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ORIGINAL RESEARCH

Clinical factors, including All Patient Refined Diagnosis Related Group severity, as predictors of early rehospitalization after COPD exacerbation

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Abbreviations

ACE, angiotensin-converting enzyme; APR-DRG, All Patient Refined Diagnosis Related Group; ARB, angiotensin II receptor blocker; CHF, congestive heart failure; CMS, Centers for Medicare and Medicaid; COPD, chronic obstructive pulmonary disease; DRG, Diagnosis Related Group; HMO, health maintenance organization; ICS, inhaled corticosteroid; LAMA, long-acting muscarinic antagonist; NDI, National Death Index; OD, odds ratio; OCS, oral corticosteroid; SABA, short-acting beta-agonist; SAMA, short-acting muscarinic antagonist; SOI, severity of illness

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Abstract

Background: Patients hospitalized for chronic obstructive pulmonary disease (COPD) exacerbations carry a high risk for early rehospitalization. We wished to identify the basic clinical factors associated with a high risk of rehospitalization, and to see how well the standardized All Patient Refined Diagnosis Related Group (APR-DRG) severity of illness (SOI) subclassification predicted rehospitalization if combined with other simple clinical measures.

Methods: We identified adult patients aged ≥40 years discharged from a major hospital in the Southwestern USA with a COPD discharge diagnosis during the study index period (1 October 2009 to 30 September 2010). Patients readmitted within 30 days ("early rehospitalization") and 90 days ("any rehospitalization") were each compared with those not rehospitalized. Clinical parameters (including demographics, comorbidities) and recent healthcare utilization were examined for their association with rehospitalization. Factors independently associated with rehospitalization were then combined with the index admission APR-DRG SOI assessment using conditional linear regression to find the best models in terms of the highest C-statistic.

Results: Among 306 patients hospitalized for COPD, 62 (20.3%) had a rehospitalization within 90 days and 28 (9.2%), an early readmission. An APR-DRG SOI subclassification ≥3 was a modest independent predictor of early or any readmission, with adjusted odds ratios ranging from 2.09 to 3.33. Models that combined the APR-DRG SOI subclassification with clinical factors present before the index hospitalization had strong C-statistics of ≥0.80. Good models without the APR-DRG SOI subclassification but including a history of recent hospitalizations before the index hospitalization were also identified.

Conclusions: An APR-DRG SOI subclassification of ≥3 for the index COPD admission is associated with an increased risk of early rehospitalizations, and can be combined with a few historical clinical factors to create strong predictive models for rehospitalization. This study demonstrates that hospitals can use commonly collected clinical information to help identify COPD patients at a high risk of failure after discharge.

Keywords: pulmonary disease, chronic obstructive; lung diseases, obstructive; patient readmission; hospitalization.

Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by persistent obstruction of expiratory airflow. COPD is associated with an enhanced chronic inflammatory response in the lungs to cigarette smoke and other noxious exposures [1]. In addition to lung damage, it is also associated with adverse systemic effects and comorbidities that contribute to its overall impact on health [2–4].

COPD is a major cause of chronic morbidity and mortality worldwide, affecting more than 210 million individuals [5]. In 2010, it was one of the top six leading causes of death [6]. COPD has been projected to become the third leading cause of death worldwide by 2030 [7].

Patients with COPD often experience acute worsening of respiratory symptoms ("exacerbations") that range in severity from mild events that can be managed at home to severe episodes that require hospitalization and can result in death. Recurrent exacerbations of COPD (particularly those requiring hospitalization) have been shown to hasten a decline in lung function, to impact negatively on quality of life and to increase mortality [8–10]. COPD patients with more severe airflow obstruction, worse debility, chronic symptoms, and advanced age carry a higher risk for acute exacerbations, increased healthcare cost, and death [11].

COPD-related hospitalizations account for the largest portion of the increased direct medical costs found among COPD patients. In 2008, the USA spent US$53.7 billion on COPD/asthma treatment, of which US$13.1 billion was a result of inpatient hospitalization [12]. COPD is also one of the major causes of early rehospitalization, with approximately one of every five Medicare patients hospitalized for COPD being readmitted within 30 days of hospital discharge [13]. Healthcare policymakers have identified reduction of hospital readmissions as a potential way of improving healthcare quality while reducing costs. In the USA, the Centers for Medicare and Medicaid (CMS) has implemented a policy wherein payments will be reduced to hospitals with excess readmissions relating to an initial hospitalization for acute myocardial infarction, congestive heart failure, pneumonia, or COPD [14]. A "readmission" is defined as hospital admission within 30 days of discharge from hospital. This policy has been implemented despite a lack of specific interventions proven to reduce COPD rehospitalization [15]. Hospitals are now highly motivated to identify COPD patients who are at highest risk for hospital readmission, and to implement interventions that reduce the risk of readmission.

The basic classification system created by the Diagnosis Related Group (DRG) was implemented by CMS as a way of reimbursing hospitals providing inpatient care for Medicare beneficiaries. This system is used to classify inpatient procedures and principal diagnoses into major diagnostic categories. The All Patient Refined Diagnosis Related Group (APR-DRG) classification scheme is a more expansive classification scheme of DRGs than the basic DRGs used by CMS. APR-DRGs are designed to include populations not normally covered by Medicare (e.g., pediatric). Each APR-DRG has four classes of severity of illness (SOI) to characterize patients further. The SOI classification system captures the extent of physiologic decompensation or loss of function in an organ system. The four SOI classes correlate to minor, moderate, major, or extreme severity. Severity classes are not considered to be scores because SOI classification levels are not comparable across APR-DRGs. The SOI classification system utilizes information on comorbidities, age, principal diagnosis, and the presence of specific operating-room and non-operating-room procedures to determine the SOI value [16].

We wished to identify basic clinical factors that a hospital could use efficiently during or soon after a COPD-related hospitalization to identify those who have the highest risk of rehospitalization. To accomplish this aim, a retrospective analysis of COPD patients treated by a large, integrated medical system in Southwestern USA was undertaken to capture all individuals hospitalized primarily for COPD exacerbations during a 12-month period. Data from administrative databases and chart reviews were used to examine a spectrum of clinical characteristics (e.g., demographic factors, comorbidities, medications) and healthcare utilization to identify those associated with hospital readmission within 30 days or 90 days after discharge. In particular, we wanted to ascertain if the standardized APR-DRG SOI subclassification could help to predict the risk of rehospitalization. We speculated that this information might be useful not only for identifying patients at risk of hospitalization, but also to provide insight into potentially modifiable risk factors.

Methods

This study was conducted among patients treated by a major hospital that is part of a non-profit regional medical system with hospitals, clinics, and staff located primarily in Albuquerque (NM, USA). Eligible patients were identified by reviewing ICD-9 codes from inpatient billing records to identify hospitalizations that were primarily for a COPD exacerbation. Most data on utilization and demographics were captured from administrative files and billing files, with review of hospital medical records used to validate cases and to collect clinical information not found in billing data. This project was approved by and supervised by the Presbyterian Health Systems Human Research Review Committee.

For study inclusion, patients had to be: hospitalized with a primary discharge code for COPD (ICD-9 491.x, 492.x, or 496) or a secondary discharge diagnosis of COPD with a primary diagnosis of respiratory failure (ICD-9 518.81, 518.82, 518.84, 799.1); discharged alive; aged ≥40 years at the index date. There were no exclusion criteria. The "index date" was defined as the discharge date from the first COPD-related hospitalization ("index admission") during the 12-month "index admission period" (1 October 2009 until 30 September 2010). Hospital records were reviewed for healthcare utilization and prescription medication before being admitted for the index admission. The "follow-up period" was the 90-day interval after the index date. This period was reviewed by billing records for evidence of any rehospitalization. "Any rehospitalization" was a rehospitalization occurring within 90 days after the index date. "Early rehospitalizations" were defined as those occurring within 30 days after the index date.

Mortality data

A subset of patients was enrolled in a managed care health plan from a health maintenance organization (HMO) affiliated with the hospital. For these patients, deaths within 90 days post-discharge were identified using the US National Death Index (NDI). The purpose of collecting mortality data was to determine the proportion of patients who expired during follow-up but were not readmitted to hospital.

Study variables

Information collected about the study subjects at the index hospitalization included: demographic variables (age, sex, Hispanic ethnicity, marital status); smoking status (current, former, never); vaccination history (influenza, pneumonia);

existing comorbidities; medications and respiratory therapy used before the initial hospitalization. Information collected about the initial hospitalization comprised: duration of stay; events during the admission (procedures and respiratory therapy); medications administered during the admission and those present at discharge. Information about the patient's care setting after discharge (e.g., home or another facility [step-down, rehabilitation, nursing, hospice care]) and care ordered at discharge (follow-up appointment, in-home care, in-home respiratory care) was also included.

Statistical analyses

Distributions of clinical and treatment prognostic factors of interest for patients in the study cohort were stratified by readmission status within each outcome evaluation interval (0–30 days and 0–90 days). Values for the mean and standard deviation were used for continuous variables. The number of study subjects and percentage of individuals with that characteristic were employed for categorical variables. The Student's t-test was used to compare continuous data. Pearson's chi-square test was employed to compare categorical data. $P<0.20$ was utilized for assessing significance for univariate models, and to determine potential factors to include in multiple regression models. Otherwise, $p\leq0.05$ was considered significant. We did not adjust for multiple testing.

One can reasonably expect many clinical factors to be highly correlated. Therefore, to assess factors that have the strongest relationship with readmission (at 30 days and 90 days), multiple logistic regression models were utilized to determine associated odds ratio (OR) and associated 95% confidence interval (95% CI) for estimation of the risk of readmission. Logistic models were constructed using an iterative method. Initial models were constructed from factors in univariate analyses that were estimated to be associated significantly with readmission using $p\leq0.20$. Factors were retained in multiple logistic regression models if factor effect estimates had an associated $p<0.30$. Different logistic models were compared using the C-statistic: an "area under the curve" measurement. C-statistic values of 0.50 are considered representative of an outcome probability equivalent to tossing a coin. Larger C-statistic values, ≥0.75, are considered indicative of more informative predictive models. Statistical analyses were carried out using SAS v9.2 software (SAS, Cary, NC, USA).

Results

Over the index admission period, 306 individuals were discharged alive after a hospitalization primarily for COPD. Of these, 62 (20.3%) were readmitted within 90 days, and 28 (9.2%) within 30 days (Table 1). Information regarding death was obtained for the subset of patients who belonged to the affiliated managed care HMO (n=93). For this subset of patients, readmission percentages were similar to those for the overall group. For the subset of patients, 18 (19.3%) were readmitted within 90 days, and 8 (8.6%) were readmitted within 30 days. None of the subset of patients died within 30 days of discharge, although 8 (8.6%) died within 90 days.

After discharge from the initial COPD hospitalization, respiratory illness was the primary discharge diagnosis for ≈50% of readmissions occurring within 30 days and 90 days. In particular, for approximately one-third of those readmitted, the readmission discharge diagnosis was obstructive bronchitis. The remaining respiratory-illness readmissions were attributed to pneumonia and respiratory failure. Finally, of the patients readmitted within 30 days, 2 (7.1%) died after readmission and, of the patients readmitted within 90 days, 3 (4.8%) died after readmission.

Table 1 provides a summary of all COPD-related medications used in the baseline period as well as baseline factors found to be significantly different between patients readmitted and not readmitted using p=0.20. Table 2 provides a similar summary, but for the initial COPD hospitalization. Table 3 provides a summary of post-discharge events.

Table 1. Baseline characteristics of patients discharged from a hospitalization for COPD (stratified by readmission within 90 days and within 30 days).

	≤90 days			≤30 days		
	No	**Yes**	**p**	**No**	**Yes**	**p**
Number of patients	244 (79.7)	62 (20.3)		278 (90.8)	28 (9.2)	
Age [mean (SD)] years	70.2 (12.3)	70.8 (12.6)	0.71	69.9 (12.5)	74.5 (10.1)	0.06
Male, N (%)	113 (84.3)	21 (15.7)	0.08	124 (92.5)	10 (7.5)	0.37
Prior hospitalizations, N (%)						
hospitalized within previous 12 months	75 (63.6)	43 (36.4)	<0.0001	99 (83.9)	19 (16.1)	0.0008
hospitalized within previous 90 days	29 (55.8)	23 (44.2)	<0.0001	38 (73.1)	14 (26.9)	<0.0001
Pneumonia vaccinations current at admission	57 (80.3)	14 (19.7)	0.8966	68 (95.8)	3 (4.2)	0.10

(*Continued*)

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Table 1. Baseline characteristics of patients discharged from a hospitalization for COPD (stratified by readmission within 90 days and within 30 days) (continued).

	≤90 days			≤30 days		
	No	**Yes**	**p**	**No**	**Yes**	**p**
Previous medications use, N (%)						
SAMA	11 (47.8)	12 (52.2)	<0.0001	17 (73.9)	6 (26.1)	0.003
SABA	91 (75.8)	29 (24.2)	0.17	108 (90.0)	12 (10.0)	0.68
combination SAMA/SABA	37 (77.1)	11 (22.9)	0.62	42 (87.5)	6 (12.5)	0.38
LAMA	39 (79.6)	10 (20.4)	0.98	44 (89.8)	5 (10.2)	0.78
LABA	74 (69.2)	33 (30.8)	0.0007	94 (87.9)	13 (12.1)	0.18
oral corticosteroids	49 (79.0)	13 (21.0)	0.88	54 (87.1)	8 (12.9)	0.25
inhaled corticosteroids	83 (69.2)	37 (30.8)	0.0002	103 (85.8)	17 (14.2)	0.01
methylxanthines	5 (62.5)	3 (37.5)	0.22	6 (75.0)	2 (25.0)	0.12
insulin	9 (45.0)	11 (55.0)	<0.0001	16 (80.0)	4 (20.0)	0.08
angiotensin II receptor blocker	16 (94.1)	1 (5.9)	0.13	17 (100.0)	0 (0.0)	0.18
beta blocker	58 (74.4)	20 (25.6)	0.17	67 (85.9)	11 (14.1)	0.08
calcium channel blocker	56 (72.7)	21 (27.3)	0.08	67 (87.0)	10 (13.0)	0.18
narcotic pain medication	44 (66.7)	22 (33.3)	0.003	58 (87.9)	8 (12.1)	0.34
immunosuppressants	1 (33.3)	2 (66.7)	0.04	3 (100.0)	0 (0.0)	0.58
chemotherapy	5 (62.5)	3 (37.5)	0.20	6 (75.0)	2 (25.0)	0.12
Existing comorbidities, N (%)						
depression	38 (74.5)	13 (25.5)	0.31	49 (96.1)	2 (3.9)	0.16
hematologic malignancy	3 (42.9)	4 (57.1)	0.01	4 (57.1)	3 (42.9)	0.002
immunosuppression	2 (33.3)	4 (66.7)	0.004	4 (66.7)	2 (33.3)	0.04
anemia	40 (71.4)	16 (28.6)	0.09	49 (87.5)	7 (12.5)	0.34
connective tissue/rheumatologic disease	3 (37.5)	5 (62.5)	0.003	8 (100.0)	0 (0.0)	0.36
diabetes	63 (73.3)	23 (26.7)	0.08	76 (88.4)	10 (11.6)	0.35
gastro-esophageal reflux disease	50 (89.3)	6 (10.7)	0.05	54 (96.4)	2 (3.6)	0.11
hypertension	122 (78.7)	33 (21.3)	0.65	137 (88.4)	18 (11.6)	0.13
pulmonary hypertension	13 (61.9)	8 (38.1)	0.04	19 (90.5)	2 (9.5)	0.95
myocardial infarction	17 (81.0)	4 (19.0)	0.89	19 (90.5)	2 (9.5)	0.95
non-ST elevation	0 (0.0)	1 (100.0)		0 (0.0)	1 (100.0)	
congestive heart failure	33 (73.3)	12 (26.7)	0.25	39 (86.7)	6 (13.3)	0.29
diastolic dysfunction	1 (20.0)	4 (80.0)		2 (40.0)	3 (60.0)	
right-sided heart failure or cor pulmonale	10 (58.8)	7 (41.2)	0.03	14 (82.4)	3 (17.6)	0.21
thrombo-embolic disease	14 (60.9)	9 (39.1)	0.02	21 (91.3)	2 (8.7)	0.94
cerebrovascular disease	27 (84.4)	5 (15.6)	0.49	32 (100.0)		0.06
supraventricular arrhythmia	31 (72.1)	12 (27.9)	0.18	36 (83.7)	7 (16.3)	0.08
pacemaker/other	3 (60.0)	2 (40.0)	0.27	3 (60.0)	2 (40.0)	0.02
Past COPD-related symptoms/diagnoses, N (%)						
sputum production	115 (81.6)	26 (18.4)	0.46	132 (93.6)	9 (6.4)	0.12
chronic hypercapnia	46 (73.0)	17 (27.0)	0.14	54 (85.7)	9 (14.3)	0.11
pneumonia	69 (85.2)	12 (14.8)	0.16	78 (96.3)	3 (3.7)	0.05
Past respiratory therapy, N (%)						
ventilation support by intubation	6 (54.5)	5 (45.5)	0.03	9 (81.8)	2 (18.2)	0.29
long-term oxygen treatment	141 (75.8)	45 (24.2)	0.03	166 (89.2)	20 (10.8)	0.23
non-invasive positive-pressure ventilation required at night	19 (67.9)	9 (32.1)	0.10	23 (82.1)	5 (17.9)	0.09

Percentages are row percentages.
COPD, chronic obstructive pulmonary disease; LABA, long-acting beta-agonist; LAMA, long-acting muscarinic antagonist; SABA, short-acting beta-agonist; SAMA, short-acting muscarinic antagonist; SD, standard deviation.

Table 2. Medications received at the initial hospitalization for COPD (stratified by readmission within 90 days and within 30 days).

	≤90 days			≤30 days		
	No	**Yes**	**p**	**No**	**Yes**	**p**
Number of patients, N (%)	244 (79.7)	62 (20.3)		278 (90.8)	28 (9.2)	
Medications administered during admission, N (%)						
SAMA	10 (62.5)	6 (37.5)	0.08	12 (75.0)	4 (25.0)	0.02
SABA	78 (79.6)	20 (20.4)	0.95	91 (92.9)	7 (7.1)	0.40
combination SAMA/SABA	186 (79.1)	49 (20.9)	0.64	216 (91.9)	19 (8.1)	0.24
LAMA	48 (72.7)	18 (27.3)	0.11	55 (83.3)	11 (16.7)	0.017
LABA	114 (75.5)	37 (24.5)	0.07	135 (89.4)	16 (10.6)	0.39
leukotriene receptor	5 (41.7)	7 (58.3)	0.0008	9 (75.0)	3 (25.0)	0.05
oral corticosteroids	161 (79.3)	42 (20.7)	0.79	186 (91.6)	17 (8.4)	0.51
inhaled corticosteroids	134 (77.0)	40 (23.0)	0.17	157 (90.2)	17 (9.8)	0.67
methylxanthines	4 (57.1)	3 (42.9)	0.13	5 (71.4)	2 (28.6)	0.07
insulin	71 (73.2)	26 (26.8)	0.05	87 (89.7)	10 (10.3)	0.63
non-insulin diabetic medications	21 (63.6)	12 (36.4)	0.01	28 (84.8)	5 (15.2)	0.21
diurectic	79 (71.8)	31 (28.2)	0.01	98 (89.1)	12 (10.9)	0.42
calcium channel blocker	65 (73.9)	23 (26.1)	0.1043	78 (88.6)	10 (11.4)	0.39
narcotic pain medication	90 (70.9)	37 (29.1)	0.001	114 (89.8)	13 (10.2)	0.58
immunosuppressants	0 (0.0)	3 (100.0)	0.0006	2 (66.7)	1 (33.3)	0.14
chemotherapy	2 (66.7)	1 (33.3)	0.57	2 (66.7)	1 (33.3)	0.14
Medications present at discharge, N (%)						
SAMA	23 (79.3)	6 (20.7)	0.95	26 (89.7)	3 (10.3)	0.81
SABA	104 (83.9)	20 (16.1)	0.14	116 (93.5)	8 (6.5)	0.18
combination SAMA/SABA	101 (78.9)	27 (21.1)	0.76	115 (89.8)	13 (10.2)	0.60
LAMA	41 (70.7)	17 (29.3)	0.06	50 (86.2)	8 (13.8)	0.17
LABA	116 (74.4)	40 (25.6)	0.02	139 (89.1)	17 (10.9)	0.28
leukotriene receptor	4 (40.0)	6 (60.0)	0.002	7 (70.0)	3 (30.0)	0.02
anti-asthmatic drug	2 (40.0)	3 (60.0)	0.03	3 (60.0)	2 (40.0)	0.02
oral corticosteroids	191 (81.3)	44 (18.7)	0.22	218 (92.8)	17 (7.2)	0.03
inhaled corticosteroids	124 (72.9)	46 (27.1)	0.0009	149 (87.6)	21 (12.4)	0.03
methylxanthines	4 (57.1)	3 (42.9)	0.13	5 (71.4)	2 (28.6)	0.07
insulin	17 (60.7)	11 (39.3)	0.009	24 (85.7)	4 (14.3)	0.32
diurectic	60 (72.3)	23 (27.7)	0.05	73 (88.0)	10 (12.0)	0.28
calcium channel blocker	53 (70.7)	22 (29.3)	0.02	64 (85.3)	11 (14.7)	0.06
narcotic pain medication	51 (71.8)	20 (28.2)	0.06	63 (88.7)	8 (11.3)	0.48
sedative/hypnotic	71 (74.0)	25 (26.0)	0.09	87 (90.6)	9 (9.4)	0.97
oral antibiotics	157 (83.1)	32 (16.9)	0.07	177 (93.7)	12 (6.3)	0.03
immunosuppressants	1 (25.0)	3 (75.0)	0.006	3 (75.0)	1 (25.0)	0.27
anti-coagulant	25 (67.6)	12 (32.4)	0.05	32 (86.5)	5 (13.5)	0.33

COPD, chronic obstructive pulmonary disease; LABA, long-acting beta-agonist; LAMA, long-acting muscarinic antagonist; SABA, short-acting beta-agonist; SAMA, short-acting muscarinic antagonist; SD, standard deviation.

The characteristics most significantly associated with both 30-day and 90-day readmissions based on univariate analyses were (Tables 1–3): (i) all-cause hospitalizations in the previous 12 months; (ii) all-cause hospitalizations in the previous 90 days; (iii) pre-admission indicators of greater disease severity (i.e., use of short-acting antimuscarinic agent; inhaled corticosteroid (ICS) use; hematologic malignancy at admission; inhaled corticosteroids present at discharge); (iv) asthmatic medications present at discharge (i.e., leukotriene receptor; anti-asthmatic drugs); (v) hip fracture noted at discharge; (vi) congestive heart failure noted at discharge.

Table 3. Characteristics of the initial hospitalization for COPD (stratified by readmission within 90 days and within 30 days).

	≤90 days			≤30 days		
	No	**Yes**	**p**	**No**	**Yes**	**p**
Number of patients, N (%)	244 (79.7)	62 (20.3)		278 (90.8)	28 (9.2)	
APR-DRG Severity classification, N (%)			0.002			0.05
1 – Minor	35 (87.5)	5 (12.5)		39 (97.5)	1 (2.5)	
2 – Moderate	127 (85.8)	21 (14.2)		139 (93.9)	9 (6.1)	
3 – Major	63 (66.3)	32 (33.7)		80 (84.2)	15 (15.8)	
4 – Extreme	9 (75.0)	3 (25.0)		10 (83.3)	2 (16.7)	
Unknown	10 (90.9)	1 (9.1)		10 (90.9)	1 (9.1)	
Duration of stay, N (%)			0.1582			0.5377
1 day	45 (90.0)	5 (10.0)		46 (92.0)	4 (8.0)	
2 days	52 (80.0)	13 (20.0)		58 (89.2)	7 (10.8)	
3 days	47 (83.9)	9 (16.1)		53 (94.6)	3 (5.4)	
4 days	35 (72.9)	13 (27.1)		40 (83.3)	8 (16.7)	
5 days	28 (80.0)	7 (20.0)		34 (97.1)	1 (2.9)	
6 days	12 (75.0)	4 (25.0)		14 (87.5)	2 (12.5)	
7 days	12 (80.0)	3 (20.0)		13 (86.7)	2 (13.3)	
8+ days	13 (61.9)	8 (38.1)		20 (95.2)	1 (4.8)	
Noted at discharge, N (%)						
Comorbidities						
hematologic malignancy	1 (20.0)	4 (80.0)	0.0008	2 (40.0)	3 (60.0)	<.0001
immunosuppression	1 (25.0)	3 (75.0)	0.006	3 (75.0)	1 (25.0)	0.27
connective tissue or rheumatologic disease	5 (55.6)	4 (44.4)	0.07	9 (100.0)	0 (0.0)	0.33
hip fracture	0 (0.0)	2 (100.0)	0.005	1 (50.0)	1 (50.0)	0.04
congestive heart failure	21 (65.6)	11 (34.4)	0.04	26 (81.3)	6 (18.8)	0.05
systolic dysfunction	2 (50.0)	2 (50.0)		3 (75.0)	1 (25.0)	
diastolic dysfunction	3 (33.3)	6 (66.7)		6 (66.7)	3 (33.3)	
right-sided heart failure or cor pulmonale	7 (50.0)	7 (50.0)	0.0046	12 (85.7)	2 (14.3)	0.50
thrombo-embolic disease	5 (35.7)	9 (64.3)	<0.0001	12 (85.7)	2 (14.3)	0.50
pacemarker/other	2 (50.0)	2 (50.0)	0.14	2 (50.0)	2 (50.0)	0.004
COPD-related symptoms/diagnoses						
sputum production	46 (83.6)	9 (16.4)	0.43	55 (100.0)	0 (0.0)	0.009
chronic hypercapnia	8 (61.5)	5 (38.5)	0.10	12 (92.3)	1 (7.7)	0.85
Respiratory therapy						
ventilation support by intubation	2 (50.0)	2 (50.0)	0.14	3 (75.0)	1 (25.0)	0.27
non-invasive positive pressure ventilation required at night	15 (68.2)	7 (31.8)	0.16	19 (86.4)	3 (13.6)	0.45

APR-DRG, All Patient Refined Diagnosis Related Group (3M, Salt Lake City, UT, USA); COPD, chronic obstructive pulmonary disease; SD, standard deviation.

All study patients were identified using primary diagnosis codes for the visit. For 288 (94.1%) of the study patients, the APR-DRG code assigned to the initial hospitalization was 140, COPD. No APR-DRG code was assigned for 11 (3.6%) of the study patients. For the other 7 (2.3%) study patients, the assigned APR-DRG codes were for tracheostomy with long-term mechanical ventilation, respiratory system diagnosis with ventilation, other pneumonia, acute myocardial infarction, heart failure, septicemia and disseminated infections. There were 95 patients with an APR-DRG SOI major subclassification (SOI=3) and 12 with an extreme subclassification (SOI=4), almost of all which had an APR-DRG code for COPD. The 2 patients with APR-DRG

codes relating to tracheostomy and septicemia had an extreme SOI subclassification, and the 3 patients with APR-DRG codes relating to a respiratory-system diagnosis with ventilation, acute myocardial infarction, and heart failure all had major SOI subclassifications. As expected, the higher APR-DRG SOI subclassifications for the index admission were associated with a greater likelihood of readmission for both 30 day and 90 day periods (Table 3).

Many of the measured factors were not found to be significantly associated with readmission at 30 days or 90 days in this population ($p>0.2$), as shown below.

- Demographic factors of Hispanic ethnicity, marital status, and smoking status.
- Existing comorbidities of: anxiety, solid tumor malignancy, lung cancer, acute renal failure, chronic kidney disease, hyponatremia, osteoporosis, previous hip fracture, cirrhosis, gastric ulcer, coronary artery disease, peripheral vascular disease, myocardial infarction (other than non-ST elevation myocardial infarction), ventricular arrhythmia, and congestive heart failure (CHF, other than diastolic dysfunction). These were also not significantly associated with readmission when noted at discharge, with the exception of CHF and previous hip fracture, which were significantly associated with readmission in 30 days ($p<0.05$) and readmission in 90 days ($p<0.05$) (see Table 3). In addition, the following diagnoses noted at discharge were not significantly associated with readmission: depression, anemia, diabetes, gastro-esophageal reflux disease, hypertension, pulmonary hypertension, cerebrovascular disease, and supraventricular arrhythmia.
- Previous COPD diagnoses of asthma and emphysema (these were also not significant when noted at discharge).
- Use of the following medications before the initial admission: long-acting muscarinic antagonist (LAMA) inhalers, combination short-acting muscarinic antagonist (SAMA)/short-acting beta-agonist (SABA) inhalers, oral corticosteroids (OCS), non-insulin diabetic medications, angiotensin-converting enzyme (ACE) inhibitors, diuretics, sedatives, antidepressants, antibiotics, vasodilators, anti-platelets, and anti-coagulants.
- Medications administered during the initial hospitalization: combination SAMA/SABA inhalers, OCS, ace-inhibitors, angiotensin II receptor blockers (ARBs), vasodilators, beta-blockers, intravenous corticosteroids, intravenous and/or oral antibiotics, sedatives, antidepressants, anti-platelets, and anti-coagulants (when these were noted as being present at discharge they were also not significantly associated with readmission, with the exception of OCS medications, sedatives, and anti-coagulants).
- Pneumonia and long-term oxygen treatment when noted at discharge.
- Being up-to-date for influenza vaccination at admission, receiving an influenza vaccination during hospitalization, and receiving a pneumonia vaccination during hospitalization.

Adjusted models for 90-day readmission

Table 4 summarizes the adjusted logistic models constructed for readmission within 90 days. Models 1, 3, and 4 included the APR-DRG SOI subclassifications 3 and 4 (major and extreme) as a factor. The C-statistic for readmission based on this factor and male sex was 0.66 (model 1). Adding whether the patient was hospitalized in the 12 months before the current discharge, and medications pre-index (inhaled corticosteroids, insulin, and ARBs) increased the C-statistic to 0.80, which is indicative of a strong model. Adding medications at discharge increased the C-statistic slightly to 0.82.

If the APR-DRG SOI subclassification is not included as a factor, and instead only male sex and whether the patient was hospitalized in the 12 months before the current discharge, then the model C-statistic is 0.71 (Model 2). The OR estimate for previous hospitalization and APR-DRG SOI subclassification changed when used concurrently, and with other clinical and comorbidity information, suggesting a strong interaction with these factors (Table 4).

Model 5 in Table 4 does not include the APR-DRG SOI subclassification, but includes factors from model 4 and, additionally, comorbidities that were not included in model 3 because the APR-DRG SOI subclassification considers comorbidities. This model had a C-statistic of 0.82. Previous hospitalization was the factor with the strongest relationship (OR, 3.99; 95% CI, 2.04–7.80; $p<0.0001$). Use of ICS and insulin were also associated with a higher risk of readmission in 90 days. Patients using ARBs before admission, comorbid gastro-esophageal reflux disease (GERD), and oral corticosteroids noted at discharge all had a reduced risk of readmission, although these factors were not significant using $p<0.05$.

An additional regression analysis was conducted using the subset of patients enrolled in the HMO. ORs were estimated for the combined event of readmission or death in the 90 days post-discharge. Because of the small sample size, only two models were constructed, equivalent to model 1 and model 2 in Table 4. For the subset of 93 patients, 26 (28.0%) had a combined event in 90 days. Among the 40 patients with a major or severe subclassification, 18 (45.0%) had a combined event, with an OR estimate, adjusted for male sex, of 4.52 (95% CI, 1.74–12.6; $p<0.0001$). The model C-statistic was 0.70. Among the 35 patients hospitalized in the previous 12 months, 16 (45.7%) had a combined event, with an OR estimate, adjusted for male sex, of 4.03 (95% CI, 1.60–10.83; $p<0.0001$). The model C-statistic was 0.69.

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Table 4. Multiple logistic regression models – readmission in 90 days.

	Model 1		Model 2		Model 3		Model 4		Model 5	
	OR (95% CI)	**p***	**OR (95% CI)**	**p***	**OR (95% CI)**	**p***	**OR (95% CI)**	**p***	**OR (95% CI)**	**p***
Model C-statistic	*0.66*		*0.71*		*0.80*		*0.82*		*0.82*	
Male	0.58 (0.32–1.06)	0.08	0.65 (0.36–1.20)	0.17	0.55 (0.29–1.06)	0.08	0.64 (0.33–1.26)	0.20	0.60 (0.30–1.19)	0.15
APR-DRG SOI subclassification >/= 3	3.23 (1.81–5.76)	<0.0001			2.77 (1.46–5.24)	0.002	2.70 (1.41–5.17)	0.003		
Hospitalized in previous 12 months			5.07 (2.76–9.29)	<0.0001	3.73 (1.94–7.19)	<0.0001	3.84 (1.97–7.51)	<0.0001	3.99 (2.04–7.80)	<0.0001
Medications pre-admission										
inhaled corticosteroids					3.06 (1.60–5.86)	0.0007	2.40 (1.17–4.94)	0.02	2.34 (1.14–4.80)	0.02
insulin					3.47 (1.13–10.61)	0.03	3.19 (1.01–10.07)	0.05	3.35 (1.07–10.48)	0.04
angiotensin II receptor blocker					0.25 (0.03–2.04)	0.20	0.24 (0.03–2.07)	0.19	0.20 (0.02–2.27)	0.20
Comorbidities										
hematologic malignancy									6.85 (0.95–49.27)	0.06
GERD									0.36 (0.13–1.02)	0.05
right-sided heard failure or cor pulmonale									2.27 (0.66–7.79)	0.19
Medications at discharge										
LABA							0.87 (0.37–2.07)	0.75	1.60 (0.73–3.51)	0.24
inhaled corticosteroids							2.33 (0.91–5.97)	0.08	2.00 (0.93–4.30)	0.08
oral corticosteroids							0.57 (0.27–1.19)	0.13	0.55 (0.26–1.17)	0.12
calcium channel blockers							1.60 (0.78–3.29)	0.20	1.74 (0.84–3.58)	0.13

*p for statistical significance of OR estimate; determined using Wald-Chi Square.
APR-DRG, All Patient Refined Diagnosis Related Group; GERD, gastroesophageal reflux disease; LABA, long-acting beta-agonist; SOI, severity of illness.

Table 5. Multiple logistic regression models – readmission in 30 days.

	Model 1		Model 2		Model 3		Model 4		Model 5	
	OR (95% CI)	**p***	**OR (95% CI)**	**p***	**OR (95% CI)**	**p***	**OR (95% CI)**	**p***	**OR (95% CI)**	**p***
Model C-statistic	0.66		0.69		0.83		0.85		0.87	
Male	0.63 (0.28–1.43)	0.27	0.82 (0.35–1.91)	0.6465	0.57 (0.22–1.45)	0.24	0.73 (0.29–1.88)	0.52	0.58 (0.22–1.56)	0.28
APR-DRG SOI subclassification >/= 3	3.33 (1.49–7.42)	0.003			2.09 (0.81–5.37)	0.13	2.55 (1.03–6.33)	0.04		
Hospitalized 90 days pre-admission			6.16 (2.71–14.02)	<0.0001	4.88 (1.91–12.43)	0.0009	5.11 (1.98–13.16)	0.0007	5.70 (2.19–14.80)	0.0004
Medications pre-admission										
SAMA					6.67 (1.82–24.46)	0.004	6.54 (1.84–23.23)	0.004	6.69 (1.86–24.09)	0.004
LABA					0.55 (0.17–1.84)	0.34				
leukotriene modifiers					2.72 (0.44–16.84)	0.28				
inhaled corticosteroids					2.46 (0.76–7.95)	0.13	2.02 (0.80–5.11)	0.14	2.20 (0.84–5.77)	0.11
beta blockers					1.77 (0.66–4.75)	0.26			1.98 (0.76–5.19)	0.16
Up to date pneumonia vaccination					0.30 (0.08–1.12)	0.07	0.30 (0.08–1.15)	0.08	0.31 (0.08–1.16)	0.08
LAMA during hospitalization					2.49 (0.96–6.42)	0.06	2.35 (0.92–6.03)	0.07	2.47 (0.95–6.44)	0.06
Comorbidities										
hematologic malignancy									3.77 (0.56–25.50)	0.17
GERD									0.25 (0.05–1.35)	0.11
Medications at discharge										
leukotriene modifiers							4.06 (0.87–18.89)	0.07	4.40 (0.95–20.29)	0.06
oral corticosteroids							0.29 (0.11–0.78)	0.01	0.28 (0.11–0.77)	0.01

*p for statistical significance of OR estimate; determined using Wald-Chi Square.
APR-DRG, All Patient Refined Diagnosis Related Group; GERD, gastroesophageal reflux disease; LABA, long-acting beta-agonist; LAMA, long-acting muscarinic antagonist; SAMA, short-acting muscarinic antagonist; SOI, severity of illness.

Adjusted models for 30-day readmission

Table 5 summarizes the adjusted logistic models that were constructed for readmission within 30 days. Models 1, 3 and 4 included APR-DRG SOI subclassifications 3 and 4. The C-statistic for readmission based on this factor (model 1) adjusting for male sex, was 0.66, almost equivalent to that for readmission within 90 days.

The C-statistic was increased to 0.83 (indicating a strong model) after adding factors for whether the patient was hospitalized in the 90 days before the current discharge; medications pre-index of SAMAs, LABAs, leukotriene modifiers, inhaled corticosteroids, and beta blockers; being up-to-date with pneumonia vaccination; receipt of LAMA during hospitalization. Dropping the medications pre-admission that had $p<0.20$ and adding the medications leukotriene modifiers and oral corticosteroids noted at discharge increased the C-statistic to 0.85 (model 4).

Models 2 and 5 do not include the APR-DRG SOI subclassification factor. The C-statistic for model 2 (which includes only whether the patient was male or not, and was hospitalized in the 90 days before the index admission) had a C-statistic of 0.69, again similar to the 90-day readmission model. In model 5, the OR estimate for previous hospitalization increased from the estimates for model 3 and 4 once the APR-DRG severity factor was omitted, again suggesting an interaction between the two factors. Patients hospitalized in the 90 days before the index hospitalization had odds of readmission within 30 days that were 5.7-times greater than those not hospitalized. Patients using SAMA pre-admission had odds that were 6.7-times greater. As in the 90-day readmission model, patients noted to have oral corticosteroids at discharge had odds of readmission within 30 days that were less than one-third those not receiving oral corticosteroids.

Discussion

We wished to identify factors associated with early hospital readmissions after a hospitalization primarily for COPD. In comparing patients who had any rehospitalization within 90 days or an early rehospitalization to those who were not readmitted, we found several clinical factors associated with readmission.

In general, factors tended to be associated with either more severe COPD, such as increased use of medication during the baseline period, more serious comorbidities (e.g., hematologic malignancies, heart disease, pulmonary hypertension) or more frequent previous hospitalizations. The APR-DRG SOI subclassification was also a good univariate predictor of readmission. Using a binary measure for the subclassifications of major/extreme severity of illness and combining that with a few simple clinical measures (e.g., previous admission history, previous use of respiratory medication), the predictive models had very strong C-statistics of ≥0.80. We did not include comorbidities or age in our models that included APR-DRG SOI subclassification as a factor because these are considered in the subclassification determination. Solid models without the APR-DRG SOI subclassification were also developed, and were based primarily on the history of hospitalizations and use of respiratory medication before the index hospitalization. These analyses suggest that very good predictive models for COPD rehospitalizations can be developed using locally collected hospital data. Furthermore, even if the APR-DRG SOI subclassification is not used by a hospital, a similar combination of severity measures for the index hospitalization plus simple historical data on utilization before the admission can be used to identify high-risk patients.

In our database, the 30- and 90-day all-cause rehospitalization rates (9.2% and 20.3%, respectively) were similar to those reported in other recent analyses. In an analysis of the 2003–2004 US Medicare fee-for-service population, the 30-day all-cause rehospitalization rate after a COPD admission was 22.6%, with 8.2% readmitted primarily for COPD [13]. In a limited analysis of 2008 fee-for-service data, the 30-day all-cause rehospitalization rate after a COPD admission was 20.5%, with 7.1% readmitted primarily for COPD [17]. A follow-up analysis of the same database for the calendar year 2010 found a similar 30-day readmission rate of 20.9% [18]. The 2008 estimate was based on 39,100 readmissions following 190,700 hospitalizations in which COPD was the principal diagnosis. The 2010 estimate was based on 126,443 readmissions after 606,186 hospitalizations. In an analysis of another US database of patients aged 40–65 years hospitalized for COPD between 2008 and 2010, the 30-day and 90-day all-cause rehospitalization rates after a COPD admission were 8.2% and 17.5%, respectively [19]. In an audit sample of COPD admissions in the UK in 2008, 90-day all-cause readmissions were 34% (2971 of 8677 patients) [20]. In a study of hospital readmissions in Denmark and in the US Kaiser Permanente system from 2002 to 2007, all-cause 30 day readmission rates after a COPD hospitalization were 20.7–24.1% in Denmark, and 19.4–21.4% in Kaiser Permanente [21]. Among these, the only study to conduct an analysis similar to ours also identified pre-index hospitalization healthcare utilization and severe comorbidities as factors associated with an increased risk of rehospitalization [19].

In the present study, the APR-DRG SOI subclassifications of major and extreme risk were strongly associated with all-cause readmission in 30 days and 90 days. Studies that have used the APR-DRG SOI subclassification to adjust for confounding in comparative effectiveness studies have found similar results. Bollu and colleagues estimated a 30-day all-cause readmission rate of 10.9% among patients discharged from a hospitalization for COPD, and treated with arformoterol or nebulized SABA. In a regression model for readmission, the strongest factors associated with readmission were an APR-DRG SOI subclassification of "major" (OR, 1.89; 95% CI,

1.02–3.49; p=0.04) and a subclassification of "extreme" (2.49; 1.28–4.85; 0.007) [22]. Similarly, Averill and colleagues showed, in their study of 30-day readmissions for Florida hospitals in 2004–2005, that estimates for potentially preventable readmissions after a hospitalization for COPD increased with increasing levels of the APR-DRG SOI subclassification, increasing from 12.2% for SOI subclassification level 1 to 21.1% for subclassification level 4 [23].

There is a need to better understand the factors associated with the risk of readmission after a hospitalization for COPD. In the USA, this need has been heightened since CMS added COPD to its Hospital Readmission Reduction Program as one of the conditions for which hospitals would be evaluated with respect to a risk-adjusted 30-day all-cause readmission rate. Concern has been voiced about including COPD [14], including uncertainty regarding the preventability of readmissions and the lack of evidence that decreasing readmissions results in improved outcomes [24]. CMS adjusts rates for risk by including age and comorbidities in its estimations for readmission rates, but including these as individual elements does not allow easy identification of which group of patients is being impacted by intervention measures designed to reduce readmission rates. Use of a risk classification scheme similar to the APR-DRG SOI subclassification levels offers this ability.

Our subset analysis also highlights the importance of obtaining information on death when conducting studies on individuals discharged from a COPD exacerbation. Estimated 30-day and 90-day readmission rates were similar between our main analysis and our subset analysis. However, in the subset analysis, beyond the 20% readmitted to the hospital within 90 days, an additional 9% died, making the percentage that died or were readmitted within 90 days of discharge almost 30%.

Our study has limitations. Administrative data are based on claim payments and ICD-9 codes, which may not accurately reflect the main reasons a patient was hospitalized, or even that the diagnosis of COPD is confirmed. We captured as broad a range of variables as possible based on what was available in the administrative database. We recognize, however, that there may be other variables that might predict hospitalization that were not available in the database. All readmissions may not have been captured, in which case our readmission percentages would be underestimated. In addition, information on inpatient stay may not have completely captured hospitalization treatments. For example, patients may have had existing therapy such as a continuous positive-airway pressure device before the index hospitalization, and its use during the hospitalization might not be captured by billing records. The extent to which coding within hospitals' charge description masters accurately reflect the care that a patient receives is not known, but our cases were reviewed by abstraction of medical records, and all were validated as having a physician's diagnosis confirming that the hospitalization was for COPD. The study population is from one hospital, discharges occurred over a 12-month period ending in 2010, and the study sample size was small, particularly for the subset analysis that included post-discharge mortality. Statistically significant findings were recorded, but the results from our study need to be replicated and, ideally, expanded upon, using larger study samples. Finally, the demographic characteristics of our patients and treatment habits of the providers in this system are likely to be different than those found in other systems. Hence, we encourage other hospitals to develop their own predictive models for COPD rehospitalization whenever feasible.

Conclusions

In the present study, patients who experienced a COPD-related rehospitalization were significantly different from those who did not according to several pre-index hospitalization factors. A strong predictor was previous hospitalization, particularly within 90 days of the index hospitalization. An APR-DRG SOI subclassification of ≥3 for the index COPD admission is associated with increased risk for early rehospitalizations, and can be combined with a few historical clinical factors to create strong predictive models for rehospitalization. Prospective analyses can focus on the parameters that were most strongly associated with rehospitalization to develop risk stratification systems, and to develop specific interventions that might reduce the risk of rehospitalizations. Ultimately, healthcare quality will be improved by further research into high risk factors that can be alleviated to reduce the risk of readmissions.

Contributions

The authors meet criteria for authorship as recommended by the International Committee of Medical Journal Editors and were fully responsible for all content and editorial decisions, and were involved at all stages of manuscript development.

Potential conflicts of Interest

The International Committee of Medical Journal Editors' (ICMJE) Potential Conflicts of Interests forms for the authors are available for download at: http://www.drugsincontext.com/wp-content/uploads/2015/03/dic.212278-COI.pdf

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Janice Beene has no conflicts of interest to declare.

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