Incidence and risk factors for deep infection after primary shoulder arthroplasty: a meta-analysis


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Abstract. – OBJECTIVE: Many risk factors associated with deep infections after primary shoulder arthroplasty remain controversial and have not yet been summarized. As such, the aim of the present study was to quantitatively summarize the risk factors associated with deep infections after primary shoulder arthroplasty.

MATERIALS AND METHODS: Computerized and additional manual searches on the Medline, Embase, Chinese National Knowledge Infrastructure (CNKI), and Cochrane central database for potential studies, published from inception to March 2022, were performed. All studies that assessed risk factors for deep infection after primary shoulder arthroplasty were selected without language restrictions. Eligible studies were required to fulfill quality assessment criteria from the Consort statement and to evaluate risk factors for deep infection after primary shoulder arthroplasty. Two reviewers independently extracted the relevant data, with disagreements resolved by consensus. Statistical analyses were performed using Stata version 11.0 (Statacorp LLC, College Station, TX, USA).

RESULTS: Seven studies including 493,148 patients who underwent primary shoulder arthroplasty, among whom 1,314 experienced infection (0.3%), were eligible and included in this meta-analysis. Meta-analysis revealed that significantly increased risk factors for infection after primary shoulder arthroplasty included male sex (odds ratio [OR] 1.79 [95% confidence interval (CI) 1.23-2.60]), avascular necrosis (OR 2.64 [95% CI 1.61-4.34]), rotator cuff arthropathy (OR 2.14 [95% CI 1.55-2.95]), proximal humerus fracture (OR 2.68 [95% CI 1.93-3.73]), and non-union of humerus fracture (OR 5.32 [95% CI 3.52-8.02]). In contrast, advanced age was associated with a decreased likelihood for development of infection (OR 0.97 [95% CI 0.94-1]).

CONCLUSIONS: Surgeons should devote close attention to the above-mentioned medical conditions to reduce deep infection after primary shoulder arthroplasty.

Key Words: Deep infection, Shoulder arthroplasty, Risk factors, Meta-analysis.

Introduction

Shoulder arthroplasty is a common surgical treatment for various conditions affecting the glenohumeral joint, including arthritis, rotator cuff disease, trauma, and tumors. Infections associated with such surgical treatment can cause pain and disability, implant failure and, occasionally, septicemia. The rate of deep infections has been reported to be 0.4% to 2.9% after total shoulder arthroplasty (TSA)1,2, 3.3% to 5.0% after reverse TSA (RTSA)3,4 and 1.0% in hemiarthroplasty (HSA)5. Previous epidemiological studies have investigated and assessed factors associated with shoulder arthroplasty infection, such as rheumatoid arthritis, obesity, and revision of previous failed arthroplasty6-8. However, some limitations exist in individual studies, including small sample sizes and the assessment of a single or very few potential risk factors. Therefore, the capacity of these factors identified from individual studies to predict infection after shoulder arthroplasty remains uncertain.

To our knowledge, no quantitative assessment has been performed to summarize these risk factors for this critical issue. As such, we performed a meta-analysis using data reported in previous original studies to summarize these factors, which we anticipate will aid clinicians in identifying patients at risk for infection when designing treatment and management strategies.

Materials and Methods

Literature Search

A computerized literature search on the Medline, Embase, Chinese National Knowledge Infrastructure (CNKI), and Cochrane Central databases for studies exploring risk factors for infection after shoulder arthroplasty, published from incep-
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Incidence and risk factors for deep infection after primary shoulder arthroplasty, was performed. The following search terms and Boolean operators were used: (“deep infection” or “surgical site infection” or “prosthetic infection” or “SSI” or “PJI” or “prosthetic joint infection”) and (“TSA” or “RTSA” or “HSA” or “total shoulder arthroplasty” or “reverse total shoulder arthroplasty” or “hemiarthroplasty”). A manual search of the reference lists of the retrieved articles and systematic reviews was performed to identify additional potentially eligible studies for inclusion.

Two reviewers (TP Cheng and LL Guo) independently evaluated the titles and abstracts of the selected studies. Only full-text studies, without language restrictions, were included in this meta-analysis. The inclusion criteria were as follows: cohort or observational study, or randomized controlled trial was performed to explore risk factors for infection after shoulder arthroplasty; cases and controls were defined based on the presence or absence of infections after shoulder arthroplasty, respectively; sufficient data were published for estimating odds ratio (OR) or hazard ratio (HR) with corresponding 95% confidence interval (CI).

Quality of Included Studies

The quality of the included studies was evaluated using the Newcastle-Ottawa Scale (NOS) based on three main items, with a perfect score of 9: selection of the study groups (0-4 points); comparability of the groups (0-2 points); and determination of either the exposure or outcome of interest (0-3 points).

Data Extraction

All data were carefully and independently extracted from all eligible articles by the two reviewers. The following data were extracted from each study: first author; year of publication; country; significant risk factors; definitions and numbers of patients with and without infection after shoulder arthroplasty; and number of citations for each potential risk factor for infection. Due to discrimination of the presentation of deep infection among the articles, the studies included in the present review were separated into prosthetic joint infection (PJI), deep infection, and surgical site infection (SSI). The original definitions of PJI, deep infection, and SSI from each article were accepted, and were diagnosed based on clinical manifestations or bacterial cultures. Any disagreements were resolved by consensus discussion. This meta-analysis was in accordance with the referred Reporting Items for Systematic Reviews and Meta-Analyses (i.e., PRISMA) and Assessment of Multiple Systematic Reviews (i.e., AMSTAR) guidelines.

Statistical Analysis

For each risk factor, attempts were made to extract the adjusted OR (from the multivariate analysis model) and corresponding 95% CI in the original study. When the adjusted OR was not provided, crude ORs were calculated based on the given frequency. The abstracted ORs were pooled across studies to assess the associations between different variables and the risk for infection, with \( p < 0.05 \) indicating a statistically significant difference. Heterogeneity among the studies was qualitatively tested using Q-test statistics, with significance set at \( p < 0.10 \). The \( I^2 \) statistic was used as a quantitative measure of heterogeneity, with \( I^2 > 50\% \) indicating significant inconsistency. A random effects model was adopted to calculate pooled ORs in the case of significant heterogeneity (\( p < 0.10 \) or \( I^2 > 50\% \)); otherwise, a fixed-effects model was used. Meta-analysis of the significant risk factors was summarized graphically using a forest plot. Publication bias was assessed using Begg’s test and graphed using a funnel plot; \( p < 0.10 \) was considered to be statistically significant. Furthermore, to explore the sources of heterogeneity, sensitivity analysis was performed for selected risk factors according to the following features: inclusion criteria; lower methodological quality of the included study; larger confidence interval size; and other elements. All analyses were performed using Stata version 11.0 (Statacorp, College Station, TX, USA).

Results

Characteristics of the Included Studies

The initial literature search retrieved 233 relevant publications, of which 226 were excluded for duplicates and miscellaneous reasons (reviews, letters, or not relevant to the study) based on the title, abstract, and full text (Figure 1). The remaining seven studies were included in the final analysis, all of which were published in English between 2012 and 2022. These seven studies included 493,148 patients with primary shoulder arthroplasty, among which 1,314 cases of infection occurred, corresponding to an accumulated incidence of 0.3%. The rates of deep infection were 1.1% after TSA, 2.8% after RTSA, and 1.0% in HSA. Detailed information regarding these studies is summarized in Table I.
The outcome of quality assessment for these studies (i.e., NOS score) included six that scored 8\textsuperscript{5,5,11-14} and one that scored 7\textsuperscript{15}.

A meta-analysis of combinable data was conducted to analyze risk factors for infection after primary shoulder arthroplasty; the main results are summarized in Table II. The combined ORs ranged from 0.86 to 5.32. Significant heterogeneity was observed among the studies when evaluating potential risk factors, including male sex and age, on the basis of the combined ORs and corresponding 95% CIs. Significant risk factors included male sex (OR 1.79 [95% CI 1.23-2.60]), avascular necrosis (OR 2.64 [95% CI 1.61-4.34]), rotator cuff arthropathy (OR 2.14 [95% CI 1.55-2.95]), proximal humerus fracture (OR 2.68 [95% CI 1.93-3.73]), and non-union of humerus fracture (OR 5.32 [95% CI 3.52-8.02]). In contrast, advanced age was associated with decreased likelihood for the development of infection (OR 0.97 [95% CI 0.94-1]). The outcome of the analysis for some of the variables described above as significant risks are presented using forest plots (Figure 2). Other variables, including body mass index (BMI), diabetes mellitus, rheumatoid arthritis, instability arthritis, and American Society of Anesthesiologists (ASA) score, were not identified as risk factors for infection after shoulder arthroplasty ($p > 0.05$).

A sensitivity analysis was performed for risk factors (male sex and age), demonstrating significant heterogeneity by excluding outlier studies due to poorer assessment quality or wider CIs for some ORs. Results revealed that the $I^2$ value decreased to $< 50\%$; however, meta-analysis’ results for these factors did not alter significance, indicating that results were robust. Detailed information regarding the sensitivity analysis is presented in Supplementary Table. Begg’s funnel plot for publication bias (with 95% pseudo confidence

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**Table I.** The detailed information for characteristics of the 7 eligible studies.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Publication</th>
<th>Country</th>
<th>Control</th>
<th>Case</th>
<th>Total</th>
<th>Age (y)</th>
<th>Significant factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Singh et al\textsuperscript{5}</td>
<td>2012</td>
<td>USA</td>
<td>1,417</td>
<td>14</td>
<td>1,431</td>
<td>63±16</td>
<td>Trauma</td>
</tr>
<tr>
<td>Singh et al\textsuperscript{11}</td>
<td>2012</td>
<td>USA</td>
<td>2,556</td>
<td>32</td>
<td>2,588</td>
<td>65±12</td>
<td>Male gender and younger age</td>
</tr>
<tr>
<td>Richards et al\textsuperscript{12}</td>
<td>2014</td>
<td>USA</td>
<td>4,483</td>
<td>45</td>
<td>4,528</td>
<td>69.7±10.3</td>
<td>Male</td>
</tr>
<tr>
<td>Morris et al\textsuperscript{4}</td>
<td>2015</td>
<td>USA</td>
<td>286</td>
<td>15</td>
<td>301</td>
<td>68.3±11.3</td>
<td>History of a prior failed arthroplasty and age younger than 65 years</td>
</tr>
<tr>
<td>Smucny et al\textsuperscript{13}</td>
<td>2015</td>
<td>USA</td>
<td>400,604</td>
<td>384</td>
<td>400,988</td>
<td>NA</td>
<td>Medicaid insurance, fracture nonunion, avascular necrosis, proximal humeral fracture, comorbidities, in-hospital events, and increased duration of hospital stay</td>
</tr>
<tr>
<td>Padegimas et al\textsuperscript{14}</td>
<td>2015</td>
<td>USA</td>
<td>81,690</td>
<td>808</td>
<td>82,498</td>
<td>NA</td>
<td>Male gender, younger age, preoperative anemia, drug abuse, and recent weight loss/nutritional deficiency</td>
</tr>
<tr>
<td>Florschütz et al\textsuperscript{15}</td>
<td>2015</td>
<td>USA</td>
<td>798</td>
<td>16</td>
<td>814</td>
<td>65±13</td>
<td>Previous non-arthroplasty operative history</td>
</tr>
</tbody>
</table>

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Discussion

Complication rates after primary shoulder arthroplasty have been reported to be between 19% and 75% and include prosthesis loosening, periprosthetic infection, hematoma, fracture, and nerve injury. Among these complications, periprosthetic infection remains a challenge, which can cause pain and disability, implant failure, and occasionally, septicemia. Diagnosis is not always easy and mostly consists of a combination of laboratory tests, clinical symptoms, and radiological examinations including routine radiography, indium scans, and microbiological swabs. After primary shoulder arthroplasty, every painful shoulder should be considered potentially infected, and an immediate detailed diagnostic examination is imperative. In these studies, C-reactive protein level among those with infected implants was often increased, while white blood cell count was not.

Florschütz et al reported an overall infection rate of 2.0% after primary TSA or RTSA, without a significant difference between TSA (1.7%) and RTSA (2.2%). In evaluating a large series of patients who underwent shoulder arthroplasty with a long-term follow-up period between 1976 and 2008, Singh et al reported a deep periprosthetic infection rate of 1.2% after primary TSA and 1.0% after primary shoulder HSA. As the number of shoulder arthroplasties performed worldwide continues to increase, identification of factors associated with infection may lead to more effective preventive interventions. In this systematic review and meta-analysis, the cumulative incidence of overall infection after primary shoulder arthroplasty was 0.3%, and multiple risk factors were found to be associated with this complication. By excluding a study investigating surgical site infection after shoulder arthroplasty, for which TSA could not be separated from RTSA, the rate of deep infection was 1.1% after TSA, 2.8% after RTSA, and 1.0% in HSA. Some surgeons prefer to adopt HSA because it has a lower complication rate; however, the poor healing condition and osteolysis of the tuberosities compromise this advantage. Similarly, the advantages of avoiding osteolysis of the tuberosities and the disadvantage of the associated high complication rate were observed in the RTSA group. Some studies have proposed that the higher RTSA infection rate can be attributed to the larger dead space and decreased viable soft tissue coverage around the prosthesis, which facilitates bacterial colonization of the implant.

In this meta-analysis, significant risk factors with high associations for infection included male sex, younger age, avascular necrosis, rotator cuff arthropathy, proximal humerus fracture, and non-union of humerus fracture.

Among patient-related demographic factors, male sex and younger age were associated with...
Singh et al\textsuperscript{11} reported that men had a higher risk for infection than women who underwent TSA; however, sex was not a risk factor for infection among patients who underwent HSA at the same institution\textsuperscript{5}. Although it is unclear why male patients were at higher risk than female patients, males without signs of infections have a much greater increased risk for bacterial cultures positive for \textit{Propionibacterium acnes}\textsuperscript{24,26}. Younger individuals were much more likely to have rheumatoid arthritis or previous trauma, and younger men were more likely to have experienced serious trauma\textsuperscript{11}. Perhaps the poorer tissue quality in patients with previous trauma or drug therapy and the
systemic effects in patients with rheumatoid arthritis play a role, despite diagnostic considerations being not significant when immediately tested.

Morbid obesity was associated with a higher risk for deep periprosthetic infection after knee or hip arthroplasty. Results of the present meta-analysis suggested that a BMI ≥ 30 kg/m² demonstrated a non-significant trend toward an association with a greater risk for infection after primary shoulder arthroplasty. This may be due to the small number of infections in our analysis, making it underpowered to detect such differences in the etiology of infection.

Surgical indications for shoulder arthroplasty included osteoarthrosis, proximal humeral fracture, avascular necrosis, fracture non-union, rheumatoid arthritis, and rotator cuff arthropathy. Nevertheless, proximal humeral fracture (OR 2.68 [95% CI 1.93-3.73]), avascular necrosis (OR 2.64 [95% CI 1.61-4.34]), fracture non-union (OR 5.32 [95% CI 3.52-8.02]), and cuff tear arthropathy (OR 2.14 [95% CI 1.55-2.95]) were associated with an increased risk for infection after primary shoulder arthroplasty (Table II).

Rotator cuff arthropathy describes pathoanatomical changes associated with chronic full thickness rotator cuff tears, which included erosions of osseous structures, humeral osteopenia, and restricted shoulder motion; as such, it has a poor preoperative condition, which results in a higher incidence of infection. Patients with a fracture non-union may have a higher risk for infection due to previous failed internal fixation, indolent infection, or poor soft tissue condition for wound healing. Confounding was also possible, because patients with positive cultures at the fracture non-union site may have been coded as an infection without the patients developing acute infections during hospital care. Florschütz et al reported that shoulders with previous operations undergoing primary shoulder arthroplasty demonstrated a significantly higher infection rate (4.3%) compared to shoulders without previous operations (1.3%), exhibiting a 3.35-fold higher risk compared to those undergoing arthroplasty for osteoarthritis. This may be due to soft tissue trauma occurring with fracture simultaneously, leading to increased bleeding, increased operative duration for prosthetic height adjustment or tuberosity reconstruction, and/or increased hematoma formation before and after trauma.

A previous review based on a small series suggested that the underlying diagnosis of rheumatoid arthritis, presence of diabetes mellitus, use of immunosuppressive or systemic corticosteroid medications, previous shoulder operations, or repeated intra-articular corticosteroid injections were risk factors for periprosthetic infections. In our review, we examined both underlying diagnoses and medical comorbidities, including rheumatoid arthritis, diabetes mellitus, ASA class, and obesity; however, we did not find any significant association with the risk for deep periprosthetic infections (Table II).

In the field of infected hip and knee prostheses, most experience has been with two-stage exchange, which is considered to be the standard procedure. With infected shoulder prostheses, most cases reported in the literature have been treated using two-stage exchanges. Two-stage exchange appears to be the best, since it addresses limited function and represents a reliable way to avoid/eradicate infection after surgery. Although one-stage exchange ensures better functional results, it is associated with a higher risk for persistent infection. Only the findings reported by Ince et al demonstrated sufficient eradication of infection after this treatment option.

**Limitations**

The present review had several limitations. First, one weakness of this study lies in the fact that not all ORs regarding the potential risk factors applied in the meta-analysis were adjusted because several studies provided only univariate rather than multivariate statistics. Similarly, some researchers may have chosen not to report results of no interest or those that were insignificant, potentially leading to a considerable amount of missing data. Thus, our overall effect was more likely to overestimate or underestimate the actual situation. Moreover, most of the included studies were retrospective in design and, therefore, had interviewer biases, which may have affected the associations between risk and infection. Finally, the measurements of risk factors differed from one another, and the follow-up periods ranged widely, from one year to decades; as such, significant heterogeneity was unavoidable in this meta-analysis. However, after sensitivity analyses, heterogeneity was resolved (I² < 50%), demonstrating that the analyses were robust, and the results were reliable. Despite these limitations, results of this study are, nevertheless, clinically valuable.
Conclusions

In summary, results of this meta-analysis suggest that male sex, younger age, avascular necrosis, rotator cuff arthropathy, proximal humerus fracture, and non-union of humerus fracture are significant risk factors for infection after primary shoulder arthroplasty.

Patients with these medical conditions should be carefully monitored by surgeons to reduce deep infection after primary shoulder arthroplasty.

Conflict of Interest
The authors declare that they have no conflict of interest.

Ethics Approval and Informed consent
Not required.

Availability of Data and Materials
All data are fully available without restriction.

Financial Support
None.

Authors’ Contribution
All authors contributed equally.

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