Does Chronic Corticosteroid Use Increase Risks of Readmission, Thromboembolism, and Revision After THA?

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Abstract

Background Systemic corticosteroids are commonly used to treat autoimmune and inflammatory diseases, but they can be associated with various musculoskeletal problems and disorders. There currently is a limited amount of data describing the postoperative complications of THA associated specifically with chronic corticosteroid use.

Questions/purposes For chronic corticosteroid users undergoing THA, we asked: (1) What is the risk of hospital readmission at 30 and 90 days after surgery? (2) What is the risk of venous thromboembolism at 30 and 90 days after surgery? (3) What is the risk of revision hip arthroplasty at 12 and 24 months after surgery?

Methods We identified patients in the Statewide Planning and Research Cooperative System who underwent primary THA between January 2003 and December 2010. This

database provides hospital discharge abstracts for all admissions in the state of New York each year. We used propensity scores to three-to-one match the 402 chronic corticosteroid users with a comparison cohort of 1206 patients according to age, sex, race, comorbidity score, year of surgery, and hip osteonecrosis. The risk of each outcome was compared between chronic corticosteroid users and the matched cohort. Because multiple comparisons were made, we considered p less than 0.008 as statistically significant.

Results Readmission was more common for corticosteroid users at 30 days (odds ratio [OR], 1.45; 95% CI, 1.14–1.85; $p = 0.003$) and 90 days (OR, 1.37; 95% CI, 1.09–1.73; $p = 0.007$). Venous thromboembolism was not more frequent in corticosteroid users at 30 days (OR, 2.39; 95% CI, 1.08–5.26; $p = 0.031$) or 90 days (OR, 1.91; 95%

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CI, 1.03–3.53; $p = 0.039$). Revision arthroplasty was more common in corticosteroid users at 12 months (OR, 2.49; 95% CI, 1.35–4.59; $p = 0.004$), but not 24 months (OR, 2.04; 95% CI, 1.19–3.50; $p = 0.010$).

Conclusions After THA, chronic corticosteroid use is associated with an increased risk of readmission at 30 and 90 days and revision hip arthroplasty at 12 months in corticosteroid users. Patients and providers should discuss these risks before surgery. Insurers should consider incorporating chronic corticosteroid use as a comorbidity in bundled payments for THA, since this patient population is more likely to return to their provider for care during the postoperative period.

Level of Evidence Level III, therapeutic study.

Introduction

Systemic corticosteroids are commonly used to treat various autoimmune and inflammatory diseases. An estimated 0.5% to 1% of patients in the general population and as many as 2.5% of older adults are characterized as chronic corticosteroid users [6]. Although systemic corticosteroids have proven short-term immunosuppressant and anti-inflammatory effects, the long-term use of these agents is associated with a myriad of complications including central obesity, skin thinning, fluid and electrolyte imbalance, adrenal insufficiency, and psychological disturbance [23].

THA often is indicated for chronic corticosteroid users with symptomatic degenerative hip disease. There is currently a limited amount of data that describes the postoperative complications of THA associated specifically with chronic corticosteroid use. Some studies have found that patients who take corticosteroids chronically are at increased risk for readmission [16], implant failure [15] and postoperative infection [5, 13, 22] after THA. However, other studies found no increases in the likelihood of readmissions for complications, including periprosthetic joint infection [2] and implant failure [4], after THA in this population. Moreover, the effect of chronic corticosteroid use on venous thromboembolism in this THA population is unknown and has been studied only indirectly in the context of how the specific inflammatory disease affects venous thromboembolism [13, 21]. These studies were either single-center analyses limited by relatively small sample sizes and questionable generalizability, or large database studies documenting corticosteroid use but not performing further subanalyses using matched cohorts that make inferences regarding readmission or revision rates or complications like venous thromboembolism [2, 4, 5, 13, 15, 16, 21, 22]. We therefore sought to use a large, multi-hospital, statewide healthcare database to investigate whether chronic corticosteroid use would be associated

with an increased risk of complications after THA by case-matching patients receiving long-term corticosteroids who underwent THA with patients who were not taking corticosteroids at the time of their hip procedures.

Specifically, we asked: (1) What is the risk of hospital readmission at 30 and 90 days after surgery for chronic corticosteroid users? (2) What is the risk of venous thromboembolism at 30 and 90 days after surgery for chronic corticosteroid users? (3) What is the risk of revision hip arthroplasty at 12 and 24 months after surgery for chronic corticosteroid users?

Patients and Methods

The New York Statewide Planning and Research Cooperative System (SPARCS) is a comprehensive healthcare data reporting system established by the New York State Department of Health (<https://www.health.ny.gov/statistics/sparcs/>). This database contains a census of all hospital admissions and ambulatory surgical procedures performed in the state of New York annually. Each record includes data on patient demographics, medical diagnoses, and surgical procedures. Hospital admissions use International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes for diagnoses and procedures, whereas ambulatory records use ICD-9 diagnosis codes and current procedure terminology codes (Current Procedural Terminology, Fourth Revision). This database includes a unique encrypted identification code for each patient, which allows researchers to track patients across multiple encounters and perform retrospective cohort analyses. Our version of the database did not contain any patient identifiers and, therefore, this study was given an exemption by the institutional review board.

The study cohort consisted of 105,122 patients who underwent primary THA in New York between January 2003 and December 2010. We initially identified the 125,306 patient records with an ICD-9 procedure code for primary THA (81.51, 00.74, 00.75, 00.76, 00.77) during this time. We then excluded 899 (< 1%) patient records with an unspecified identification code and 88 (< 1%) patient records with an unspecified date of surgery. We also excluded the 11,279 (9%) patient records specifying a history of hip arthroplasty (ICD-9 diagnosis code V43.64) at the time of the THA admission. For the 113,127 remaining patient records (87 (< 1%) patient records contained more than one exclusion), we considered only the first THA admission for each of the 105,122 patients and excluded the remaining 8005 (7%) patient records. We did not exclude any records owing to missing patient data. Those with incomplete data only had ‘race’ missing (see paragraph on this topic that follows later in Patients and

Methods). We were unable to identify patients who sought followup care outside New York or who died during followup.

Demographic variables for each admission, including age (in years), sex (male, female), race (white, nonwhite, missing), and year of admission (2003–2010), were extracted. Comorbidities were assessed using the Charlson and Deyo scoring method for ICD-9 coding [8]. The 17 comorbidities (with point value in parentheses) included: congestive heart failure (1), peripheral vascular disease (1), dementia (1), cerebrovascular disease (1), chronic pulmonary disease (1), rheumatologic disease (1), peptic ulcer disease (1), mild liver disease (1), past myocardial infarct (1), uncomplicated diabetes (1), hemiplegia or paraplegia (2), renal disease (2), malignancy including leukemia and lymphoma (2), diabetes with end organ damage (2), moderate or severe liver disease (3), metastatic solid tumor (6), and HIV infection (6). Patients with none of these comorbidities received a score of 0 points. For each patient, the length of stay for the primary THA admission also was extracted. We used diagnosis codes to identify patients with osteonecrosis of the hip at the time of the primary THA (ICD-9 diagnoses 733.40, 733.42, 733.49).

We identified 402 patients (ICD-9 diagnosis V58.65) who were chronic corticosteroid users at the time of their admission for primary THA. Patients without a documented diagnosis of chronic corticosteroid use were assigned to the comparison cohort. We used ICD-9 diagnosis codes to identify comorbid conditions that are commonly associated with chronic corticosteroid therapy, including rheumatoid arthritis (714), chronic obstructive pulmonary disease (490, 491, 492, 494, 496), asthma (493), polymyalgia rheumatica (725), systemic lupus erythematosus (710.0), vasculitis (446), psoriasis (696), and history of renal transplant (V42.0) (Table 1).

A matched comparison cohort then was created to minimize the confounding bias of demographic variables on the outcome data. Using propensity scores [19], we

matched patients in the comparison cohort with corticosteroid users in a three-to-one ratio. Matching variables included age, sex, race, Charlson and Deyo comorbidity score, year of admission, and hip osteonecrosis. However, when performing the matching algorithm, the database had some gaps. For example, a small number of patients had a ‘missing’ race, and we ran an additional analysis excluding these patients. However, we elected to match the small subset of chronic corticosteroid users and control subjects with missing race, since the exclusion of these patients would reduce the power of our outcome analyses, and we used these results for our conclusions. Fisher’s exact tests (sex, hip osteonecrosis), chi-square tests (race), and independent sample t-tests (age, Charlson and Deyo comorbidity score) were used to calculate the significance of demographic differences between chronic corticosteroid users and the comparison cohort. : Chronic corticosteroid users were younger (mean, 63 [SD, 16] vs mean, 65 [SD, 14] years, $p = 0.005$), more commonly female (65% vs 57%; $p < 0.001$), more commonly white race (84% vs 82%; $p = 0.004$), had a higher Charlson and Deyo comorbidity score (mean, 1.2 [SD, 0.9] vs mean, 0.5 [SD, 0.9]; $p < 0.001$), and more likely to have hip osteonecrosis (30% vs 7%; $p < 0.001$). After matching 1206 patients in the comparison cohort with the 402 chronic corticosteroid users, there were no differences according to sex ($p = 0.904$), race ($p = 0.130$), year of surgery ($p = 0.999$), or hip osteonecrosis ($p = 0.273$). However, chronic corticosteroid users were younger (mean, 63 [SD, 16] vs mean, 65 [SD, 14] years; $p = 0.012$) and had a lower Charlson and Deyo comorbidity score (mean, 1.2 [SD, 0.9] vs mean, 1.3 [SD, 1.4]; $p = 0.012$) (Table 2). There were no differences in the mean lengths of stay ($p = 0.350$) for chronic corticosteroid users (mean, 4.34 days; 95% CI, 4.13–4.54 days) compared with the matched comparison cohort (mean, 4.48 days; 95% CI, 4.25–4.71 days).

Using the patient identification code, we retrospectively evaluated patients for the subsequent 24 months after their primary THA. We identified patients who were admitted during this period for any cause, venous thromboembolism (ICD-9 diagnoses 415.11, 415.13, 415.19, 451.11, 451.19, 451.2, 451.81, 451.9, 453.1, 453.2, 453.40, 453.41, 453.42, 453.8, 453.89, 453.9), and revision hip arthroplasty (ICD-9 procedure codes 81.53, 00.70, 00.71, 00.72, 00.73, 80.05).

We compared the date of the primary THA with the date of hospital admission (readmission, venous thromboembolism) or the date of surgery (revision hip arthroplasty) to identify the duration between the primary THA and the outcomes of interest. Endpoints for readmission and venous thromboembolism included 30 and 90 days. Endpoints for revision hip arthroplasty included 12 and 24 months.

Table 1. Comorbid conditions among chronic corticosteroid users

Comorbid condition	Prevalence (percent of patients)
Rheumatoid arthritis	29
Chronic obstructive pulmonary disease	16
Asthma	15
Polymyalgia rheumatica	13
Systemic lupus erythematosus	7
Vasculitis	3
Psoriasis	2
History of renal transplant	2

Table 2. Patient demographics of study cohort

Demographic	Chronic corticosteroid users	Comparison cohort	p value	Matched comparison cohort	p value
Admissions, number	402	104,720		1206	
Age (years), mean	63	65	0.005	65	0.012
Sex (%)					
Male	35	43	< 0.001	35	0.904
Female	65	57		65	
Race (%)					
White	84	82	0.004	80	0.130
Nonwhite	14	12		17	
Missing	2	5		3	
Charlson and Deyo score, mean	1.2	0.5	< 0.001	1.3	0.012
Hip osteonecrosis (%)					
No	70	93	< 0.001	73	0.273
Yes	30	7		27	
Year of surgery			< 0.001		0.999

Statistical Analysis

The incidence of each outcome was calculated using frequency tables for chronic corticosteroid users and the matched comparison cohort. The risk of each outcome then was modeled with logistic regression used to calculate the odds ratio (OR) and 95% CI for chronic corticosteroid users compared with the matched comparison cohort. We controlled for age and Charlson and Deyo comorbidity score in all regression models, since a significant difference remained between the cohorts after matching. However, the models were not adjusted for sex, race, year of surgery, or hip osteonecrosis, because matching on these variables had minimized their associated confounding effects. Per the guidelines of our data use agreement for the SPARCS database, which required at least 10 events for each complication, we were unable to specifically analyze the subpopulation of chronic corticosteroid users with osteonecrosis because of the small sample size and the low incidence of each of the studied postoperative complications of THA. The reason for this SPARCS database guideline is to protect patient confidentiality where there are very few events of a particular type. In addition, we were unable to evaluate indications for corticosteroid use or revision surgery.

Statistical analyses were performed using SAS[®] Version 9.4 (SAS Institute Inc, Cary, NC, USA). Figures were generated using Microsoft[®] Excel[®] 2010 (Microsoft Corporation, Redmond, WA, USA). All p values were two-tailed. We applied the Bonferroni correction to our outcome analyses to avoid the problem of multiple comparisons. Since there were six total endpoints, we interpreted p less than 0.008 (0.05/6) as statistically significant.

Results

Readmission was more common for chronic corticosteroid users compared with the matched comparison cohort. In regression models, the ORs of readmission for chronic corticosteroid users were 1.45 (95% CI, 1.14–1.85; $p = 0.003$) at 30 days and 1.37 (95% CI, 1.09–1.73; $p = 0.007$) at 90 days (Fig. 1). When excluding subjects with a missing race classification, the ORs of readmission at 30 and 90 days were 1.32 (95% CI, 1.05–1.67; $p = 0.020$) and 1.29 (95% CI, 1.03–1.62; $p = 0.025$).

There was no difference in the risk of venous thromboembolism for chronic corticosteroid users compared with the matched comparison cohort. In regression models, the ORs of venous thromboembolism for chronic corticosteroid users were 2.39 (95% CI, 1.08–5.26; $p = 0.031$) at 30 days and 1.91 (95% CI, 1.03–3.53; $p = 0.039$) at 90 days (Fig. 2), which based on our Bonferroni correction do not represent significant differences. On exclusion of patients with undocumented race, the ORs of venous thromboembolism at 30 and 90 days were 1.76 (95% CI, 0.86–3.61; $p = 0.121$) and 1.83 (95% CI, 1.02–3.28; $p = 0.042$), which based on our Bonferroni correction do not represent significant differences.

Revision hip arthroplasty was more common for chronic corticosteroid users compared with the matched comparison cohort. In regression models, the ORs of revision hip arthroplasty for chronic corticosteroid users were 2.49 (95% CI, 1.35–4.59; $p = 0.004$) at 12 months and 2.04 (95% CI, 1.19–3.50; $p = 0.010$) at 24 months (Fig. 3). When excluding subjects with a missing race classification, the ORs of revision at 12 and 24 months were 2.76 (95% CI, 1.52–5.00; $p = 0.001$) and 2.16 (95% CI, 1.28–3.63; $p = 0.004$).

Fig. 1 The odds ratio of readmission after THA is shown.

Fig. 2 The odds ratio of venous thromboembolism (VTE) after THA is shown.

Discussion

In patients with degenerative disease of the hip, THA often is indicated to decrease pain and improve quality of life. The information we have regarding complications after THA in chronic corticosteroid users, particularly venous thromboembolism, readmission, and revision, are limited and contradictory [2, 4, 5, 13, 15, 16, 22]. Some studies were single-center analyses limited by relatively small sample sizes and questionable generalizability [4, 5, 13, 15]. Additionally, large-database studies either documented

corticosteroid use but did not perform further subanalyses using matched cohort analysis to make inferences regarding complications [16], or they addressed postoperative complications in populations with inflammatory arthritides, who presumably used chronic corticosteroid therapy, but did not further stratify analyses based on corticosteroid use [21]. Therefore, using a large, statewide sample of patients who underwent THA during an 8-year period, we evaluated the risk of common postoperative complications for chronic corticosteroid users versus a matched comparison cohort. We found that this patient population had an

Fig. 3 The odds ratio of revision after THA is shown.

increased risk of hospital readmission and revision hip arthroplasty, but not venous thromboembolism.

Our study has several limitations. The database we used (SPARCS) does not contain data regarding dosage, duration, or indication of chronic corticosteroid therapy; the cause of hip osteonecrosis (idiopathic, steroid-associated, alcohol-associated, traumatic); intraoperative exposures, including surgical approach, incision time, and implant type; or postoperative variables, including pain, function, and indication for revision. Lack of information regarding corticosteroid dose and duration, in particular, is a limitation when evaluating the correlation of use of these drugs with complications. Although an “associated condition” is provided for each corticosteroid user, we cannot verify that this is the primary indication for use. Furthermore, if we had chosen to stratify based on “associated condition”, these subgroups would have been statistically underpowered. However, our study showed that chronic use is associated with higher readmission and revision rates. This conclusion can provide an impetus for further work focusing on the role of dosage and duration of corticosteroid use. Ultimately, given the paucity of data on this subject, we think this study is a valuable addition even in the absence of dosage and duration of use. Furthermore, there was insufficient sample size to stratify our analyses of venous thromboembolism into deep venous thrombosis and pulmonary embolism, study the complications of periprosthetic joint infection, stratify our analyses according to comorbid conditions that commonly are associated with chronic corticosteroid use, or perform a stratified analysis of each outcome for chronic corticosteroid users with osteonecrosis. However, it is important for future

evaluations, either with the use of larger databases or as a multicenter study, to evaluate the correlation of corticosteroid use with other complications, such as postoperative infection. We also were unable to identify patients who sought followup care outside New York and patients who died during followup. Further limitations of database use include the inconsistencies of data collection and reporting. For example, patients’ race was missing for 2% of chronic corticosteroid users and 3% of the matched comparison cohort. However, the *p* value of this difference was not significant, suggesting that the confounding effect of race was minimized through matching. Another limitation is the use of comorbidity index scores to match patients. These scoring systems are nonspecific, and it is difficult to compare different comorbidities between patients. However, unlike the Elixhauser system which is unweighted and additive, the Charlson and Deyo score is well known to readers and assigns weights to medical comorbidities. To our knowledge, this is currently the best way to compare overall comorbid status of patients, as doing this by individual disease is beyond our scope and also flawed given that with each disease, severity will likely vary among patients. Given the small sample size, and the large number of potential comorbidities to match on, we elected to use the Charlson and Deyo score for our final analysis. Further study may be warranted to develop a more accurate measure of comparing comorbid status among patients.

The risk of readmission was greater for chronic corticosteroid users at 1 to 3 months after THA. This is consistent with a prior database study, which found that corticosteroid users were nearly three times as likely to be readmitted within 30 days as the comparison cohort [16].

However, the validity of that study's finding is enshrouded by a multivariate logistic regression model containing greater than 25 predictor variables, thus increasing the rate of a false-positive finding. Moreover, comparisons were made between readmitted and nonreadmitted subjects, who were statistically different in terms of comorbidities and age and thus could not have made a more unbiased measurement than our study did with a matched-pair analysis. Nonetheless, we not only confirmed an increase in 1-month readmission rates, but also showed that readmission rates in chronic corticosteroid users continued to remain higher than the comparison cohort at 3 months postoperatively, the latter finding being particularly important for hospital systems participating in Medicare bundled care plans that further ensure 90-day postoperative treatment. Readmission rates for both matched cohorts were high. Although the exact reason is unknown, we postulate that this may be attributable to the comorbidities present in the two groups. With mean Charlson and Deyo scores greater than 1, these patients generally are more medically infirm than the average patient undergoing THA. Despite this, our study showed an increased risk of all-cause readmission among chronic corticosteroid users, but further study is needed to clarify whether the readmission was associated with a postoperative complication of THA versus the patient's comorbid conditions.

There was no difference in the risk of venous thromboembolism among chronic corticosteroid users at 1 to 3 months postoperatively. This finding is not consistent with prior studies, although those data were not specific to THA. Endogenous corticosteroid excess was associated with an increased risk of venous thromboembolism [25], and the risk of pulmonary embolism increased with higher doses and decreased with duration of use [24]. Mechanistically, corticosteroids can decrease serum levels of cytokines that cause reactive inflammation and hypercoagulability in the immediate postoperative period [11, 12, 14, 26]. However, corticosteroids also can increase the synthesis and release of clotting factors and fibrinolysis inhibitors, thereby enhancing coagulation [9, 10, 18]. Therefore, further study is indicated to explore the topic of thromboembolic events in chronic corticosteroid users. Specifically, these should focus on stratifying corticosteroid users based on individual conditions to evaluate differences in venous thromboembolism rates. This may aid in determining whether the corticosteroids, or possibly the associated chronic conditions, influence the venous thromboembolism rates.

Chronic corticosteroid use and its association with risk of revision after THA is controversial and data have been limited to those from underpowered studies. Our study is the first large, multihospital, statewide healthcare database study with sufficient power to investigate the influence of chronic corticosteroid use on THA revision risk, which we

found was statistically greater for chronic corticosteroid users at 6, 12, 18, and 24 months followup. At 12 months, the 1.91% incidence of revision hip arthroplasty among our matched comparison cohort is similar to the 2.03% cumulative incidence of revision reported from a large Medicare database study [3], thus supporting the findings in our comparison cohort and our study's external validity. A prior case series of corticosteroid users undergoing THA showed postoperative complications requiring reoperation included periprosthetic fracture, recurrent hip dislocation, and persistent deep infection [20]. Potential mechanisms for the association between corticosteroids and revision include poor bone formation secondary to suppression of osteoblasts [7], poor bone stock increasing the risk for fracture and prosthesis loosening [7], inhibition of collagen deposition and secretion of growth factors leading to impaired wound healing [27], and weakened immune function leading to infection [1, 17]. In a future study, long-term followup of chronic corticosteroid users at 5-year and 10-year endpoints would be useful to comprehensively assess implant survival in this patient population.

Orthopaedic surgeons should be aware of the increased risk of readmission and revision hip arthroplasty after THA in patients who are chronic corticosteroid users. Discussion of these potential complications in the consultation setting will help chronic corticosteroid users and their providers better evaluate the risks and benefits of surgery. Insurers should consider incorporating chronic corticosteroid use as a comorbidity in the calculation of bundled payments for THA, because our study found that this patient population is more likely to return to their providers for care during the postoperative period.

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