Prevalence and influence of chronic obstructive pulmonary disease on stroke outcomes in hospitalized stroke patients

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) and stroke are important causes of death. COPD patients are at higher risk of cerebral hypoxia and aspiration. Yet, relatively little is known about the prevalence of COPD among stroke patients or its impact on outcomes after an index stroke. We assess the prevalence of COPD among hospitalized stroke patients in a nationally representative sample and examine the effect of COPD with mortality risk in the hospital after a stroke.

Methods: Using the National Inpatient Sample, a nationally representative dataset of US hospital admissions between January 2004 and December 2009 (n = 48,087,002), we assessed Crude and age-adjusted COPD prevalence among stroke patients and in-hospital mortality rates by COPD status. Independent associations of COPD with in-hospital mortality following stroke were evaluated using multivariable logistic regression.

Results: 11.71% (95% CI: 11.48–11.94%) of all adult patients hospitalized for stroke had COPD. The crude and age-adjusted in-hospital mortality rates for these patients were 6.33% (95% CI: 6.14–6.53%) and 5.99% (95% CI: 4.05–7.94%), respectively. On multivariable analyses, COPD was modestly associated with overall stroke mortality (OR 1.03; 95% CI 1.01–1.06; p = 0.018). The greater risks of mortality were seen among those with intracerebral hemorrhage (OR: 1.12; 95% CI 1.03–1.20; p = 0.005) and ischemic stroke patients (OR 1.08; 95% CI 1.03–1.13, p = 0.001).

Conclusions: 12% of hospitalized stroke patients have COPD. The presence of COPD is independently associated with higher odds of dying during stroke. Prospective studies are needed to identify any modifiable risk factors contributing to this deleterious relationship.

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1. Introduction

The prevalence and mortality of stroke and chronic obstructive pulmonary disease (COPD) remain high. In 2011, COPD was the third leading cause of death and the estimated crude prevalence of COPD was 6.3% (95% CI: 6.2–6.4) [1]. Likewise, the burden of stroke in the United States remains significant despite recent prevention advances notably the change from the 3rd to the 4th cause of mortality [2]. Interestingly, both conditions are closely interrelated. For example, smoking is an important risk factor for stroke and the strongest determinant of COPD. In addition, Patients with severe COPD have chronic hypoxemia at and hypercapnia that could potentially put them at greater risk of cerebral insults in the event that they have an acute stroke. Furthermore, patients with stroke and COPD are at increased risk of risk of aspiration, a leading cause of death among patients with stroke [3,4]. Given all of the aforementioned issues, it is conceivable that the prevalence of COPD might be elevated in stroke patients and that COPD may confer a higher risk of early mortality after stroke. Despite these epidemiological and pathophysiological considerations, there is scarcity of data on COPD prevalence among stroke patients and mortality risk in COPD patients after an acute stroke.

In this study, we hypothesized that COPD is highly prevalent among individuals with stroke and that COPD patients are at increased risk of death after a stroke.

2. Methods

2.1. Study population

Data were obtained from all US states that contributed to the National Inpatient Sample for adult patients, 18 years and older, admitted to US non-federal hospitals between January 2004 and December 2009 (n = 48,087,002). Briefly, the National Inpatient Sample (NIS), the largest publicly available all-payer inpatient care database in the United States. The NIS contains data from ≈8 million-de-identified hospital stays a year and approximates a 20% stratified sample of nonfederal US hospitals. The majority (≥97%) of the hospitals in the United States is nonfederal and include government hospitals operated by the city, county, and

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state, as well as hospitals operated by for-profit and nonprofit organizations. The database sampling strategy allows for extrapolation from the sample to represent all US hospitalizations nationwide, using sampling weights. The National Healthcare Cost Utilization Project of the Agency maintains the database for Healthcare Research and Quality. Detailed information on the design of the NIS is available at www.hcup-us. ahrq.gov. The study qualified for Institutional Review Board waiver.

2.2. Diagnosis of stroke and COPD

Primary discharge diagnoses of stroke were identified using the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) diagnosis codes 430–432 and 433–436, of which a subset with co-existing COPD were defined with secondary ICD-9-CM diagnoses codes 490–492, 494, and 496.

2.3. Statistical analysis

We computed crude and age-adjusted prevalence of stroke and stroke subtypes in the whole database as well as prevalence of COPD prevalence among stroke patients overall and stroke patients in each subtype. Crude and age-adjusted in-hospital mortality rates were also calculated. Independent associations of COPD with in-hospital mortality following stroke were evaluated using multivariable logistic regression. The following were included as co-variates in the logistic regression analyses: 1) Age [18–44 years (reference), 45–64 years, 65–84 years, >85 years], 2) Gender [Male (reference), Female], 3) Race/Ethnicity [White Non-Hispanic (reference), Black Non-Hispanic, Hispanic, Others], 4) Residential zip code median income divided in quartiles with the highest quartile as reference, 5) Admission day [Weekday (reference), Weekend], 6) Source of admission [Routine (reference), Emergency department, Other Hospital, Other Health facility/Law enforcement], 7) Hospital size [Large (reference), Medium, Small], 8) Hospital location/teaching hospital status [Urban Teaching (reference), Urban non-Teaching, Rural], 9) Hospital census region [West (reference), Northeast, Midwest, South], 10) Primary payer [Medicare/Medicaid (reference), Private Insurance, Self-pay, No charge], and 11) Charlson co-morbidity index (CCI) grouped into 3 categories: 0 (reference), 1, and ≥2. CCI is a weighted score of 17 conditions including congestive heart failure, myocardial infarction, chronic pulmonary disease, cerebrovascular disease, dementia, diabetes without complications, mild liver disease, peptic ulcer disease, peripheral vascular disease, and connective tissue disease (weight 1); hemiplegia or paraplegia, diabetes with complications, malignancy, renal disease (weight 2); moderate or severe liver disease (weight 3); metastatic solid tumor and HIV/AIDS (weight 6) [5].

We also tested for statistically significant interactions between COPD and age, gender, or race/ethnicity. Appropriate survey weights were applied in estimating the population-based rates, odds ratios (OR), and confidence intervals (CI). Statistical hypotheses were tested with p < 0.05 as the level of statistical significance.

3. Results

We identified 33,053,263 NIS participants ≥18 years of whom overall 2.65% (unadjusted) (95% CI: 2.61%–2.70%) were hospitalized for acute stroke. Ischemic strokes, hemorrhagic strokes, sub-arachnoid hemorrhages, and intra-cerebral hemorrhages were present in 2.29% (2.25%–2.33%), 0.37% (0.35%–0.38%), 0.08% (0.072%–0.085%), and 0.20% (0.19%–0.21%) of participants respectively.

3.1. Overall and stroke subtypes specific COPD prevalence

Overall, the unadjusted prevalence (95% CI) of COPD among stroke patients was 11.71% (11.48%–11.94%). Corresponding figures for patients with ischemic stroke, hemorrhagic stroke, sub-arachnoid hemorrhage, and intracerebral hemorrhage were 12.16 (95% CI: 11.48%–11.94%), 8.87% (8.59%–9.16%), 7.47% (6.99%–7.95%), and 9.13% (8.82%–9.43%) respectively; Table 1.

3.2. Stroke mortality among stroke patients with COPD vs. without COPD

Concerning frequency of mortality, overall there was no difference between COPD and non-COPD stroke participants (unadjusted mortality rate 6.3%; 95% CI: 6.1%–6.5% vs. 6.1%, 95% CI: 6.0%–6.3%). Similarly, no difference in mortality rates was detected for intracerebral hemorrhage between COPD and non-COPD participants. However, frequency of mortality was significantly higher in COPD patients than non-COPD patients with hemorrhagic stroke combined (unadjusted mortality rate 25.4%; 95% CI: 24.5–26.3%, vs. 23.95%, 95% CI 23.5–24.4%), Subarachnoid hemorrhage (unadjusted mortality rate 26.9-%; 95% CI 24.8–28.9% vs. 22.2%, 95% CI 21.4–23.0%), and ischemic stroke (unadjusted mortality rate 4.11%; 95% CI 3.96–4.3% vs. 3.2%, 95% CI 3.1–3.3%). When analysis was restricted to ischemic stroke patients who received r-tPA, the excess mortality in COPD patient was no more apparent; Table 2.

3.3. Multiple logistic regression analysis of the risk of death in stroke patients by COPD status

In univariate logistic regression analysis, COPD was a predictor of stroke mortality in the entire cohort (OR 1.03, 95% CI: 1.01–1.06), ischemic stroke (1.30, 95% CI: 1.26–1.35), hemorrhagic stroke combined (1.08, 95% CI: 1.03–1.13), and subarachnoid hemorrhage (1.29, 95% CI: 1.16–1.42) but not among intracerebral hemorrhage patients (1.03, 95% CI: 0.98–1.09). As shown in Table 3, after multivariate adjustment, the association between stroke mortality and COPD persisted for stroke overall (OR 1.06, 95% CI: 1.02–1.08) and ischemic stroke (1.08, 95% CI: 1.03–1.13) while it became significant for intracerebral hemorrhage (OR 1.12, 95% CI: 1.03–1.20). There were no statistically significant interactions between COPD and age, gender, or race/ethnicity.

4. Discussion

In this study totaling over a million stroke admissions during a 5-year period, we observed that: 1) approximately 1 out of 9 hospitalized

Table 1
Stroke prevalence and COPD Prevalence.

Variables	Stroke prevalence		COPD prevalence	
	Crude survey-weighted rate % (95% CI) n (unweighted total): 33,053,263	Age-adjusted survey-weighted rate % (95% CI) N (weighted total): 162,610,833	Crude survey-weighted rate % (95% CI) n (unweighted total): 1,061,177	Age-adjusted survey-weighted rate % (95% CI) N (weighted total): 5,214,559.46
All strokes	2.65 (2.61, 2.70)	1.70 (1.63, 1.79)	11.71 (11.48, 11.94)	5.68 (5.52, 5.84)
Ischemic strokes	2.29 (2.25, 2.33)	1.39 (1.37, 1.41)	12.16 (11.93–12.31)	5.91 (5.74–6.08)
All hemorrhagic strokes	0.37 (0.35, 0.38)	0.27 (0.26, 0.29)	8.87 (8.59–9.16)	4.52 (4.31–7.73)
Sub-arachnoid hemorrhages	0.08 (0.07, 0.09)	0.08 (0.073, 0.088)	7.47 (6.99–7.95)	4.69 (4.34–5.04)
Intra-cerebral hemorrhages	0.20 (0.19, 0.21)	0.13 (0.13, 0.140)	9.13 (8.82–9.43)	4.49 (4.26–4.72)