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Outcomes of revision arthroplasty for shoulder periprosthetic joint infection: a three-stage revision protocol

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Background: This study evaluated outcomes after treatment of shoulder periprosthetic joint infection (PJI) with a 3-stage revision protocol consisting of (1) débridement, explantation, and cement spacer placement, followed by parenteral antibiotics; (2) open biopsy and débridement; and (3) reimplantation if cultures were negative. We hypothesized this protocol would eradicate persistent infection while producing excellent functional and subjective outcomes, and there would be no difference in these parameters for patients with shoulder PJI compared with patients with revision for aseptic indications.
Methods: We retrospectively analyzed a prospectively collected revision shoulder arthroplasty cohort to identify shoulder PJI patients treated with a 3-stage protocol. Demographics, culture data, range of motion, and patient-reported outcomes were collected. Outcomes for patients with shoulder PJI and revision to RTSA were compared with patients revised to RTSA for noninfectious indications. Significance was defined as $P < .05$.
Results: There were 28 cases of shoulder PJI in 27 patients (age, 66.4 ± 11.2 years,); of these, 21 shoulders were revised to RTSA, and 7 shoulders were revised to hemiarthroplasty. There was no recurrent infection at a mean 32-month follow-up. One year after surgery, mean forward flexion was 110° ± 41° and abduction was 106° ± 42°. Mean final American Shoulder and Elbow Surgeons subjective score was 66.5 ± 23.3. The 21 shoulders with PJI revised to RTSA had no differences for functional and subjective outcomes compared with revised patients without shoulder PJI.
Conclusions: A 3-stage revision protocol for shoulder PJI reliably eradicated infection. Patients with PJI revised to RTSA can have similar outcomes as patients with noninfectious revision to RTSA.
Levels of evidence: Level III; Retrospective Cohort Design; Treatment Study

Keywords: Shoulder periprosthetic infection; three-stage protocol; reverse total shoulder arthroplasty; functional outcome; patient-reported outcome; visual analog scale

The University of California San Francisco Committee on Human Research approved this study (IRB number: 10-02764).

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Shoulder arthroplasty allows for the treatment of pain and restoration of function for numerous shoulder conditions.[21,30] With increasing use of shoulder arthroplasty, the prevalence of shoulder periprosthetic joint infection (PJI) has

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increased as well.[26] The overall rate of shoulder PJI is estimated to be approximately 1% in primary shoulder arthroplasty and up to 15% in revision shoulder arthroplasty.[24] The costs of 2-staged revision surgery for shoulder PJI are approximately 2-times higher than primary shoulder arthroplasty surgery.[2]

There is no clearly accepted treatment protocol for shoulder PJI that reliably eradicates infection and restores symptom-free function.[14] Treatment with antibiotics alone has an unacceptably low success rate.[23] Surgical options include irrigation and débridement without prosthesis exchange, single-stage revision, multistage revision, or permanent spacer insertion. Dennison et al[11] reported a 30% complication rate when treated with irrigation and débridement only. Although some studies report successful treatment with a single-stage revision,[16,20] this protocol often requires long-term suppressive antibiotics, limiting the utility of this treatment for most patients.[22] With 2-stage revision, the gold standard treatment for knee and hip PJI, the functional results for shoulder PJI are suboptimal, and the reinfection rate is more than 36%.[6,27,31] Permanent cement spacer or prosthesis of antibiotic loaded acyclic cement placement has even been suggested as a possible definitive treatment, but functional results with these treatments are poor.[14,17]

Zhang et al[33] reported a series of 18 patients with deep shoulder infection treated by a 3-stage revision protocol that included open biopsy to ensure infection eradication before reimplantation. They detected a 22% rate of persistent infection at time of open biopsy that was treated with repeat irrigation and débridement. No recurrent infections were found under this revision protocol in patients with a wide array of conditions, including osteomyelitis, infection after proximal humeral fracture fixation, and shoulder PJI.[33] However, the outcomes for patients with shoulder PJI who are treated with this protocol remain unknown, especially compared with revision arthroplasty for noninfectious reasons.

For this study, we had 2 goals: (1) to report the functional and subjective outcomes of the 3-stage revision protocol for patients with shoulder PJI and (2) to compare outcomes for patients with shoulder PJI and definitive implantation of RTSA with those of patients with noninfected failed shoulder arthroplasty revised to RTSA. We hypothesized that the 3-stage protocol would eradicate persistent infection after definitive implantation while producing excellent functional and subjective outcomes. We also hypothesized that there would be no difference in final outcomes between shoulder PJI patients revised to RTSA and noninfected patients undergoing revision RTSA.

Materials and methods

Patient cohort identification

We retrospectively analyzed a prospectively collected database to identify all patients with shoulder PJI who were treated by 3 fellowship-trained surgeons (C.B.M., B.T.F., and A.L.Z.) at a single tertiary referral center from 2004 to 2016. We implemented the 3-stage revision protocol in 2004 and treated all patients with infected arthroplasties with this treatment protocol. All patients provided informed consent to participate. Inclusion criteria were a diagnosis of shoulder PJI and treatment with the 3-stage revision protocol (Fig. 1). Patients were excluded if follow-up was less than 1 year. Revision cases without a history of shoulder PJI were identified for the noninfected cohort. Patients were included if revised to RTSA and were excluded if follow-up was less than 1 year.

Demographic data were collected, including age, sex, body mass index, medical history, and self-reported smoking history. The age-adjusted Charlson Comorbidity Index was calculated from the patient's medical history.[8]

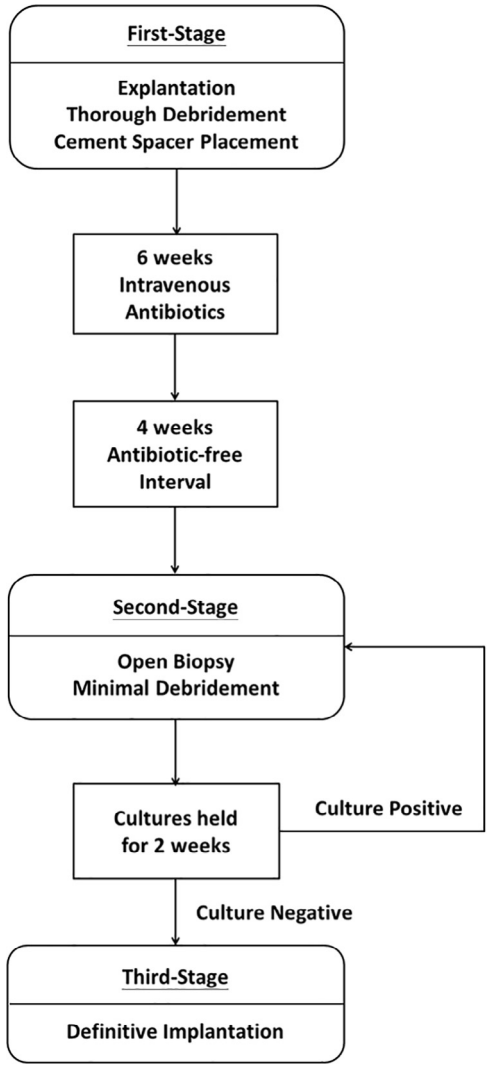

Figure 1 Flow chart shows the components of our 3-stage revision protocol for managing shoulder periprosthetic joint infection.

Diagnosis of shoulder PJI

All of the diagnosed shoulder PJIs met the definition proposed by Musculoskeletal Infection Society (MSIS) for the lower extremity, including sinus tract communicating with the prosthesis, pathogen

isolated by culture from 2 separated tissue samples, or the constellation of clinical symptoms, purulence of the joint, laboratory data (peripheral white blood cell counts, erythrocyte sedimentation rate [ESR], C-reactive protection [CRP]), and more than 5 neutrophils per high-power field in 5 high-power fields detected from histologic analysis of periprosthetic tissue at original magnification ×400.[25] The interval between the index surgery and infection was categorized according to Sperling et al,[29] with an acute infection within 3 months of the index surgery, subacute infection within 3 to 12 months, and chronic infection after more than 12 months.

Three-stage revision protocol

Shoulder PJI patients were treated with a 3-stage revision protocol (Fig. 1). First, the patient underwent prosthesis explantation and a thorough débridement, which included excision of the rotator cuff. An ultrasonic cement removal device was used to remove any residual cement mantle, if present. Three to 5 sets of cultures were taken from superficial tissue, deep tissue, and bone edges. Cultures were incubated in an aerobic and anaerobic environment and held for at least 14 days. An antibiotic-loaded (1 g vancomycin with 1.2 g tobramycin per bag of cement) cement spacer was fashioned by hand then implanted to maintain soft tissue tension and provide local infection treatment. Culture-specific intravenous antibiotics were prescribed for 6 weeks in consultation with our institution's infectious disease service, followed by a 4-week antibiotic-free interval.

For the second stage, patients underwent an open biopsy and limited débridement with cultures held for at least 14 days. A limited deltopectoral approach was used through the previous incision, and dissection was carried down to the bone-cement junction at the medial aspect of the proximal humerus. Three to 5 cultures were obtained from deep tissue and proximal humerus. If there was frank purulence or positive cultures during the second stage, an additional débridement was performed after another course of parenteral antibiotic therapy.

The final stage reimplantation was performed if there was no clinical concern for recurrent infection and open biopsy cultures remained negative. All patients in the infected group and aseptic revision group underwent definitive implantation with components from the same implant system (Zimmer Biomet, Warsaw, IN, USA), including a cemented humeral stem in all cases, and trabecular metal-backed baseplate with a central peg and 2 peripheral screws for the glenoid component.

Postoperative regimen

A standardized rehabilitation protocol was followed for all patients. In the first and second stages of the protocol for infected shoulders, patients were placed in an abduction sling for immobilization with passive range of motion only. After definitive RTSA implantation, the shoulder was immobilized for 6 weeks in an abduction sling. Formal physical therapy started after 6 weeks with passive and active range of motion. Strengthening started at 12 weeks, and patients were released to all activities after 5 months. For the hemiarthroplasty patients, the passive range of motion started once tolerated. Active range of motion started at 6 weeks, and strengthening exercise began at 12 weeks. Full activity was allowed after 5 months.

Outcome measures

Range of motion was measured with a goniometer at the 1-year follow-up visit and included forward elevation, abduction, external rotation, and internal rotation. Patient-reported outcome scores, including visual analog scale (VAS) pain scores and American Shoulder and Elbow Surgeons (ASES) subjective scores, were reported at 1 year postoperatively and at the final follow-up.

Statistical analysis

Descriptive statistics were calculated for demographic variables, range of motion measurements, and patient-reported outcomes. Demographic variables, 1-year range of motion measurements, and final VAS pain and ASES subjective scores were compared between shoulder PJI patients revised to RTSA and patients who underwent revision RTSA for noninfectious indications. Comparisons were performed with unpaired *t* tests, χ^2, and Fisher exact tests. All analyses were performed with SPSS 19.0 software (IBM, Armonk, NY, USA). Significance was defined as $P < .05$.

Results

PJI was diagnosed in 33 patients (34 shoulders) who were treated with the 3-stage revision protocol. Six patients were excluded due to inadequate follow-up (4 patients had <1 year of follow-up, and 2 patients died without adequate follow-up), leaving 27 patients with 28 (84.8%) infected shoulders included with a minimum 1-year follow-up. There were 20 patients with 21 shoulders that were revised to RTSA. A hemiarthroplasty was the definitive implant for 7 patients from the shoulder PJI group, and hemiarthroplasty was chosen due to concerns for poor glenoid bone stock. Four patients in the group revised to RTSA needed an extended humeral osteotomy to extract the original prosthesis, but there were no complications with these osteotomies. Mean follow-up for the cohort was 32.3 ± 18.9 months.

The mean age for the infected cohort was 66.4 ± 11.2 years, and 57.1% were men (Table I). The mean body mass index was 29.6 ± 5.1 kg/m^2, and the average Charlson Comorbidity Index was 4.00 ± 1.79. There were 4 acute infections, 7 subacute infections, and 17 chronic infections. The mean peripheral white blood cell counts were $7.50 \pm 1.70 \times 10^3$/μL, ESR was 44.5 ± 22.4 mm/h, and CRP was 28.2 ± 35.5 mg/L. The causative organism reported in the infected cohort was most commonly mixed *Staphylococcus epidermis* and *Cutibacterium* (formerly *Propionibacterium*) *acnes* (25.0%) or isolated *S epidermis* (25.0%). Culture results were negative for 7 patients (25.0%). Complications occurred in 4 patients (14.3%). Wound dehiscence after hemiarthroplasty in 1 patient was treated with resection arthroplasty. Dislocations occurred in 3 patients (10.7%) after RTSA. Two were managed successfully with open reduction and liner exchange. The third patient had recurrent dislocation after a liner exchange and was successfully managed with baseplate revision, lateralized glenosphere, and liner exchange. These

Table I Demographic and laboratory data for the overall infected cohort

Variable	Infected cohort (n = 27)
Affected shoulders, No.	28
Age, yr	66.4 ± 11.2
Male sex, %	59.3 (16)
Body mass index, kg/m^2	29.6 ± 5.1
Charlson Comorbidity Index	4.00 ± 1.79
Smoking, %	51.9 (14)
Follow-up, mo	32.3 ± 18.9
Laboratory data	
Peripheral WBC counts, 10^3/μL	7.50 ± 1.70
ESR, mm/h	44.5 ± 22.4
C-reactive protein, mg/L	28.2 ± 35.5
Timing of infection	
Acute (<3 months)	4 (14.3)
Subacute (3-12 months)	7 (25.0)
Chronic (>12 months)	17 (60.7)
Causative organism	
S epidermis and *C acnes*	7 (25.0)
S epidermis	7 (25.0)
C acnes	5 (17.8)
P avidum and *S epidermis*	1 (3.6)
Pseudomonas aeruginosa	1 (3.6)
No organism isolated	7 (25.0)

WBC, white blood cell; *ESR*, erythrocyte sedimentation rate; *S epidermis*, Staphylococcus epidermis; *C acnes*, Cutibacterium acnes; *P avidum*, Propionibacterium avidum.
Continuous data are presented as the mean ± standard deviation and categoric data as number (%) or as indicated.

patients' replacements were stable at recent 1.5-, 3-, and 5-year follow-up separately.

Overall range of motion for infected cohort showed forward flexion of 110° ± 41°, abduction of 106° ± 42°, external rotation of 26° ± 26°, and internal rotation to L4 at the 1-year follow-up. The ASES subjective score was 65.9 ± 23.8, and VAS pain score was 2.08 ± 2.37 at the 1-year follow-up. At the final follow-up, the ASES subjective score was 66.5 ± 23.3, and the VAS pain score was 1.95 ± 2.01.

Cultures were positive for 6 patients (21.4%) at the second stage with open biopsy, and they underwent additional débridement and open biopsy procedures. Three had isolated *C acnes* infection and the other three had mixed *S epidermis* and *C acnes* infections, which had the same organism as their first stage culture results. All had negative cultures after 1 additional open biopsy and underwent final implantation. There were no patients with recurrent infection as documented by normalized laboratory values and symptom-free clinical presentation after definitive implantation at the most recent follow-up.

A cohort of 27 patients (mean follow-up, 37.8 ± 22.6 months) with revision arthroplasty to RTSA and no history of shoulder PJI was used as a noninfected comparison group. Revision indications included rotator cuff insufficiency with prosthesis instability (70.4%), implant loosening (25.9%), and greater tuberosity nonunion (3.7%). There were no significant differences in demographics between the shoulder PJI and noninfected cohorts (Table II). There were no differences between infected and noninfected revisions in range of motion for forward flexion (121° ± 33° vs. 129° ± 30°, $P = .364$), abduction (117° ± 41° vs. 115° ± 36°, $P = .902$), external rotation (29° ± 27° vs. 35° ± 21°, $P = .427$; Fig. 2), or internal rotation (L4 vs. L2, $P = .238$). There were no statistically significant differences for VAS pain score (1.71 ± 1.76 vs. 1.33 ± 1.72, $P = .53$) (Fig. 3, *A*), 1-year ASES subjective score (68.6 ± 22.5 vs. 65.1 ± 24.6, $P = .628$), or ASES subjective score at the final follow-up (71.4 ± 22.7 vs. 74.3 ± 14.0, $P = .662$; Fig. 3, *B*).

Discussion

We have reported the outcomes of a 3-stage revision protocol for shoulder PJI. Our comparison of final revision to RTSA for patients with or without a history of shoulder PJI found no differences in range of motion, VAS pain scores, or ASES subjective scores. With this 3-stage revision protocol, no patients had recurrent infections after definitive implantation.

The key to successful management of shoulder PJI involves eradication of the infection while maintaining function. The gold standard for PJI in hip and knee arthroplasty is a 2-stage procedure.[10] In the shoulder, prior results have been discouraging for 1-stage and 2-stage revision procedures. Beekman et al[3] reported 1-stage revision results for shoulder PJI patients with Constant scores that only increased from 45 points before surgery to 55 points at the final follow-up visit.

Cuff et al[9] compared outcomes for 10 shoulders revised to RTSA with single-stage exchange and 12 shoulders with a second-stage revision. There were no differences between the 1-stage and 2-stage surgery outcomes. Both groups, however, showed limited abduction (76°), forward flexion (80°), and external rotation (25°) at the final follow-up. The mean ASES subjective score was 57.0 and VAS pain score was 3.5. In addition, the rate of reinfection, even after a 2-stage exchange, is as high as 36.8%.[31] These prior reports show that shoulder PJI is a challenging entity and that 1-stage and 2-stage procedures may not reliably provide an infection-free and functional shoulder.

Based on the risk of persistent infection and the unique pathogenic organisms present in shoulder PJI, we introduced an interim stage between the initial explantation and definitive implantation. Aspiration for synovial fluid analysis has a high false-negative rate and may not be effective in diagnosing persistent periprosthetic shoulder infection.[32] Arthroscopic biopsy could be considered an option to collect tissue sample. Dilisio et al[12] reported a positive culture rate of 47% when this procedure was performed. However, harvesting an adequate tissue sample arthroscopically with the cement spacer in place and without a normal capsular space

Table II Demographic comparisons for revision to reverse total shoulder arthroplasty for patients with and without a history of shoulder periprosthetic joint infection

Variable	Infected cohort	Noninfected cohort	*P* value
Affected shoulders, No.	21	27	
Age, yr	67.4 ± 10.0	64.3 ± 10.8	.326
Male sex, %	66.7	55.6	.435
Body mass index, kg/m^2	29.8 ± 4.6	27.5 ± 6.4	.172
Charlson Comorbidity Index	4.24 ± 1.61	3.48 ± 1.50	.100
Smoking history, %	38.1	44.4	.658
Follow-up time, mo	34.9 ± 20.4	37.8 ± 22.6	.604

Continuous data are presented as the mean ± standard deviation and categoric data as indicated.

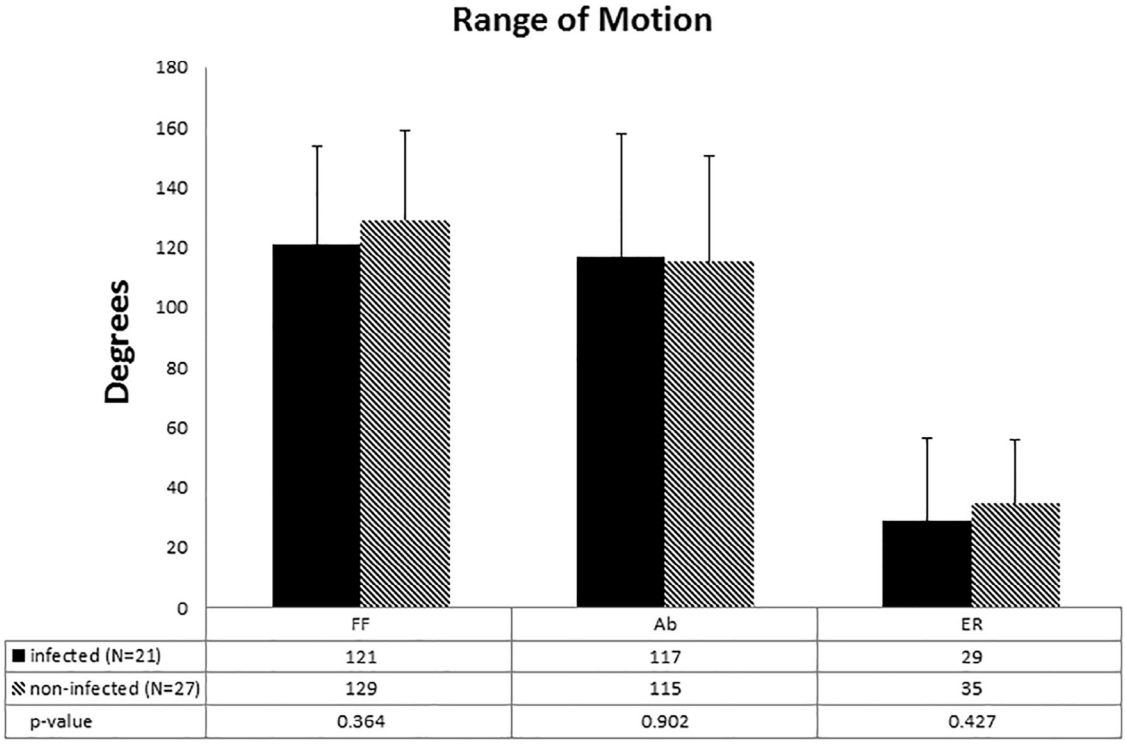

Figure 2 Active range of motion comparison for patients undergoing revision to reverse total shoulder arthroplasty with and without a history of shoulder periprosthetic joint infection. No significant differences were observed for forward flexion (*FF*), abduction (*Ab*), or external rotation (*ER*) for infected and noninfected revision cohorts. Mean data are presented with the standard deviation (*range bars*).

may be difficult. Also, some patients can have proximal humeral and glenoid bone loss, and getting to the bone and soft tissue interface for biopsy can be difficult with the arthroscopic approach.

The second-stage, which is an open biopsy and minimal débridement through the prior deltopectoral incision, may mitigate these shortcomings of an aspiration or arthroscopic biopsy. This stage is performed after a 4-week antibiotic holiday and is used to increase detection of persistent infection before reimplantation. In this series, we detected 6 patients (21.4%) with persistent infection at open biopsy, similar to the rate reported by Zhang et al.[33] These 6 patients in our series had *C acnes* infections. *C acnes*, a slow-growing microorganism, is unique to shoulder PJI and is especially difficult to eradicate.[15] Despite appropriate treatment with antibiotics and normalization of laboratory values, these patients had incomplete eradication and would have undergone reimplantation with positive cultures without this 3-stage protocol. The significance of positive cultures in shoulder surgery remains debatable; however, we believe that treating these cases as persistent infection allowed for the observed improvement in this cohort relative to prior reports.[18]

One concern of multiple-stage revision is soft tissue compromise, which may influence future functional outcomes. The comparison between 3-stage revision to RTSA and noninfected revision to RTSA revealed no significant differences in range of motion or subjective outcome scores. Our results compared favorably to prior reports of revision reverse

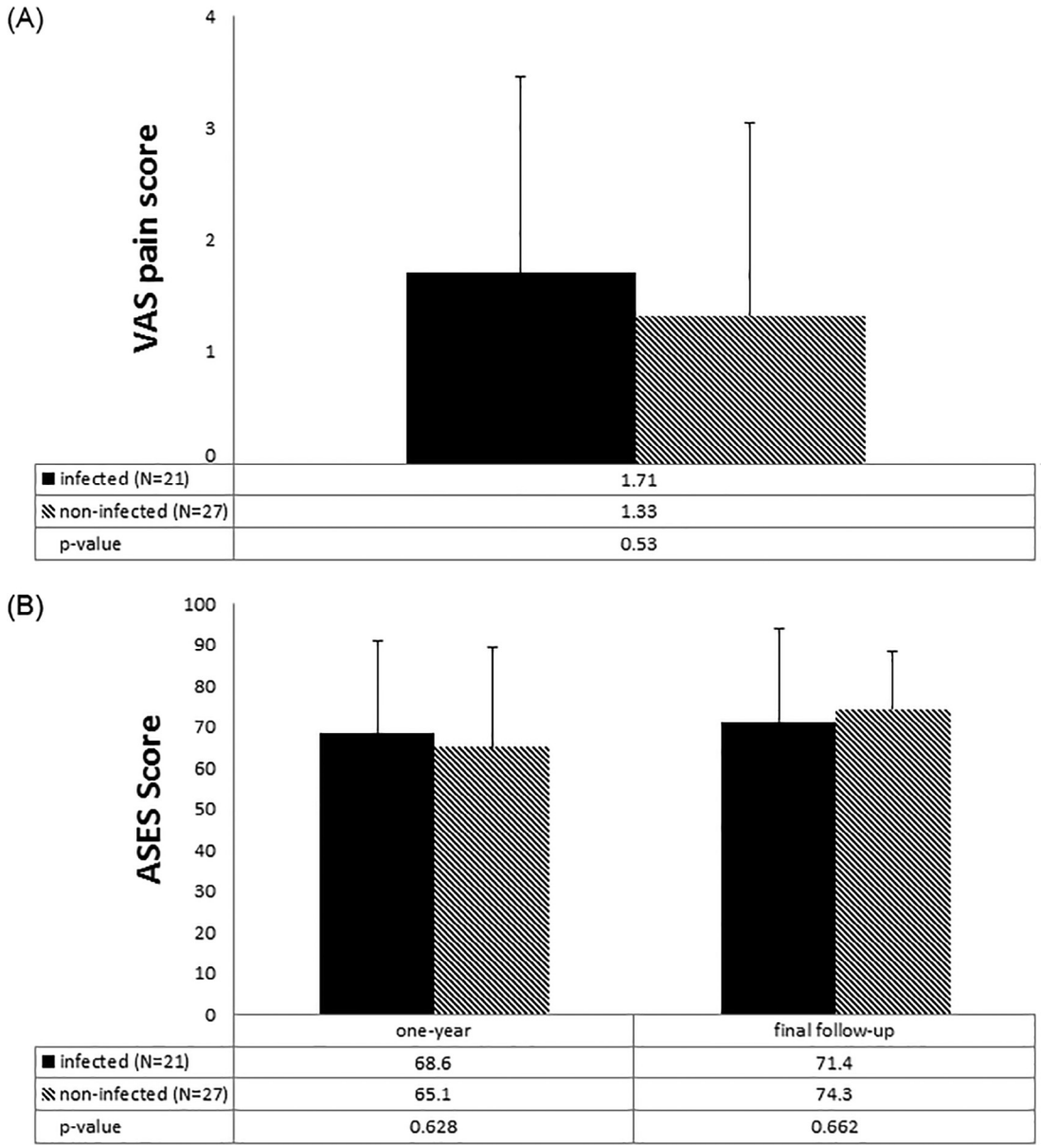

Figure 3 Patient-reported outcomes comparison for patients undergoing revision to reverse total shoulder arthroplasty, with and without a history of shoulder periprosthetic joint infection, for (**A**) visual analog scale (*VAS*) pain scores and (**B**) American Shoulder and Elbow Surgeons (ASES) subjective scores. There were no significant differences between the groups for either of the patient-reported outcome scores. Mean data are presented with the standard deviation (*range bars*).

arthroplasty. Boileau et al[4] reported mean forward elevation of 111° in a series of 37 patients who underwent revision to reverse arthroplasty with final Constant score of 47 points. Kelly et al[19] similarly reported forward flexion of 106°, abduction at 98°, and final ASES subjective score of 72 at 2 years after RTSA in 40 shoulders.

These results are similar to our results for infected and noninfected patients. There were, however, 3 dislocations (10.7%) in the shoulder PJI group after definitive RTSA implantation. The dislocation rate of revision shoulder arthroplasty after infection is high. Two studies, by Romano et al[27] and Sabesan et al,[28] reported 5 of 17 patients in their cohorts had complications of prosthesis dislocation in their 2-stage reimplantation series. The higher dislocation rate may be due to soft tissue débridement related to eradicating the infection.

The diagnosis of shoulder PJI remains a challenge.[7] No single criteria can be accepted to definitely diagnose shoulder PJI. Systemic laboratory tests, such as ESR and CRP, have been used to help with diagnosis of PJI, although they are nonspecific, can be elevated for a variety of reasons, and may also remain low or normal in the setting of an indolent infection. They should be interpreted in context with clinical symptoms and physical examination findings.[5] We adopted

the criteria set up by MSIS, which is the consensus of grouped experts in the PJI field to increase the sensitivity and specificity.[25] Cultures in 7 patients were persistently negative. These patients were included in our infection cohort because they met the definition proposed by MSIS for PJI on the basis of sinus tract formation, laboratory values, and intraoperative infected appearance. The results in this cohort were no different than those with culture-positive infection in range of motion and subjective outcomes. Advances in synovial fluid cytokine analysis (interleukin 6, tumor necrosis factor-α, etc) and the use of polymerase chain reaction technology may allow for improved diagnostic certainty when treating shoulder PJI.[1,13]

The findings of this study should be interpreted with an understanding of its limitations. First, the cohort sizes compared here are limited, and true differences may not be detected with the sample sizes available. Our cohort size is larger than most prior reports, and collecting a larger sample size will likely require larger multicenter studies. Our results reflect a single-institution experience with a single implant system, so the results described may not be generalizable. Diagnosis of PJI in the shoulder remains a challenge, as reflected by 7 patients with persistently negative cultures. We included these patients based on the constellation of infectious symptoms and signs, although there is a possibility of overtreatment.

Second, we did not obtain cultures in our aseptic revision cohort if there was no clinical concern for shoulder PJI. It is possible that patients in this group may be affected with subclinical infection or have false-positive cultures.

Third, we did not directly compare our 3-stage protocol to a 1-stage or 2-stage protocol and instead present our data compared with prior published reports.

Fourth, we treated all positive cultures in the second stage as true infections, leading to the possibility of overtreating due to false-positive culture results. We did not attempt aspiration so have no comparison to this method for potentially diagnosing persistent infection.

Lastly, we did not perform a cost-effectiveness analysis with this treatment approach, although future research should examine the effect this protocol could have on health care expenditures for patients with shoulder PJI.

Conclusions

We observed improved functional and subjective outcomes and reinfection rate with a 3-stage revision protocol compared with prior reports. We observed similar shoulder range of motion and patient-reported outcomes for patients with revision RTSA for shoulder PJI compared with patients with revision RTSA for aseptic indications. Our findings support the clinical use and further investigation of this 3-stage protocol in managing shoulder PJI.

Disclaimer

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