Chronic Corticosteroid Use as a Risk Factor for Perioperative Complications in Patients Undergoing Total Joint Arthroplasty

Abstract

Background: Osteoarthritis may be caused by or concurrent with diseases such as rheumatoid arthritis or systemic lupus erythematosus, which rely on chronic corticosteroids regimens for treatment. If a total knee or hip arthroplasty is needed, this chronic treatment method has been associated with poorer surgical outcomes.

Methods: A retrospective analysis of data collected by the American College of Surgeons National Surgical Quality Improvement Program was conducted. The Current Procedural Terminology codes were used to identify 403,566 total knee arthroplasty and total hip arthroplasty patients who were then stratified by the use of chronic corticosteroids for univariate analysis.

Results: Forteen thousand seven hundred seventy-four of the patients identified were prescribed chronic corticosteroid regimens. A statistically significant difference was observed in perioperative complications for patients prescribed with corticosteroids, including higher rates of surgical site infection ($P = 0.0001$), occurrence of deep incisional surgical site infection ($P = 0.0001$), occurrences of organ space surgical site infection ($P < 0.0001$), wound dehiscence ($P < 0.0001$), general wound infection ($P < 0.0001$), pneumonia ($P < 0.0001$), occurrences of unplanned intubation ($P = 0.0002$), urinary tract infection ($P < 0.0001$), and readmission ($P < 0.0001$). No statistically significant difference was observed in the 30-day mortality between the 2 groups (0.63), venous thromboembolic event (0.42), cerebrovascular accident (0.12), myocardial infarction (0.49), cardiac arrest (0.098), deep vein thrombosis (0.17), or sepsis (0.52).

Conclusion: Many of the notable differences in complications may be directly attributed to the immunosuppressive nature of corticosteroids. With increased knowledge of which perioperative complications to monitor, surgeons can tailor treatment strategies to this population that reduce morbidity and improve outcomes.
Total joint arthroplasty (TJA) is a procedure frequently performed for the treatment of end-stage joint osteoarthritis. The combined incidence of primary total knee arthroplasty (TKA) and total hip arthroplasty (THA) in the United States in 2010 was greater than 1 million, with a further 100,000 cases of revision knee and hip arthroplasties; this number is projected to increase with the aging population.1-3 Furthermore, it is estimated that the prevalence of corticosteroid use in the United States is nearly 1.2%.4 A number of patients presenting for TJA, such as those with rheumatoid arthritis, have comorbidities that are managed with chronic corticosteroid use resulting in notable overlap between these patient populations.5,6

Corticosteroids are used for chronic management of immune and inflammatory processes, but the same mechanisms that facilitate their anti-inflammatory and immunosuppressive effects also cause delayed wound healing.7,8 Specifically, corticosteroids decrease the ability of immune cells to infiltrate wounds via downregulation of cytokines and adhesion proteins in the endothelium (intracellular adhesion molecule [ICAM]), decrease fibroblast proliferation, and decrease the ability to perform collagen remodeling.7,9 These mechanisms are believed to contribute to the clinical finding that chronic corticosteroids result in poorer outcomes of surgical procedures, including TJAs.5,6,8,10-13

Associated complications include an increased need for revision arthroplasty, increased risk of readmission, thromboembolism, mortality, urinary tract infection (UTI), and deep and superficial wound infections.6,8,10-13

Few studies have examined the independent risk factor of chronic corticosteroid use for perioperative complications after THA and TKA,12,13 and none have examined a broad range of complications. Therefore, this study aims to determine if chronic corticosteroid utilization is associated with an increase in perioperative complications in THA, TKA, and revision knee and hip arthroplasty.

Methods

This was a retrospective analysis of prospectively collected data from the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database between 2010 and 2017. The ACS-NSQIP is a national database of 30-day postoperative morbidity and mortality outcomes from more than 500 institutions in the United States. The database includes more than 300 variables including preoperative, intraoperative, and postoperative variables. Because the ACS-NSQIP is a Health Insurance Portability and Accountability Act (HIPPA) compliant deidentified database, this study was exempt from Institutional Review Board (IRB) approval.

Patients who underwent TJA, including primary TKA, primary THA, revision TKA, and revision THA, were identified using the following Current Procedural Terminology codes: 27447, 27130, 27134, 27137, 27138, 27486, and 27487. A total of 403,566 patients were identified using the following Current Procedural Terminology code search criteria, and none were excluded.

Patient characteristics included patient demographics, medical comorbidities, preoperative condition, and surgical variables. Patient demographics included sex and age. Medical comorbidities included obesity (body mass index > 30), diabetes, current smoker within one year, pulmonary comorbidities (ventilator dependence within 48 hours before surgery or a history of chronic obstructive pulmonary disease), cardiac comorbidities (hypertension requiring medication or a history of congestive heart failure), renal comorbidities (history of acute renal failure or progressive renal insufficiency), currently requiring or on dialysis, and bleeding disorders. Preoperative conditions included American Society of Anesthesiologists (ASA) class ≥3, dyspnea at rest, poor functional status, weight loss, and patients who received preoperative transfusion of ≥1 unit of whole/packed red blood cells (RBC) in 72 hours before surgery.

The primary outcome measures for this study included mortality and perioperative complications occurring within 30 days after surgery. The perioperative complications reviewed were wound infection and complications, including surgical site infection, occurrence of deep incisional surgical site infection, occurrences of organ space surgical site infection, and wound dehiscence. Also included were pneumonia, occurrences of unplanned intubation, episode of venous thromboembolic event, failure to wean from the ventilator within 48 hours after surgery, UTI, postoperative cerebrovascular accident, cardiac arrest, myocardial infarction, deep vein thrombosis (DVT), sepsis, and readmission.

Univariate statistical analysis was performed on baseline characteristics and for mortality and perioperative complication measures. Statistical significance was set at P = 0.05. All statistical analysis were performed using the SAS University Edition using SAS Studio 3.8.

Results

In our cohort of 403,566 patients, 3.7% (14,774 of 403,566) were prescribed corticosteroids for a chronic medical condition. Some baseline patient characteristics were significantly different between patients who were prescribed corticosteroids and those who were not (Table 1). Statistically significant differences in medical comorbidities included obesity.

| Comorbidity               | Prescribed Corticosteroids | Not Prescribed Corticosteroids | P-value |
|---------------------------|---------------------------|-------------------------------|---------|
| Obesity                   | 5.1%                      | 1.9%                          | <0.01   |
| Diabetes                  | 11.6%                     | 8.2%                          | <0.01   |
| Smoker within one year    | 12.3%                     | 9.8%                          | <0.01   |
| Pulmonary Disease         | 7.8%                      | 5.5%                          | <0.01   |
| Cardiac Disease           | 12.5%                     | 9.1%                          | <0.01   |
| Renal Disease             | 7.2%                      | 4.1%                          | <0.01   |

These findings highlight the importance of considering corticosteroid use as a potential risk factor in the perioperative management of patients undergoing TJA. Further research is needed to understand the mechanisms underlying these associations and to develop strategies to mitigate their impact on patient outcomes.
(P < 0.0001), pulmonary comorbidity (P < 0.0001), cardiac comorbidity (P = 0.0035), patients on dialysis (P < 0.0001), and bleeding disorder (P < 0.0001). Regarding preoperative patient characteristics, ASA class (P < 0.0001), dyspnea at rest (P < 0.0001), poor functional status (P < 0.0001), weight loss (P < 0.0001), and preoperative transfusion of ≥1 unit of whole/packed RBCs in 72 hours before surgery (P < 0.0001) all were significantly different between the chronic corticosteroid and control groups.

The results of the univariate analysis are summarized in Table 2. No statistically significant difference was observed in the 30-day mortality between the two groups. However, a statistically significant difference was observed in perioperative complications for patients prescribed corticosteroids, including higher rates of surgical site infection (P < 0.0001), occurrence of deep incisional surgical site infection (P < 0.0001), occurrences of organ space surgical site infection (P < 0.0001), wound dehiscence (P < 0.0001), general wound infection (P < 0.0001), pneumonia (P < 0.0001), occurrences of unplanned intubation (0.0002), UTI (P < 0.0001), and re-admission (P < 0.0001).

Discussion

The aim of this study was to assess the risk of perioperative complications of TJA in patients on a regimen of corticosteroids for chronic disease. The results showed that patients undergoing chronic treatment with corticosteroids experienced a statistically significant increase in surgical site infection, deep incisional surgical site infection, organ space surgical site infection, wound dehiscence, general wound infection, pneumonia, re-intubation, UTI, and readmission. However, these patients did not

### Table 1

Baseline Patient Characteristics in the Patients Prescribed Corticosteroids for a Chronic Condition and No Corticosteroid Use Groups, Including Medical Comorbidities at the Time of Surgery, Preoperative Condition, and Operative Variables

| Patient Characteristics          | No Steroid Use (n = 388,792) | Steroid Use (n = 14,774) | P Value |
|---------------------------------|-----------------------------|--------------------------|---------|
| **Sex**                         |                             |                          |         |
| Male                            | 159,882                     | 4,808                    | 32.54   |
| Female                          | 228,728                     | 9,962                    | 67.43   |
| Age ≥ 65                        | 207,263                     | 7,357                    | 49.80   |
| **Medical comorbidities**       |                             |                          |         |
| Obesity                         | 220,208                     | 7,709                    | 52.18   | <0.0001 |
| Diabetes                        | 61,778                      | 2,334                    | 15.80   | 0.7647  |
| Smoking                         | 40,045                      | 1,562                    | 10.57   | 0.0845  |
| Pulmonary comorbidities         | 13,894                      | 1,231                    | 8.33    | <0.0001 |
| Cardiac comorbidities           | 239,939                     | 9,438                    | 63.88   | <0.0001 |
| Renal comorbidities             | 577                         | 36                       | 0.24    | 0.0035  |
| Dialysis Dependent              | 675                         | 75                       | 0.51    | <0.0001 |
| Bleeding disorder               | 8,414                       | 586                      | 3.97    | <0.0001 |
| **Preoperative condition**      |                             |                          |         |
| ASA class > 3                   | 6,695                       | 621                      | 4.20    | <0.0001 |
| Dyspnea at rest                 | 695                         | 85                       | 0.58    | <0.0001 |
| Poor functional status          | 6,067                       | 474                      | 3.21    | <0.0001 |
| Weight loss                     | 565                         | 53                       | 0.36    | <0.0001 |
| Transfusion                     | 22,521                      | 1,233                    | 8.35    | <0.0001 |
| **Surgical variables**          |                             |                          |         |
| Primary TKA                     | 225,103                     | 8,208                    | 55.56   |
| Primary THA                     | 140,374                     | 5,337                    | 36.12   |
| rTKA                            | 12,989                      | 608                      | 4.12    |
| rTHA                            | 10,326                      | 621                      | 4.20    |

ASA = American Society of Anesthesiologists, rTHA = revision total hip arthroplasty, rTKA = revision total knee arthroplasty, THA = total hip arthroplasty, TKA = total knee arthroplasty.
experience increased rates of overall mortality. We also found that the difference in baseline characteristics of patients taking regimens of chronic corticosteroids versus the control group were statistically significant, reflecting higher comorbidities in the corticosteroid group.

Our result of increased risk of perioperative infection in chronic corticosteroid users is consistent with previous findings.14-17 The goals of the previous studies were to identify risk factors for TJA infection rather than to identify complications related to chronic corticosteroid use. Therefore, previous publications do not differentiate between the types of infections caused by corticosteroids. Our results show that the rates of all types of surgical site infections are increased in TJA patients prescribed chronic corticosteroids. UTIs were also found at a higher rate in the population taking chronic corticosteroids. Although there is very little literature addressing nosocomial UTIs as a complication of arthroplasty, Alvarez et al18 did identify chronic corticosteroid use as an independent risk factor for UTI in TJA. There are also no known studies directed at exploring pneumonia as a complication of patients receiving chronic corticosteroids and receiving TJA. These complications are likely attributed to the immunosuppressive effects of corticosteroids. The decreased ability of the immune cells to infiltrate the surgical site leads to less immune activity and a greater likelihood that a pathogen will colonize the site.7,9 The systematic effects of the drug also decrease immune function in the urinary tract and respiratory system, leading to increased risk of developing an UTI or pneumonia, respectively.

Wound dehiscence was also found to be increased by a statistically significant margin in patients taking chronic corticosteroids. No previous studies exist demonstrating the relationship between dehiscence and chronic corticosteroids in arthroplasty surgeries; however, there are studies that demonstrate an increased prevalence of wound dehiscence with corticosteroid use in other surgeries, such as abdominal and colorectal incisions.19,20 Another study, completed by Ismael et al,8 used the ACS-NSQIP database and demonstrated an increase in wound dehiscence in chronic corticosteroid users across all types of surgery. This effect may be explained by the ability of corticosteroids to depress the proliferation of fibroblasts and inhibit the ability to remodel collagen.7,9

It is also notable that mortality, venous thrombus emboli (VTE), failure to be weaned from ventilation after 48 hours, postoperative cerebrovascular accident, cardiac arrest, myocardial infarction, DVT, and sepsis did not occur at a statistically significant

| Perioperative Complication                  | No Steroid Use (n = 388,792) | Steroid Use (n = 14,774) | P Value |
|--------------------------------------------|------------------------------|--------------------------|---------|
| Mortality                                  | 6                            | 0                        | 0.6326  |
| Surgical site infection                    | 2,126                        | 116                      | 0.0001  |
| Deep incisional surgical site infection    | 727                          | 54                       | <0.0001 |
| Organ space surgical site infection        | 982                          | 64                       | <0.0001 |
| Wound dehiscence                           | 668                          | 56                       | <0.0001 |
| Any wound infection                        | 4,247                        | 269                      | <0.0001 |
| Pneumonia                                  | 1,212                        | 117                      | <0.0001 |
| Reintubation                               | 583                          | 40                       | 0.0002  |
| Venous thromboembolic event                | 1,672                        | 57                       | 0.4191  |
| Failure to wean off ventilator             | 249                          | 14                       | 0.151   |
| UTI                                        | 3,120                        | 187                      | <0.0001 |
| Postoperative cerebrovascular accident     | 349                          | 19                       | 0.127   |
| Cardiac arrest                             | 297                          | 17                       | 0.098   |
| Myocardial infarction                      | 843                          | 36                       | 0.4921  |
| DVT                                        | 2,487                        | 108                      | 0.1728  |
| Sepsis                                     | 11                           | 0                        | 0.5179  |
| Readmission                                | 844                          | 50                       | <0.0001 |

DVT = deep vein thrombosis, UTI = urinary tract infection
increased rate. There is literature that shows that high concentrations of cortisol is linked to higher prevalence of both VTE and DVT.21,22 However, we found no evidence of increased risk for clotting events in our study. The only other investigation into postarthroplasty VTE and chronic corticosteroid use was also performed using the ACS-NSQIP database.13 The absence of an increased rate of perioperative sepsis is surprising. Although perioperative infection rates did increase with chronic corticosteroid use, the incidence of sepsis did not. Although there is no known literature assessing the risk of sepsis due to chronic steroid use in TJA, there are a few studies that show that there is an increased risk of sepsis in patients undergoing other surgeries who are on chronic corticosteroids.23,24 The absence of an increased risk of sepsis may be due to the immunomodulating effects of corticosteroids; although some literature has demonstrated a decrease in mortality from septic shock among corticosteroid users,25 others have shown no difference in mortality rates.26 Therefore, further study is warranted to explore the relationship between postoperative TJA sepsis and chronic corticosteroid use. This study is not without several limitations. First, the statistically significant differences existed in baseline characteristics between the control group and those who were on regimens of chronic corticosteroids. The goal of this study, however, is not to prove chronic corticosteroid use as an independent, causative risk factor for TJA complications. Instead, it demonstrates that patients receiving chronic corticosteroid treatment are associated with more comorbidities than the general population at baseline, and this population consequently features a higher risk for specific perioperative morbidities. This study is useful for surgeons, allowing them to consider a broader increased risk of specific perioperative complications in patients prescribed chronic corticosteroids. As with any large database study of this scale, it is difficult to eliminate mistakes in the recording of patient information, and a subset of patients may have been inadvertently included or excluded. Finally, there is a lack of data on the dose of corticosteroids taken by the patients. Further study in which patients are stratified by high- or low-dose chronic corticosteroids would be useful.

Conclusion

Corticosteroid use for a chronic condition for patients who underwent TJA were found to be independently associated with multiple perioperative complications. Further study of complication incidences in relation to corticosteroid use can help improve preoperative planning, optimization, and postoperative monitoring. Risk stratification can result in an improvement of postoperative complications.

References

1. Maradit Kremers H, Larson DR, Crowson CS, et al: Prevalence of total hip and knee replacement in the United States. J Bone Joint Surg Am 2015;97:1386-1397.

2. Steiner C, Andrews R, Barrett M, Weiss A: HCUP Projections: Mobility/Orthopedic Procedures 2003 to 2012. Report No.: 2012-03. Rockville, MD: US Agency for Healthcare Research and Quality (US), 2012, pp 110.

3. Inacio MCS, Paxton EW, Graves SE, Namba RS, Nemes S: Projected increase in total knee arthroplasty in the United States—An alternative projection model. Osteoarthr Cartil 2017;25:1797-1803.

4. Overman RA, Yeh JY, Deal CL: Prevalence of oral glucocorticoid usage in the United States: A general population perspective. Arthritis Care Res (Hoboken) 2013;65: 294-298.

5. Cordtz RL, Zobbe K, Hoigaard P, et al: Predictors of revision, prosthetic joint infection and mortality following total hip or total knee arthroplasty in patients with rheumatoid arthritis: A nationwide cohort study using Danish healthcare registers. Ann Rheum Dis 2018;77:281-289.

6. Somayaj R, Barnabe C, Martin L: Risk factors for infection following total joint arthroplasty in rheumatoid arthritis. Open Rheumatol J 2013;7:119-124.

7. Wang AS, Armstrong EJ, Armstrong AW: Corticosteroids and wound healing: Clinical considerations in the perioperative period. Am J Surg 2013;206:410-417.

8. Ismael H, Horst M, Farooq M, Jordon J, Patton JH, Rubinfeld IS: Adverse effects of preoperative steroid use on surgical outcomes. Am J Surg 2011;201:305-309.

9. Schäcke H, Docke WD, Asadullah K: Mechanisms involved in the side effects of glucocorticoids. Pharmacol Ther 2002;96: 23-43.

10. Salt E, Wiggins AT, Rayens MK, et al: Modulating effects of immunosuppressive medications and risk factors for postoperative joint infection following total joint arthroplasty in patients with rheumatoid arthritis or osteoarthritis. Semin Arthritis Rheum 2017;46:423-429.

11. Jørgensen CC, Pitter FT, Kehlet H: Safety aspects of preoperative high-dose glucocorticoid in primary total knee replacement. Br J Anaesth 2017;119: 267-275.

12. Boddapati V, Fu MC, Su EP, Sculco PK, Bini SA, Mayman DJ: Preoperative corticosteroid use for medical conditions is associated with increased postoperative infectious complications and readmissions after total hip arthroplasty: A propensity-matched study. Am J Orthop 2018;47:47.

13. Boylan MR, Perfetti DC, Elmallah RK, Krebs VE, Paulino CB, Mont MA: Does chronic corticosteroid use increase risks of readmission, thromboembolism, and revision after THA? Clin Orthop Relat Res 2016;474:744-751.

14. Castano-Betancourt MC, Fruschein Annichino R, de Azevedoe Souza Munhoz M, Gomes Machado E, Lipay M, Marchi E: Identification of high-risk groups for complication after arthroplasty: Predictive value of patient’s related risk factors. J Orthop Surg Res 2018;13:328.

15. Kustinor SK, Whitehouse MR, Blom AW, Beswick AD: Patient-related risk factors for periprosthetic joint infection after total joint arthroplasty: A systemic review and meta-analysis. PLoS One 2016;11:e0150866.

16. Hao L, Zhang Y, Song W, et al: Risk factors for infection following primary total knee replacement. Biomed Res 2018;29: 715-723.

17. Chen J, Cui Y, Li X, et al: Risk factors for deep infection after total knee arthroplasty: A meta-analysis. Arch Orthop Traum Surg 2013;133:675-687.

18. Alvarez AP, Demzik AL, Alvi HM, Hardt KD, Manning DW: Risk factors for postoperative urinary tract infections in
patients undergoing total joint arthroplasty. *Adv Orthop* 2016;2016:7268985.

19. Moghadamyeghaneh Z, Hanna MH, Carmichael JC, et al: Wound disruption following colorectal operations. *World J Surg* 2015;39:2999-3007.

20. Pavlidis TE, Galatianos IN, Papaziogas BT, et al: Complete dehiscence of the abdominal wound and incriminating factors. *Eur J Surg* 2001;167:351-355.

21. Bateman N: Use of glucocorticoids and risk of thromboembolism: A nationwide population-based case-control study. *Clin Otolaryngol* 2013;38:380.

22. Trementino L, Arnaldi G, Appolloni G, et al: Coagulopathy in Cushing’s syndrome. *Neuroendocrinology* 2010;92(suppl 1):53-59.

23. Abdulager AM, Uddin FJ, Johnson DJ, Burke D, Sagar PM: The influence of steroids on the risk of postoperative sepsis in patients after ileal pouch-anal procedure. *Br J Surg* 2003;90:137.

24. Szender JB, Grzankowski KS, Akers SN, Ziros EX, Odunci KO, Lele SB. Evaluation of the impact of chronic steroid use on outcomes in gynecologic cancer patients: A NSQIP database analysis. *Gynecol Oncol* 2016;141:169.

25. Annane D: Corticosteroids for severe sepsis: An evidence-based guide for physicians. *Ann Intensive Care* 2011;1:7.

26. Volbeda M, Wetterslev J, Gluud C, Zijlstra JG, van der Horst IC, Keus F: Glucocorticosteroids for sepsis: Systematic review with meta-analysis and trial sequential analysis. *Intensive Care Med* 2015;41:1220-1234.