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Risk factors for periprosthetic infection after reverse shoulder arthroplasty

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Background: Management of periprosthetic infection after reverse shoulder arthroplasty (RSA) remains a challenge. Whereas the infection rate after RSA has improved, more information would be helpful to identify patient risk factors for infection after RSA. The purpose of this study was to evaluate risk factors for infection after RSA.

Methods: We identified 301 primary RSAs with a minimum of 1-year follow-up in a prospectively collected shoulder arthroplasty registry. We performed bivariate and multivariable logistic regression analyses to assess the association between patient demographic and clinical characteristics (age, sex, smoking, diabetes, rheumatoid arthritis, body mass index, and history of prior failed hemiarthroplasty or total shoulder arthroplasty) and periprosthetic infection after RSA.

Results: There were 15 periprosthetic infections after RSA (5.0%). Patients with a history of RSA for failed arthroplasty (odds ratio, 5.75; 95% confidence interval, 2.01-16.43; $P = .001$) and patients younger than 65 years had an increased risk for development of an infection (odds ratio, 4.0; 95% confidence interval, 1.21-15.35; $P = .021$). History of smoking, diabetes, rheumatoid arthritis, or obesity did not contribute to an increased risk of infection after RSA.

Conclusions: This is the first study evaluating risk factors for infection after RSA while controlling for confounding variables with multivariable analysis. The greatest risk factors for infection after RSA were history of a prior failed arthroplasty and age younger than 65 years. Patients with these clinical characteristics should be counseled preoperatively about the increased risk for development of infection after RSA.

Level of evidence: Level III, Retrospective Cohort Design, Treatment Study.

Keywords: Infection; reverse shoulder arthroplasty

Reverse shoulder arthroplasty (RSA) is increasing as indications for its use continue to expand.[16,26] Although promising results have been reported for various pathologic processes,[4,10,12,18,21,28,30] RSA continues to have a high rate of complications.[1,7,8,19,25,29] Complications after RSA are reported to be between 19% and 75%, including instability, periprosthetic infection, hematoma, fracture,

The Institutional Review Board at the Texas Orthopedic Hospital approved this study (TOH140).

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and neurologic injury.[1,7,8,19,25,29] In particular, periprosthetic infection remains a challenging problem to treat after RSA. The historical infection rate after RSA has ranged from 1% to 10%.[7,8,28,29] Additional information is needed to characterize patient risk factors for infection after RSA.

Patient comorbid factors such as diabetes, smoking, morbid obesity, and rheumatoid arthritis have been associated with infection in orthopedic surgeries.[14,15,17,24] Rheumatoid arthritis, obesity, and revision of prior failed arthroplasty have been singled out as risk factors for periprosthetic infection after shoulder arthroplasty in several small series[2,6,14]; however, we are aware of no studies that have examined a large series of patients and controlled for confounding factors (e.g., age, diabetes, smoking, rheumatoid arthritis, obesity, failed prior arthroplasty) with multivariable analysis to confirm which variables are risk factors for infection after RSA.

The purpose of this study was to examine risk factors for periprosthetic infection after RSA. Our hypothesis was that diabetes, rheumatoid arthritis, smoking, and RSA for failed prior shoulder arthroplasty would be associated with periprosthetic infection after RSA.

Materials and methods

Patient inclusion criteria and demographics

We identified 301 primary RSAs (57.6%) with a minimum of 1-year follow-up data of a total of 518 RSAs completed from 2004 to 2011 in a prospectively collected shoulder arthroplasty registry. All cases were performed at a single, high-volume shoulder arthroplasty center by a single surgeon (T.B.E.). All patients with a history of infection in the operative shoulder and all patients undergoing revision of an existing RSA were excluded. All patients with a history of a prior failed hemiarthroplasty or total shoulder arthroplasty were included and considered a ''failed prior arthroplasty.'' A minimum of 12 months of follow-up was required for surveillance of postoperative infection. The majority of the patients were female (179; 59.5%), and the average age was 68.3 years (standard deviation, 11.3 years; range, 18-93 years). The indications for RSA included 144 rotator cuff tear arthropathies (47.8%), 61 failed prior arthroplasties (prior hemiarthroplasty or total shoulder arthroplasty; 20.3%), 22 acute proximal humeral fractures (7.3%), 24 proximal humeral nonunion or malunions (8.0%), 18 primary osteoarthritis (6.0%), 10 instability arthropathies (3.3%), 6 inflammatory arthropathies (2.0%), and 16 others (5.3%).

We reviewed prior clinic notes, outside hospital records, preoperative radiographs, and operative reports to determine how many patients had prior surgery. We determined that 99 patients had prior operations (32.89%). Sixty-one patients had prior arthroplasty (hemiarthroplasty or total shoulder arthroplasty), 27 patients had a prior rotator cuff repair, 8 patients had prior open reduction with internal fixation or intramedullary nail for proximal humerus fractures, and 3 patients had prior instability surgery. Two of the patients with instability arthropathy had prior arthroscopic procedures. One patient with instability arthropathy had a prior failed arthroscopic stabilization procedure and a prior failed coracoid transfer procedure.

Surgical technique

The operative extremity was cleaned with isopropyl alcohol and then prepared with povidone-iodine scrub and iodine paint solution (Medline Industries, Inc, Mundelein, IL, USA). Ioban 2 (3M, St Paul, MN, USA) surgical drapes were used to cover all exposed skin on the operative extremity. Surgical helmets were not used.

The Aequalis (Tornier, Inc., Bloomington, MN, USA) RSA system was used for all patients during the study period. The RSA technique used for patients during the study period is well described.[11,27] A standard deltopectoral approach was used. All patients had cemented humeral stems, and non-antibiotic-loaded cement was used. A closed suction drain was placed at the time of wound closure and removed on the first postoperative day. Sequential compression devices were routinely used for deep venous thrombosis prophylaxis; chemical prophylaxis for deep venous thrombosis was not routinely used.

Antibiotic protocol

All patients received preoperative intravenous (IV) antibiotics within 30 minutes of incision and 24 hours of IV antibiotics postoperatively. The antibiotic regimen from 2004 to 2009 was 1 g of IV cefazolin infused within 30 minutes of incision and 1 g of IV cefazolin every 8 hours postoperatively for 3 additional doses. The antibiotic regimen was changed in 2010 in response to 5 infections in 2009. The antibiotic regimen in 2010 changed to 1 g of vancomycin infused before incision and 1 g of vancomycin every 12 hours postoperatively for 2 additional doses. Furthermore, from 2010 to 2011, patients also received 300 mg of oral clindamycin after surgery every 8 hours for a total of 12 doses as additional precaution for *Propionibacterium acnes*. There were 11 infections from 2004 to 2009 compared with 4 infections from 2010 to 2011. Overall, there was no statistical difference in the infection rates from 2004 to 2009 compared with 2010 to 2011 ($P = .432$).

Postoperative rehabilitation

All patients were placed in a neutral rotation brace for 3 to 4 weeks before initiation of an aquatic physical therapy program.[20,27] Patients who were unable to participate in aquatic therapy had a similar land-based therapy regimen with the same goals.

Clinical assessment

Patients were prospectively enrolled in a shoulder arthroplasty registry and observed clinically. Patients were examined preoperatively by the senior surgeon (T.B.E.), and repeated examinations were completed postoperatively at 1 week, 6 weeks, 3 months, 6 months, 12 months, and then annually after that. Radiographs were obtained at each clinic appointment and included anteroposterior in the plane of the scapula, scapular Y, and axillary views. All intraoperative and postoperative complications were recorded.

All patients with suspected infection based on history and physical examination and all patients with preexisting hardware (prior open reduction and internal fixation, total shoulder arthroplasty, hemiarthroplasty) completed a preoperative infection workup. Similarly, all patients with a suspected infection in the postoperative period based on history and physical examination completed an infection workup. Findings that typically warranted an infection workup included obvious factors, such as an erythematous or draining wound and fluctuance, or less obvious clinical factors, such as persistent pain after surgery or new or unexplained pain. The infection workup for suspected periprosthetic infection included the following: complete blood count with differential, erythrocyte sedimentation rate, and C-reactive protein. Any elevation in erythrocyte sedimentation rate or C-reactive protein above the normal range was followed by an image-guided aspiration by a musculoskeletal radiologist. Aspirate was sent for aerobic, anaerobic, fungal, and acid-fast bacterial cultures. Cultures were held for a minimum of 21 days to detect bacteria such a *P. acnes* and *Staphylococcus epidermidis* that have a longer incubation period.[9,31] After the diagnosis of a periprosthetic infection, antibiotics were held until intraoperative culture specimens were obtained. Complete removal of RSA components was then performed along with 1 or 2 débridement procedures and antibiotic cement spacer placement. The patients were observed by infectious disease specialists as inpatients and treated with IV antibiotics in the outpatient setting for 6 weeks before the second stage with reimplantation of RSA components.

Statistical analysis

Independent sample *t* tests assuming unequal variances were used to compare age and follow-up between infection groups. Bivariate and multivariable exact logistic regression analyses were used to assess the associations between patient and clinical characteristics and periprosthetic infection. All variables significant at $P < .05$ in bivariate analyses were entered into a multivariable logistic regression model.

Results

Of 301 patients, 15 developed a periprosthetic infection (5.0%). The average clinical follow-up for the entire cohort was 38.1 months (standard deviation, 24.1 months; range, 12-111 months), and there was no statistical difference between the periprosthetic infection group and the non-periprosthetic group regarding follow-up duration ($P = .68$). The average age of the periprosthetic infection group was significantly lower at 60.6 years vs 68.6 years in the non-periprosthetic infection group ($P = .04$).

The primary indications for RSA in the periprosthetic infection group included the following: 9 failed prior arthroplasties (60.0%), 2 rotator cuff tear arthropathies (13.3%), 2 proximal humeral nonunion or malunions (13.3%), one inflammatory arthropathy (6.7%), and one instability arthropathy (6.7%).

Of the 15 patients who developed a periprosthetic infection, 1 patient developed an acute infection (<3 months after surgery), 5 patients developed a subacute infection (between 3 and 12 months after surgery), and 9 patients developed a late or chronic infection (>12 months after surgery).[3,23] Methicillin-sensitive *Staphylococcus aureus* (3 patients), methicillin-resistant *S. aureus* (2 patients), *P. acnes* (2 patients), *S. epidermidis* (1 patient), coagulase-negative *Staphylococcus* (1 patient), and *Enterobacter cloacae* (1 patient) were cultured. Five patients had no culture growth despite gross purulence noted at the time of surgery. Of the 15 patients with an infection, 6 underwent 2-stage revisions, and 4 of the 2-stage revisions were successful; 2 had a recurrence of infection and ultimately had a resection arthroplasty instead of a repeated 2-stage revision. The remaining 9 of 15 patients were given the option of a 2-stage revision and elected to undergo resection arthroplasty instead. Overall, resection arthroplasty was the final operation in 11 patients, and 4 patients currently have revised RSA implants in place after 2-stage revision.

Bivariate exact logistic regression for the association between patient demographics and clinical characteristics and periprosthetic infection was completed (Table I). History of smoking, diabetes, rheumatoid arthritis, body mass index, and duration of follow-up were not significant in bivariate analysis. Prior failed arthroplasty was significantly associated with periprosthetic infection (odds ratio [OR], 6.69; 95% confidence interval [CI], 2.03-23.90; $P = .001$), whereas rotator cuff repair ($P = .998$) and prior open reduction with internal fixation or intramedullary nail for fracture ($P = .109$) were not. Age (OR, 0.95; 95% CI, 0.91- 0.99; $P = .012$) was also found to be statistically significant for periprosthetic infection. RSA for failed arthroplasty and age were found to be statistically significant for periprosthetic infection and were entered into the multivariable exact logistic regression analysis. Both prior failed arthroplasty and age remained significant in the multivariable model, indicating that they are independent factors associated with infection risk. Patients with a history of RSA for failed arthroplasty (OR, 5.75; 95% CI, 2.01-16.43; $P = .001$) had a higher likelihood for development of an infection, after accounting for age. Increasing age was associated with a decreased likelihood for development of an infection (OR, 0.95; 95% CI, 0.91-0.99; $P = .021$), after accounting for RSA for failed prior arthroplasty. Patients younger than 65 years had a higher likelihood of infection (OR, 4.00; 95% CI, 1.21-15.35; $P = .021$) compared with patients older than 65 years.

In addition to development of a periprosthetic infection, 7 complications were noted in 5 patients in the periprosthetic infection group. Three intraoperative complications occurred: 1 suprascapular nerve injury, 1 nondisplaced greater tuberosity fracture (no treatment required), and 1 displaced greater tuberosity fracture that required cerclage wires intraoperatively. Four postoperative complications also occurred in the periprosthetic infection group: 4 anterior dislocations (1 treated with closed reduction and 3 treated with revision of components from a 36-mm to a 42-mm glenosphere).

Table I Results of bivariate exact logistic regression analyses for periprosthetic infection vs patient demographic and clinical characteristics

	Infection group, n (%)	No infection group, n (%)	Odds ratio (95% CI)	*P*
Smoking	2 (13.3)	36 (12.6)	1.07 (0.11, 5.02)	.999
Revision arthroplasty	9 (60.0)	52 (18.2)	6.69 (2.03, 23.90)	.001*
Prior rotator cuff repair	1 (6.7)	26 (9.1)	0.71 (0.02, 5.08)	.998
Prior ORIF or IMN humerus fracture	2 (13.3)	6 (2.1)	7.07 (0.64, 44.97)	.109
Diabetes	3 (20.0)	45 (15.7)	1.34 (0.23, 5.23)	.877
Rheumatoid arthritis	3 (20.0)	39 (13.6)	1.58 (0.27, 6.23)	.699
Male (female is reference)	8 (53.3)	114 (39.9)	1.72 (0.53, 5.74)	.441
BMI classification				
Healthy weight: <25 (reference)	6 (40.0)	90 (31.5)		
Overweight: 25-30	5 (33.3)	91 (31.8)	0.83 (0.19, 3.37)	.999
Obese: >30	4 (26.7)	105 (36.7)	0.76 (0.34, 1.58)	.595
Age			0.95 (0.91, 0.99)	.012*
Follow-up			1.00 (0.98, 1.02)	.717

CI, confidence interval for odds ratio; *BMI*, body mass index; *ORIF*, open reduction and internal fixation; *IMN*, intramedullary nail.
* Statistical significance for $P < .05$ and CI does not contain 1.00.

There were 74 complications in 59 patients in the non-periprosthetic infection group. Forty-four intraoperative complications occurred: 18 tuberosity or humeral shaft fractures that required cerclage cabling, 12 tuberosity fractures that required no cerclage cabling, 9 glenoid fractures, 4 nerve traction injuries, and 1 vascular injury. Thirty postoperative complications occurred: 25 anterior dislocations (18 treated with closed reduction and 7 treated with revision of components from 36-mm to 42-mm glenosphere), 3 acromial stress fractures, 1 hematoma, and 1 humeral aseptic loosening. There was no statistical difference in the number of patients who had complications between the infected (5 of 15; 33.3%) and the noninfected (59 of 286; 20.6%) groups ($P = .327$).

Discussion

Our investigation demonstrates that a failed prior arthroplasty and younger patient age (<65 years) are independent risk factors for infection after RSA. This is the first study of which we are aware reporting risk factors for infection after RSA while controlling for confounding variables with multivariable analysis.

One of the largest reported series of 199 RSAs reported a 4% overall infection rate,[28] which is similar to a recent systematic review reporting a 3.8% infection rate.[32] Our overall infection rate of 5.0% in 301 patients was similar to this historical rate.

The largest series to date of which we are aware reporting infection after RSA is a recent study describing 501 primary RSAs.[22] The study reported the effectiveness of antibiotic-impregnated cement in prevention of deep infection after primary RSA at 1-year minimum follow-up. The investigation did not perform a multivariable analysis and was unable to account for patient variables, such as smoking, diabetes, rheumatoid arthritis, or body mass index, that may contribute to infection. Antibiotic-loaded cement was not used in our study.

Of 61 patients, 9 (14.8%) in our investigation with a prior failed arthroplasty (hemiarthroplasty or total shoulder arthroplasty) developed a periprosthetic infection after RSA, and these 9 patients represented 60.0% of the entire group of patients who developed an infection. Some suspect that prior shoulder surgery leads to an increase in infection rates because of unrecognized indolent infections.[5,7] Prior surgery is also thought to create a large amount of dead space that may predispose to infection.[7]

Although recent data suggest that RSA in patients younger than 60 years may yield worse postoperative satisfaction, there are few data to suggest an increased infection rate in younger patients.[21] The average age of patients developing a periprosthetic infection in our study was 60.6 years compared with the average age of 68.6 years for patients in the non-periprosthetic group ($P = .04$).

An increased infection rate (9.5%) has been reported in a small series of 21 patients with rheumatoid arthritis after RSA[14]; however, a similar series of 18 patients with rheumatoid arthritis after RSA reported a 0% infection rate.[30] Our series included 42 patients with rheumatoid arthritis, and our analysis controlled for other confounding variables, such as diabetes, smoking, and prior failed arthroplasty. Rheumatoid arthritis was not a risk factor for infection in our patient cohort when controlling for these other variables. Likewise, diabetes is a risk factor for infection in total knee and total hip arthroplasty[15]; however, our series included 48 patients with diabetes, and it was not a risk factor for infection in our cohort when controlling for other confounding variables.

RSA in severely obese patients (>35 kg/m^2) has been shown to have a higher rate of complications with no increased risk of infection[13]; however, a recent study

reported a higher infection rate (18%) in obese patients.[2] Our investigation did not show an increased risk of infection in obese patients.

One of the strengths of this study is that it represents the largest cohort to date controlling for potential confounding variables in a multivariable analysis to determine risk factors for infection after RSA. Specifically, prior studies have discussed higher infection rates for RSA in the setting of failed prior arthroplasty; however, these studies consisted of small cohorts of patients and did not control for other clinical variables (e.g., diabetes, rheumatoid arthritis, smoking, obesity).[5,6] Additional strengths include that a single surgeon performed the same operative technique, with the same postoperative protocol and postoperative rehabilitation.

Several limitations of the study are noted. One limitation is the possibility of additional treatments for periprosthetic infection or other operations required beyond our documented clinical follow-up. The minimum follow-up time of 12 months may be considered by some to be too short; however, a minimum of 12 months of follow-up has been used for postoperative infection surveillance after RSA,[22] and the average follow-up time for the entire study population was more than 3 years (38.1 months).

Conclusions

History of a failed prior arthroplasty and younger patient age (<65 years) are independent risk factors for infection after RSA. Given the challenge of treating periprosthetic infection after RSA, this additional information will enable us to better counsel patients about risk factors for infection before surgery. We will be able to better stratify patients who are at a higher risk for development of infection after RSA.

Disclaimer

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