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Risks of chronic steroid or immunosuppressive therapy on total shoulder arthroplasty patients

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Abstract

Introduction: Patients on chronic corticosteroids/immunosuppressants (SI) undergoing orthopaedic surgery are at an increased risk for surgical complications and worse outcomes. However, whether or not chronic preoperative SI use increases the risk for 30-day complications in patients undergoing primary total shoulder arthroplasty (SA) has yet to be explored.

Methods: From 2006 to 2019, the National Surgical Quality Improvement Program (NSQIP) database was used to identify all patients who underwent primary SA (anatomic TSA and reverse TSA). Patients were stratified into two cohorts: chronic pre-operative SI users and those without use. Bivariate and multivariate analyses were utilized in this study.

Results: Of the 26,979 patients who underwent primary SA, 25,656 (95.1%) patients did not have SI usage whereas 1323 (4.9%) patients had chronic preoperative SI usage. Following adjustment on multivariate analyses, compared to the non-SI usage cohort, patients who used SI had an increased risk of urinary tract infections (UTIs) (OR 1.87; $p = 0.009$) and septic shock (OR 7.14; $p = 0.002$). There were no differences in mortality between the two cohorts ($p = 0.058$).

Discussion and Conclusion: Chronic pre-operative SI use is an independent risk factor for septic shock and UTIs following primary SA. Surgeons and patients should be aware of these risks to better inform patient counseling and surgical decision making.

Keywords

total shoulder arthroplasty, steroids, immunosuppression, complications, infection

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Introduction

Many patients use corticosteroids or other immunosuppressants chronically (oral or parenteral) for managing various systemic conditions, including rheumatoid arthritis, systemic lupus erythematous, inflammatory bowel disease, Grave's disease, and other inflammatory or autoimmune conditions.[1] An estimated 1.2% of the general U.S. population is using oral glucocorticoids with an average with a 34% increase in long-term oral glucocorticoid prescriptions (> 3 months) from 1989 to 2008 in the United Kingdom.[2,3] Long-term steroid use increases the risk for many adverse effects, including hyperlipidemia, adrenal insufficiency, growth suppression, osteoporosis, and liver damage.[4] Like other adults, these patients on chronic steroid or immunosuppressant therapies are likely to require an orthopaedic surgery as they age.[5] Thus, given the increasing prevalence and adverse-effect profile of chronic steroid/immunosuppressant (SI) use, it is important to identify and understand whether these patients are at an increased risk for surgical complications.

Prior literature has explored surgical risks in chronic SI users in both the orthopaedic and non-orthopaedic setting.[6–14] In one study of over 5 million orthopaedic

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and non-orthopaedic surgical patients, chronic steroid use was found to be an independent risk factor for perioperative complications, with a 58% increase in risk for readmission and a 32% increase in risk for death.[13] Likewise, Weisberger et al. showed that chronic steroid use increased the risk for major bleeding complications by four times following microvascular free tissue transfer procedures.[9] In the orthopaedic setting, chronic pre-operative steroid use was found to be an independent risk factor for septic shock and a prolonged hospital length of stay following revision total knee arthroplasty (rTKA).[14] Moreover, chronic corticosteroid use increases the risk of 30-day readmission, 90-day readmission, and revision hip arthroplasty at 12 months following primary THA.[15] Similarly, chronic preoperative steroid use was found to be an independent risk factor for readmission, pulmonary embolism, and surgical site infection within 30-days following elective posterior lumbar spinal fusion.[12] Moreover, in a study of 15, 015 patients who underwent shoulder arthroscopy, chronic steroid use was shown to be an independent risk factor for 30-day readmission.[16] Importantly, steroid use was found to be an independent predictor of any complication, bleeding resulting in transfusion, and minor morbidity in a study of 1922 patients undergoing primary total shoulder arthroplasty (TSA).[17]

However, prior literature has not thoroughly explored potential differences in risk for chronic SI users across a broad range of complications in the acute post-operative setting following primary SA (anatomic TSA (aTSA) and reverse TSA (rTSA)) using a large multi-institutional database. Thus, the purpose of this study is to explore whether chronic SI users are at an increased risk for 30-day morbidity or mortality following primary TSA compared to their non-SI user counterparts.

Methods

For this retrospective cohort study, the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database was utilized.[18] The ACS-NSQIP is a national database that contains deidentified patient data from over 600 participating hospitals. This database includes many different variables, such as preoperative, intraoperative, and postoperative variables. This database is maintained by trained surgical clinical reviewers and it has high inter-rater reliability with data collection.[19,20] In addition, this database has been used in a variety of orthopaedic and non-orthopaedic research studies to track the clinical course of individual patients.[21,22]

Patient selection

All patients who underwent primary SA (aTSA or rTSA) from the years 2006 to 2019 were identified using current procedural terminology (CPT) code 23472. Patients with missing baseline values were excluded from the study, as well as patients under the age of 18 years. Two patient groups were defined in this study: patients without chronic preoperative SI usage and patients with chronic preoperative SI usage. Chronic preoperative SI usage was defined as patients who required regular administration of parenteral or oral corticosteroid medications or immunosuppressant

Table 1. Demographics and clinical characteristics Among patients undergoing primary total shoulder arthroplasty.

Demographics	No Steroid Use (N = 25,656)	Steroid Use (N = 1323)	*P*-Value
Age[a] (year)	69.33 ± 9.61	68.17 ± 10.43	**< 0.001***
Sex[b]			**< 0.001****
Male	11,449 (44.6)	412 (31.1)	
Female	14,207 (55.4)	911 (68.9)	
Race[b]			**< 0.001****
White	22,917 (89.3)	1140 (86.2)	
Black	1286 (5.0)	79 (6.0)	
Hispanic	1140 (4.4)	69 (5.2)	
American Indian	107 (0.4)	11 (0.8)	
Asian	176 (0.7)	21 (1.6)	
Hawaiian	30 (0.1)	3 (0.2)	
BMI[a] (kg/m^2)	31.18 ± 6.85	30.29 ± 7.02	**< 0.001***
ASA Classification[b]			**< 0.001****
ASA I	363 (1.4)	2 (0.2)	
ASA II	10,931 (42.6)	338 (25.5)	
ASA III	13,637 (53.2)	914 (69.1)	
ASA IV	703 (2.7)	69 (5.2)	
ASA V	4 (0.0)	0 (0.0)	

BMI: body mass index; ASA: American Society of Anesthesiologists.
Bolding equals significance $p < 0.05$.
*Analysis of variance.
**Pearson's chi-squared test.
[a]The values represent the mean and the standard deviation.
[b]The values represent the number of patients, with the percentage indicated in parentheses.

Table 2. Comorbidities Among patients undergoing primary total shoulder arthroplasty.

Comorbidities[a]	No Steroid Use (N = 25,656)	Steroid Use (N = 1323)	*P*-Value*
COPD	1639 (6.4)	193 (14.6)	**< 0.001**
CHF	153 (0.6)	21 (1.6)	**< 0.001**
Hypertension	17,395 (67.8)	900 (68.0)	0.864
Dialysis	91 (0.4)	9 (0.7)	0.057
Weight loss	48 (0.2)	5 (0.4)	0.126
Bleeding disorder	660 (2.6)	62 (4.7)	**< 0.001**
Preoperative Transfusion	53 (0.2)	1 (0.1)	0.299
Smoker	2663 (10.4)	136 (10.3)	0.907
Functional status preoperative			**< 0.001**
Independent	24,839 (97.6)	1252 (95.8)	
Partially dependent	568 (2.2)	54 (4.1)	
Totally dependent	31 (0.1)	1 (0.1)	
DM status			0.074
No DM	21,059 (82.1)	1112 (84.1)	
Noninsulin-dependent DM	3263 (12.7)	140 (10.6)	
Insulin-dependent DM	1334 (5.2)	71 (5.4)	
Dyspnea			**< 0.001**
No dyspnea	24,000 (93.5)	1147 (86.7)	
Moderate exertion	1574 (6.1)	165 (12.5)	
At rest	82 (0.3)	11 (0.8)	
Anesthesia type			0.729
General	24,882 (97.1)	1286 (97.3)	
Neuraxial	47 (0.2)	2 (0.2)	
Regional	429 (1.7)	24 (1.8)	
MAC	187 (0.7)	5 (0.4)	

*Pearson's chi-squared test.
Bolding equals significance $p < 0.05$.
COPD: chronic obstructive pulmonary disease; CHF: congestive heart failure; DM: diabetes mellitus; MAC: monitored anesthetic care.
[a]The values represent the number of patients, with the percentage indicated in parentheses.

medications in the thirty days before surgery for a chronic medical condition (e.g. COPD, inflammatory bowel disease, rheumatologic disease).[18] A one-time pulse limited short course of corticosteroids, or a taper, of less than 10 days duration did not qualify. Topical corticosteroids or corticosteroids administered by inhalation or rectally did not qualify.

Patient characteristics

Patients' demographics and clinical characteristics extracted from the database included age, sex, race, body mass index (BMI), and American Society of Anesthesiologists (ASA) classification. Patients' medical comorbidities and intraoperative variables assessed included chronic obstructive

Table 3. Bivariate analysis of postoperative complications of patients following primary total shoulder arthroplasty.

30-Day Outcomes[a]	No Steroid Use (N = 25,656)	Steroid Use (N = 1323)	*P*-Value*
Operative Complications			
Superficial Surgical Site Infection	48 (0.2)	3 (0.2)	0.746
Deep Surgical Site Infection	19 (0.1)	1 (0.1)	0.984
Organ Space Infection	46 (0.2)	1 (0.1)	0.378
Wound Dehiscence	17 (0.1)	0 (0.0)	0.349
Non-Operative Complications			
Pneumonia	117 (0.5)	9 (0.7)	0.243
Renal Insufficiency	22 (0.1)	2 (0.2)	0.436
Pulmonary Embolism	75 (0.3)	4 (0.3)	0.948
Urinary Tract Infection	177 (0.7)	21 (1.6)	**< 0.001**
Stroke	22 (0.1)	1 (0.1)	0.902
Myocardial Infarction	63 (0.2)	5 (0.4)	0.349
Requiring Transfusion	620 (2.4)	49 (3.7)	**0.003**
Deep Vein Thrombosis	89 (0.3)	7 (0.5)	0.278
Septic Shock	9 (0.0)	4 (0.3)	**< 0.001**
Extended Length of Stay (>2 days)	4437 (17.3)	289 (21.9)	**< 0.001**
Readmission	694 (3.5)	53 (5.1)	**0.010**
Reoperation	340 (1.3)	23 (1.7)	0.203
Death	41 (0.2)	6 (0.5)	**0.012**

*Pearson's chi-squared test.
Bolding equals significance $p < 0.05$.
[a]The values represent the number of patients, with the percentage indicated in parentheses.

pulmonary disease (COPD), congestive heart failure (CHF), hypertension, requirement for dialysis, weight loss in the past six months, bleeding disorder, preoperative transfusion requirement, smoking status, functional status, diabetes mellitus, dyspnea, and type of anesthesia.

Postoperative outcomes

The thirty-day complications evaluated in this study included superficial and deep surgical site infections (SSIs), organ space infections, wound dehiscence, pneumonia, renal insufficiency, pulmonary embolism, urinary tract infection, stroke, myocardial infarction, bleeding requiring postoperative transfusion, deep vein thrombosis, septic shock, extended length of hospital stay, readmission, reoperation, and mortality. Extended length of stay was defined as more than 2 days based on previous studies.[23,24]

Statistical analysis

Patient demographics, medical comorbidities, and postoperative outcomes were analyzed between the non-SI cohort and the SI cohort using bivariate analyses. Pearson's Chi-squared test and one-way analysis of variance were utilized where appropriate. To control for covariates, demographic and comorbidity variables were included in the multivariate analyses for p-values < 0.20.[25,26] Postoperative outcome variables with a p-value < 0.05 were chosen for multivariate analyses. Multivariate logistic regression analyses were performed to identify the independent effects of steroid use for these postoperative complications. The value for statistical significance was a p-value of < 0.05 in this study. Statistical Package for the Social Sciences (SPSS; Version 28; Armonk, NY) software was utilized to conduct the various statistical analyses.

Table 4. Multivariate analysis of postoperative complications of patients following primary total shoulder arthroplasty.

Steroid Use (versus No Steroid Use) 30-Day Outcomes	Odds Ratio	95% CI		*P*-Value
Urinary Tract Infection	1.874	1.173	2.994	**0.009**
Requiring Transfusion	1.151	0.845	1.567	0.374
Septic Shock	7.142	2.060	24.764	**0.002**
Extended Length of Stay (>2 days)	1.073	0.929	1.240	0.339
Readmission	1.232	0.918	1.652	0.164
Death	2.359	0.970	5.736	0.058

CI: confidence interval.
Bolding equals significance $p < 0.05$.

Results

Demographics

In total, 26,979 patients who underwent primary SA were included in the analysis. 25,656 (95.1%) patients did not have chronic preoperative SI usage and 1323 (4.9%) patients had chronic preoperative SI usage. Compared to patients who did not use SI, those with chronic SI usage were more likely to be female (68.9% vs 55.4; $p < 0.001$), Black (6.0% vs 5.0%; $p < 0.001$), have a lower BMI (30.3 vs 31.2 kg/m^2; $p < 0.001$) and have an ASA class of III (69.1% vs 53.2%; $p < 0.001$) (Table 1).

Comorbidities

Relative to patients in the non-SI usage cohort, patients who were chronic preoperative SI users were more likely to have medical comorbidities, including COPD (14.6% vs 6.4%; $p < 0.001$), CHF (1.6% vs 0.6%; $p < 0.001$), bleeding disorders (4.7% vs 2.6%; $p < 0.001$), have a dependent functional status (4.2% vs 2.3%; $p < 0.001$), and dyspnea on moderate exertion (12.5% vs 6.1%; $p < 0.001$) (Table 2).

Outcomes

On bivariate analysis, compared to patients who did not have chronic preoperative SI usage, patients with SI usage were more likely to develop urinary tract infections (1.6% vs 0.7%; $p < 0.001$), bleeding requiring transfusion (3.7% vs 2.4%; $p = 0.003$), septic shock (0.3% vs 0.0%; $p < 0.001$), have an extended length of stay greater than 2 days (21.9% vs 17.3%; $p < 0.001$), require readmission to the hospital (5.1% vs 3.5%; $p = 0.010$), and have a higher mortality rate (0.5% vs 0.2%; $p = 0.012$) (Table 3). Patients with chronic preoperative SI use did not have an increased risk for superficial SSIs (0.2% vs 0.2%; $p = 0.746$) or deep SSIs (0.1% vs 0.1%; $p = 0.984$).

To control for the differences in demographics and comorbidities between the non-steroid usage cohort and SI usage cohort, multivariate analyses were performed which showed that patients who used SI had increased risk of urinary tract infections (OR 1.87; 95% CI 1.17 to 2.99; $p = 0.009$) and septic shock (OR 7.14; 95% CI 2.06 to 24.76; $p = 0.002$) compared to patients who did not use SI. There were no differences in length of stay ($p = 0.339$), readmission ($p = 0.164$), or mortality ($p = 0.058$) between the two cohorts following adjustment on multivariate analysis (Table 4).

Discussion

Chronic SI use patients are at an increased risk for surgical and medical complications, worse functional outcomes, and readmissions following various orthopaedic and non-orthopaedic surgeries.[6–14] It is important to understand these differences in risks to better optimize their care, reduce costs, and improve outcomes. This study showed for the first time that among primary SA patients, chronic pre-operative SI use is an independent risk factor for septic shock and UTIs post-operatively but not readmission or mortality. Most importantly, chronic preoperative SI use is not an independent risk factor for superficial or deep SSIs following primary SA.

Although we found an increased risk for UTIs and septic shock, these findings may not be as clinically significant today. Urinary catheters are not used as frequently today by orthopaedic surgeons, and thus the risks of a UTI are already minimal.[27–29] Prior research has shown that reducing indwelling urinary catheter use may reduce UTI risk in the orthopaedic setting.[27–29] Likewise, a recent meta-analysis highlighted that urinary catheterization during total joint arthroplasty (TJA) can increase the risk for post-operative UTI and may not be required routinely.[30] As such, simply not using a urinary catheter at the time of surgery may reduce any differences in risk for UTI or septic shock to nearly zero between chronic preoperative SI users and patients without chronic SI use. Nonetheless, it is possible that the UTI and septic shock risk is partly due to the immunosuppressive and anti-inflammatory effects of corticosteroids and other immunosuppressant medications. This is because corticosteroids alter the way our body's immune system responds to infections.[31] Mechanistically, corticosteroids sequester CD4+ T-lymphocytes, alter the transcription of cytokines, and influence neutrophil migration.[32,33] Further research is needed to better understand the underlying causes for the increased UTI and septic shock risks, as this may necessitate further collaboration between orthopaedic surgeons and medical teams on peri-operative SI dosing, antibiotic

management, and more. Additionally, the increased UTI and septic shock risks are not consistent with all previous literature. For example, one study found no increased risk in peri-operative sepsis or septic shock following total joint arthroplasty (primary or revision THA and TKA). Moreover, the risks of UTI and septic shock were not found to be increased in chronic steroid use patients following anterior lumbar fusion.[34]

Our finding of no increased risk for superficial or deep SSIs in chronic SI users undergoing primary SA is consistent with a study by Fassihi et al.[14] Using a large national database study of over 10,000 patients undergoing revision TKA, Fassihi et al. found that patients with chronic preoperative steroid use were not at an increased risk for SSIs compared to those patients without chronic preoperative steroid use.[14] However, there are many studies in contrary to our findings regarding SSI risks. In a large database study of 99,970 patients undergoing arthroscopic and open rotator cuff repair, shoulder stabilization, and other associated procedures, chronic steroid use was found to be an independent risk factor for infectious complications.[10] Likewise, in a study of around 15,000 patients undergoing shoulder and knee arthroscopic procedures, chronic steroid use was found to be an independent risk factor for readmission, most commonly due to surgical-site infections.[35] Contrary findings are also seen in hip and knee arthroplasty literature. Kittle et al. conducted a retrospective analysis of over 400,000 patients who underwent total joint arthroplasty, including primary TKA, primary total hip arthroplasty (THA), revision TKA, and revision THA.[11] Among these patients, chronic corticosteroid use was found to increase the post-operative risk for superficial SSIs, deep SSIs, and readmission compared to non-steroid use patients.[11] Similarly, Boddapati et al. also showed that chronic steroid users undergoing primary THA are at an increased risk post-operatively for superficial SSIs.[36] Finally, a meta-analysis found steroid therapy to be associated with deep infection following total knee arthroplasty.[37] Similar findings are also seen in spine literature. For example, an increased risk for deep SSIs was found among chronic pre-operative steroid users following elective anterior lumbar fusion (ALF).[34]

Further research is necessary to understand why our study found no increased superficial or deep SSI risk in chronic SI users undergoing primary SA, which is in contrary to most hip and knee literature. Such contrast in risks, however, is consistent with prior studies showing lower risks of morbidity and mortality following SA relative to hip and knee arthroplasty.[38,39] For example, Farmer et al. found that patients who had shoulder arthroplasties had no in-hospital deaths and, on average, lower complication rates, shorter length of stays, and fewer total charges compared to patients who underwent hip or knee arthroplasties.[39] Similarly, in a large study of US veterans, those undergoing TSAs were almost 70% less likely to have any postoperative complication compared to THAs or TKAs.[38]

This study is not without limitations. A large database such as the NSQIP database used in this study may have errors with data omission or erroneous data entry, although it is unlikely to be at a high enough rate to significantly impact our results. Additionally, the types and classes of immunosuppressants or corticosteroids used were not available. Furthermore, the database did not provide further specifications regarding the exact length of SI use. Future studies should evaluate differences in risk based on length of SI use, such as for those using SI for more than 1 year, more than 2 years, and longer. Moreover, we were unable to discern the dosage of SI due to the database's limitations, which may influence the risks. Studies exploring risk differences based on high-dose or low-dose SI and specific medications is warranted. The risks also could not be further stratified by underlying indication for SI use (rheumatoid arthritis, inflammatory bowel disease, transplant recipient, etc.) due to the database and should be further explored. The database also did not allow for us to differentiate between patients who underwent anatomic TSA or reverse TSA. Despite these limitations, this is the first well-powered, multi-institutional database study to evaluate the risks of chronic pre-operative SI use on primary TSA patients.

Conclusion

Chronic preoperative corticosteroid/immunosuppressant use does not increase the risk for superficial or deep SSIs, readmissions, or mortality following primary TSA. Chronic SI use increases the risk for UTIs and septic shock, although this may not be as clinically significant. It is important for both surgeons and patients to be aware of these risks to guide shared surgical decision making. Surgeons should consider additional modifications to their pre- or post-operative protocols for these patients to better prevent and manage these complications.

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