

Original Research

Corticosteroid Dosing and Glucose Levels in COPD Patients Are Not Associated with Increased Readmissions

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Abstract

Introduction: Hospital admissions and readmissions for chronic obstructive pulmonary disease (COPD) exacerbations are associated with increased mortality and higher cost. The management of exacerbations with a shortened course of systemic corticosteroids has similar efficacy as compared to longer steroid courses, but actual overall steroid dose given is still variable. The outcomes associated with steroid side effects, such as hyperglycemia, need further evaluation. We hypothesized that the use of higher doses of corticosteroids, and the subsequent hyperglycemia, contributes to readmission.

Methods: This is a retrospective study at a tertiary care referral center in central Texas between February 2014 and July 2016. Daily corticosteroid dose, blood glucose levels, and readmission rates at 30 and 31-90 days were recorded. Sample characteristics are described using descriptive statistics. A chi-square test or student's *t*-test were used to test for associations in bivariate comparisons. Multivariable logistic regression assessed the association between readmission rate and demographic and clinical characteristics.

Results: There were 1120 patients admitted for COPD exacerbation between February 2014 and July 2016. A total of 57% were female, mean age was 69 years (standard deviation [SD] 12), and average body mass index (BMI) was 29.4 (SD 9.8). Of the total, 349 (31%) had diabetes prior to admission. The 30-day readmission rate was 16%, and the readmission rate from 31-90 days was 14%. The average prednisone equivalent dose per day during hospitalization was 86 mg (SD 52). A multivariable logistic regression model did not show any significant association between readmission and average daily glucose, high maximum glucose (>180mg/dL on any reading), or prednisone equivalent administered per day.

Conclusion: Corticosteroid dose and hyperglycemia were not associated with an increased 30-day or 31-90-day readmission rate after COPD exacerbation discharge. In addition, using higher doses of corticosteroids instead of standard-of-care (prednisone 40mg per day for a 5-day period) did not appear to affect the readmission rate in this cohort.

Abbreviations: chronic obstructive pulmonary disease, **COPD**; standard deviation, **SD**; body mass index, **BMI**; analysis of variance, **ANOVA**; odds ratio, **OR**

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Introduction

Acute exacerbations of chronic obstructive pulmonary disease (COPD) lead to increased mortality and morbidity, and frequently require hospitalization.¹ The greatest risk factor for future hospitalization for COPD exacerbation is a history of hospitalization for exacerbation,¹ so optimization of care during the hospital stay is critical to help reduce the burden of readmissions.

One of the mainstay treatments used in patients admitted to the hospital is systemic corticosteroids, both oral and parenteral. Early investigations into corticosteroid use for COPD exacerbation supported using corticosteroids over placebo to shorten a hospital stay as well as reduce rate of treatment failure (death, readmission, intubation) at 30 and 90 days, though it was noted that the patients who received glucocorticoid therapy were more likely to have hyperglycemia requiring therapy than those who received the placebo.^{2,3} In recent years, there has been a trend toward reducing the amount of corticosteroids administered to patients, with the finding that lower doses can still adequately treat the patient. The Reduction in the Use of Corticosteroids in Exacerbated COPD (REDUCE) trial found that a 5-day course of oral corticosteroids was noninferior to a 7-14 day course, and that a 5-day course of treatment was associated with overall shorter hospital length of stay.⁴

Providing the lowest corticosteroid dose can decrease the risk of complications including

hyperglycemia, osteoporosis, fractures, obesity, and susceptibility to infections, among others.⁵ Moreover, it is estimated that 28% of patients admitted for COPD exacerbation suffer from diabetes.⁶ Although the current literature recommends prednisone 40mg per day for a 5-day period,⁴ actual dose given and length of treatment are highly variable.

Given the known risk of hyperglycemia with corticosteroid use, we hypothesized that higher doses of corticosteroids will lead to increased readmissions, due to complications of hyperglycemia. The objective of this study was to assess rates of corticosteroid overuse in hospitalized COPD exacerbation patients admitted to a tertiary care referral center in central Texas, and to determine if corticosteroid exposure and average blood glucose had any effect on hospital readmission.

Methods**Study Design and Data Collection**

A retrospective study of patients above 18 years old admitted for COPD exacerbation was conducted at a tertiary care referral center in central Texas between February 2014 and July 2016. A COPD exacerbation was defined in 2 ways based on Center for Medicare and Medicaid Services guidelines (Supplement A in the online supplement). Data collection included demographics, age, sex, body mass index (BMI), daily corticosteroid dosing, average daily blood glucose level, emergency department admission, length of hospitalization, and discharge disposition. The primary outcomes studied were readmission rates at 30 and 31-90 days. Prednisone equivalent dosage was calculated for each different type of corticosteroid administered per individual during hospitalization.⁷ The average daily glucose was determined as the mean of glucose levels per day during hospitalization and high maximum glucose was recorded as an indicator of whether the patient had any glucose level reading over 180 mg/dL during hospitalization. Discharge disposition was grouped into 4 categories: home, home with home health, post-hospital facility, and other (court/law enforcement, home with hospice, inpatient hospice, and left against medical advice).

Statistical Analysis

Sample characteristics are described using descriptive statistics. Frequencies and percentages

are used to describe categorical variables. Means and standard deviations (or medians and ranges where appropriate) are used to describe continuous variables. A chi-square test (or Fisher's exact test where appropriate) and student's *t*-test (or their non-parametric equivalents) were used to assess outcomes among different patient groups. An analysis of variance (ANOVA) model (or Kruskal-Wallis test when appropriate) was used to test for differences in continuous variables between the 3+ groups. The post-hoc Tukey's test was used for pairwise comparisons when the ANOVA test showed a statistically significant result. Multivariable logistic regression assessed the association between readmission rate, glucose, and prednisone equivalent dosage adjusting for age, sex, BMI, history of diabetes, emergency department admission, and discharge disposition. The regression model variables were selected to control for potential confounding factors that were of interest. The average daily glucose and high maximum glucose were used in separate regression models due to the high correlation. A subgroup analysis of this study was conducted which considered only patients carrying a diagnosis of diabetes in the year prior to their first COPD admission.

All analyses were performed using SAS, Version 9.4 (SAS Institute, Cary, North Carolina). Research was approved by the local institutional review board (protocol number 160323), and the need for consent was waived, due to the retrospective nature of the study.

Results

Patient Characteristics

A total of 1120 individuals were included in this study. The mean age was 69.2 years old (SD 11.6), average BMI was 29.4 (SD 9.8), and the majority were female (57%). The median for hospital length of stay was 3 days (range 1-35) and 89% were admitted through the emergency department. Of the total, 349 (31%) had diabetes prior to admission. The average prednisone equivalent dose per day was 86.0 mg (SD 52.1). Guideline-based dosing of prednisone equivalent 40mg per day was seen in 201 patients (18%).

The average daily glucose level was 151.0mg/dL (SD 52.1). Only 38% had an average glucose of less than 120mg/dL during their stay. Another 42% had

averages between 120mg/dL and 180mg/dL, and the rest had an average above 180mg/dL. There were 446 patients (40%) with high maximum glucose (>180mg/dL on any reading) (Table 1). Patients with diabetes prior to admission were the majority of the high maximum glucose group at 76% (Table 2). Patients with an average daily glucose <120mg/dL received less prednisone equivalent compared to those >120mg/dL (77.4mg versus 90.9mg, $p<0.001$).

Outcomes

The 30-day and 31-90-day readmission rates were 16% and 14% respectively and in-hospital mortality rate was 1.5%. In decreasing order, patients were

Table 1. Overall Demographics and Outcomes

	Overall Demographics (N=1120) Mean (SD), N(%), Median (min-max)
Age	69.2 (11.6)
Female	638 (57%)
BMI	29.4 (9.8)
Underweight (BMI <18.5)	102 (9%)
Normal (18.5 ≤ BMI <25)	330 (30%)
Overweight (25 ≤ BMI <30)	237 (21%)
Obese (BMI >30)	451 (40%)
Diabetes Diagnosis	349 (31%)
Emergency Department Admission	997 (89%)
	Overall Outcomes
Hospitalization Length	3 (1 - 35)
30-Day Readmission	181 (16%)
31-90-Day Readmission	159 (14%)
Discharge Disposition	
Home	702 (63%)
Home with home health	216 (19%)
Post-hospital facility	147 (13%)
Other	55 (5%)
Average Daily Prednisone Equivalent	85.8 (52.1)
Average Daily Glucose Level	151 (52.1)
High Maximum Glucose^a	446 (40%)
In-hospital Mortality^b	17 (1.5%)

^aNumber of patients with any glucose level reading over 180mg/dL during hospitalization.

^bNumber of patients who died during hospitalization

SD=standard deviation; BMI=body mass index

Table 2. Patient With Diabetes Demographics and Outcomes Comparison

	Patient with Diabetes (N=349)	Patient without Diabetes (N=771)	P-value
	Mean (SD), N(%), Median (min-max)		
Age	69.7 (11.0)	69.0 (11.9)	0.2
Female	208 (60%)	429 (56%)	0.2
BMI	34.2 (10.3)	27.2 (8.7)	<0.001 ^a
Overall Outcomes			
Hospitalization length (days)	3 (1 - 19)	3 (0 - 35)	0.5
30-day Readmission	69 (20%)	112 (15%)	0.03 ^b
31-90-day Readmission	55 (16%)	104 (14%)	0.3
Emergency Department Admission	315 (90%)	682 (88%)	0.4
Discharge Disposition			0.6
Home	210 (60%)	492 (64%)	
Home with home health	74 (21%)	142 (18%)	
Post hospital facility	49 (14%)	98 (13%)	
Other	16 (5%)	39 (5%)	
Average Daily Prednisone Equivalent	84.2 (55.0)	86.5 (50.7)	0.2
Average Daily Glucose Level	197.7 (63.0)	129.9 (26.8)	<0.001 ^a
High Maximum Glucose	266 (76%)	180 (23%)	<0.001 ^a
In-hospital Mortality	5 (1.4%)	12 (1.6%)	0.8

^a $p < 0.001$

^b $p < 0.05$

SD=standard deviation; BMI=body mass index

discharged to home (63%), home with home health (19%), post-hospital facility (13%), and other locations (5%) (Table 1).

Prednisone equivalent dosage was similar for those discharged to a post-hospital facility (86.5mg daily) and those discharged to home with or without home health (84.0mg daily). Patients discharged to home with home health or a post-hospital facility were more likely to be readmitted within 30 days in comparison to those discharged home without home health (unadjusted odds ratio [OR]=1.60, 95% CI [1.15, 2.23], $p < 0.01$).

Average daily glucose and guideline-based dosing of prednisone equivalent 40 mg per day were not found to be associated with 30-day or 31-90-day readmission rates. However, 31-90-day readmission had a borderline significant association with high maximum glucose (unadjusted OR=1.37, 95% CI [0.98, 1.93], $p = 0.07$).

In the multivariable logistic regression (Table 3), the odds of a 30-day readmission for the obese group (BMI>30) was lower than the normal group

($18.5 \leq \text{BMI} < 25$) (adjusted OR=0.56, 95% CI [0.37, 0.86], $p < 0.05$) and the odds of readmission for patients discharged to home with home health (adjusted OR=1.68, 95% CI [1.12, 2.50], $p < 0.05$) or post-hospital facility (adjusted OR=1.64, 95% CI [1.02, 2.64], $p < 0.05$) was higher than those discharged to home without help. The regression models did not show any significant associations between 30-day readmission and average daily glucose, high maximum glucose, or prednisone equivalents per day after controlling for potential confounding factors. In accordance with the unadjusted model, the risk of readmission at 31-90 days had a borderline significant association with high maximum glucose (adjusted OR=1.44, 95% CI [0.97, 2.14], $p = 0.07$) as demonstrated in Table 4.

Subanalysis

A subanalysis was conducted on 349 individuals with a diagnosis of diabetes. This subgroup of patients had a higher BMI (34.2 versus 27.2, $p < 0.001$) and average daily glucose level (197.7

versus 129.9, $p < 0.001$) in comparison to the non-diabetic group. Also, high maximum glucose was prevailing (76%) in this subgroup of patients. The 30-day readmission rate was higher among patients with diabetes in comparison to others (20% versus 15%, $p = 0.02$). The hospital length of stay, emergency department admission rate, average prednisone equivalent, 31-90-day readmission rate, and discharge disposition were similar to the non-diabetic group (Table 2). Both unadjusted and adjusted models did not show any association between 30-day or 31-90-day readmission rates and glucose levels or prednisone equivalent doses in this specific group of individuals.

Discussion

We found that guideline discordant dosing of corticosteroids in the treatment of COPD exacerbation did not impact 30-day or 31-90-day readmission rates after discharge from the hospital. Additionally, average glucose level during the initial

Table 3. 30-Day Readmission Multivariable Logistic Regression

Variable	Odds Ratio	95% Confidence Limits		P-value
Age	0.98	0.84	1.14	0.8
Female	0.86	0.62	1.19	0.4
Underweight (BMI<18.5)	0.56	0.28	1.10	0.09 ^a
Overweight (25≤BMI<30)	0.84	0.54	1.30	0.4
Obese (BMI>30)	0.56	0.37	0.86	0.007 ^b
History of Diabetes	1.79	1.17	2.75	0.008 ^b
120<Glucose Average<180	1.09	0.74	1.59	0.6
180<Glucose Average	0.84	0.48	1.47	0.5
Prednisone Equivalent	1.02	0.99	1.05	0.2
Discharge to Home Health	1.68	1.12	2.50	0.01 ^b
Discharge to Post-Hospital Facility	1.64	1.02	2.64	0.04 ^b
Discharge to Other	0.31	0.09	1.04	0.06 ^a
Emergency Department Admission	1.03	0.61	1.75	0.9

^ap<0.1
^bp<0.05

BMI=body mass index

Table 4. 31-90-Day Readmission Multivariable Logistic Regression

Variable	Odds Ratio	95% Confidence Limits		P-value
Age	0.93	0.79	1.09	0.4
Female	1.17	0.82	1.66	0.4
Underweight (BMI<18.5)	1.56	0.83	2.92	0.2
Overweight (25≤BMI<30)	1.33	0.82	2.18	0.3
Obese (BMI>30)	1.04	0.66	1.64	0.8
History of Diabetes	1.01	0.66	1.55	0.9
High Maximum Glucose^a	1.44	0.97	2.14	0.07 ^b
Prednisone Equivalent	0.99	0.96	1.03	0.7
Discharge to Home Health	1.01	0.65	1.57	0.9
Discharge to Post-Hospital Facility	1.14	0.68	1.92	0.6
Discharge to Other	0.11	0.02	0.84	0.03 ^c
Emergency Department Admission	2.24	1.10	4.55	0.02

^aHigh maximum glucose replaced average daily glucose

^bp<0.1
^cp<0.05

BMI=body mass index

hospital stay did not impact 30- day or 31-90-day readmission rates after discharge. These findings suggest that strict adherence to guideline-based corticosteroid dosing during hospitalization for COPD exacerbation may not impact the patient's risk of readmission in the immediate or 3-month periods and this heterogeneity in steroid prescribing practice is consistent with other literature. We did find that

patients discharged home with home health or a post hospital facility were more likely to be readmitted within 30 days compared to those discharged home without home health (21% versus 14%, $p<0.01$), which may be a major factor to total cost of care.

Our findings do not give license to use of higher doses of steroids, as this study was not designed to evaluate the effectiveness of current corticosteroid recommendations. Risk of hyperglycemia from higher doses of corticosteroids should continue to be a consideration for clinicians. Umpierrez et al showed that patients with new onset hyperglycemia on admission had increased mortality and length of stay compared to those with normoglycemia on admission,⁸ though glucose levels at readmission was not studied in our data. Additionally, new onset diabetes has been observed to occur in up to 46% of patients after initiation of corticosteroid therapy.⁹ Furthermore, Blackburn et al found that the risk of diabetes was even higher in the elderly population when initiated on a corticosteroid.¹⁰

We did perform a subgroup analysis consisting of those carrying a diagnosis of diabetes prior to their initial admission, but the analysis did not show any significant trend regarding readmission rates. Breakey et al showed similar outcomes when they found that glucocorticoid use increased the risk of hyperglycemia in admitted patients with respiratory diseases except in those previously carrying a diagnosis of diabetes.¹¹ This is somewhat counterintuitive, as one would expect those who already have insulin resistance and depletion would be more likely to develop hyperglycemia from a trigger. It is possible that glucose levels during admission are more aggressively managed in those who

have been identified to clinicians as diabetics.

Our current study has design limitations and the findings of this study should be interpreted within the appropriate context. The study was retrospective which should be considered before generalization. Another limitation is the lack of protocolized management of COPD exacerbation and variability in steroid administration, although order sets are

available to encourage standardization of care. Finally, data regarding past history related to COPD and the severity were not available secondary to study design.

Additional research is needed to understand if, and how, in-hospital treatment of COPD exacerbation impacts functional status, and health, after discharge.

Conclusion

We conclude that guideline discordant dosing of corticosteroids and the average daily glucose level in the treatment of COPD exacerbation did not impact 30-day or 31-90-day readmission rates after discharge from the hospital.

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Declaration of Interest

The authors have no conflicts of interest to disclose.

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