SN Comprehensive Clinical Medicine (2023) 5:156
https://doi.org/10.1007/s42399-023-01493-1

REVIEW

Do Patient-reported Allergies Lead to Poor Outcomes Following Shoulder Arthroplasty? A Systematic Review

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Accepted: 24 May 2023 / Published online: 5 June 2023

Abstract

Total shoulder arthroplasty (TSA) is growing more widespread, with over 100,000 TSA cases each year in the USA. Previous research shows increasing number of patient-reported allergies is associated with worse surgical outcomes following orthopedic procedures. This study systematically reviewed the association of patient-reported allergies to outcomes following TSA. A comprehensive review of the PubMed, EBSCO host, Medline, and Google Scholar electronic databases was conducted identifying all studies reporting on the association of patient-reported allergies to TSA outcomes between January 1, 2000 and June 1, 2022. The following keywords and MeSH terms were utilized in combination with "AND" or "OR" Boolean operators: "shoulder arthroplasty," "shoulder replacement," "allergy," "allergies," and "hypersensitivity." The final analysis included 8 studies with a total of 166,303 patients. Four studies looked at all types of allergies, 2 studies looked at drug allergies, and 2 studies looked at antibiotic allergies. Of the 8 articles included in the study, 6 reported having more reported allergies is associated with worse outcomes. Patients in the better outcome group reported an average of 1.6 allergies, while those in the worse outcome group reported an average of 3.3 allergies. Patients with more reported antibiotic allergies are at a higher risk of PJIs. Furthermore, patients with more reported allergies were at an increased risk of pain intensity, length of stay (LOS), and worse patient-reported outcomes. In conclusion, a higher number of patient reported allergies is associated with worse outcomes following TSA. Although patient-reported allergies may not always be accurate, they could still serve as a preliminary screening tool to identify patients who require further diagnostic testing to confirm the presence of allergies.

Keywords Shoulder arthroplasty · Allergies · Prosthetic joint infection · Screening tool · Complications

Introduction

Shoulder arthroplasty (SA) is a viable treatment for end-stage degenerative shoulder pathology, with notable improvements in pain, mobility, and quality of life. Total shoulder arthroplasty (TSA) is growing more widespread, with over 100,000 TSA cases each year in the USA [1, 2]. However, even though there are generally positive outcomes, the prevalence of chronic pain following TSA can be as high as 22% [3]. In addition to lack of motion and pain, some negative outcomes include structural complications, periprosthetic joint infection (PJI), surgical site infection (SSI), postoperative anemia, deep vein thrombosis, and pulmonary emboli [4, 5]. Therefore, identifying risk factors for poor outcomes is critical.

Multiple patient characteristics have been linked to poor outcomes after SA such as prior shoulder surgery [6], increased number of medical comorbidities [7], sex, and advanced age [8]. Previous research has also linked various allergens and the number of allergies to poor surgical outcomes following orthopedic surgery [9–11]. For instance, Fisher et al. reported that patients who underwent revision total joint arthroplasty (TJA) for infection had a significantly higher number of reported allergies [12]. According to a recent study by Graves et al., patients who reported four or more allergies experienced worse outcomes after hip and knee replacement surgery [13]. The authors contended that multiple reported allergies could serve as a surrogate for a mental

This article is part of the Topical Collection on *Surgery*

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health survey, assisting in the identification of patients at high risk of poor postoperative outcomes.

Few studies have examined the impact of patient allergies on SA outcomes. The purpose of this study was to perform a systematic review to evaluate the association of allergies with shoulder arthroplasty. Specifically, we asked: (1) How are different types of allergens associated with the outcomes of SA? (2) Is an increased number of allergies associated with worse outcomes following SA?

Materials and Methods

Search Strategy

A comprehensive review of the PubMed, EBSCO host, Medline, and Google Scholar electronic databases was conducted to identify all studies that reported on the association of allergies to shoulder arthroplasty between January 1, 2000 and June 1, 2022. The following keywords and MeSH terms were utilized in combination with "AND" or "OR" Boolean operators: "shoulder arthroplasty," "shoulder replacement," "allergy," "allergies," "hypersensitivity," and "patch test."

Eligibility Criteria

Articles were included if full-text articles in the English language were available; the study reported on the relationship between allergies and the outcomes of shoulder arthroplasty. Exclusion criteria were employed to ensure the scientific rigor of the study selection process. Studies that did not meet the following criteria were excluded: (1) not published in the English language, (2) conducted on animal models, (3) presented as case reports, (4) only available as abstracts, and (5) duplicates identified across multiple databases.

Study Selection

Two reviewers (AK and MS) independently assessed each article's eligibility for inclusion in our review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) criteria. Disagreements were resolved via discussion to reach a consensus. The initial query generated 200 articles, which were then screened for appropriate studies that were relevant to the purpose of our study. After removing duplicates and reading each abstract, we selected 11 studies for further consideration. The full text of each article was then reviewed, 8 of which fulfilled our inclusion criteria. A thorough review of each study's reference list did not yield any additional articles (Fig. 1).

Data Collection

A collaborative online spreadsheet (Google Sheets), arranged by two reviewers prior to starting, facilitated data extraction. Reviewers (AK and MS) performed data extraction on duplicates and findings were compared for verification. Details regarding study design, methodology, patient demographics, outcomes, and the number and type of allergy were documented.

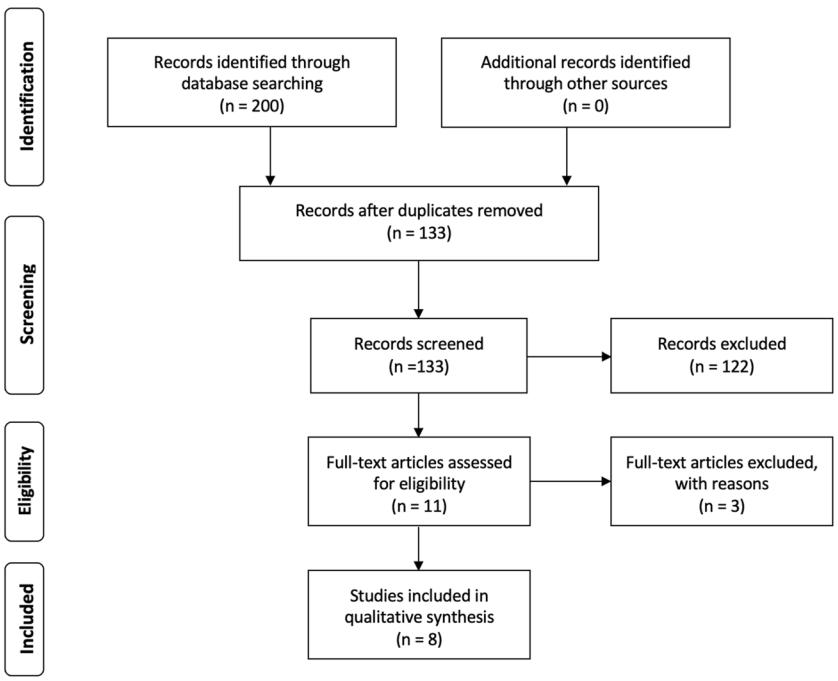

Fig. 1 PRISMA diagram

Methodological Quality Assessment

Two reviewers (AK and MS) independently evaluated the quality of included studies using the Methodological Index for Nonrandomized Studies tool (MINORS). This is a validated assessment tool that grades non-comparative studies from 0 to 16 based on eight criteria and 0 to 24 for comparative studies based on twelve categories related to study design, outcomes assessed, and follow-up. Each domain is scored 0 if not reported, 1 when reported but inadequate, and 2 when reported and adequate, such that higher scores represent better study quality. Disagreements were resolved via discussion to reach a consensus. In this systematic review, a predefined scoring system was utilized to assess the quality of included non-comparative and comparative studies. For non-comparative studies, a score of ≤ 8 was deemed to be of poor quality, 9–14 was considered to be of moderate quality, and a score of 15–16 was deemed to be of good quality. For comparative studies, the predefined cutoff points were ≤ 14 for poor quality, 15–22 for moderate quality, and 23–24 for good quality.

Results

The final analysis included 8 studies (Table 1) with a total of 166,303 patients and a mean age of 68.8 years. Of the studies that reported sex, there were 38,530 males (44%) and 48,996 females (56%). All studies had a retrospective design. Four (4/8) studies reported on all types of allergens, two reported on drug allergies and another two studies reported specifically on antibiotic allergies. All the articles studied patient-reported allergies and did not medically validate the existence of the allergy. The mean MINORs score was 18.4 ± 0.7. Four articles reported differences in the number of allergies between two groups: a poor outcome group and a good outcome group. The articles used different criteria to separate patients into the good and poor outcome groups. One used American Shoulder and Elbow Surgeons (ASES scores), one used VAS scores, one used length of stay, and the last one used severe postoperative pain. The pooled results between these four studies show that patients in the good outcome group reported an average of 1.6 allergies, while those in the poor outcome group reported an average of 3.3 allergies (Table 2).

Six of the 8 articles in this study reported that certain types of allergies or the number of reported allergies is associated with worse outcomes. Two of the six studies reported on the association between self-reported penicillin allergy and the risk of PJIs. Wu et al. [14] reported that patients with a penicillin allergy had an odds ratio (OR) of 3.9 for developing PJI within 1 year of total shoulder arthroplasty compared to those who did not. Similarly, Bahoravitch et al. [15] reported that patients with antibiotic allergies had a higher risk of PJI within 30 days, 1 year, and 2 years of surgery with the highest risk being within 30 days. Further analysis revealed that patients with a penicillin allergy had a higher rate of revision surgery due to PJI at 30 days, 90 days, 1 year, and 2 years. The authors also reported patients had a higher risk for readmission, postoperative anemia, and blood transfusions within 90 days [15]. Two other studies evaluated the preoperative factors associated with ASES after a minimum of 2 years after TSA.

Forlizzi et al. stated that patients in the bottom quartile of ASES scores had a significantly higher number of reported allergies (3.4 ± 4.9) compared to those in the upper quartile (1.4 ± 1.9) [16]. While Elrick et al. found a similar trend that an increased number of drug or latex allergies was associated with a trend of worse ASES, Single Assessment Numerical Evaluation (SANE) score, and 12-Item Short Form Health Survey (SF-12), the differences were not statistically significant [17]. The only outcome measure that was significantly correlated with the number of allergies was the QuickDASH score. Those with two reported allergies scored significantly higher on the QuickDASH scale than those with no allergies. Menedez et al. reported patients with a higher number of allergies experienced severe postoperative pain defined as peak pain intensity $\geq$ 75th percentile with OR of 1.28 per 1-unit increase [18]. Another study by the same group found a greater number of patient-reported allergies had the strongest association with extended LOS (defined as LOS > 75th percentile) [19].

The two studies that reported no association existed between allergies and SA outcomes were by Puzzitiello et al. and Rosenthal et al. [20, 21]. Puzzitiello et al. stated that patients with persistent pain after 2 years following rTSA were more likely to have a higher number of self-reported allergies (3.0 ± 4.8 vs. 1.9 ± 2.3), but no association was found after controlling for potential confounding effects [20]. Similarly, Rosenthal et al. reported that the number of drug allergies was not associated with poorer Simple Shoulder Test (SST) score, Visual Analogue Scale (VAS) pain score, or active forward flexion after TSA. However, it is important to note that these two studies had the smallest two patient populations [21].

Discussion

The results of our study suggest that a higher number of patient-reported antibiotic allergies is associated with a higher risk of PJI. Six of the 8 studies revealed association between patient-reported allergies and poor patient-reported outcomes, PJI, and prolonged hospitalization. However, two of the eight studies were not able to identify an association. Patients in the poor outcome group had an average of 3.3 allergies, which is more than twice as many as the number of allergies reported in the good outcome group with an

Table 1 Characteristics of articles included in final analysis

Title	Author, year	Study design	Allergen	How were allergens determined	Sample size (*N*)	Sex (%male)	Mean age	Minors score
Total shoulder arthroplasty: antibiotic allergies increase risk of postoperative complications	Bahoravitch et al. [15] (2022)	Retrospective study	Antibiotic (penicillin, sulfonamide, or other antibiotic allergies)	Patient-reported	85,606	44%	67.7 ± 8.1	18
Predictors of poor and excellent outcomes after reverse total shoulder arthroplasty	Forlizzi et al. [16] (2022)	Retrospective study	All types	Patient-reported	338	39.10%	71.5	17
Patient-reported drug and latex allergies negatively affect outcomes after total and reverse shoulder arthroplasty	Elrick et al. [17] (2021)	Retrospective Study	Drug and Latex allergies	Patient-reported	411	64.50%	66.5	19
Prevalence and predictors of persistent pain 2 years after total shoulder arthroplasty	Puzzitiello et al. [20] (2021)	Retrospective study	All types	Patient-reported	244	38.50%	68.8 ± 8.4	18
Is patient-reported penicillin allergy independently associated with increased risk of prosthetic joint infection after total joint arthroplasty of the hip, knee, and shoulder?	Wu et al. [14] (2020)	Retrospective study	Antibiotic (penicillin) allergy	Patient-reported	78,776	N/A	N/A	18
Delayed hospital discharge after total shoulder arthroplasty: why, and who is at risk?	Menendez et al. [19] (2019)	Retrospective study	All types	Patient-reported	415	39%	68.8 ± 8.4	19
High pain intensity after total shoulder arthroplasty	Menendez et al. [18] (2018)	Retrospective study	All types	Patient-reported	415	39%	68.8 ± 8.4	19
Shoulder arthroplasty outcomes in patients with multiple reported drug allergies: does number of drug allergies have an effect on outcome?	Rosenthal et al. [21] (2016)	Retrospective study	Drug allergies	Patient-reported	98	50%	67.7	19

Table 2 Outcomes of the studies

Author, year	Number of allergies in the good outcome group	Number of allergies in the poor outcome group	Follow-up period	Outcomes
Bahoravitch et al. [15] (2022)	N/A	N/A	2 years	Patients who had antibiotic allergies had a higher risk of PJI within 30 days, 1 year, and 2 years of surgery. Patients who had antibiotic allergies were more likely to have postoperative anemia, blood transfusions, and readmission within 90 days of surgery. Patients with penicillin allergy had a higher rate of PJI revision at 30 days, 90 days, 1 year, and 2 years
Forlizzi et al. [16] (2022)	1.4 ± 1.9	3.4 ± 4.9	Average of 28.3 months	Patients with an increasing number of reported allergies are more likely to achieve poor outcomes (ASES) after reverse shoulder arthroplasty
Elrick et al. [17] (2021)	N/A	N/A	Average of 1.9 ± 1.2 years	Only the QuickDASH score showed a statistically significant difference between allergy groups, while other postoperative PROs (ASES, SANE, SF-12 MCS, and SF-12 PCS) represented a pattern of worse outcomes with greater allergies. In particular, the group with 2 allergies had a considerably higher QuickDASH score than the group with 0 allergies, which was indicative of worse outcomes. After age, arthroplasty type, and baseline QuickDASH score, allergy group was the fourth most significant independent predictor of postoperative QuickDASH scores. In addition, higher number of allergies was the most influential independent predictor of postoperative patient satisfaction
Puzzitiello et al. [20] (2021)	1.9 ± 2.3	3.0 ± 4.8	2 years	Patients with persistent pain were more likely to have a higher number of self-reported allergies. However, after controlling for potential confounding effects no association was found
Wu et al. [14] (2020)	N/A	N/A	N/A	Patients who reported a penicillin allergy had a higher risk of PJI within 1 year of total shoulder arthroplasty than those who did not report a penicillin allergy (1.5% versus 0.4%)

Table 2 (continued)

Author, year	Number of allergies in the good outcome group	Number of allergies in the poor outcome group	Follow-up period	Outcomes
Menendez et al. [19] (2019)	1.6 ± 2.1	3.3 ± 3.8	N/A	Patients with extended LOS were more likely to have more self-reported allergies. After adjustment for potential confounding effects in multivariable modeling, the preoperative patient characteristics that had the strongest association with extended LOS was greater number of patient-reported allergies with an odds ratio of 1.22 per 1-unit increase
Menendez et al. [18] (2018)	1.5 ± 2.0	3.4 ± 3.7	N/A	Severe postoperative pain, defined as peak pain intensity ≥ 75th percentile (9–10 of 10 possible), was independently associated with a greater number of patient-reported allergies (OR, 1.28 per 1-unit increase)
Rosenthal et al. [21] (2016)	N/A	N/A	1.50 ± 0.79 years	The presence of single or multiple drug allergies is not associated with poorer SST score, VAS pain score, or active forward flexion after total shoulder arthroplasty

average of 1.6 allergies (Table 2). This result is supported by available literature; multiple studies have reported the association of the number of self-reported allergies with poor postoperative functional outcomes and quality of life after total joint arthroplasty [9, 13, 22]. Higher pain intensity and the poor patient-reported outcome can in turn result in an increased length of stay as these patients might require longer observation prior to discharge.

PJIs impose a large financial burden for payers as well as a health burden for patients. PJI after total joint arthroplasty can cost up to $93,000 due to the need for revision and increases the average length of stay by around 5 days [23–26]. Previous research has indicated that up to 95% of self-reported penicillin allergies were found to be incorrect when patients were tested [27-29]. This would mean that a considerable number of patients who may benefit from penicillin are instead receiving second-line antibiotics, putting them at a higher risk of PJI. This emphasizes the need of having allergy testing done prior to surgery in order to determine the correct course of treatment for the patient.

Penicillin allergy is one of the most prevalent self-reported allergies, with roughly 10% of patients reporting that they are allergic [11, 30]. Penicillin-reported allergies frequently prevent the use of penicillins and other beta-lactams and instead result in the administration of second-line antibiotics (i.e., clarithromycin, azithromycin, amoxicillin-clavulanate, cephalosporin, or fluoroquinolone) and broad-spectrum antibiotics, which are associated with toxicity, the development of antimicrobial resistance, and adverse events [31]. Additionally, second-line antibiotics can result in an increase of between 32 and 50% in the likelihood of PJIs [32, 33].

Moreover, patients who report a higher number of allergies may be allergic to substances that are not commonly known to them, such as metals used in surgery. Nam et al. reported a 2.3% increase in metal allergy reporting after the introduction of a metal allergy-specific question on preoperative questionnaires, and patients who reported metal allergies had decreased functional outcomes after total knee arthroplasty (TKA) and decreased mental health scores after total hip arthroplasty [34]. However, diagnosing metal implant allergy remains challenging due to the need to exclude differential diagnoses and the requirement for a combination of different allergy diagnostic tools. We propose that the number of patient-reported allergies can be used as a screening tool to identify patients at risk of having unknown allergies to metals or prosthetics. Such patients can then be evaluated using various diagnostic tools, such as a skin patch test, to confirm the presence of an allergy. If an allergy is confirmed, treatment with hypoallergenic materials can be considered. This approach has the potential to improve patient outcomes and reduce the risk of implant failure or adverse events due to undiagnosed allergies.

Prior investigations have noted the quantity of self-reported allergies is a possible indicator of psychological distress, depression, anxiety, and functional somatic syndrome [35–37]. Several studies have found that individuals experiencing psychological distress had poorer self-perceived outcomes following total joint arthroplasty [38–40]. According to Moverman et al., functional somatic symptoms are widespread in patients receiving shoulder arthroplasty and are associated with poorer outcomes [41]. For instance, Werner et al. reported that patients with depression achieved lower final ASES scores and SF-12 PCS scores as well as lower satisfaction levels at 2 years compared to those without depression [42]. This emphasizes the significance of screening for patient-reported allergies as they might indicate an underlying psychiatric health condition that might negatively impact the outcomes of SA.

This systematic review has several limitations. The number of research articles included in this systematic review was restricted, and a larger body of data might alter the outcome findings. Furthermore, all the articles studied patient-reported allergies and did not medically validate the existence of the allergies, which may weaken the associations of our results. In addition, three of the studies included in our study are from the same study group which decreases the generalizability of our study. Moreover, all the articles included in our study utilized patient-reported allergies, without confirming true allergies, which allows room for confounding errors. Additionally, it should be noted that all studies included in this systematic review have a retrospective design, which poses limitations to establishing causality between patient-reported allergies and outcomes of shoulder arthroplasty. Finally, the average MINORS score of 18.4 ± 0.7 is considered a low score for comparative studies, which suggests that the quality of the studies included does not have the highest power and good quality studies are needed to strengthen the association of allergies with SA. More studies assessing the association between the number of allergies and the type of allergies with SA are needed in order to better risk stratify patients and counsel them accordingly.

Conclusion

Patients with a higher number of reported antibiotic allergies are at potential risk for PJI after SA. Several studies also found an association between patient-reported allergies and increased postoperative pain, increased hospital length of stay, and poor patient-reported outcomes. Although patient-reported allergies may not always be accurate, they could still serve as a preliminary screening tool to identify patients who require further diagnostic testing to confirm the presence of allergies. Future studies should focus on evaluating the effectiveness and accuracy of allergy diagnostic tools in patients undergoing SA. Additionally, investigating if the use of hypoallergenic materials in patients with reported metal or prosthetic allergies could lead to improved outcomes.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s42399-023-01493-1.

Author Contribution A.K and J.L were involved in the design and conception of this manuscript. A.K and J.L performed the literature search, gathered all data, compiled the primary manuscript, and compiled the figures. M.S critically revised the manuscript. All authors have approved the manuscript as it is written.

Funding Open access funding provided by SCELC, Statewide California Electronic Library Consortium

Data Availability All data pertaining to this research article are included within the manuscript as written.

Code Availability All data pertaining to this research article are included within the manuscript as written.

Declarations

Ethics Approval Not applicable.

Consent to Participate Not applicable.

Written Consent for Publication Not applicable.

Conflict of Interest The authors declare no competing interests.

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