



## Chronic steroid use as an independent risk factor for perioperative complications



Fouad Chouairi, BS, Sina J. Torabi, BA, Michael R. Mercier, BA, Kyle S. Gabrick, MD, Michael Alperovich, MD, MSc\*

Department of Surgery, Yale University School of Medicine, New Haven, CT

### ARTICLE INFO

#### Article history:

Accepted 21 December 2018

Available online 11 February 2019

### ABSTRACT

**Background:** Corticosteroid use continues to rise nationally. Studies have evaluated the impact of chronic steroid use on surgical outcomes in smaller populations. This study investigated the impact of chronic steroid use on perioperative surgical outcomes in a surgical cohort of more than 5 million surgical patients, using a statistically rigorous methodology.

**Methods:** The National Surgical Quality Improvement Program Database was queried 2008–2016 to evaluate chronic steroid use. Patient demographics, comorbidities, and outcomes were compared, using  $\chi^2$  and *t* test analysis, and then repeated after propensity score matching. Finally, a double-adjustment logistic regression was utilized, yielding odds ratios to assess the effect of chronic steroids on perioperative outcomes within the matched population.

**Results:** Between 2008 and 2016, a total of 5,244,588 patients met inclusion criteria, of whom 181,901 (3.5%) were taking steroids for a minimum of 30 days before surgery. Patients on chronic steroids had significantly more comorbidities compared with the remaining population. After propensity score matching and double-adjusted logistic regression, chronic steroid use was found to be associated with increased surgical complications and poorer surgical outcomes. Chronic steroid use significantly increased a patient's risk of having a hospital stay longer than 30 days by 19%, risk of readmission within 30 days by 58%, risk of reoperation by 21%, and risk of death by 32%.

**Conclusion:** After controlling for differences in comorbidities and demographics, patients on chronic steroids have significantly poorer perioperative outcomes. Chronic steroid use should be evaluated and, if possible, addressed before surgery, given their significant impact on surgical outcomes.

© 2018 Elsevier Inc. All rights reserved.

### Introduction

An estimated 0.5%–1% of patients in the general population, and 2.5% of older adults receive prolonged courses of steroids.<sup>1,2</sup> Despite the increasing availability of more targeted therapies, chronic corticosteroid use has continued to steadily rise, with an estimated 34% increase from 1989 to 2008.<sup>3–5</sup> Their broad immune inhibitory effect has made them favorable for the management of multiple inflammatory and autoimmune disorders.<sup>6,7</sup>

Complications from chronic steroid use include central obesity, adrenal insufficiency, fluid/electrolyte imbalances, and psychiatric disturbances.<sup>2,8,9</sup> Perioperatively, chronic steroid use is associated with impaired wound healing, surgical site dehiscence, and

increased risk of wound infection.<sup>10,11</sup> Research has documented the higher rates of postoperative wound infections and increased intestinal anastomotic failure among chronic steroid users.<sup>12,13</sup>

Clinical studies have examined the effects of chronic steroids in limited sample sizes or limited patient populations. This study evaluated the perioperative outcomes from chronic steroid use across all surgeries in more than 5 million surgical patients, using a national, well-validated, audited database with demographic, perioperative, and postoperative data from more than 650 hospitals in the United States.<sup>10,14</sup> The findings from this study inform the impact of chronic steroids on perioperative complications.

### Methods and Materials

#### Inclusion criteria

Data were extracted from the National Surgical Quality Improvement Program (NSQIP) database between 2008 and 2016.

\* Reprint requests: Michael Alperovich, MD, MSc, Assistant Professor of Plastic Surgery, Yale University School of Medicine, Section of Plastic and Reconstructive Surgery, 330 Cedar St. Boardman Building, 3rd Fl., New Haven, CT 06510.

E-mail address: [Michael.Alperovich@yale.edu](mailto:Michael.Alperovich@yale.edu) (M. Alperovich).

**Table 1**  
Demographics and comorbidities of the chronic steroid patient population

Demographic	Chronic steroid use	Remaining cohort	P value
N (number of patients)	181,901	5,062,687	
Female (%)	103,626 (57.0)	2,882,449 (57.0)	.870
Race (%)			< .001
White	138,742 (79.3)	3,728,134 (77.2)	
Black	19,232 (11.0)	497,856 (10.3)	
Asian	3,590 (2.1)	135,439 (2.8)	
Native American/Alaskan Native Americans	826 (0.5)	22,383 (0.5)	
Hawaiian/Pacific Islander	442 (0.3)	19,124 (0.4)	
Unknown/Not reported	12,029 (6.9)	425,112 (8.8)	
Comorbidities			
Insulin-dependent diabetes	19,929 (11.0)	285,840 (5.7)	< .001
Non-insulin-dependent diabetes	14,408 (8.0)	429,129 (8.6)	< .001
Current smoker	29,677 (16.3)	939,723 (18.6)	< .001
Dyspnea on exertion	20,810 (11.4)	304,417 (6.0)	< .001
Dyspnea at rest	4,303 (2.4)	31,025 (0.6)	< .001
Ventilator dependence	2,520 (1.4)	22,201 (0.4)	< .001
Severe COPD	23,299 (12.8)	219,674 (4.3)	< .001
Ascites	1,656 (0.9)	19,696 (0.4)	< .001
CHF 30 days before surgery	3,323 (1.8)	36,081 (0.7)	< .001
Hypertension requiring meds	101,499 (55.8)	2,287,780 (45.2)	< .001
Dialysis	6,010 (3.3)	62,927 (1.2)	< .001
Disseminated cancer	10,269 (5.6)	104,162 (2.1)	< .001
Open wound	12,973 (7.1)	163,432 (3.2)	< .001
>10% Weight loss	6,990 (3.8)	67,901 (1.3)	< .001
Bleeding disorders	18,271 (10.0)	221,959 (4.4)	< .001
Transfusion > 1 unit	4,507 (2.5)	45,419 (0.9)	< .001
Systemic sepsis			
Sepsis	8,040 (4.5)	101,949 (2.0)	< .001
Septic shock	1,903 (1.1)	15,134 (0.3)	< .001
SIRS	9,485 (5.3)	164,997 (3.3)	< .001
ASA classification			< .001
I	1,429 (0.8)	477,084 (9.5)	
II	47,715 (26.3)	2,314,068 (45.9)	
III	104,976 (57.9)	1,949,390 (38.6)	
IV	26,167 (14.4)	296,517 (5.9)	
V	1,013 (0.6)	9,717 (0.2)	
Functional health			
Independent	166,657 (92.3)	4,865,979 (96.4)	< .001
Partially dependent	10,007 (5.5)	120,453 (2.4)	< .001
Totally dependent	2,737 (1.5)	32,648 (0.6)	< .001
Age (years)	59.3 (15.9)	56.1 (16.7)	< .001
Operation time (minutes)	125.5 (98.3)	110.3 (92.7)	< .001
Total length of stay (days)	6.2 (11.2)	3.3 (7.7)	< .001

COPD, chronic obstructive pulmonary disease; CHF, congestive heart failure; SIRS, systemic inflammatory response syndrome.

NSQIP collects outcomes from more than 650 hospitals in the United States and includes more than 200 variables, including demographics, comorbidities, complications, and outcomes.

#### Statistical analysis

Patient demographics were analyzed using basic frequency statistical tests. Demographics, comorbidities, surgical factors, and outcomes were compared between the steroid and nonsteroid populations through  $\chi^2$  and Fisher exact tests for categorical variables and *t* tests for continuous variables.

Propensity scores for steroid use were calculated based on a binary logistic regression, including variables such as comorbidities, sex, race, surgical specialty, American Society of Anesthesiologists (ASA), wound classification, operation time, age, body mass index (BMI), functional status, operative year, and elective surgery status. Propensity scores were then one-to-one matched without replacement between the steroid and nonsteroid group, with a caliper of 0.001 maximizing execution performance. After matching, steroid and nonsteroid complication rates were compared. The  $\chi^2$  and Fisher exact tests were used for categorical variables.

Before and after propensity score matching, standardized differences were calculated in all variables before and after propensity

score matching to assess matching fidelity.<sup>15</sup> Any variable with a standardized difference above 0.10 after matching was further included as a control variable in a logistic regression calculating the effect of steroids on complications, readmission, and reoperation. This process of double adjustment further isolated the effect of steroid use on outcomes from potential confounders.<sup>15,16</sup> Double-adjusted odds ratios and confidence intervals for steroid effects were calculated.

## Results

### Patient demographics of patients on chronic steroids

Between 2008 and 2016, a total of 5,244,588 patients met inclusion criteria, of whom 181,901 (3.5%) were taking steroids for a minimum of 30 days before surgery. The chronic steroid population was more likely to be older (59.3 years vs 56.1 years;  $P < .001$ ) and white or black, but less likely to be Asian or another race ( $P < .001$ ). The chronic steroid population also was significantly more likely to have insulin-dependent diabetes ( $P < .001$ ), dyspnea on exertion and rest ( $P < .001$  for both), ventilator dependence ( $P < .001$ ), severe chronic obstructive pulmonary disease ([COPD]  $P < .001$ ), ascites ( $P < .001$ ), congestive heart failure ( $P < .001$ ), hypertension

**Table II**  
Complication profile of the chronic steroid patient population

Complication	Chronic steroid use	Remaining cohort	P value
N (number of patients)	181,901	5,062,687	
In hospital >30 days	1,882 (1.3)	18,749 (0.5)	< .001
Death in 30 days	6,263 (3.4)	53,458 (1.1)	< .001
Superficial incisional SSI	5,106 (2.8)	88,756 (1.8)	< .001
Deep incisional SSI	2,039 (1.1)	29,115 (0.6)	< .001
Organ SSI	4,967 (2.7)	59,243 (1.2)	< .001
Deep wound dehiscence	1,917 (1.1)	20,657 (0.4)	< .001
Pneumonia	5,871 (3.2)	60,885 (1.2)	< .001
Unplanned intubation	3,826 (2.1)	39,397 (0.8)	< .001
Pulmonary embolism	1,167 (0.6)	16,280 (0.3)	< .001
DVT/thrombophlebitis	2,812 (1.5)	28,859 (0.6)	< .001
Postoperative ventilator	6,183 (3.4)	60,699 (1.2)	< .001
Renal insufficiency	988 (0.5)	12,219 (0.2)	< .001
Renal failure	1,396 (0.8)	13,875 (0.3)	< .001
Urinary Tract infection	4,633 (2.5)	699,234 (1.4)	< .001
CVA/stroke	668 (0.4)	10,388 (0.2)	< .001
Cardiac arrest	1,079 (0.6)	12,267 (0.2)	< .001
Bleeding	18,798 (10.3)	260,674 (5.2)	< .001
Sepsis	6,983 (3.8)	78,511 (1.6)	< .001
Septic shock	4,661 (2.6)	39,018 (0.8)	< .001
C. diff infection	507 (0.7)	5,720 (0.3)	< .001
Readmission	15,167 (10.9)	194,528 (5.3)	< .001
Reoperation	7,470 (5.3)	104,503 (2.8)	< .001

SSI, surgical site infection.

requiring medication ( $P < .001$ ), dialysis ( $P < .001$ ), disseminated cancer ( $P < .001$ ), open wounds ( $P < .001$ ), >10% recent weight loss ( $P < .001$ ), bleeding disorders ( $P < .001$ ), preoperative transfusion > 1 unit ( $P < .001$ ), preoperative sepsis ( $P < .001$ ), preoperative septic shock ( $P < .001$ ), and preoperative systemic inflammatory response syndrome ([SIRS]  $P < .001$ ). Compared with the remaining cohort, patients on chronic steroids were less likely to have non-insulin-dependent diabetes ( $P < .001$ ) or be smokers ( $P < .001$ ). The chronic steroid population also had significantly higher proportions of anesthesia classification ASA 3 (57.9% vs 38.6%), ASA 4 (14.4% vs 5.9%), and ASA 5 (0.6% vs 0.2%) patients ( $P < .001$ ). Patients on chronic steroids were more likely to be partially ( $P < .001$ ) or totally dependent ( $P < .001$ ) in terms of functional health. With respect to surgery, the chronic steroid population had significantly longer operative times (125.5 minutes vs 110.3 minutes;  $P < .001$ ) and hospital length of stay (6.2 days vs 3.3 days;  $P < .001$ ; Table I).

#### Analysis of complications for patients on chronic steroids

Patients on chronic steroids had significantly more hospital stays longer than 30 days ( $P < .001$ ), more superficial and deep surgical site infections ( $P < .001$  for both), more organ surgical site infections ( $P < .001$ ), more deep wound dehiscence ( $P < .001$ ), more pneumonia ( $P < .001$ ), more unplanned intubations ( $P < .001$ ), more pulmonary embolisms ( $P < .001$ ), higher rates of deep vein thrombosis (DVT)/thrombophlebitis ( $P < .001$ ), more postoperative ventilator dependence ( $P < .001$ ), more renal insufficiency ( $P < .001$ ), more renal failure ( $P < .001$ ), more urinary tract infections ( $P < .001$ ), more cerebrovascular accident (CVA)/stroke ( $P < .001$ ), more cardiac arrest requiring cardiopulmonary resuscitation ([CPR]  $P < .001$ ), more bleeding ( $P < .001$ ), more sepsis ( $P < .001$ ), more septic shock ( $P < .001$ ), more *Clostridium difficile* infections ( $P < .001$ ), more readmissions ( $P < .001$ ), more reoperations ( $P < .001$ ), and higher rates of death ( $P < .001$ ; Table II).

#### Propensity score matched–complication analysis

Given the significant differences between the chronic steroid subgroup and the remaining population, propensity score

**Table III**  
Propensity score matched–complication profile between the chronic steroid population and the remaining cohort

Complication	Chronic steroid use	Remaining cohort	P value
N (number of patients)	141,924	141,924	
Complications			
In hospital >30 days	1,516 (1.2)	1,105 (0.9)	< .001
Death in 30 days	3,703 (2.6)	1,789 (1.3)	< .001
Superficial incisional SSI	3,578 (2.5)	3,942 (2.8)	< .001
Deep incisional SSI	1,506 (1.1)	1,575 (1.1)	.211
Organ SSI	3,742 (2.6)	2,029 (1.4)	< .001
Deep wound dehiscence	1,297 (0.9)	1,032 (0.7)	< .001
Pneumonia	4,122 (2.9)	2,077 (1.5)	< .001
Unplanned intubation	2,507 (1.8)	1,570 (1.1)	< .001
Pulmonary embolism	874 (0.6)	673 (0.5)	< .001
DVT/thrombophlebitis	2,041 (1.4)	1,089 (0.8)	< .001
Postoperative ventilator	3,546 (2.5)	3,164 (2.2)	< .001
Renal insufficiency	687 (0.5)	716 (0.6)	.439
Renal failure	826 (0.6)	808 (0.6)	.652
Urinary tract infection	3,262 (2.3)	2,262 (1.6)	< .001
CVA/stroke	462 (0.3)	242 (0.2)	< .001
Cardiac arrest	703 (0.5)	520 (0.4)	< .001
Bleeding	15,289 (10.8)	7,944 (5.6)	< .001
Sepsis	5,193 (3.7)	3,482 (2.5)	< .001
Septic shock	2,913 (2.1)	2,243 (1.6)	< .001
C. diff infection	481 (0.7)	251 (0.4)	< .001
Readmission	13,867 (10.8)	8,983 (7.1)	< .001
Reoperation	6,661 (5.2)	4,822 (3.8)	< .001

SSI, surgical site infection.

matching was used to match 141,924 patients from the chronic steroid and general populations. After propensity score matching, patients on steroids were more likely to have hospital stays longer than 30 days ( $P < .001$ ), more organ surgical site infections ( $P < .001$ ), more deep wound dehiscence ( $P < .001$ ), more pneumonia ( $P < .001$ ), more unplanned intubation ( $P < .001$ ), more pulmonary embolisms ( $P < .001$ ), more DVT/thrombophlebitis ( $P < .001$ ), more postoperative ventilator dependence ( $P < .001$ ), more urinary tract infections ( $P < .001$ ), more CVA/stroke ( $P < .001$ ), more cardiac arrests requiring CPR ( $P < .001$ ), more bleeding ( $P < .001$ ), more sepsis ( $P < .001$ ), more septic shock ( $P < .001$ ), more *Clostridium difficile* infections ( $P < .001$ ), more readmissions ( $P < .001$ ), more reoperations ( $P < .001$ ), and higher rates of death ( $P < .001$ ; Table III).

#### Double-adjustment of propensity score matched population

On standardized difference analysis, BMI, age, sex, disseminated cancer, >10% weight loss, bleeding disorders, elective surgery, race, surgical specialty, diabetes treatment, dyspnea, ASA class, and wound class had a standardized difference still above 0.10 between the chronic steroid and remaining population using propensity score matching. These variables were controlled for in a double-adjusted propensity score matching binary logistic regression to isolate the impact of chronic steroid use alone (Table IV).

#### Double-adjusted binary logistic regression analysis of complications

After double adjusting the propensity score–matched population, using binary logistic regression, chronic steroid use was found to be associated with hospital stays longer than 30 days (OR: 1.19;  $P < .001$ ), organ surgical site infections (OR: 1.89;  $P < .001$ ), deep wound dehiscence (OR: 1.25;  $P < .001$ ), pneumonia (OR: 1.56;  $P < .001$ ), unplanned intubation (OR: 1.34;  $P < .001$ ), DVT/thrombophlebitis (OR: 1.61;  $P < .001$ ), urinary tract infection (OR: 1.35;  $P < .001$ ), CVA/stroke (OR: 1.34;  $P < .001$ ), bleeding (OR: 1.55;  $P < .001$ ), sepsis (OR: 1.49;  $P < .001$ ), septic shock (OR: 1.17;  $P < .001$ ), *Clostridium difficile* infection (OR: 1.75;  $P < .001$ ),

**Table IV**  
Standardized differences in the propensity score model

Demographic	Standard difference
Operative time	0.0821
<b>BMI</b>	<b>1.9059</b>
Age	<b>0.8421</b>
<b>Sex</b>	<b>0.3554</b>
Current smoker	0.0621
Ventilator dependence	0.0057
Severe COPD	0.0439
Ascites	0.0493
CHF 30 days before surgery	0.0024
Hypertension requiring meds	0.0980
Renal failure	0
Dialysis	0.0399
<b>Disseminated cancer</b>	<b>0.1661</b>
Open wound	0.0008
<b>&gt;10% weight loss</b>	<b>0.1748</b>
<b>Bleeding disorders</b>	<b>0.1068</b>
Transfusion >1 unit	0.0638
<b>Elective surgery</b>	<b>0.1812</b>
Race	
<b>White</b>	<b>0.1164</b>
<b>Black</b>	<b>0.2073</b>
<b>Asian</b>	<b>0.1371</b>
Native American	0.0090
Hawaiian	0.0561
Unknown	0.0521
Surgical specialty	
Otolaryngology	0.0083
Plastic surgery	0.0414
<b>General surgery</b>	<b>0.2988</b>
Cardiac surgery	0.0406
<b>Obstetrics/gynecology</b>	<b>0.1657</b>
<b>Neurosurgery</b>	<b>0.1494</b>
<b>Orthopedic surgery</b>	<b>0.4521</b>
<b>Thoracic surgery</b>	<b>0.1139</b>
<b>Urology</b>	<b>0.1281</b>
<b>Vascular surgery</b>	<b>0.3991</b>
Interventional radiology	0.0198
Diabetes	
<b>No</b>	<b>0.2780</b>
<b>Insulin therapy</b>	<b>0.1315</b>
<b>Non-insulin therapy</b>	<b>0.2305</b>
Dyspnea	
<b>No</b>	<b>0.1787</b>
<b>Moderate exertion</b>	<b>0.1816</b>
Rest	0.0172
Functional status	
Independent	0.0529
Partially dependent	0.0433
Totally dependent	0.0376
Unknown	0.0047
PR sepsis	
No	0.0498
Sepsis	0.0239
Septic shock	0.0058
SIRS	0.0491
ASA	
Class 1	0.0069
<b>Class 2</b>	<b>0.2317</b>
<b>Class 3</b>	<b>0.2101</b>
Class 4	0.0063
<b>Class 5</b>	<b>0.4532</b>
Operative year	
2011	0.0328
2012	0.0281
2013	0.0110
2014	0.0010
2015	0
2016	0.0334
Wound class	
<b>Class 1</b>	<b>0.2966</b>
<b>Class 2</b>	<b>0.3570</b>
Class 3	0.0692
Class 4	0.0301

CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; SIRS, systemic inflammatory response syndrome.

**Table V**  
Double adjusted logistic regression comparing complication profiles between the chronic steroid population and the remaining cohort

Complication	Odds ratio	95% CI	P value
Complications			
In hospital >30 days	<b>1.19</b>	<b>1.08–1.32</b>	< .001
Death in 30 days	<b>1.32</b>	<b>1.23–1.42</b>	< .001
Superficial incisional SSI	1.03	0.97–1.10	.382
Deep incisional SSI	1.04	0.95–1.16	.393
Organ SSI	<b>1.89</b>	<b>1.76–2.03</b>	< .001
Deep wound dehiscence	<b>1.25</b>	<b>1.12–1.40</b>	< .001
Pneumonia	<b>1.56</b>	<b>1.46–1.67</b>	< .001
Unplanned intubation	<b>1.34</b>	<b>1.23–1.45</b>	< .001
Pulmonary embolism	1.10	0.96–1.27	.175
DVT/thrombophlebitis	<b>1.61</b>	<b>1.46–1.77</b>	< .001
Postoperative ventilator	0.98	0.92–1.05	.534
Renal insufficiency	0.94	0.81–1.09	.402
Renal failure	0.99	0.87–1.12	.870
Urinary tract infection	<b>1.35</b>	<b>1.26–1.45</b>	< .001
CVA/stroke	<b>1.34</b>	<b>1.10–1.63</b>	.004
Cardiac arrest	1.06	0.91–1.22	.459
Bleeding	<b>1.55</b>	<b>1.49–1.61</b>	< .001
Sepsis	<b>1.49</b>	<b>1.41–1.58</b>	< .001
Septic shock	<b>1.17</b>	<b>1.08–1.26</b>	< .001
C. diff infection	<b>1.75</b>	<b>1.44–2.12</b>	< .001
Readmission	<b>1.58</b>	<b>1.52–1.64</b>	< .001
Reoperation	<b>1.21</b>	<b>1.15–1.28</b>	< .001

SSI, surgical site infection.

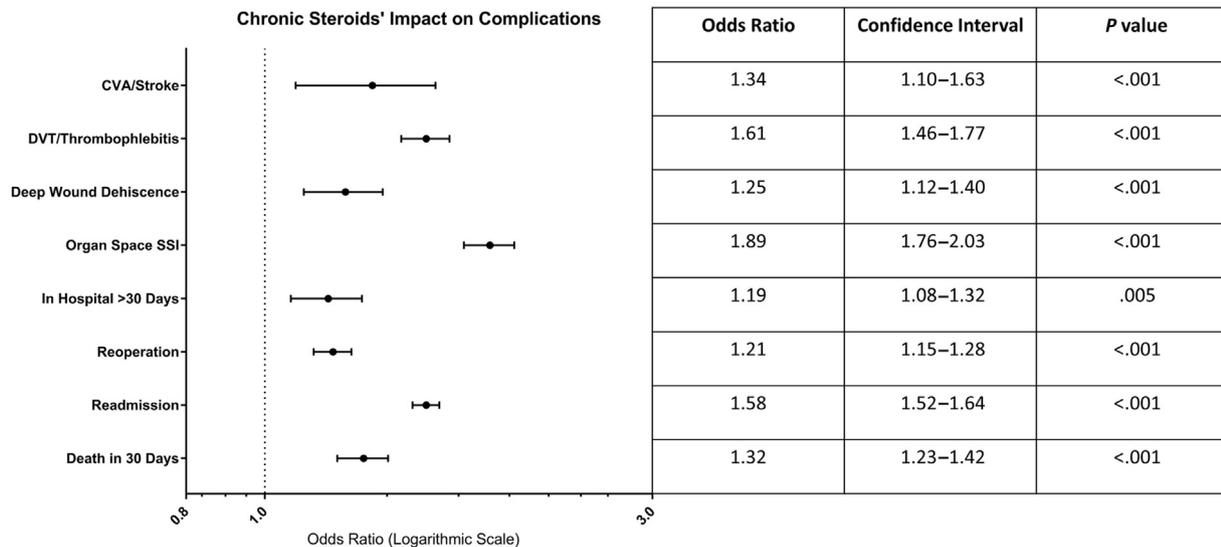
readmission (OR: 1.58;  $P < .001$ ), reoperation (OR: 1.21;  $P < .001$ ), and death (OR: 1.32;  $P < .001$ ; Table V).

## Discussion

Although studies have evaluated the impact of chronic steroids in limited sample sizes or surgical populations, this is the first study to critically evaluate the impact of chronic steroid use across all surgeries in more than 181,000 patients. Furthermore, using double-adjusted propensity score matching, the impact of chronic steroid use on perioperative complications was isolated using rigorous statistical methodology.<sup>10</sup> To our knowledge, this is the first analysis that utilizes this statistical paradigm in a heterogeneous surgical outcomes database of this sample size.

In total, 3.5% of patients were on chronic steroids, which is slightly higher than the weighted national average of 1.2% reported elsewhere.<sup>17</sup> Patients requiring chronic steroids are more likely to have comorbidities that may require surgery compared with the remaining population. The proportion of patients on chronic steroids in a surgical database would be higher than the incidence in a general national cohort. After both propensity score matching and double-adjusted binary logistic regression, chronic steroid use significantly increased a patient's risk of having a hospital stay longer than 30 days by 19%, a risk of readmission within 30 days by 58%, reoperation risk by 21%, and risk of death by 32% (Figure). Compared with all other covariates, steroid use was one of the 10 strongest correlates for the main perioperative complications. Steroid use had the fourth strongest correlation to readmission, fifth strongest correlation to organ space surgical site infection, and sixth strongest correlation to deep surgical site infection.

Chronic steroid therapy has been shown to inhibit the hypothalamic-pituitary axis, which impairs the body's response to physiologic stress from surgery.<sup>18</sup> Furthermore, chronic steroids impair wound healing and increase susceptibility to metabolic derangement and infection postoperatively.<sup>19–22</sup> In this study, steroid use was associated with a higher incidence of postoperative deep wound dehiscence, organ surgical site infection, and reoperation.



**Figure.** The impact of chronic steroids on complications. A double adjusted binary logistic model controls for age, BMI, sex, disseminated cancer, <10% weight loss, bleeding disorders, elective surgery status, race, specialty, diabetes therapy, dyspnea, ASA, and wound class within a propensity score–matched population.

Our findings are consistent with studies that documented an increased risk of surgical site infections, wound dehiscence, and mortality in patients on chronic steroids.<sup>10</sup> Specialty-specific studies have also shown increased risks from chronic steroids within plastic surgery, orthopedic surgery, and patients with inflammatory bowel disease.<sup>2,23,24</sup>

Chronic steroid use also accelerates atherosclerosis. Thromboembolic events have been shown to be more frequent among patients taking glucocorticoids.<sup>25–29</sup> In this study, higher rates of thrombotic and cardiovascular complications were identified in the chronic steroid cohort.<sup>30,31</sup> Although both basic science and clinical studies have identified similar physiologic risks associated with chronic steroid use, none have been as adequately powered or as statistically rigorous to separate chronic steroid use from its associated comorbidities.

Our findings support the routine implementation of pathways to anticipate or counteract the impact of chronic steroids on the postoperative course. Some centers have advocated for the administration of suprathreshold perioperative stress dose protocols.<sup>23,32–38</sup> The decision to implement this protocol is dependent on the patient's history of steroid use as well as on the duration and invasiveness of the planned surgery.<sup>39</sup> Patients who display no hypothalamic-pituitary axis suppression can continue the prescribed steroid dose, and suprathreshold doses can be given in instances of suppression.<sup>40–42</sup>

No consensus exists regarding the precise dose or duration of chronic steroid use that impacts the hypothalamic-pituitary axis or the period of time of steroid cessation required to reverse the effects on the endocrine system.<sup>43</sup> More recent analyses have questioned the dogma that increasing steroid dosing perioperatively improves physiologic outcomes and, in more minor surgical procedures, can have a deleterious effect.<sup>44</sup> A multi-center randomized controlled trial comparing steroid doses perioperatively in chronic steroid use patients is needed to address best practices.

As this study evaluates perioperative complications related to chronic steroids across a broad range of surgical procedures, developing risk-reduction protocols will depend on the individual requirements of each surgical specialty. In cases that are elective, deferring intervention until the patient is no longer on steroids would be advisable. For patients who are on chronic steroids,

vitamin A supplementation can partially restore steroid-related wound healing impairment.<sup>45</sup>

Limitations of this study include the lack of data on outcomes outside 30 days. Furthermore, because the population includes all surgical procedures, there is inherent heterogeneity in the samples. However, stringent efforts were made to match the cohorts and control for comorbidities. The database queried does not record short-term steroid use or provide more detail regarding the actual length of chronic steroid use beyond the greater than 30-day metric. As a function of a large well-powered database, there was high significance in *P* values across multiple variables. However, after double adjustment, significant odds ratios related the effect size of chronic steroid use on perioperative complications. Despite these limitations, this study represents the largest powered study to date regarding the incidence of postoperative complications after steroid use in surgical patients.

In conclusion, after controlling for demographics, surgical factors, and comorbidities in more than 5 million surgical patients, chronic steroid use is associated with significantly higher rates of surgical and medical perioperative complications. As a result, physicians should likely be wary in recommending elective surgeries to patients with extensive history of steroid use.

#### NSQIP disclosure

The American College of Surgeons National Surgical Quality Improvement Program and the hospitals participating in the ACS NSQIP are the source of the data used herein; they have not verified and are not responsible for the statistical validity of the data analysis or the conclusions derived by the authors.

#### References

- Curtis JR, Westfall AO, Allison J, et al. Population-based assessment of adverse events associated with long-term glucocorticoid use. *Arthritis Rheum.* 2006;55:420–426.
- 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.
- Narula N, Borges L, Steinhart AH, Colomel JF. Trends in narcotic and corticosteroid prescriptions in patients with inflammatory bowel disease in the United States ambulatory care setting from 2003 to 2011. *Inflamm Bowel Dis.* 2017;23:868–874.

4. Fardet L, Petersen I, Nazareth I. Prevalence of long-term oral glucocorticoid prescriptions in the UK over the past 20 years. *Rheumatology (Oxford)*. 2011;50:1982–1990.
5. Hoes JN, Jacobs JW, Bijlsma JW. Glucocorticoids are forever? *Rheumatology (Oxford)*. 2011;50:1940–1941.
6. Fauci AS. Mechanisms of corticosteroid action on lymphocyte subpopulations. II. Differential effects of in vivo hydrocortisone, prednisone and dexamethasone on in vitro expression of lymphocyte function. *Clin Exp Immunol*. 1976;24:54–62.
7. Schäcke H, Döcke WD, Asadullah K. Mechanisms involved in the side effects of glucocorticoids. *Pharmacol Ther*. 2002;96:23–43.
8. Stanbury RM, Graham EM. Systemic corticosteroid therapy—Side effects and their management. *Br J Ophthalmol*. 1998;82:704–708.
9. Liu D, Ahmet A, Ward L, et al. A practical guide to the monitoring and management of the complications of systemic corticosteroid therapy. *Allergy Asthma Clin Immunol*. 2013;9:30.
10. 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;201:305–308; discussion 308–309.
11. Anstead GM. Steroids, retinoids, and wound healing. *Adv Wound Care*. 1998;11:277–285.
12. Hasselgren PO, Säljö A, Fornander J, Lundstam S, Seeman T. Postoperative wound infections in patients with long preoperative hospital stay. *Acta Chir Scand*. 1982;148:473–477.
13. Golub R, Golub RW, Cantu Jr R, Stein HD. A multivariate analysis of factors contributing to leakage of intestinal anastomoses. *J Am Coll Surg*. 1997;184:364–372.
14. Davenport DL, Henderson WG, Khuri SF, Mentzer Jr RM. Preoperative risk factors and surgical complexity are more predictive of costs than postoperative complications: a case study using the National Surgical Quality Improvement Program (NSQIP) database. *Ann Surg*. 2005;242:463–468; discussion 8–71.
15. Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. *Stat Med*. 2009;28:3083–3107.
16. Nguyen T-L, Collins GS, Spence J, et al. Double-adjustment in propensity score matching analysis: Choosing a threshold for considering residual imbalance. *BMC Med Res Methodol*. 2017;17:78.
17. 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.
18. Reding R, Michel LA, Donckier J, de Canniere L, Jamart J. Surgery in patients on long-term steroid therapy: a tentative model for risk assessment. *Br J Surg*. 1990;77:1175–1178.
19. Streefen DH. Corticosteroid therapy. II. Complications and therapeutic indications. *JAMA*. 1975;232:1046–1049.
20. Streefen DH. Corticosteroid therapy. I. Pharmacological properties and principles of corticosteroid use. *JAMA*. 1975;232:944–947.
21. Udelsman R, Goldstein DS, Loriaux DL, Chrousos GP. Catecholamine-glucocorticoid interactions during surgical stress. *J Surg Res*. 1987;43:539–545.
22. Udelsman R, Norton JA, Jelenich SE, et al. Responses of the hypothalamic-pituitary-adrenal and renin-angiotensin axes and the sympathetic system during controlled surgical and anesthetic stress. *J Clin Endocrinol Metab*. 1987;64:986–994.
23. Barcha CP, Ranzer MJ. Impact of chronic steroid use on plastic surgery outcomes: Analysis of 94,140 cases. *Plast Reconstr Surg*. 2018;142:770e–779e.
24. Subramanian V, Saxena S, Kang JY, Pollak RC. Preoperative steroid use and risk of postoperative complications in patients with inflammatory bowel disease undergoing abdominal surgery. *Am J Gastroenterol*. 2008;103:2373–2381.
25. Calvo-Alen J, Toloza SM, Fernandez M, et al. Systemic lupus erythematosus in a multiethnic US cohort (LUMINA). XXV. Smoking, older age, disease activity, lupus anticoagulant, and glucocorticoid dose as risk factors for the occurrence of venous thrombosis in lupus patients. *Arthritis Rheum*. 2005;52:2060–2068.
26. Stolz E, Klotzsch C, Schlachetzki F, Rahimi A. High-dose corticosteroid treatment is associated with an increased risk of developing cerebral venous thrombosis. *Eur Neurol*. 2003;49:247–248.
27. Van Zaane B, Nur E, Squizzato A, et al. Hypercoagulable state in Cushing's syndrome: a systematic review. *J Clin Endocrinol Metab*. 2009;94:2743–2750.
28. van Zaane B, Nur E, Squizzato A, et al. Systematic review on the effect of glucocorticoid use on procoagulant, anti-coagulant and fibrinolytic factors. *J Thromb Haemost*. 2010;8:2483–2493.
29. Yale SH, Medlin SC, Liang H, Peters T, Glurich I, Mazza JJ. Risk assessment model for venothromboembolism in post-hospitalized patients. *Int Angiol*. 2005;24:250–254.
30. Albiger N, Testa RM, Almoto B, et al. Patients with Cushing's syndrome have increased intimal media thickness at different vascular levels: comparison with a population matched for similar cardiovascular risk factors. *Horm Metab Res*. 2006;38:405–410.
31. de Prada TP, Pozzi AO, Coronado MT, et al. Atherogenesis takes place in cholesterol-fed rabbits when circulating concentrations of endogenous cortisol are increased and inflammation suppressed. *Atherosclerosis*. 2007;191:333–339.
32. de Lange DW, Kars M. Perioperative glucocorticosteroid supplementation is not supported by evidence. *Eur J Intern Med*. 2008;19:461–467.
33. Lamberts SW, Bruining HA, de Jong FH. Corticosteroid therapy in severe illness. *N Engl J Med*. 1997;337:1285–1292.
34. Coursin DB, Wood KE. Corticosteroid supplementation for adrenal insufficiency. *JAMA*. 2002;287:236–240.
35. Salem M, Tainsh Jr RE, Bromberg J, Loriaux DL, Chernow B. Perioperative glucocorticoid coverage: a reassessment 42 years after emergence of a problem. *Ann Surg*. 1994;219:416–425.
36. Friedman RJ, Schiff CF, Bromberg JS. Use of supplemental steroids in patients having orthopaedic operations. *J Bone Joint Surg Am*. 1995;77:1801–1806.
37. Mathis AS, Shah NK, Mulgaonkar S. Stress dose steroids in renal transplant patients undergoing lymphocele surgery. *Transplant Proc*. 2004;36:3042–3045.
38. Bromberg JS, Baliga P, Cofer JB, Rajagopalan PR, Friedman RJ. Stress steroids are not required for patients receiving a renal allograft and undergoing operation. *J Am Coll Surg*. 1995;180:532–536.
39. Hoes JN, Jacobs JW, Boers M, et al. EULAR evidence-based recommendations on the management of systemic glucocorticoid therapy in rheumatic diseases. *Ann Rheum Dis*. 2007;66:1560–1567.
40. Kehlet H, Binder C. Adrenocortical function and clinical course during and after surgery in unsupplemented glucocorticoid-treated patients. *Br J Anaesth*. 1973;45:1043–1108.
41. Kehlet H, Binder C. Value of an ACTH test in assessing hypothalamic-pituitary-adrenocortical function in glucocorticoid-treated patients. *Br Med J*. 1973;2:147–149.
42. Hagg E, Asplund K, Lithner F. Value of basal plasma cortisol assays in the assessment of pituitary-adrenal insufficiency. *Clin Endocrinol (Oxf)*. 1987;26:221–226.
43. Jabbour SA. Steroids and the surgical patient. *Med Clin North Am*. 2001;85:1311–1317.
44. Brown CJ, Buie WD. Perioperative stress dose steroids: Do they make a difference? *J Am Coll Surg*. 2001;193:678–686.
45. Hunt TK. Vitamin A and wound healing. *J Am Acad Dermatol*. 1986;15:817–821.