-operative range of motion (ROM) were frequently reported.

In order to perform this analysis, the data we reviewed were:

- Number of patients
- Single- or double-stage exchange
- In case of double-stage exchange, the kind of spacer: static or articulating
- The rate of eradication of infection
- The functional knee score: KSS, OKS, HSS
- The range of motion after the whole procedure

Results

Thirty-two original articles describing the management of periprosthetic joint infection around the knee were included: 14 articles for the single-stage exchange procedure and 18 for the two-stage procedure. Our review reported the results of 1773 surgical procedures: 687 for one-stage exchange and 1086 for two-stage exchange. The range in the number of cases was from 10 to 177 and the range of follow up was from six months to 10.5 years.

Eradication rate

The eradication rate after the one-stage procedure ranged from 67% to 100% with an average rate of 87.1%. The eradication rate after the double-stage procedure ranged from 54% to 100% with an average rate of 84.8%. In the double-stage exchange group, 34.5% of patients underwent the procedure with a static spacer and 65.5% with an articulating spacer. The eradication rate was higher in the articulating spacer group compared with the static spacer group: 92.5% vs 74%. The results are reported in Table 1.

Functional outcomes

The functional outcomes were similar in both groups. The studies reporting single-stage exchange gave a Knee Society Score ranging from 72 to 88 with an average score of 80. The studies reporting double-stage exchange reported a Knee Society Score ranging from 63.8 to 86.0 with an average score of 77.8. The average range of motion was 91.4° (76°–100°) in the single-stage group and 97.8° (86°–112°) in the double-stage group. The results are reported in Table 2.

Discussion

Our study reported no statistical difference between the single-stage exchange group and the two-stage exchange in terms of functional outcome and eradication rates. Considering the fact that single-stage exchange is much more comfortable for the patients and allows the hospital to reduce the costs associated with periprosthetic joint infection, single-stage exchange appears to be a viable alternative to double-stage exchange surgery. However, some of the studies were small with very short (six months) follow-up.

Table 1. Eradication rates of single- and double-stage exchange

Author	Single/double stage	Year	Revue	Patients	FU	Eradication rate %
Buechel et al[39]	Single	2004	*American Journal of Orthopedics*	22	10.2	90.9
Göksan and Freeman[12]	Single	1992	*JBJS Br*	18	5.0	77.0
Jenny et al [20]	Single	2013	*Clinical Orthopedics*	47	3.0	87.0
Silva et al[26]	Single	2002	*Clinical Orthopedics*	37	4.0	89.2
Singer et al[17]	Single	2012	*Clinical Orthopedics*	63	24.0	95.0
Tibrewal et al[40]	Single	2014	*BJJ*	50	10.5	92.0
Jenny et al[19]	Single	2016	*Knee*	130	3.2	81.0
Antony et al[41]	Single	2015	*Infectious Disease*	37	1.0	89.0
Zahar et al[42]	Single	2015	*Clinical Orthopedics*	70	9.0	93.0
Massin et al[25]	Single	2016	*KSSTA*	108	3.5	77.0
Bauer et al[43]	Single	2006	*RCOT*	30	4.5	67.0
Castellani et al[44]	Single	2017	*HSS Journal*	14	1.0	94.2
Haddad et al[16]	Single	2015	*Clinical Orthopedics*	28	6.5	100.0
Cuckler et al[45]	Double	2005	*JOA*	44	5.4	98.0
Durbhakula et al[46]	Double	2004	*JOA*	24	2.8	92.0
Fehring et al[47]	Double	2000	*Clinical Orthopedics*	55	3.0	90.0
Ford et al[28]	Double	2018	*JOA*	56	3.3	54.0
Frank et al[38]	Double	2017	*Clinical Orthopedics*	57	1.0	88.0
Hofmann et al[48]	Double	2005	*Clinical Orthopedics*	50	6.0	88.0
Hsu et al[49]	Double	2007	*JOA*	28	2.0	87.0
Huang et al[50]	Double	2006	*JOA*	21	4.5	96.5
Jämsen et al[23]	Double	2006	*International Orthopedics*	34	2.8	85.0
Lichstein et al[22]	Double	2016	*Clinical Orthopedics*	121	3.7	94.0
Mortazavi et al[27]	Double	2011	*Clinical Orthopedics*	117	3.8	72.0
Siebel et al[51]	Double	2002	*Acta Orthopedica Belgica*	10	1.5	100.0
Massin et al[25]	Double	2016	*KSSTA*	177	55.0	69.0
Bauer et al[43]	Double	2006	*RCOT*	77	4.5	67.0
Castellani et al[44]	Double	2017	*HSS Journal*	52	1.0	84.0
Haddad et al[16]	Double	2015	*Clinical Orthopedics*	74	6.5	93.0

Note. FU, follow up; ER, eradication rate.

Recently, Kunutsor et al[14] performed a meta-analysis comparing single- and two-stage exchange for knee revision in cases of infectious disease. Their article included 10 studies for single-stage (423 patients), and 108 studies for double-stage exchange (5129 patients). They reported lower re-infection rates for single-stage exchange compared with two-stage exchange: 7.6% (95% CI 3.4–13.1) vs 8.8% (95% CI 7.2–10.6). As in our review, the functional outcomes were similar in terms of clinical score and range of motion. The knee society knee score was 80.3 (74.8–86.5) in the single-stage group and 82.1 (76.0–86.0) in the double-stage exchange group. The average range of motion was 97.5° (93.8°–100.5°) in the one-stage revision group and 97.8° (93.7°–104.0°) in the two-stage revision group.

Nagra et al[15] published their review in 2016 including 231 patients: 46 single-stage and 185 double-stage with a minimum of two years follow up. The rate of re-infection was 4.3% in their single-stage group, and 13.5% in the double-stage but without statistically significant difference: OR –0.06 (95% CI –0.13 to 0.01). In their subgroup analyses, the studies performed after 2000 reported significantly better rates for the single-stage group (OR –0.08; 95% CI –0.20 to 0.00). Considering the functional outcomes they reported the results of Haddad et al[16] with an increase of 56 points in the Knee Society Score for single-stage compared with 45 points for the two-stage revision group.

In 2012, Romanò et al[17] published a systematic review. Their results included a comparison between static and articulating spacers in cases of two-stage revision. In their review, 204 patients underwent single-stage exchange in six studies from 1966 to 2011 and 1421 patients underwent two-stage exchange in 38 studies. The eradication rate was higher in the two-stage exchange group: 89.8% with 40 months of follow-up versus 81.9% with 44 months of follow-up in the single-stage exchange group. In cases of two-stage revision, they recommended using an articulating spacer to improve the eradication rate: 91.2% versus 87.0% in cases of static spacer.

Jämsen et al[13] in 2009 published a systematic review in which they included 31 articles from 1980 to 2005: 154 cases underwent single-stage exchange with eradication rates ranging from 73% to 100%; 956 cases underwent two-stage exchange with eradication rates ranging from 82% to 100%. The lowest rates were reported for the series with two-stage exchange using an articulating spacer as reported by Romanò et al.[17] Their functional results were similar to ours with no difference in terms of clinical score or range of motion between the single- and two-stage revision groups.

Table 2. Functional outcomes of single- and double-stage exchange

Author	Year	Revue	Patients	Follow up (yrs)	KSS before	KSS after	HSS before	HSS after	OKS before	OKS after	ROM before	ROM after
Buechel et al[39]	2004	*American Journal of Orthopedics*	22	10.2		79.5						
Göksan and Freeman[12]	1992	*JBJS Br*	18	5.0								
Jenny et al[20]	2013	*Clinical Orthopedics*	47	3.0		85.0						100.0
Silva et al[26]	2002	*Clinical Orthopedics*	37	4.0								
Singer et al[17]	2012	*Clinical Orthopedics*	63	24.0		72.0						
Tibrewal et al[40]	2014	*BJJ*	50	10.5					14.5	34.5		
Jenny et al[19]	2016	*The Knee*	130	3.2								
Antony et al[41]	2015	*Infectious Disease*	37	1.0								
Zahar et al[42]	2015	*Clinical Orthopedics*	70	9.0			35	69.6			50	76.0
Baker et al[52]	2013	*KSSTA*	33	0.6						24.9		
Massin et al[25]	2016	*KSSTA*	108	3.5								97.0
Bauer et al[43]	2006	*RCOT*	30	4.5		75.5						92.5
Castellani et al[44]	2017	*HSS Journal*	14	1.0								
Haddad et al[16]	2015	*Clinical Orthopedics*	28	6.5	32	88.0						
Cuckler et al[45]	2005	*Journal of Arthroplasty*	44	5.4	36	84.0						112.0
Durbhakula et al[46]	2004	*Journal of Arthroplasty*	24	2.8				82.0				104.0
Ferhing et al[47]	2000	*Clinical Orthopedics*	55	3.0				83.0				102.0
Ford et al[28]	2018	*Journal of Arthroplasty*	56	3.3								
Frank et al[38]	2017	*Clinical Orthopedics*	57	1.0								
Hofmann et al[48]	2005	*Clinical Orthopedics*	50	6.0								104.0
Hsu et al[49]	2007	*Journal of Arthroplasty*	28	2.0								86.0
Huang et al[50]	2006	*Journal of Arthroplasty*	21	4.5	60	80.0						97.6
Jämsen et al[23]	2006	*International Orthopedics*	34	2.8	38	80.0						100.0
Lichstein et al[22]	2016	*Clinical Orthopedics*	121	3.7	36	86.0						100.0
Mortazavi et al[27]	2011	*Clinical Orthopedics*	117	3.8								
Siebel et al[51]	2002	*Acta Orthopedica Belgica*	10	1.5	39	63.8						86.5
Baker et al[52]	2013	*KSSTA*	89	0.6						22.8		
Massin et al[25]	2016	*KSSTA*	177	55								91.0
Bauer et al[43]	2006	*RCOT*	77	4.5		74.8						93.0
Castellani et al[44]	2017	*HSS Journal*	52	1.0								
Haddad et al[16]	2015	*Clinical Orthopedics*	74	6.5	31	76.0						

Note. KSS, Knee Society Score; HSS, Hospital for Special Surgery Score; OKS, Oxford Knee Score; ROM, range of motion.

Selection criteria for single-stage surgery

The above studies are encouraging when considering single-stage exchange in cases of periprosthetic joint infection around the knee. However, many of them do not describe comparable patient groups and the criteria for selection of single- or two-stage revision are not defined precisely.

Following Gehrke et al,[18] we consider that each procedure should be performed considering various selection criteria and considering contra-indications. Single-stage exchange should not be considered in any of the following situations:

- Failure of ⩾ two previous one-staged procedures.
- Infection spreading to the neurovascular bundle.
- Unclear pre-operative bacterial specification.
- Non-availability of appropriate antibiotics.
- High antibiotic resistance.
- Sinus tract with unclear bacterial specification.

Jenny el al[19] published a study in 2016 in which they claimed the opposite: they compared a single-stage revision group without selection criteria (54 cases) with another one including only selected patients (77 cases). The selection criteria were: good general patient condition, non-acute infection, responsible pathogens sensitive to standard antibiotic treatment, and good bone stock without the need for bone grafting. In their study the rate of infection-free patients at 38 months' follow-up was 85% in the group without selection and 78% in the selected group. Their conclusion was that selection of patients for single-stage exchange does not improve the eradication rate. Jenny et al[20] previously published on the subject a series describing 47 patients who underwent single-stage exchange for revision knee arthroplasty: the minimum follow-up was three years, the eradication rate was 87%, and 56% of the patients had a Knee Society Score of more than 150 points. Their findings were similar to ours: single-stage exchange gave the same results as double-stage exchange, but no benefits were demonstrated in functional outcomes.

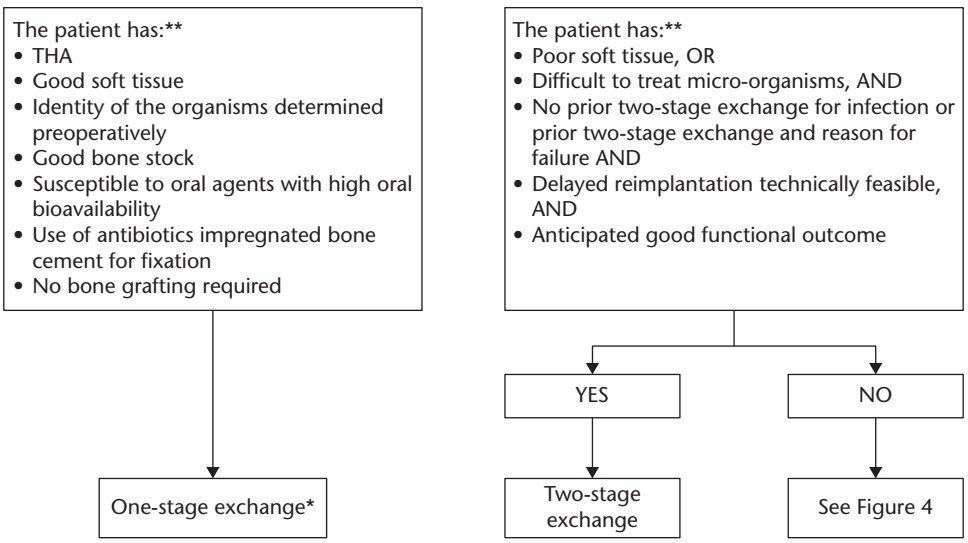

Fig. 1 Guidelines of the Infectious Disease Society of America

Today the choice between single- and two-stage exchange remains, in most cases, the decision of the surgeon and depends on the habits of the institution. In order to help surgeons choose wisely, the Infectious Disease Society of America has published guidelines[21] explaining what the present indications are for single- and two-stage exchange for periprosthetic joint infection (Fig. 1).

Types of spacers

In the case of two-stage exchange, the studies so far are unanimous: the articulating spacer improves the eradication rates and the functional outcomes compared with static spacers. Lichstein et al[22] reported the results of 121 infected TKAs treated with two-stage exchange and articulating spacer from 1999 to 2011. The median range of motion was 100° (60°–139°) and 94% patients were free of infection at 3.7 years of follow-up. The results of Romanò et al[17] showed an eradication rate of 91.2% for articulating spacers vs 87.0% in cases treated with a static spacer as mentioned previously.

An alternative to the cement spacer is described by Jämsen et al,[23] using re-sterilized prosthetic components as spacers. In their study, 24 patients underwent exchange with this kind of spacer compared with 10 patients in a control group with a static spacer. The rate of re-infection was similar in the two groups. During the interim period, the patients with re-sterilized prosthesis spacers had a greater range of motion: mean 89±18° vs 17±13° ($p < 0.001$) in patients with cement spacers.

Finally, the last advantage of the articulating spacer is that it can be left in place if the patient is medically unfit for repeated surgery. Siddiqi et al[24] published a series of 29 patients who underwent only the first stage of a double-stage exchange and kept their spacer. Their results showed 79.3% success, 13.8% chronic wound drainage and 6.9% requiring a later multiple-spacer exchange.

Risks factors for PJI

The risks factors for PJI are well known, Pulido et al[1] described them as high American Society of Anesthesiologists (ASA) score, obesity, blood transfusion, atrial fibrillation, myocardial infarction, urinary infection or longer hospital stay, whereas Bohl et al[2] cited great age, male gender, diabetes, high blood pressure, smoking habit, high operating time and pneumonia. Considering the choice between single-stage surgery or double-stage for PJI around the knee, we must consider the risk factors of recrudescence of the infection. Massin et al[25] described the global risk factors of failure for PJI as fistula, gram-negative bacteria and two-stage exchange with a static spacer. Silva et al[26] reported factors associated with successful single-stage exchange as gram-positive organism, absence of sinus tract, aggressive debridement of infected tissue, antibiotics-impregnated cement and long-term antibiotic therapy, whereas rheumatoid arthritis and corticosteroid were associated with higher rates of failure. Mortazavi et al[27] published a series of 117 patients who underwent two-stage exchange to identify the risks factor for failure. Their rate of failure was 28% with three identified risks factors: negative culture and methicillin-resistant organism and increased operative time.

Infectious organism

The infectious agent also needs to be known to be able to choose between single- and double-stage exchange. In their series, Ford et al[28] described 68.75% of Staphylococci with higher risks of re-offending bacteria in cases of Coagulase negative or Methicillin resistant organism. The results of Klatte et al[29] on single-stage exchange with fungal infection do not encourage us to perform these procedures in the presence of fungal infection.

Periprosthetic joint infection in unicompartmental knee arthroplasty (UKA)

Chronic infection in UKA is not a common mode of failure. The three main reasons are loosening, wear and progression of osteoarthritis.[30] Nevertheless, the incidence of infection in cases of failure for UKA should force us to consider it as a diagnosis option. Epinette et al describe it as the cause of 1.9% of failures[31] and Sierra et al as 3%.[30] The Society of Unicondylar Research reported it to be the cause of 10% of re-interventions after UKA.[32] In their article, they claim that surgeons do not think about this diagnosis and thus, 40% of the failures of UKA have an incomplete PJI evaluation before re-intervention. They published a list of tools which should be used in case of UKA failure: An Erythrocyte Sedimentation Rate $>$ 27 mm/H, C-Reactive Protein $>$ 14 mg/mL and white blood cell count in synovial fluid 6200/µL is the cut-off value for which PJI should be considered. The white blood cell count in synovial fluid has a sensitivity of 90% and specificity of 96%.

Only one series has been published for infected UKA management: Labruyère et al[33] reported nine cases of single-stage exchange of UKA to TKA. The average International Knee Society (IKS) knee score was 60 before surgery and 75 after surgery. The average IKS function score was 50 before surgery and 60 after surgery. They explained that in cases of PJI, cartilage and ligaments are so destroyed that a revision implant or rotating hinge is needed. Khan et al[34] published a series of 201 revision UKAs treated by TKR, in which they insisted on the need for augments and bone grafting.

Surgical technique: debridement

Surgical debridement is one of the keys for the success of either single- or double-stage exchange. George and Haddad[35] published an update of the surgical technique for single-stage exchange emphasizing that it should be aggressive considering the fact that it is a 'one shot' procedure. The debridement should be performed in cases of single-stage exchange as follows: all hardware and remaining cement should be removed as well as non-bleeding tissue and related bone, if necessary with intramedullary reaming. Chemical debridement with 12 L of sodium chloride 0.9%, povidone iodine and hydrogen peroxide should follow. Gehrke et al[18] state clearly in their article that single-stage exchange must be considered as a 'short double stage'. This involves closing the wound after debridement, the whole surgical team re-scrubbing and the use of new instruments for re-implantation.

In cases of double-stage exchange, the principles of debridement remain the same except for two differences: a second debridement may be necessary before re-implantation during the second stage,[36] and bone loss needs to be considered after removal of the cement spacer. Calton et al[10] demonstrated in their report that bone loss is caused directly by removal of the spacer. A small spacer and long period between two surgeries are directly correlated with higher bone loss.

Antibiotic therapy

Finally, a well conducted surgical procedure will be useless without a documented and wisely chosen antibiotic regime, guided by expert microbiologists. The length and timing of this antibiotic therapy still varies from one team to another. Osmon et al[21] in their guidelines for the Infectious Disease Society of America recommend generally four to six weeks of IV antibiotic therapy followed by oral antibiotic therapy for a total of three months. Laffer et al[37] considered that there is no need to have longer antibiotic therapy than six months. Recently, Frank et al[38] performed a randomized controlled trial for double-stage exchange; the control group had no antibiotics after re-implantation and the other group had three months antibiotic therapy after re-implantation. The rates of re-infection were totally different: 19% of re-infection in the control group and 5% in the antibiotic group (hazard ratio, 4.37; 95% CI, 1.297–19.748; $p = 0.0162$).

Conclusions

The results of this systematic review should help us to decide whether single- or double-stage exchange is the most indicated procedure for chronic periprosthetic infection around the knee. Our results show that there are no clear benefits in terms of eradication rates or functional outcomes. Single-stage exchange appears to be a viable alternative to double-stage exchange, provided there are no contra-indications, with reduced morbidity and costs. The decision should be based upon the risk factors related to the patient and infectious organism and the contra-indication previously mentioned. In cases of double-stage exchange, articulating spacers show higher eradication rates and better functional outcomes.

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ICMJE CONFLICT OF INTEREST STATEMENT

MO reports consultancy to Arthrex, Stryker and New-clip outside the submitted work.
JNA reports board membership of the Journal of Bone and Joint Surgery and consultancy to Zimmer, Adler and Symbios outside the submitted work.
CP declares no conflict of interest relevant to this work.

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