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Impact of pulmonary hypertension in patients with acute exacerbation of chronic obstructive pulmonary disease and its effect on healthcare utilization

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Abstract

We aim to study the impact of pulmonary hypertension on acutely exacerbated chronic obstructive pulmonary disease (AECOPD). We used the 2016 and 2017 National Readmission Database with an inclusion criterion of AECOPD as a primary and pulmonary hypertension as a secondary diagnosis using ICD 10-CM codes. Exclusion criteria were age under 18 years, non-elective admission, and discharge in December. The primary outcome was in-hospital mortality during the index admission. Secondary outcomes were 30-day readmission rate, resource utilization, and instrument utilization including intubation, prolonged invasive mechanical ventilation >96 h (PIMV), tracheostomy, chest tube placement, and bronchoscopy during the index admission. A total of 627,848 patients with AECOPD were included in the study, and 68,429 (10.90%) patients had a diagnosis of pulmonary hypertension. Pulmonary hypertension was more common among females (61.14%) with a mean age of 71 ± 11.66, Medicare recipients (79.5%), higher Charlson comorbidity index, and treatment in an urban teaching hospital. Pulmonary hypertension was associated with greater mortality (adjusted odds ratio (aOR) 1.89, $p < 0.001$), higher 30-day readmission (aOR 1.24, $p < 0.001$), higher cost (adjusted mean difference (aMD) $2785, $p < 0.01$), length of stay (aMD 1.09, $p < 0.001$), and higher instrument utilization including intubation (aOR 199, $p < 0.001$), PIMV (aOR 2.12, $p < 0.001$), tracheostomy (aOR 2.1, $p < 0.001$), bronchoscopy (aOR 1.46, $p = 0.007$), and chest tube placement (aOR 1.39 $p < 0.004$). We found that pulmonary hypertension is related to higher in-hospital mortality, length of stay, increased instrument utilization, readmission, and costs. Our study aims to shed light on the impact of pulmonary hypertension on AECOPD in hopes to improve future management.

Keywords

acutely exacerbated chronic obstructive pulmonary disease, pulmonary hypertension, chronic obstructive pulmonary disease (COPD) readmission, hypoxia

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Introduction

Chronic obstructive pulmonary disease (COPD) is one of the leading pulmonary pathologies in the United States. It is characterized by progressive airway obstruction and can present in an array of ways such as emphysema, chronic bronchitis, or mixed.[1] Occasionally, these patients

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experience an acute deterioration in their respiratory system (termed exacerbation) and often require hospitalization.[1] Pulmonary hypertension (PH) is a common sequela of COPD and is classified as World Health Organization (WHO) group 3 for cause of PH.[2] The primary investigated structural basis of PH in COPD are remodeling of pulmonary arteries and arterioles.[3]

PH in COPD patients is associated with shorter life expectancy, higher healthcare utilization, and readmission rates.[3–5] Some studies have indicated that the direct costs of COPD (attributable to healthcare expenditures) were estimated to be over net $50 billion in 2010.[6] Our study aims to analyze outcomes, 30-day readmission rates, and healthcare resource utilization associated with PH in patients with acutely exacerbated COPD (AECOPD).

Methods

Data source

The study cohort was acquired from the 2016–2017 National Readmission Database (NRD). The NRD is a part of the Healthcare Cost and Utilization Project (HCUP), organized and supported by the Agency for Healthcare Research and Quality. The NRD is one of the largest all-payer publicly accessible healthcare databases in the US. It comprises data of both weighted and unweighted hospital encounters each year. The initial data provided to researchers are unweighted, and using an algorithm provided by the HCUP, it is converted to weighted data which allows for measuring national estimates.[7] The unweighted data consists of roughly 20% of national hospital inpatient data and weighting allows for performing analysis on a national level.[7]

Study population

International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes were used to identify adults. Inclusion criteria for the study were admission with AECOPD as a primary diagnosis and PH as a secondary diagnosis using ICD-10-CM codes from the year 2016–2017. Exclusion criteria were age under 18 years, non-elective admission such as urgent or emergent admissions (to better assess re-admission outcomes), and discharge in December, since looking at 30-day readmission is not possible for December admissions. The primary outcome was in-hospital mortality during the index admission. Secondary outcomes were 30-day readmission rates, resource utilization, intubation rates, prolonged invasive mechanical ventilation >96 h (PIMV), tracheostomy rate (TR), chest tube placement rate, and bronchoscopy rate (BR) during the index admission.

Statistical analyses

The Pearson chi-square test and Student's t-test were utilized for assessing categorical and continuous variables, respectively. The trends in the readmission of AECOPD were analyzed by the linear-by-linear association test. After adjusting for baseline characteristics and comorbidities, a two-step hierarchical multivariate regression model using variables with a $p < 0.2$ on a univariate regression analysis was used to measure the risk of hospitalization outcomes among patients with AECOPD and PH. Variables used in the multivariate regression analysis included PH, insurance status, age, gender, race, hospital bed size (since certain events can vary based on hospital bed size),[8,9] Charlson comorbidity index (CCI), day of admission, hospital region, hospital location (rural or urban), teaching or non-teaching hospital, and median household income, as these factors can impact outcomes in COPD and PH. COPD severity could not be used in the multivariate regression analysis, as there are no ICD-10 codes demonstrating disease severity. Stata Version 16.1 by StataCorp LLC (College Station, TX) was utilized for all statistical analyses.

Results

A total of 627,848 patients with AECOPD were included in the study and 68,429 (10.9%) patients had a secondary diagnosis of PH. PH was more common among elderly females ((61.1%); with a mean age of 71 ± 11.66), Medicare recipients (79.47%), higher CCI, and treatment at an urban teaching hospital (Table 1). PH was associated with greater in-hospital mortality (adjusted odds ratio (aOR) 1.89, $p < 0.01$), higher length of stay (LOS) (adjusted mean difference (aMD) 1.09 ± 0.03)), higher hospital-related costs (aMD $2785, $p < 0.001$), and higher 30-day readmission rate (aOR 1.24, $p < 0.001$) compared to patients without PH (Table 2). In addition, PH was associated with higher incidence of intubation rate (aOR 1.99, $p < 0.001$), PIMV >96 h (aOR 2.12, $p < 0.001$), TR (aOR 2.15, $p < 0.001$), chest tube placement (aOR 1.39, $p < 0.004$), and BR (aOR 1.46, $p = 0.007$) (Table 2).

Discussion

PH is associated with poorer outcomes, decreased functional capacity, impaired quality of life, increased oxygen requirement, and increased mortality.[2,10] Mortality in COPD and PH has significantly improved due to advances made in the field and the expanded knowledge in the pathophysiology and the treatment of PH.[11] Typically, PH develops when airflow limitation is severe and results in chronic hypoxemia secondary to chronic alveolar hypoxia and pulmonary vasoconstriction.[3] PH is defined as a resting mean pulmonary arterial pressure (mPAP) > 20 mm Hg with a pulmonary vascular resistance greater than 3 Wood Units[12] and is associated with increased morbidity and

Table 1. Comparison of baseline characteristics in acutely exacerbated COPD patients without and with pulmonary hypertension.

Variable	COPD without PH (%)	COPD with PH (%)	p-Value
Total (N – 627,848)	559,599 (89.1%)	68,429 (10.9%)	
Gender			<0.001
Male	42.45	38.86	
Female	57.55	61.14	
Mean age (±SD)	68 (±11.97)	71(±11.66)	<0.001
Age group			<0.001
30–40 year	0.8	0.5	
40–50 year	5.3	2.9	
50–65 year	27.2	19.21	
>65 year	66.5	77.2	
Length of stay (LOS)			<0.001
<3 days	35.6	22.6	
3–7 days	51.09	52.7	
>7 days	13.3	24.5	
Insurance provider			<0.001
Medicare	71.49	79.47	
Medicaid	15.09	11.51	
Private	10.62	7.89	
Uninsured	2.8	1.13	
Charlson comorbidity index			<0.001
1	37.09	16.67	
2	25.77	26.17	
3 or more	37.14	57.16	
Substance abuse			<0.001
Opioid use	2.4	2.0	
Cocaine use	1.4	1.1	
Smoking	30.6	22.5	
Alcohol	5.4	4.0	
Medical disorders			<0.001
HIV	0.3	0.2	
Schizophrenia	1.6	1.2	
Depression	17.6	17.4	
Chronic pain	13.1	11.8	
Cannabis	1.4	1.1	
Hospital teaching status			<0.001
Non-teaching	46.6	39.56	
Teaching	53.36	60.44	
Hospital location			<0.001
Rural	16.52	11.77	
Urban	83.48	88.23	

Table 2. Odds ratio and mean differences in acutely exacerbated COPD with pulmonary hypertension as compared to without pulmonary hypertension.[a]

Outcomes	Adjusted odds ratio (aOR); adjusted mean difference (aMD)	95% Confidence interval (CI)	p-Value
Mortality	1.89	1.73–2.07	<0.001
30-Day readmission rate	1.24	1.21–1.28	<0.001
Intubation	1.99	1.85–2.14	<0.001
Prolonged invasive mechanical ventilation	2.12	1.89–2.38	<0.001
Chest tube placement	1.39	1.11–1.74	<0.004
Tracheostomy	2.15	1.53–2.9	<0.001
Bronchoscopy	1.46	1.11–1.94	0.007
Length of stay (LOS)	1.09 days	1.02–1.15	<0.001
Total hospital cost	$2785	$2602–$2967	<0.001

[a]Adjusted model using variables with p<0.2 such as hospital characteristics, Charlson comorbidity index, age, gender, hospital teaching status, and race.

mortality.[3] Currently, PH is divided into five groups based on the WHO classifications, with COPD resulting in PH classified as WHO group 3.[12] PH in COPD is usually of moderate severity and does not alter right ventricular function in most cases.[13] The major cause for PH in COPD is due to pulmonary vascular remodeling.[13] However, the exact pathophysiology behind the development of PH in COPD is not completely understood.

Determining the prevalence of PH in COPD patients has been difficult owing to a lack of right heart catheterization due to ethical reasons (for the sole purpose of diagnosis without any clinical benefit to the patient) and subjective errors in echocardiography.[14] Some studies have indicated that the prevalence of PH in COPD patients is >35%, though these numbers have likely increased over time.[15] In a study by Chaouat et al., the researchers found that the prevalence of PH in hospitalized COPD patients was nearly 50%.[16] It is safe to conclude that PH is prevalent in COPD patients and is associated with higher hospitalization rates. In our study, we found that PH was prevalent in 8.33% patients who presented with AECOPD, lower than previously found. The lower prevalence could be due in part to the advances in medicine, improved understanding of the disease process, prompt treatment, and the design of this study.

Various treatment options are available to address PH in COPD; however, oxygen therapy is a favorable means of treatment for these patients, as it has been shown to improve PH-related symptoms and decrease the chance of developing right heart failure.[3] Surgical options are available as well. In patients with advanced emphysema, lung volume reduction surgery (LVRS) can be a viable option, though there are some controversies relating to this option.[17] In one study, the researchers found that LVRS can yield favorable pulmonary hemodynamic outcomes by improving pulmonary function and arterial blood gas dynamics in patients with emphysema,[17] though there is no direct study done to assess LVRS in patients with COPD and PH. Moreover, LVRS is a double-edged sword and may result in the reduction of the pulmonary vascular tree and have damaging effects.[3] In patients with advanced COPD and PH, lung transplantation should be considered. In a study by Bjørtuft et al., patients with advanced COPD and mild-to-moderate PH who received single lung transplant showed an improvement in mPAP (roughly 10 mmHg decrease) with similar decreases in pulmonary vascular resistance, and these results were maintained after two years of follow-up treatment.[18] All in all, though there are some controversies in the management of PH in COPD, oxygen therapy and lung transplantation remain the definite treatment of choice in these patients depending on the disease severity, with referral to specialized PH centers.

In our study, we found an increase in the frequency of PH in the elderly. Our observed prevalence of PH in the elderly is due to higher likelihood of cardiopulmonary comorbidities in this population (Table 1). There is a progressive decline in lung function that has been observed with normal aging because of alteration in the static elastic recoil of the lung, chest wall stiffness, decreased strength in the respiratory muscles, and loss of total lung capillary volume.[19] A combination of these factors likely leads to increased prevalence of PH in the elderly.[19] Furthermore, it has been demonstrated that there is roughly a 1 mmHg increase in systolic pulmonary arterial pressure with each 10-year increase in age.[19] Therefore, it is important to address any modifiable factors to prevent PH in the elderly, particularly those with COPD.

It is crucial to understand the increasing economic burden and readmissions associated with COPD. Our study showed that there was a near $3000 additional hospital charge associated with patients who had PH in comparison to patients without PH. Some of the contributing reasons for this added cost were increased instrumentation seen in patients with PH such as intubation, PIMV, tracheostomy, chest tube, and bronchoscopy, as well as increased LOS (9% increase in LOS among AECOPD and PH patients). One study by Iheanacho et al. found that overall direct costs were found to generally increase with COPD severity, exacerbation frequency, and severity of COPD symptoms.[20] They also found a higher rate of healthcare resource utilization for patients with more severe COPD, more frequent COPD exacerbations, and more severe COPD symptoms.[20] Furthermore, in our study we found that patients with PH had 24% higher odds of being readmitted within 30 days (aOR 1.24, $p < 0.001$). With increased readmission comes increased resource utilization and economic burden on our healthcare system. In addition, these factors can have a detrimental effect on a patient's well-being and impact their quality of life.

PH in COPD has been demonstrated to have higher mortality and in-hospital complications. A study by Balasubramanian et al. found that over a course of 1, 3, and 5 years the survival was 87%, 60%, and 51%, respectively, among COPD patients with PH.[21] This indicates that over time the survival rate decreases for patients with COPD and PH. Our study indicates that patients with AECOPD and PH had an increased LOS and higher odds of mortality. This can be explained due to the higher procedure utilization seen among patients with PH, since this cohort had higher odds of intubation, tracheostomy, bronchoscopy, chest tube placement, and PIMV. The requirement of these procedures indicates that patients with COPD and PH have higher complications requiring such interventions. Furthermore, it has been established that the presence of PH has a higher association with mortality in COPD than forced expiratory volume in one second or other gas exchange variables.[17] PH in COPD has also been linked to increased morbidity and adverse events leading to increased hospitalization.[17] Therefore, it is no surprise that

we observed a higher mortality among patients with COPD and PH as compared to COPD without PH.

Limitations to this study include the nature of the dataset, diagnostic coding errors, inability to trace specific patient encounters longitudinally, administrative nature of the dataset, and the possibility of inaccurate calculation of the disease burden due to multiple inpatient admissions of the same patient. This dataset uses ICD-10 codes, and it is quite possible that PH maybe have been documented inaccurately. Due to the nature of the dataset, discharge ICD-10 codes are not provided and only principal diagnosis and events occurring in the hospital or previous history of a certain diagnosis are recorded using ICD-10 codes. Furthermore, it is difficult to assess the nature and severity of PH as limited by ICD-10 coding and therefore the adjusted model could not take into consideration the COPD disease severity. Disease severity among COPD patients can have different outcomes, with more severe COPD patients having worse outcomes. A study in the future with variables that can account for COPD severity would further elaborate the findings of this paper. In addition, certain information was not available to us such as current smoking status, laboratory values, imaging, pulmonary function testing values, medication use, and COPD staging. Furthermore, readmission was analyzed from 2016 to 2017 and is limited to that timeframe, and the NRD is constructed from State Inpatient Databases and does not include readmissions occurring in a different state. However, this is one of the largest nationally representative US datasets and one of the few that allows for analysis of readmissions.

Conclusion

Our study indicates that PH is associated with greater in-hospital mortality, LOS, and 30-day readmission among patients with AECOPD. It is also associated with increased procedure utilization and higher healthcare resource utilization leading to increased hospital expenses. Prompt diagnosis and appropriate treatment of PH in patients with COPD may improve outcomes of these patients.

Highlights

- Pulmonary hypertension is associated with worse outcomes in COPD patients.
- Pulmonary hypertension is associated with higher 30-day readmission.
- Age 30–50, LOS > 3 days, Medicare, higher CCI are predictors of higher readmission.
- Pulmonary hypertension is associated with increased instrumentation and costs.

Disclaimer

The views expressed in this article are his or her own.

Conflict of interest

The author(s) declare that there is no conflict of interest.

Authors' contributions

- Rezwan F. Munshi: Conceptualization, resources, writing – original draft, writing – review and editing.
- James R. Pellegrini Jr.: Conceptualization, resources, writing – original draft, writing – review and editing.
- Pranavi Patel: Writing – original draft; writing – review and editing, resources.
- Maxim Kashin: Writing – original draft; writing – review and editing, resources.
- James Kang: Writing – original draft; writing – review and editing, resources.
- Robert Sexton: Writing – original draft; writing – review and editing, resources.
- Jose R. Russe: Writing – original draft; writing – review and editing, resources.
- Amgad N. Makaryus: Conceptualization, writing – original draft; writing – review and editing, resources.
- Palakkumar Patel: Resources, methodology, formal analysis, software analysis, data curation.
- Samarthkumar Thakkar: Writing – original draft; writing – review and editing, resources.
- Brandon Pelletier: Writing – original draft; writing – review and editing, resources.
- Tinu Abraham: Writing – original draft; writing – review and editing, resources.
- Muhammad Tiwana: Writing – original draft; writing – review and editing, resources.
- Fatima Anjum: Conceptualization, methodology, validation, resources, writing – review and editing, visualization, supervision, project administration.

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