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Single-stage versus two-stage revision for shoulder periprosthetic joint infection: a systematic review and meta-analysis

Elshaday S. Belay, MD^{a,}[*,](#page-0-0) Richard Danilkowicz, MD^a, Garrett Bullock, PT, DPT^{[b](#page-0-1)}, Kevin Wall, MD^{[c](#page-0-2)}, Grant E. Garrigues, MD^{[d](#page-0-3)}

^aDepartment of Orthopaedic Surgery, Duke University Medical Center, Durham, NC, USA ^bNuffield Department of Orthopaedics, Rheumatology, and Musculoskeletal Sciences, University of Oxford, Oxford, UK ^cDepartment of Orthopaedic Surgery, University of Alabama at Birmingham School of Medicine, Birmingham, AL, USA ^dMidwest Orthopaedics at Rush, Rush University Medical Center, Chicago, IL, USA

Background: Shoulder periprosthetic joint infection (PJI) is a significant complication after arthroplasty with high morbidity. An evidence-based algorithm for the treatment of shoulder PJI is lacking in current practice. The purpose of this systematic review and meta-analysis was to understand and compare the role of single- and 2-stage shoulder arthroplasty revision for PJI.

Methods: A comprehensive literature review was performed to identify all studies related to shoulder arthroplasty for PJI in PubMed, Scopus, and EMBASE. Inclusion criteria for this systematic review were studies that reported on single- or 2-stage revision, with infection eradication and a minimum follow-up of 12 months and a minimum of 5 patients for analysis. A random-effects meta-analysis was performed, and heterogeneity was assessed with Cochrane Q and I2.

Results: A total of 13 studies reporting on single-stage revision and 30 studies reporting on 2-stage revision were included in final analysis. The majority of positive cultures from single-stage revision for PJI resulted in *Cutibacterium acnes* with 113 of 232 (48.7%) reported cases compared with 190 of 566 (33.7%) reported cases for 2-stage revision. However, there was a lower percentage of methicillin-resistant Staphylococcus aureus positive cultures, with 2.5% for single-stage compared with 9.7% for 2-stage revision. The overall pooled randomeffect reinfection incidence was 0.05 (95% confidence interval: 0.02-0.08), with moderate heterogeneity ($I^2 = 34\%$, $P = .02$). The reinfection rate was 6.3% for single-stage and 10.1% for 2-stage revision, but this was not significant ($Q = 0.9$ and $P = .40$).

Conclusion: Based on a systematic review with meta-analysis, single-stage revision for shoulder PJI is an effective treatment. Indeed, our analysis showed single-stage to be more effective than 2-stage, but this is likely confounded by a treatment bias given the higher propensity of virulent and drug-resistant bacteria treated with 2-stage in the published literature. This implies that shoulder surgeons treating PJI can be reassured of a low recurrence rate (6.3%) when using single-stage treatment for C acnes or other sensitive, low-virulence organisms. Level of evidence: Level IV; Systematic Review

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Keywords: Shoulder periprosthetic infection; shoulder arthroplasty; single-stage revision; two-stage revision; staphylococcus aureus; cutibacterium acnes

Institutional review board approval was not required for this systematic review.

*Reprint requests: Elshaday S. Belay, MD, Department of Orthopaedic Surgery, Duke University Medical Center, DUMC 104002, Durham, NC 27710, USA.

E-mail address: Elshaday.Belay@duke.edu (E.S. Belay).

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Shoulder periprosthetic joint infection (PJI) is a devastating complication with significant morbidity. The incidence of PJI after primary shoulder arthroplasty has been reported to range from 1% to 4% after primary and up to 4% -15% after revision arthroplasty.^{[11](#page-8-0)[,36](#page-9-0)} Factors associated with an increased risk for shoulder PJI include medical comorbidities such as diabetes, inflammatory disease, obesity, and chemotherapy, as well as previous corticosteroid injections.[4](#page-8-1),[13](#page-8-2)[,53](#page-9-1) Studies have also shown a connection between PJI and male gender, prior failed arthroplasty, arthroplasty for trauma, and age under $65.^{30,37}$ $65.^{30,37}$ $65.^{30,37}$ $65.^{30,37}$ Shoulder arthroplasty infection can broadly be categorized as acute $(<$ 3 months), subacute (3-12 months), or chronic (>12) months) based on the time from initial surgery.^{[53](#page-9-1)} Common organisms involved in shoulder PJI have been identified as Coagulase-negative staphylococcus (CoNS), Cutibacterium acnes, Staphylococcus aureus, and Staphylococcus epidermidis.^{[11](#page-8-0),[61](#page-10-0)} Because of the absence of a reliable preor intraoperative test for the most common organism, C acnes, the diagnosis of shoulder PJI, and thus also the treatment, represents one of the greatest challenges in shoulder arthroplasty.^{[36](#page-9-0)}

Historically, shoulder PJI management has drawn on evidence from hip and knee arthroplasty infection.^{[7](#page-8-3)[,8](#page-8-4)} However, given the lack of a reliable and consistent definition of shoulder PJI, the treatment approaches have been disparate. Recently, the recommendations of the International Conference for Periprosthetic Infection included a consensus definition for shoulder PJI derived through systematic literature review and a Delphi process. Definite PJI can be identified by the presence of a sinus tract, intraarticular pus, or 2 positive cultures with phenotypically identical organisms. Probable infection and possible infection are referenced based on a scoring rubric of minor criteria.^{[17](#page-8-5)} However, given proximity of this publication, the definition described by the ICM for shoulder PJI has only recently been put into clinical use and was not included in any of the articles assessed; thus we used each author's own, highly variable, definitions for infection in each article reviewed.^{[17](#page-8-5)}

Treatment options for an infected shoulder arthroplasty include irrigation and debridement (I&D) with implant retention, 1- or 2-stage exchange arthroplasty, implantation of a permanent spacer, or a resection arthroplasty.^{[7](#page-8-3)} As is the case with hip and knee periprosthetic infection, 2-stage exchange arthroplasty has been suggested as the gold standard for shoulder PJI.^{[8](#page-8-4)} Specifically, implant removal, I&D, insertion of antibiotic spacer, followed by delayed reimplantation, have been favored over single-stage ex-change revision arthroplasty.^{[7](#page-8-3)[,8,](#page-8-4)[36](#page-9-0)}

To date, the evidence has been conflicting between 1- and 2-stage revision for shoulder PJI. The purpose of this systematic review is to study the pathogens involved in shoulder periprosthetic infections, rate of infection eradication, functional outcomes, and complications with singlevs. 2-stage revision. The purpose of the meta-analysis is to compare these 2 treatment modalities and determine whether there is a difference in eradication of infection and ultimately minimize the uncertainty that exists with clinical decision making for the treatment of shoulder PJI.

Methods

A comprehensive literature review was performed to identify all studies on revision shoulder arthroplasty for PJI. Terms used for the search included ''infection'' or ''reinfection'' or ''positive culture'' or ''prosthesis-related infection'' AND ''shoulder joint'' or ''shoulder'' AND ''arthroplasty, replacement,'' or ''arthroplasty'' or ''total joint'' or ''periprosthetic'' or ''replacement'' or "shoulder prosthesis" AND "1-stage" or "2-stage" or "onestage'' or ''two-stage'' or ''single stage'' or ''resection'' or ''exchange'' or ''explant'' or ''re-implantation'' or ''spacer'' AND English [lang] in PubMed, Scopus, and EMBASE from database inception through July 2019. Inclusion criteria for our systematic review were all English studies (Level I-IV evidence) that reported on single- or 2-stage revision, with eradication of shoulder arthroplasty infection with a minimum follow-up of 12 months and a minimum of 5 patients for analysis. Exclusion criteria for our review were all non-English studies, papers that exclude single- or 2-stage exchange, review papers, case reports, or technique articles without outcome data. Preferred reporting items for systematic review and meta-analysis criteria were applied. 12

Using the systematic review tool, Covidence ([https://www.](https://www.covidence.org) [covidence.org](https://www.covidence.org)), 2 independent investigators (ESB and KW) screened the titles, abstracts, and full-text articles. A third investigator (senior author GEG) adjudicated any conflicts and determined final inclusion. In line with previous systematic review on revision shoulder arthroplasty, data were obtained for demographics (age and gender), time to infection, pathogen, procedure, antibiotics, laboratory values, reinfection or infection eradication rates, functional outcomes, and length of follow-up.

Study quality was assessed with level of evidence (Level I-IV) based on the American Academy of Orthopaedic Surgeons classification system. 22 22 22 The methodological index for nonrandomized studies (MINORS) criteria were scored for each study with 2 independent reviewers. As such, a comparative study has a maximum score of 24, and a noncomparative study has a score of 16.[52](#page-9-5)[,53](#page-9-1) Intraclass correlation coefficient was calculated for the quality assessment.^{[31](#page-9-6)}

Outcomes and infection data were initially analyzed through descriptive analyses. Infections were then calculated per 100 component years. Before meta-analyses, the data were stabilized via a Turkey double arcsine transformation.^{[35](#page-9-7)} The binomial distribution domain data were then analyzed through a random-effects analysis, with Clopper-Pearson 95% confidence intervals $(95\% \text{ CIs})$.^{[60](#page-10-1)} A sensitivity analysis was then performed in which studies with at least 10 patients were included. Studies that reported more than 1 individual cohort were each calculated as individual studies. Heterogeneity was assessed with the Cochrane Q and I^2 , with high heterogeneity designated by a Q P-value <.10 and I2 > 50% ^{[23](#page-9-8)} Data subdivisions were compared between stage 1 and stage 2 using Cochrane's Q test ($P < .05$).^{[48](#page-9-9)} Funnel plots were used to assess the presence of publication bias. All metaanalyses were performed in R version 3.5.1 (R Core Team (2013). R: A language and environment for statistical computing.

Figure 1 Summary of systematic review and meta-analysis.

R Foundation for Statistical Computing, Vienna, Austria. [http://](http://www.r-project.org/) [www.R-project.org/\)](http://www.r-project.org/) using the *meta* package.^{[47](#page-9-10)}

Results

Search strategy

A total of 297 titles and 297 abstracts were initially screened. Eligibility for inclusion was assessed in all 297 abstracts. This resulted in 73 articles for full-text review followed by 36 articles, which met inclusion criteria for systematic review and meta-analysis [\(Fig. 1](#page-2-0)).

Risk of bias

Two independent reviewers assessed a total of 36 nonrandomized studies using the MINORS criteria [\(Table I](#page-3-0)).^{[1-3,](#page-8-7)[5](#page-8-8)[,6](#page-8-9),[10](#page-8-10)[,11,](#page-8-0)[16](#page-8-11),[19-21](#page-9-11)[,23,](#page-9-8)[25](#page-9-12),[27-30](#page-9-13)[,33,](#page-9-14)[34](#page-9-15),[39-42](#page-9-16)[,45,](#page-9-17)[46](#page-9-18)[,49](#page-9-19)[,54-58,](#page-9-20)[61](#page-10-0)} Of these, 8 studies were Level III, 10,39,41,42,45,53,55,56 10,39,41,42,45,53,55,56 10,39,41,42,45,53,55,56 10,39,41,42,45,53,55,56 10,39,41,42,45,53,55,56 10,39,41,42,45,53,55,56 10,39,41,42,45,53,55,56 10,39,41,42,45,53,55,56 10,39,41,42,45,53,55,56 whereas the remaining 28 studies were Level IV[.1-3](#page-8-7)[,5](#page-8-8)[,6](#page-8-9),[11](#page-8-0),[16](#page-8-11),[19-21,](#page-9-11)[23,](#page-9-8)[25,](#page-9-12)[27-30](#page-9-13)[,33](#page-9-14)[,34,](#page-9-15)[40,](#page-9-24)[46,](#page-9-18)[49,](#page-9-19)[54,](#page-9-20)[57,](#page-10-3)[58](#page-10-4),[61](#page-10-0) The median MINORS score for the 8 comparative studies was 16 of $24, \frac{10,39,41,42,45,53,55,56}{1000}$ whereas the median MINORS score for the 28 noncomparative studies was 10 of 16[.1-3,](#page-8-7)[5](#page-8-8)[,6,](#page-8-9)[11,](#page-8-0)[16,](#page-8-11)[19-21,](#page-9-11)[23](#page-9-8)[,25](#page-9-12)[,27-30](#page-9-13)[,33](#page-9-14)[,34](#page-9-15)[,40,](#page-9-24)[43,](#page-9-25)[44](#page-9-26)[,46](#page-9-18)[,48](#page-9-9)[,49,](#page-9-19)[54,](#page-9-20)[57,](#page-10-3)[58,](#page-10-4)[61](#page-10-0) All studies included in this review had a minimum follow-up of 2 years. No studies used a prior sample size calculation. The majority of studies, 32 of 36 (89%), used infection clearance as a stated endpoint, whereas only 2 studies had a less specific endpoint. $16,20$ $16,20$ Overall, there was substantial interrater agreement for the MINORS scoring with an intraclass correlation coefficient of 0.95 (95% CI: 0.83-1).

Demographics

Shoulder periprosthetic infection was managed with singleor 2-stage revision arthroplasty in a total of 652 shoulders. Using our inclusion criteria, 13 studies of single-stage revision and 30 studies of 2-stage revision were used for analysis. Of the included studies, 8 studies reported on outcomes for both single- and 2-stage revision.^{[10](#page-8-10),[39](#page-9-16)[,41,](#page-9-21)[42](#page-9-22),[45](#page-9-17)[,53,](#page-9-1)[55](#page-9-23)[,56](#page-10-2)} For single-stage revision, there were 264 shoulders in 264 patients. Of these, 154 were male (62.6%) and 92 female (37.4%) with an average age of 66.5 years. For 2-stage revision, there were 406 shoulders in 406 patients. Of these, 195 were male (48.0%) and 211 female (52.0%) with an average age of 65.5 years ([Table II](#page-4-0)). Potentially relevant baseline information such as preoperative anatomic shoulder arthroplasty (ASA) classification, body mass index, and medical comorbidities including smoking, diabetes, and heart disease were rarely

Table I Risk of bias

Study (year)	Level of evidence	MINORS criteria
Acherman et al $(2013)^1$	Retrospective case series (IV)	10/16
Assenmacher et al $(2017)^2$	Retrospective case series (IV)	10/16
Beekman et al $(2010)^3$	Retrospective case series (IV)	9/16
Boileau et al $(2013)^5$	Retrospective case series (IV)	10/16
Buchalter et al (2017) ⁶	Retrospective case series (IV)	10/16
Costourus (2017)	Retrospective case series (IV)	10/16
Cuff et al $(2008)^{10}$	Retrospective cohort (III)	16/24
Dodson (2009)	Retrospective case series (IV)	10/16
Friedman et al $(2008)^{16}$	Retrospective case series (IV)	7/16
Fritz $(2019)^{17}$	Retrospective case series (IV)	0/16
Ghijselings et al (2013) ¹⁹	Retrospective case series (IV)	10/16
Goorman (2006)	Retrospective case series (IV)	10/16
Grosso (2012)	Retrospective case series (IV)	10/16
Hsu et al $(2016)^{23}$	Retrospective case series (IV)	11/16
Ince et al $(2005)^{25}$	Retrospective case series (IV)	8/16
Jaquout (2015)	Retrospective case series (IV)	9/16
Jawa et al (2011) ²⁸	Retrospective case series (IV)	10/16
Jerosch and Schneppenheim $(2003)^{29}$	Retrospective case series (IV)	10/16
Lee (2017)	Retrospective case series (IV)	10/16
Merolla et al (2018) ³³	Retrospective case series (IV)	10/16
Middernacht et al $(2014)^{34}$	Retrospective case series (IV)	10/16
Ortmaeir (2014)	Retrospective cohort (III)	16/24
Padegimas (2017)	Retrospective case series (IV)	10/16
Patrick et al $(2019)^{41}$	Retrospective cohort (III)	16/24
Pelligrini (2019)	Retrospective cohort (III)	15/24
Renz (2016) ⁴³	Retrospective case series (IV)	5/16
Romano et al $(2012)^{45}$	Retrospective cohort (III)	14/24
Sabesan et al $(2011)^{46}$	Retrospective case series (IV)	10/16
Sevelda and Fink $(2018)^{49}$	Retrospective case series (IV)	10/16
Sperling et al $(2001)^{54}$	Retrospective cohort (III)	13/24
Stephens et al (2016) ⁵⁵	Retrospective case series (IV)	10/16
Stine (2009)	Retrospective cohort (III)	13/24
Stone (2016)	Retrospective cohort (III)	16/24
Strickland (2016)	Retrospective case series (IV)	10/16
Twiss $(2010)^{59}$	Retrospective case series (IV)	9/16
Weber et al $(2011)^{62}$	Retrospective case series (IV)	9/16

MINORS, methodological index for nonrandomized studies.

reported in the studies reviewed and thus not included in final analysis.

Diagnostic evaluation

Less than 10% of single-stage revision studies and 0% of 2-stage revision studies reported an abnormal white blood cell count (WBC) in their patients. 11 Of the 8 studies that reported both single- and 2-stage revision, only 2 studies reported the erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and aspirations for each group.^{[10](#page-8-10)[,11](#page-8-0)} In addition, of the 5 studies that only report on single-stage revision, 2 studies reported ESR, CRP, and aspirations.^{[19](#page-9-11)[,22](#page-9-4)} In 2-stage revision studies, 5 of the 22 studies reported ESR, CRP, and aspiration outcomes.^{[1,](#page-8-7)[2](#page-8-12)[,6,](#page-8-9)[13](#page-8-2)[,25](#page-9-12)} In total, ESR was more uniformly reported and was found to be abnormal in 63.2% of single-stage revision patients and 60.5% of 2-stage revision patients. CRP was also more widely reported, with an abnormal CRP reported in 74.1% of single-stage revisions, 46.5% of 2-stage, and 55.0% in which the number of stages was not specified. Regarding shoulder aspiration, the identified studies provided minimal detail, which precluded effective grouping and large-scale analysis.

Pathogens

Microbiological data were reported in the majority of studies and are summarized in [Table II.](#page-4-0) In the single-stage studies, the most common organism was C acnes with 113

C acnes, Cutibacterium acnes; CoNS, Coagulase-negative staphylococcus; MSSA, methicillin-sensitive Staphylococcus aureus; MRSA, methicillin-resistant Staphylococcus aureus; GNR, gram-negative rods.

of 232 (48.7%) reported cases. This was followed in frequency by CoNS, which represented 54 of 232 (23.2%) of all identified organisms. Methicillin-sensitive S aureus was more commonly reported than methicillin-resistant S aureus (MRSA) with 26 of 232 (11.2%) and 6 of 232 (2.6%) reported cases, respectively. In the 2-stage revision groups, the most common organism was also C acnes with 190 of 566 (33.7%) reported cases, followed by CoNS with 115 of 556 (20.3%) cases. Methicillin-sensitive S aureus was reported in 95 of 566 (16.8%) cases, whereas MRSA was found in 55 of 566 (9.7%) cases. In both singlestage and 2-stage, at least 2 organisms (poly-microbial) were identified with 24 of 232 (10.3%) and 31 of 566 (5.5%) cases, respectively ([Table II\)](#page-4-0). American Shoulder and Elbow Score (ASES), Simple Shoulder Test (SST), and Disabilities of Arm, Shoulder and Hand (DASH).

Outcomes

For all shoulder revision related to periprosthetic infection treated with either single- or 2-stage revision arthroplasty, the reported reinfection rate was 8.9%. On examining each group, the overall reinfection rate was 6.3% for single-stage studies and 10.1% for 2-stage revision studies ([Table III](#page-4-1)). The overall pooled random-effect reinfection incidence was 0.05 (95% CI: 0.02-0.08), and heterogeneity was moderate to high with $\tau^2 = 0.001$, $I^2 = 33.9\%$ (95% CI: 4.2-54.4), P $= .02$. In subgroup analysis, pooled single-stage reinfection incidence was 0.02 (95% CI: 0.0004-0.07) with low heterogeneity (Q) = 12.4, $\tau^2 = 0.001$, $I^2 = 3.8\%$. For 2-stage revision, the pooled reinfection incidence was 0.05 (95% CI: 0.02-0.1) with heterogeneity (Q) = 51.5, $\tau^2 = 0.01$, I² $= 41.8\%$ [\(Figs. 2](#page-5-0) and [3](#page-6-0)). There was no significant difference between single- and 2-stage reinfection with $Q = 0.9$ and $P = .4$. A sensitivity analysis was performed in which

only studies with at least 10 patients were included. The combined pooled random effect for studies with at least 10 patients was 0.06 (95% CI: 0.03-0.1), and heterogeneity was moderate to high with $\tau^2 = 0.02$, $I^2 = 52.8\%$ (95% CI: 25.6-70.1), $P = .001$. In subgroup analysis for single-stage sensitivity analysis for studies with at least 10 patients, the k proportion was 0.04 (95% CI: 0.01-0.09) with low heterogeneity (Q) = 6.5, $\tau^2 = 0$, I² = 0%. For 2-stage revision, the k proportion was 0.06 (95% CI: 0.02-0.1) with hetero-geneity (Q) = 4[3](#page-6-0).8, $\tau^2 = 0.01$, $I^2 = 63.5\%$ [\(Figs. 2](#page-5-0) and 3). Heterogeneity was increased from moderate to high for the 2-stage group, whereas overall heterogeneity was still small for the 1-stage group. No publication bias was detected (Supplementary Appendix S1).

Functional outcome evaluations of single-stage and 2 stage were inconsistent. Using frequency-weighted mean, the Constant score, forward flexion, abduction, and external rotation were summarized, as shown in [Table IV.](#page-6-1) Neer, ASES, SST, and DASH scores were reported with low fidelity and not included in final analysis. For single-stage revision, the average Constant score was 52.9 compared with 51.8 for 2-stage revision. In addition, there was inconsistency with range of motion data in both singlestage and 2-stage revision. Forward flexion was an average of 81.9 \degree for single-stage revision and 96.5 \degree for 2stage revision. Abduction and external rotation was higher for 2-stage (66.3 $^{\circ}$ and 27.5 $^{\circ}$, respectively) compared with single-stage $(62.2^{\circ}$ and 25.4° , respectively).

Complications related to revision arthroplasty were most frequently caused by hematoma, perioperative fracture, instability, or nerve injury. There was inconsistent reporting from all studies with specific and limited meta-analysis for each type of complication. When comparing interventions, single-stage revision had 9 of 79 (11.4%) cases with complications and 2-stage revision had 58 of 258 (22.5%) cases reporting at least 1 complication.

Discussion

Infection after shoulder arthroplasty is a rare, but potentially debilitating complication, with an incidence in the literature of up to 3.8% in primary cases and over 15% in revision cases.^{[7,](#page-8-3)[14](#page-8-14)} It is the main cause of revision within the first few years postoperatively.^{[7-11](#page-8-10)} With shoulder arthroplasty expected to rise in demand over the next decade, and a consensus diagnostic definition for shoulder PJI, working toward a consensus management algorithm for shoulder

Figure 2 Full meta-analysis for shoulder periprosthetic joint infection. CI, confidence interval.

periprosthetic infection is increasingly relevant and important.[3](#page-8-13),[12](#page-8-6)[,17](#page-8-5) The British Elbow and Shoulder Society created an evidence-based algorithm ([Fig. 4](#page-7-0)), but they highlight a limitation of their recommendation noting limited evidence of comparative analyses between 1-stage and 2-stage revision.^{[43](#page-9-25)} In 2016, George et al^{[18](#page-9-30)} and Nelson et al^{38} al^{38} al^{38} each conducted systematic reviews that found comparable outcomes for infection eradication and functional outcomes between multiple treatment modalities including resection or arthrodesis, I&D with implant

Study	Events Total		Proportion	95%-CI Weight			
Type = Stage One							
Cuff et al. 2008	0	$10 -$		0.00 [0.00; 0.31]	3.0%		
Beekman et al. 2010	1	11		0.09 $[0.00; 0.41]$	3.2%		
Grosso et al. 2012	1	17		0.06 $[0.00; 0.29]$	4.0%		
Middemacht et al. 2014	2	19		0.11 [0.01; 0.33]	4.2%		
Hsu et al. 2016	0	$27 -$		0.00 $[0.00; 0.13]$	4.9%		
Stephens et al. 2016	1	13		0.08 [0.00; 0.36]	3.5%		
Stone et al. 2016	2	40		0.05 [0.01; 0.17]	5.5%		
Sevelda et al. 2018	$\overline{2}$	14		0.14 [0.02; 0.43]	3.6%		
Random effects model		151		0.04 $[0.01; 0.09]$	32.0%		
Heterogeneity: $l^2 = 0\%$, $\tau^2 = 0$, $p = 0.49$							
$Type = Stage Two$							
Goorman et al. 2006	0	$20 -$		0.00 [0.00; 0.17]	4.3%		
Cuff et al. 2008	0	$12 -$		0.00 $[0.00; 0.26]$	3.3%		
Friedman et al. 2008	1	11		0.09 [0.00; 0.41]	3.2%		
Stine et al. 2009	0	$12 -$		0.00 $[0.00; 0.26]$	3.3%		
Pellegrini et al. 2010	0	$11 -$		0.00 $[0.00; 0.28]$	3.2%		
Twiss et al. 2010	0	$20 -$		0.00 [0.00; 0.17]	4.3%		
Jawa et al. 2011	3	16		0.19 $[0.04; 0.46]$	3.9%		
Sabesan et al. 2011	1	17		0.06 [0.00; 0.29]	4.0%		
Romano et al. 2012	0	$17 -$		0.00 $[0.00; 0.20]$	4.0%		
Jaquout et al. 2015	5	14		0.36 $[0.13; 0.65]$	3.6%		
Renz et al. 2016	2	17		0.12 [0.01; 0.36]	4.0%		
Strickland et al. 2016	7	19		0.37 [0.16; 0.62]	4.2%		
Assenmacher et al. 2017	5	35		0.14 [0.05; 0.30]	5.3%		
Buchalter et al. 2017	5	19		0.26 [0.09; 0.51]	4.2%		
Lee et al. 2017	0	$12 -$		0.00 $[0.00; 0.26]$	3.3%		
Padegimas et al. 2017	0	$27 -$		0.00 $[0.00; 0.13]$	4.9%		
Patrick et al. 2019	$\overline{2}$	27		0.07 [0.01; 0.24]	4.9%		
Random effects model		306		0.06 [0.02; 0.13]	68.0%		
Heterogeneity: $l^2 = 63\%$, $\tau^2 = 0.0236$, $p < 0.01$							
Random effects model		457 ◇					
0.06 [0.03; 0.10] 100.0% Heterogeneity: l^2 = 53%, τ^2 = 0.0150, $p < 0.01$							
Residual heterogeneity: $l^2 = 54\%$, $p < 0.01$ 0 0.2 0.3 0.4 0.1 $0.5\quad 0.6$							

Figure 3 Sensitivity analysis with studies with at least 10 patients. CI, confidence interval.

retention, antibiotic spacer, and single-stage or 2-stage revision arthroplasty with approximately 30 studies in total. Since that time, there has been an increase in literature for shoulder periprosthetic infection, and thus our study has 30 studies evaluating 2-stage revision and 13 studies evaluating single-stage revision. The aim of this systematic review and meta-analysis was to provide insight into the strengths and weaknesses of the current landscape for management of shoulder PJI and compare outcomes specifically between 1-stage and 2-stage revision arthroplasty. In addition to the breadth of review, this study has included a quality assessment for risk of bias and performed meta-analysis, which has not previously been achieved on this topic.

One of many controversial and challenging features of managing shoulder arthroplasty infection is the limitation in diagnostic abilities—both with regard to timeliness and definitiveness. An accurate diagnosis is critical for determining the surgical indications for patients with possible infection, and ideally this decision can be made pre- or intraoperatively before decision regarding removal and/or reinsertion of components are made by the surgeon. 32 An incomplete or inaccurate evaluation can lead to either a missed diagnosis or overdiagnosis, both of which can have significant morbidity for patients. The frequently cited standard workup for suspected shoulder arthroplasty infection is plain film views of the shoulder and a series of inflammatory and infectious labs, including WBC, ESR, CRP, and an aspirate of the joint in question to send for cell

Figure 4 British Elbow and Shoulder Society periprosthetic joint infection management algorithm. CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; DAIR, Debridement, Antibiotics and Implant Retention.

count, culture, and crystals.^{[17](#page-8-5),[43](#page-9-25)} Even with this workup, the results are often unreliable based on low sensitivities of the inflammatory markers in the shoulder and the high false-negative rates in aspiration.^{[58](#page-10-4)} Dodson et al^{[11](#page-8-0)} demonstrated similar challenges in diagnostic evaluation for shoulder PJI. In their series of shoulder PJI case, the mean ESR was 33 mm/h and CRP 2 mg/dL. 11 11 11 Coste et al^{[8](#page-8-4)} demonstrated that preoperative aspiration only correlated with positive intraoperative cultures in 50% of shoulder PJI cases. This weakness in diagnostic evaluation has led to newer studies such as alpha-defensin being proposed for the standard workup of shoulder PJI.^{62,[63](#page-10-7)} In addition, with C acnes being a common organism in shoulder PJI, cultures may be initially negative for over 5 days. As such, cultures for shoulder PJI should be observed for a minimum of 7 days.^{[11](#page-8-0),[36](#page-9-0)} Further complicating the issue is the lack of detailed diagnostic evaluation that is reported in the current literature. In the studies identified for this review, only a small number reported their diagnostic values with enough detail to allow proper aggregation and higher-level statistical analysis to draw concrete conclusions. This lack of a diagnostic definition has been a major limitation in the current literature and is a key area of improvement for future studies as the ICM consensus definition is incorporated into both diagnostic evaluation and research reporting.[15](#page-8-15)[,50,](#page-9-33)[52](#page-9-5)[,59](#page-10-5)

There are underwhelming data with patient-reported outcomes and functional outcomes to support single-stage over 2-stage revision. The postoperative range of motion measurements was greater for 2-stage revision in forward flexion, external rotation, and abduction, but the differences are minimal enough to question the clinical significance of this finding. Although the functional outcomes for singleand 2-stage revision may be similar, they are far inferior to functional outcomes after primary shoulder arthroplasty.^{[36](#page-9-0)} The most compelling outcome measure found in this analysis is the infection eradication rates. The single-stage approach appears to have a lower rate of reinfection when compared with 2-stage revision (6.3% vs. 10.1%). However, after meta-analysis with a random-effects model, this difference was not found to be significant with moderate heterogeneity in the data ($Q = 0.9$, $P = .4$). This limitation is due to a greater number of studies reporting 2-stage revision, significant heterogeneity with each subgroup, and likely reporting bias that favors reporting smaller infection rates.[26](#page-9-34) In addition, a weakness of the current literature exists with a majority of studies reporting 12-month success rates for infection eradication. Future studies may be directed to compare the long-term success of single- or 2 stage revision in shoulder PJI for infection eradication and alternative techniques to measure overall infection eradication, as this has not yet been reported.

These overall findings suggest 1-stage to be as effective as 2-stage in a select group of patients to reduce the need for additional surgery, costs, and risk for patients. However, there must be caution interpreting these findings, as there is inherent selection bias with regard to patient-specific factors that guide treatment including timing of infection, severity of infection, perioperative clinical findings, and long-term infection clearance. For reference, the 1-stage group had a higher percentage of C acnes (48.7% vs. 33.6%) and acute or subacute infections (63% vs. 46.1%), and the 2-stage group had a higher percentage of virulent infections (MRSA) (10% vs. 2.6%) and chronic infections (53.9% vs. 37%). This likely represents a significant selection bias by the treating surgeons and highlights the significant limitation of the interpretation from such meta-analysis data but lays the foundation for future prospective studies that control for such variables and eliminate this selection bias. Specifically, future observational studies should include rigorous diagnostic parameters such as those described by ICM for shoulder PJI with the presence of sinus tract, drainage, ESR, CRP,WBC, aspiration data, culture data, and potential use of newer serum or synovial diagnostic tools.

Conclusion

Based on a systematic review with meta-analysis, singlestage revision for shoulder PJI is an effective treatment. Indeed, our analysis showed single-stage to be more effective than 2-stage, but this is likely confounded by a treatment bias given the higher propensity of virulent and drug-resistant bacteria treated with 2-stage in the published literature. This implies that shoulder surgeons treating PJI can be reassured of a low recurrence rate (6.3%) when using single-stage treatment for C *acnes* or other sensitive, low-virulence organisms. Future studies should aim to control for patient-specific variables and diagnostic features to create an evidence-based algorithm to guide the treatment of shoulder PJI.

Disclaimer

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Supplementary Data

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