Original Article

Association of preoperative systemic corticosteroid therapy with surgical outcomes in chronic obstructive pulmonary disease patients

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Abstract:

BACKGROUND: Chronic obstructive pulmonary disease (COPD) patients are at an increased risk of postoperative pulmonary complications (PPCs). The purpose of this study is to evaluate the risks and benefits associated with preoperative steroids in COPD patients.

METHODS: The National Surgical Quality Improved Program database was used to identify 92 COPD patients who underwent surgery at the American University of Beirut Medical Center between 2009 and 2013. COPD was diagnosed based on postbronchodilator forced expiratory volume in 1 s to forced vital capacity ratio <0.7 and a history of smoking. The exposure of interest was preoperative systemic corticosteroid therapy. The primary outcomes were PPCs and wound complications. Cardiac and urinary complications along with unplanned readmission or reoperation and death were also evaluated.

RESULTS: Overall 42.4% of patients received preoperative systemic corticosteroids. Postoperative wound complications were significantly more frequent in COPD patients who received preoperative systemic corticosteroids compared to patients who did not (10.3% vs. none, respectively, $P = 0.03$). However, PPCs were not significantly different between patients who received preoperative systemic corticosteroids and patients who did not (17.9% vs. 13.2%, respectively, $P = 0.53$). There were no significant differences in the secondary outcomes.

CONCLUSIONS: This study suggests that preoperative administration of systemic corticosteroids in stable COPD patients is associated with an increased risk of postoperative wound complications but may not reduce PPCs.

Keywords:

Chronic obstructive pulmonary disease, corticosteroids, postoperative pulmonary complications, postoperative wound complications

Chronic obstructive pulmonary disease (COPD) patients are at an increased risk of postoperative pulmonary complications (PPCs).[1] PPCs increase the length of hospital stay, morbidity, mortality, and total health cost and are at least as common as cardiac complications in nonthoracic surgeries.[2-4] Preoperative interventions aimed to decrease the risk of PPC in these patients include smoking cessation, inhaled bronchodilators, and in case of severe uncontrolled symptoms, systemic corticosteroids.[5]

Systemic corticosteroids are thought to decrease airway bronchospasm and inflammation and are part of the mainstay treatment of COPD exacerbations.[6] Given the low incidence of acute side effects when used preoperatively in asthmatics, systemic corticosteroids are also commonly used preoperatively in stable COPD patients in an

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attempt to reduce PPCs with little evidence to support their use.[7]

Some studies suggested that perioperative systemic corticosteroids are possibly beneficial in COPD patients undergoing coronary artery bypass graft (CABG) surgeries and associated with lower PPC or a shorter intensive care unit and hospital stay.[8,9] However, other studies suggested increased risk of wound complications associated with steroid therapy.[10-12] To our knowledge, the use of preoperative corticosteroids has not been well studied in COPD patients undergoing noncardiothoracic surgery.

In general, some pulmonary physicians systematically prescribe preoperative systemic corticosteroids for stable COPD patients and some do not. This study aimed to evaluate the risks and benefits associated with preoperative systemic corticosteroids. We specifically compared the incidence of PPC and wound complications in COPD patients treated with systemic corticosteroids preoperatively versus COPD patients who were not.

Methods

Sample

The National Surgical Quality Improvement Program (NSQIP) database was used to identify patients who underwent surgery at the American University of Beirut Medical Center (a participating center in the NSQIP database) between 2009 and 2013. Out of the 4708 surgeries performed during that period, 327 patients underwent pulmonary function test, of which 92 patients had irreversible airway obstruction diagnostic of COPD. COPD was diagnosed based on postbronchodilator forced expiratory volume in 1 s to forced vital capacity ratio <0.7 and a history of smoking following the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines.[6] The study was approved by the Institutional Review Board at the American University of Beirut Medical Center (IM.HC.08).

Exposure and outcome assessment

Postoperative outcomes and all patient (habits and demographic and baseline comorbidities) and surgical characteristics (type, year, anesthesia type and length, wound classification, etc.) were obtained from the NSQIP where they were recorded prospectively following standard NSQIP definitions and procedures.[13] Cardiovascular comorbidities assessment included presence of congestive heart failure (CHP) within 30 days, myocardial infarction within 6 months, angina within 30 days, prior angioplasty or cardiac surgery, and hypertension requiring medical therapy. Central nervous system (CNS) disorder assessment included impaired sensorium within 48 h, coma, and history of transient ischemic attack history, cerebrovascular accident with or without neurologic deficit, CNS tumors, hemiplegia/hemiparesis, paraplegia/paraparesis, and quadriplegia/quadriparesis. Participants were also assessed for a history of diabetes and presence of sepsis within 48 h, current pneumonia, and ventilator dependence within 48 h from surgery.

PPC or respiratory occurrences included unplanned re-intubation, failure to wean from ventilator for more than 48 h, pneumonia atelectasis, and pulmonary embolism. Wound complications/occurrences included superficial surgical-site infection, deep-incisional surgical-site infection, organ-space surgical-site infection, and wound disruption.

Other NSQIP-recorded postoperative complications/occurrences included urinary tract, CNS, and cardiac complications (arrhythmia, myocardial ischemia, and CHP), along with mortality, length of hospital stay, and any unplanned reoperation or hospital readmission likely related to the principal procedure within 30 days.

The American College of Surgeon-estimated probability of morbidity and mortality for patients in the NSQIP database is calculated using parameters with a random intercept, fixed-slope hierarchical model, including a series of 21 preoperative risk factors.[14] The factors include age, sex, functional status, emergency case, ASA class, steroid use for chronic conditions, ventilator dependence, presence of ascites, sepsis, disseminated malignancy, diabetes, treated hypertension, previous cardiac event, CHF within 30 days, dyspnea, current smoking, history of COPD, hemodialysis, acute renal failure, body mass index status, and type of surgery.

Data on perioperative corticosteroid therapy (systemic vs. inhaled vs. none) were collected from medical records. Information on systemic steroid therapy included type, dose, and duration. Intake of chronic steroids for chronic condition defined as regular use of systemic corticosteroids for more than 10 days within 30 days preoperatively was obtained from NSQIP.[13] Spirometric measures were performed following American Thoracic Society/European Respiratory Society guidelines and criteria and obtained from the pulmonary function laboratory database.[15]

Statistical analysis

The exposure of interest was preoperative systemic corticosteroid therapy categorized as treatment or no treatment. Therapy was further categorized into secondary analyses by median duration (1 day vs. >1 day) and by median cumulative dose (equivalent to ≤ vs. >60 mg of methylprednisolone). The primary outcomes of interest were PPC and wound complications. Cardiac and urinary complications, along with unplanned

readmission or reoperation and death, were considered secondary outcomes. Outcomes were compared between patients who received preoperative systemic corticosteroids and those who did not. Student's *t*-test and Chi-square or Fisher's exact test were used to compare the difference in continuous and categorical outcomes between the exposure groups. Multivariable logistic regression models adjusted for significant bivariate predictors of PPC in our sample included duration of anesthesia and probability of morbidity. Adjusted odds ratio (OR) and a 95% confidence interval were reported. Analyses were performed using SAS software, version 9.4 (SAS Inc, Cary NC USA). $P < 0.05$ was considered statistically significant.

Results

Characteristics of the sample are presented in Table 1. Thirty-nine patients (42.4%) received systemic corticosteroids preoperatively, whereas 53 did not (57.6%). These two groups were similar in terms of demographic characteristics and preoperative comorbidities, including age, sex distribution, functional status, and prevalence of diabetes and cardiovascular diseases. The severity of airway obstruction did not vary significantly between patients who received systemic corticosteroids and those who did not (59.0 vs. 52.8% GOLD Class 1, respectively, $P = 0.25$), whereas the difference in the proportion of current smokers did not reach statistical significance (46.2 vs. 28.3%, respectively, $P = 0.08$). Patients who received preoperative systemic corticosteroids were more likely to be on chronic inhaled corticosteroids (41.0 vs. 18.9% of patients, $P = 0.02$) and more likely to have received preoperative bronchodilators (87.2 vs. 32.1%, $P < 0.001$) than the patients who did not. Two participants in our study sample had taken steroids for chronic conditions for more than 10 days within 30 days prior to surgery for a chronic medical condition. One of those participants continued corticosteroid therapy preoperatively and received prednisone at 20 mg/day for 21 days, whereas the other had the steroids stopped prior to hospitalization for surgery. The majority of patients treated with preoperative corticosteroids received intravenous methylprednisolone ($n = 35$, 89.7%), at a median dose of 60 mg/day (range: 20–240 mg/day) for a median duration of 1 day and a range of 1–13 days. Three patients (7.7%) received dexamethasone and one patient received prednisone. Overall 43.5% received preoperative corticosteroids for >1 day and 46.2% received a cumulative dose equivalent to >60 mg of methylprednisolone.

Patients who received preoperative systemic corticosteroids had higher estimated probability of morbidity than the other group (0.17 vs. 0.11, $P = 0.04$) [Table 2]. All surgeries were major procedures; primarily performed electively under general anesthesia with a minority performed using endoscopy [Table 2]. These characteristics including surgery type and anesthesia techniques were not significantly different between patients who received preoperative systemic corticosteroids and those who did not [Table 2]. Although the average duration of anesthesia was significantly longer in patients who received preoperative corticosteroids (247.2 vs. 192.65 min, $P = 0.02$), the proportion who received prolonged anesthesia (≥270 min) was not significantly different between the two groups [Table 2]. There was no significant difference in the surgical wound classification between the two groups either.

No statistically significant difference was found in the rate of PPC between patients who received preoperative systemic corticosteroids and patients who did not (17.9% vs. 13.2%, respectively, $P = 0.53$) [Table 3]. No significant difference was noted in the subtypes of PPC either including unplanned intubation and failure to wean from mechanical ventilation for >48 h. Furthermore, adjusting for the baseline probability of morbidity and for the duration of anesthesia (both significantly higher in patients who received corticosteroids) did not impact this finding (adjusted OR of PPC = 0.98, 95% confidence interval [CI]: 0.25–3.86, $P = 0.93$ vs. unadjusted OR of PPC = 0.70, 95% CI: 0.22–2.18; $P = 0.53$). However, the postoperative wound complications were significantly more common in patients who received systemic corticosteroids (10.3% vs. none, $P = 0.03$). These wound complications included primarily superficial surgical-site infection (7.5%) and deep-incisional surgical-site infection (2.5%). There was no statistically significant difference in other assessed secondary outcomes including unplanned readmission, return to operation room, death, cardiac complications, and urinary occurrences [Table 3].

There was no significant difference in postoperative outcomes between patients who received corticosteroid treatment for 1 day vs. >1 day or between patients who received a cumulative corticosteroid dose of equivalent to ≤ vs. >60 mg of methylprednisolone (results not shown).

Discussion

In 92 patients with stable COPD diagnosed by spirometry who underwent surgery at a single tertiary center, preoperative systemic steroid therapy was associated with a significantly higher rate of wound complications but no significant difference in PPC or nonpulmonary complications.

Previous studies have similarly shown that patients treated preoperatively with systemic corticosteroids

Table 1: Sample characteristics stratified by preoperative intake of systemic corticosteroid therapy

	Preoperative systemic corticosteroid therapy		*P*
	Yes	No	
n (%)	39 (42.4)	53 (57.6)	
Demographic characteristics			
Age (years), mean±SD	68.5±11.9	69.5±11.8	0.68
Sex, females (%)	12 (30.8)	20 (37.7)	0.49
Weight (kg), mean±SD	64.4±5.7	64.4±4.0	0.13
BMI (kg/m^2), mean±SD	31.3±8.3	28.9±6.0	0.07
Current smoker within 1 year, (%)	18 (46.2)	15 (28.3)	0.08
Pack-year cigarette history, mean±SD	34.2±62.0	22.8±43.8	0.55
Current alcohol drinker (>2 drinks per day) (%)	0	1 (4.6)	1.00*
Functional health status prior to surgery			
Partially dependent	6 (15.3)	7 (13.2)	0.42*
Totally dependent	1 (2.6)	0	
Preoperative comorbidities			
Dyspnea with moderate exertion or at rest (%)	1 (2.6)	1 (1.9)	0.35
Pulmonary disease			
Ventilator dependent (within 48 h)	0	0	
Current pneumonia	0	0	
History of severe COPD (%)	14 (35.9)	11 (20.8)	0.11
Baseline airway obstruction severity			0.25
GOLD Class 1: FEV1 ≥80	23 (59.0)	28 (52.8)	
GOLD Class 2: FEV1=79-50	11 (28.2)	22 (41.5)	
GOLD Class 3: FEV1=49-30	4 (10.3)	3 (5.7)	
GOLD Class 4: FEV1 <30	1 (2.6)	0	
Diabetes (oral/insulin) (%)	9 (23.1)	13 (24.5)	0.87
Any cardiovascular diseases** (%)	22 (73.3)	37 (88.1)	0.11
Any CNS disorders*** (%)	1 (5.6)	0	0.45*
Sepsis within 48 h (systemic inflammatory response syndrome or sepsis or septic shock)	0	0	
Do not resuscitate status	0	0	
Preoperative therapies			
Systemic corticosteroid type			
Methylprednisolone (%)	35 (89.7)		
Duration, median (range)	1 day (1-13)		
Daily dose, median (range)	60 mg (20-240)		
Prednisone (%)	1 (2.6)		
Duration	21 days		
Daily dose	20 mg		
Dexamethasone (%)	3 (7.7)		
Duration median (range)	3 days (1-5)		
Daily dose	16 mg		
Systemic corticosteroid duration >1 day	17 (43.5)		
Systemic corticosteroid cumulative dose			
>60 mg of methylprednisolone	18 (46.2)		
Steroid use for chronic condition**** (%)	1 (2.6)	1 (1.9)	1.00*
Use of inhaled corticosteroids at home (%)	16 (41.0)	10 (18.9)	0.02
Use of inhaled corticosteroids at the hospital (%)	26 (66.7)	6 (11.3)	<0.0001
Use of bronchodilator at the hospital (%)	34 (87.2)	17 (32.1)	<0.0001

*Fisher's exact test, **History of cardiovascular diseases includes congestive heart failure (within 30 days) (*n*=3), myocardial infarction (within 6 months) (*n*=0), percutaneous coronary intervention (previous procedure) (*n*=0), cardiac surgery (previous) (*n*=1), history of angina (within 30 days) (*n*=0), hypertension requiring medical therapy (*n*=59), ***History of CNS disorders includes impaired sensorium (within 48 h) (*n*=0), coma (*n*=0), hemiplegia/hemiparesis (*n*=0), transient ischemic attack (history) (*n*=0), cerebrovascular accident/residual neurologic deficit (history) (*n*=1), CVA/no neurologic deficit (history) (*n*=0), tumor-involving CNS (*n*=0), paraplegia/paraparesis (*n*=0), quadriplegia/quadriparesis (*n*=0), ****Regular administration of systemic corticosteroids for >10 days within 30 days preoperatively. BMI=Body mass index, SD=Standard deviation, COPD=Chronic obstructive pulmonary disease, GOLD=Global Initiative for Chronic Obstructive Lung Disease, CNS=Central nervous system, CVA=Cerebrovascular accident, FEV1=Forced expiratory volume in 1 s

are more prone to surgical wound complications.[10-12] Nevertheless, one study reported a higher rate of postoperative wound complications in patients who did not receive preoperative systemic corticosteroids.[9]

Table 2: Operative characteristics and occurrences stratified by preoperative intake of systemic corticosteroid therapy

	Preoperative systemic corticosteroid therapy		*P*
	Yes (*n*=39)	No (*n*=53)	
Patient status, inpatient (%)	39 (100)	53 (100)	
Year of operation (%)			
2009	4 (10.3)	7 (13.2)	0.61
2010	9 (23.1)	9 (17.0)	
2011	13 (33.3)	12 (22.6)	
2012	6 (15.4)	10 (18.9)	
2013	7 (18.0)	15 (28.3)	
Surgical subspecialty (%)			
Cardiac surgery	0	1 (1.9)	0.52
General surgery	17 (43.6)	27 (50.9)	
Neurosurgery	3 (7.7)	1 (1.9)	
Orthopedics	4 (10.3)	10 (18.9)	
Thoracic	6 (15.4)	7 (13.2)	
Urology	3 (7.7)	2 (3.8)	
Vascular	6 (15.4)	5 (9.4)	
Elective surgery (%)	17 (85.0)	24 (77.2)	0.72*
Endoscopic/laparoscopic	8 (21.6)	10 (19.6)	
Minor	0	0	
Anesthesia type (% general)	37 (94.9)	39 (73.6)	0.10
Total duration of anesthesia (min), mean±SD	247.2±113.8	192.7±108.7	0.023
Anesthesia duration ≥270 min	14 (35.9)	12 (23.5)	0.20
Wound classification (%)			0.51
Clean	23 (59.0)	31 (58.5)	
Clean/contaminated	11 (28.2)	18 (34.0)	
Contaminated	5 (12.8)	3 (5.7)	
Dirty/infected	0	1 (1.9)	
Estimated probability of mortality, mean±SD	0.02±0.04	0.02±0.06	0.99
Estimated probability of morbidity, mean±SD	0.17±0.1	0.11±0.1	0.04

*Fisher's exact test. SD=Standard deviation

While another study found that corticosteroid therapy for <10 days before surgery had no impact on postoperative surgical wound complications.[16] Although the results of those studies contradict, corticosteroids were shown to decrease collagen formation during wound healing by suppressing tumor growth factor-β and insulin growth factor-I expression. Thus, administration of systemic corticosteroids acutely before surgery is likely to impair surgical wound healing and increase the risk of wound complications.[11]

The main risk factors for wound healing and infection include systemic factors: older age, diabetes, medications, obesity, alcohol consumption, smoking, and nutrition.[17] In our sample, these risk factors were not significantly different between patients who received preoperative corticosteroids and those who did not.

The lack of association between systemic corticosteroid therapy and PPC in our study is consistent with the findings of a study of COPD patients undergoing CABG.[9] In contrast, another study showed an improvement in lung volumes and a shorter intubation time when patients with COPD undergoing CABG were given corticosteroids preoperatively.[8] A single high dose of methylprednisolone before surgery also reduced PPC in non-COPD patients with multiple fractures but did not affect the occurrence of nonpulmonary postoperative complications.[18] In another study including 86 COPD patients in South Korea, patients who took systemic corticosteroids had higher nonpulmonary complications (23% of the steroid group vs. 7.1% of the nonsteroid group, $P = 0.032$), primarily due to wound dehiscence (10% vs. 1.8%), whereas the odds of pulmonary complications only became significant with adjustment for the underlying propensity score.[19]

The incidence of PPC in our study was comparable to the incidence reported in literature (10%–30%).[2,20] The main risk factors for PPC include type of surgery, anatomic site, duration of anesthesia, and smoking status.[21,22] Thoracic and abdominal surgeries are associated with the highest rate of PPC, with an incidence ranging from 20% to 70%.[23,24] Surgical procedures lasting >270 min are associated with a higher incidence of PPC and those lasting >4 h are associated with higher rate of postoperative

Table 3: Postoperative occurrences stratified by preoperative intake of systemic corticosteroid therapy

	Preoperative systemic corticosteroid therapy		*P*
	Yes (*n*=39)	No (*n*=53)	
Length of total hospital stay (days), mean±SD	9.2±9.2	8.4±13.5	0.74
Any wound occurrences (%)	4 (10.3)	0	0.03*
Superficial surgical-site infection	3 (7.5)	0	
Deep-incisional surgical-site infection	1 (2.5)	0	
Organ-space surgical-site infection	0	0	
Wound disruption	0	0	
Respiratory occurrences (%)	7 (17.9)	7 (13.2)	0.53
Pneumonia	1 (2.6)	4 (7.6)	0.39*
Atelectasis	3 (13.6)	4 (14.3)	1
Unplanned intubation	1 (2.6)	1 (1.9)	1.00*
Pulmonary embolism	2 (5.1)	0	0.18*
On ventilator >48 h	2 (5.1)	1 (1.9)	0.57*
Urinary tract occurrences (%)			
Acute renal failure	0	1 (1.9)	1.00*
Urinary tract infection	0	2 (3.8)	0.51*
CNS occurrences (%)	0	0	
Any cardiac occurrences** (%)	1 (2.6)	1 (1.9)	1.00*
Discharge destination (%)			0.42
Home	37 (97.4)	53 (100)	
Expired	1 (2.6)	0	
Return to operating room within 30 days*** (%)	3 (7.7)	1 (1.9)	0.31*
Postoperative death within 30 days (%)	0	0	0.71
Unplanned readmission within 30 days**** (%)	6 (15.4)	3 (5.7)	0.16*
COPD exacerbation	2 (5.1)	0	0.18
GI symptoms: Vomiting, diarrhea, abdominal pain	0	3 (5.7)	0.26
Acute febrile illness	2 (5.1)	0	0.18
Wound complication	2 (5.1)	0	0.18
Syncope	1 (2.6)	0	0.42

*Fisher's exact test, **Included cardiac arrest (*n*=1) and myocardial infarction (*n*=1), ***For any cause included: resection of ischemic bowel (*n*=1), obstructive incisional hernia (*n*=1), thoracotomy in the preoperative corticosteroid therapy group (*n*=1), and transurethral resection of prostate (*n*=1) in the no preoperative corticosteroid therapy group, ****Likely related to primary operative procedure. COPD=Chronic obstructive pulmonary disease, CNS=Central nervous system, SD=Standard deviation, GI=Gastrointestinal

pneumonia.[1,21] Although the average duration of anesthesia was significantly higher in patients who received preoperative systemic corticosteroids, the proportion of patients with anesthesia duration ≥270 min was not significantly different between the two groups. Furthermore, adjustment for anesthesia duration and baseline preoperative risk of morbidity that was also higher in patients who received preoperative systemic corticosteroids did not impact the lack of association with PPC. There was no significant difference in the other risk factors of PPC between patients who received preoperative systemic corticosteroids and those who did not.

Our study is limited by the small study sample that provided limited statistical power (β = 0.38) to detect a 10% difference in PPC. Thus, although the complication rate was not significantly different between patients who received preoperative systemic corticosteroids and those who did not, we cannot rule out a protective effect of preoperative systemic corticosteroids. Furthermore, information on some predictors of wound and respiratory complications such as perioperative alimentation and rehabilitation were not available. Finally, the observational design does not allow firm conclusion regarding causality; a randomized controlled trial that would randomly assign patients to preoperative corticosteroid therapy would provide superior evidence. Balancing these limitations is the use of the NSQIP database, which is a well-described database with standardized prospective ascertainment of exposure and outcomes.

Conclusion

This study suggests that preoperative administration of systemic corticosteroids in stable COPD patients may be associated with an increased risk of postoperative wound complications and may not be of benefit in reducing PPC. A large-scale randomized clinical trial is needed to better assess the risks and benefit of preoperative steroid therapy in COPD patients undergoing surgery.

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Conflicts of interest

There are no conflicts of interest.

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