Hospital Noninvasive Ventilation Case Volume and Outcomes of Acute Exacerbations of Chronic Obstructive Pulmonary Disease

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Abstract

Rationale: Higher hospital case volume may produce local expertise ("practice makes perfect"), resulting in better patient outcomes. Associations between hospital noninvasive ventilation (NIV) case volume and outcomes for patients with acute exacerbations of chronic obstructive pulmonary disease (COPD) are unclear.

Objectives: To determine associations between total hospital NIV case volume for all indications and NIV failure and hospital mortality among patients with acute exacerbations of COPD.

Methods: Using the 2011 California State Inpatient Database and multivariable hierarchical logistic regression, we calculated hospital-level risk-adjusted rates for NIV failure (progression from NIV to invasive mechanical ventilation) and hospital mortality among patients with acute exacerbations of COPD.

Measurements and Main Results: We identified 37,516 hospitalizations for acute exacerbations of COPD in 252 California hospitals in 2011. Total hospital NIV use for all indications ranged from 2 to 565 cases (median, 64; interquartile range, 96). Hospital NIV failure rates for acute exacerbations of COPD ranged from 3.7 to 31.3% (median, 8.5%; interquartile range, 4.2). At the hospital level, higher total hospital NIV case volume was weakly associated with higher hospital NIV failure rates for acute exacerbations of COPD ($r = 0.13$; $P = 0.03$). Higher hospital NIV failure rates were weakly associated with higher hospital mortality rates for acute exacerbations of COPD ($r = 0.15$; $P = 0.02$), but higher total hospital NIV case volume was not associated with hospital mortality for exacerbations of COPD ($r = -0.11$; $P = 0.08$). At the patient level, patients admitted to high-NIV versus low-NIV case-volume hospitals had greater odds of NIV failure (quartile 4 vs. quartile 1 adjusted odds ratio [aOR], 1.95; 95% confidence interval [CI], 1.12–3.40). Compared with initial treatment with invasive mechanical ventilation, NIV failure was associated with higher odds of death (aOR, 1.81; 95% CI, 1.35–2.44). However, admission to high-NIV versus low-NIV case-volume hospitals was not significantly associated with patient in-hospital mortality (quartile 4 vs. quartile 1 aOR, 0.76; 95% CI, 0.57–1.02).

Conclusions: Despite strong evidence for use of NIV in the management of acute exacerbations of COPD, we observed no significant mortality benefit and higher rates of NIV failure in high-NIV case-volume hospitals. Further investigation of patient selection and hospital factors associated with NIV failure is needed to maximize favorable patient outcomes associated with use of NIV for acute exacerbations of COPD.

Keywords: chronic obstructive pulmonary disease; noninvasive ventilation; critical care outcomes; invasive mechanical ventilation; health care outcome assessment

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Acute exacerbations of chronic obstructive pulmonary disease (AECOPD) lead to more than 800,000 hospitalizations per year, and they are the third leading cause of death in the United States (1–3). Noninvasive ventilation (NIV) and invasive mechanical ventilation (IMV) are frequently used for respiratory support during AECOPD with severe respiratory distress (4, 5).

Evidence derived from randomized trials demonstrated that NIV use early during severe chronic obstructive pulmonary disease (COPD) exacerbations reduced the need for IMV, length of stay, and hospital mortality as compared with usual medical care (4, 6–9). AECOPD remains one of the few conditions with high-level evidence demonstrating benefits of NIV in patients with respiratory distress. Following trial benefits, epidemiologic studies (10, 11) demonstrated a large population-level increase in the use of NIV for AECOPD, with a concomitant decrease in IMV use.

However, NIV use in acute respiratory failure involves processes of care that require careful patient selection, monitoring, and titration by a multidisciplinary team of nurses (12), respiratory therapists (13), and physicians (14), often across multiple hospital care settings. Hospitals that care for a greater number of patients may develop local expertise ("practice makes perfect") that results in better patient outcomes, as has been demonstrated across other critical care conditions and procedures (15), including IMV (16–18), sepsis (19), and surgery (20, 21). Alternatively, higher hospital case volume may result from suboptimal patient selection or result in strain on an understaffed or underprepared health care system, producing poor outcomes (22–24).

Because of the complex care processes involved with NIV, associations between hospital NIV case volume and outcomes are currently unclear. We sought to investigate associations between hospital NIV case volume and outcomes among patients with AECOPD, a condition with strong evidence for NIV use. We hypothesized that greater hospital NIV experience and case volume would be associated with lower NIV failure rates and improved patient outcomes for patients with AECOPD. Some of the results of these studies have been reported previously in the form of an abstract (25).

Methods

Study Subjects

Using the Healthcare Cost and Utilization Project California State Inpatient Database (26), we analyzed adult patients who were at least 40 years old and hospitalized in 2011 with AECOPD. We identified patients hospitalized with AECOPD with an International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM), principal diagnosis of COPD or a principal diagnosis of acute respiratory failure and a secondary diagnosis of AECOPD present on admission (27, 28) (*see* Table E1 in the online supplement).

We excluded patients with admission Do Not Resuscitate (DNR) orders (29, 30), patients transferred to or from another acute care hospital, patients with comorbid obstructive sleep apnea, patients admitted to hospitals with fewer than 25 AECOPD-related hospitalizations during the year 2011, and patients admitted to hospitals with no cases of NIV for AECOPD. We used previously validated ICD-9-CM procedure codes 93.90 (28) and 96.7x (31, 32) to identify NIV and IMV, respectively. NIV exposure was defined as only patients whose initial ventilatory treatment was NIV. NIV failure was defined as a patient having received NIV on or before the first day of IMV.

Exposures and Outcomes

Our primary exposure variable was total hospital NIV case-volume count for all indications. We chose total hospital NIV case volume rather than NIV for COPD case volume because hospital experience with NIV is likely driven by total use and not use for one specific condition.

Our primary outcome was hospital risk-adjusted NIV failure rate (number of NIV failure cases per 100 NIV cases for AECOPD), and our secondary outcomes were IMV rate (number of IMV per 100 AECOPD hospitalizations) and hospital mortality. We chose NIV failure rate as our primary outcome because several studies have shown that patients with NIV failure have higher mortality than patients who initially received IMV (11, 28, 33–35), and NIV failure is more proximal in the causal pathway of NIV-specific processes of care than hospital mortality.

In a secondary analysis, we examined the association of hospital NIV case volume with patient-level outcomes (NIV failure, IMV, in-hospital death) to avoid an ecological fallacy (36). We also calculated hospital risk-adjusted NIV rates among patients with COPD (number of NIV per 100 AECOPD hospitalizations) to describe between-hospital variation in NIV use for AECOPD. Patients could contribute multiple hospitalizations to analyses related to our primary analysis.

Statistical Analysis

We compared continuous variables with Student's *t* test, Wilcoxon rank-sum tests, and linear regression as appropriate, and we analyzed categorical variables with Mantel-Haenszel chi-square and Cochran-Armitage tests for trends. We used multivariable hierarchical logistic regression (37) with hospital-level random intercepts to calculate hospital NIV, NIV failure, IMV, and mortality rates for patients with AECOPD, adjusting for patient demographics, individual Elixhauser comorbidities (38, 39), and acute organ failures (40, 41) (Table E2) present on admission (29). To assess the association of hospital practice patterns with individual patient outcomes, we performed multivariable hierarchical logistic regression with patient-level outcomes to determine the association of hospital NIV case-volume quartile with patient-level NIV failure, IMV use, and in-hospital mortality.

We estimated between-hospital variation in NIV failure attributable to unmeasured hospital factors using intraclass correlation coefficients derived from hospital intercept variance estimates (42, 43). We used Spearman's correlations to determine the correlation between hospital total NIV case volume with risk-adjusted NIV failure, IMV, and hospital mortality rates, and we used cubic spline regression to visualize the relationships.

Sensitivity Analysis

We conducted a sensitivity analysis to determine the association between NIV case volume and NIV failure rate, excluding patients with NIV and IMV initiated on the same hospital day because we could not clearly determine which mode of ventilation was initiated first. Furthermore, as NIV case volume may affect only NIV mortality, we conducted an additional sensitivity analysis to determine the association of NIV case volume and hospital mortality only for

patients receiving NIV. We created hospital total NIV case-volume quartiles with equal numbers of patients (21).

An alternative approach was to create quartiles with equal numbers of hospitals in each quartile (16). Thus, we performed a sensitivity analysis on patient-level outcomes where the primary exposure was hospital total NIV case-volume quartile using quartiles constructed with equal numbers of hospitals. Finally, as our mortality analysis could be subject to survivor bias for patients with multiple hospitalizations for AECOPD during 2011, as these patients must necessarily have survived admissions earlier in the year to have admissions later in the year, we conducted an additional sensitivity analysis on the secondary outcome of mortality in which we included only the last hospitalization for patients with multiple hospitalizations for AECOPD.

Statistical testing was two-tailed with an α-value of 0.05 and conducted with SAS versions 9.3 and 9.4 software (SAS Institute, Cary, NC). This study of de-identified data was deemed exempt from review by the Boston University Medical Campus Institutional Review Board.

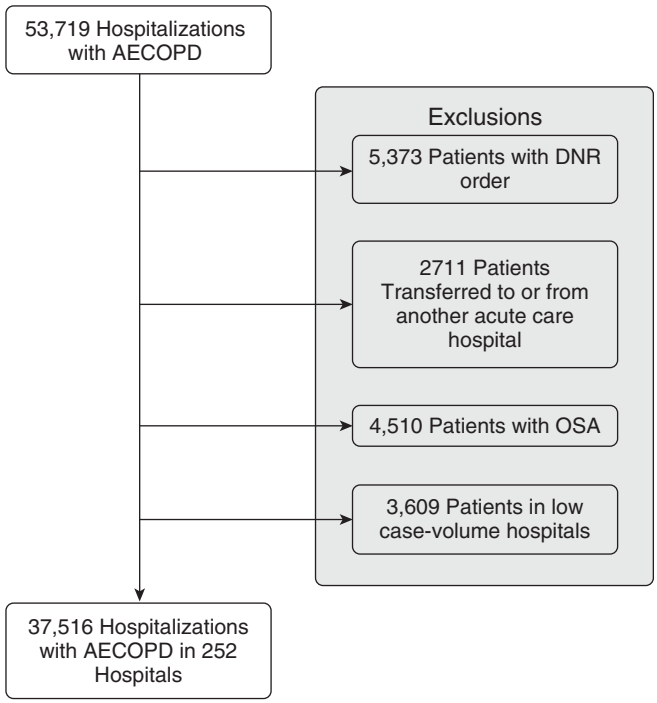

Figure 1. Study design. Patients with DNR orders at admission, who were transferred to or from another acute care hospital, with comorbid OSA, and who were admitted to low AECOPD case-volume hospitals or hospitals with no NIV for AECOPD cases were excluded. AECOPD = acute exacerbation of chronic obstructive pulmonary disease; DNR = Do Not Resuscitate; NIV = noninvasive ventilation; OSA = obstructive sleep apnea.

Results

Study Subjects

We identified 37,516 hospitalizations for AECOPD across 252 hospitals in California in 2011 (Figure 1). The average age of patients admitted with AECOPD was 69.7 years (SD, 11.9). The majority of patients were female (54.3%), white (65.4%), and had Medicare as their primary payer (68.3%). Overall, 9.3% of hospitalizations for AECOPD received NIV and 6.9% received IMV. Hospital mortality for hospitalizations for AECOPD was 1.8%, that for AECOPD with NIV was 4.9%, and that for AECOPD and IMV was 15.8%. Median total hospital NIV case volume for all indications was 64 cases (IQR, 96).

Hospitals that used more NIV for all diagnoses tended to use more NIV for COPD ($r = 0.84$; $P < 0.0001$) (Figure E1). High-NIV-use hospitals compared with low-NIV-use hospitals tended to admit more women, black patients, patients with Medicaid, and patients with indices suggestive of greater severity of illness (Table 1) (44).

Variation in NIV Use

Hospital risk-adjusted NIV rates for AECOPD (median, 10.0%; interquartile range, 10.0; range, 1.6–35.7) varied widely, with 40% of hospitals significantly deviating from the average hospital NIV use rate for AECOPD (Figure E2). Unmeasured hospital factors accounted for 17.4% (95% confidence interval [CI], 14.5–21.2) of the between-hospital variation in risk-adjusted NIV rates.

Variation in NIV Failure

Among patients receiving NIV for AECOPD, NIV failed in 10.4% and progressed to IMV. Patient demographics were not associated with NIV failure, but chronic comorbidities and acute organ failures present on admission were associated with increased odds of NIV failure (Table E3). Hospital risk-adjusted NIV failure rates varied widely between different institutions (median, 8.5%; interquartile range, 4.2; range, 3.7–31.3) (Figure E3). Unmeasured hospital factors accounted for 15.4% (95% CI, 9.8–26.7) of the between-hospital variation in NIV failure. Total hospital NIV case volume explained 14.3% of the between-hospital variation in NIV failure rates in our model.

Hospital-Level Associations

Similar to individual patient–level analysis, total hospital NIV case volume was associated with higher hospital risk-adjusted NIV failure rates for AECOPD ($r = 0.13$; $P = 0.03$) (Figure 2), but not with hospital risk-adjusted IMV rates ($r = -0.05$; $P = 0.43$) or hospital risk-adjusted mortality rates ($r = -0.11$; $P = 0.08$). Additionally, higher hospital risk-adjusted NIV failure rates were associated with higher hospital risk-adjusted mortality rates for AECOPD ($r = 0.15$; $P = 0.02$) (Figure 3, Table 2).

Patient-Level Associations

For an individual patient with AECOPD, admission to a high-NIV versus low-NIV case-volume hospital was associated with higher odds of NIV failure (quartile 4 vs. quartile 1 aOR, 1.95; 95% CI, 1.12–3.40) (Table 3), and NIV failure was associated with higher odds of death compared with initial treatment with IMV (aOR, 1.81; 95% CI, 1.35–2.44). However, admission to a high-NIV versus low-NIV case-volume

Table 1. Characteristics of patients with acute exacerbations of chronic obstructive pulmonary disease, by hospital total noninvasive ventilation quartile

	Hospital NIV Quartile 1 (*n* = 9,069)	Hospital NIV Quartile 2 (*n* = 9,389)	Hospital NIV Quartile 3 (*n* = 9,075)	Hospital NIV Quartile 4 (*n* = 9,983)	*P* Value*
Number of hospitals	88	67	52	45	NA
Total hospital NIV case volume, median (range)	25 (2–43)	62 (44–89)	114 (90–159)	235 (163–565)	NA
NIV for AECOPD, %	4.0	7.1	9.9	15.7	<0.0001
Age, yr, mean (SD)	70.1 (12.0)	69.8 (11.7)	69.6 (11.9)	69.4 (12.0)	<0.0001
Female sex, %	52.4	55.1	54.7	55.1	0.001
Race/ethnicity, %					0.0001
White	66.7	65.1	66.4	63.7	
Black	7.6	14.1	11.7	16.2	
Hispanic	11.9	11.4	12.4	10.1	
Other†	13.8	9.4	9.6	10.0	
Primary payer, %					<0.0001
Medicare	70.9	68.0	68.1	66.3	
Medicaid	16.2	16.3	18.0	19.5	
Private insurance	8.1	10.4	8.2	8.2	
Other†	4.8	5.2	5.7	6.0	
Median income of patient ZIP code, %					0.001
Level 1	34.3	33.3	34.2	36.8	
Level 2	27.8	24.5	26.9	26.7	
Level 3	23.1	23.3	24.7	19.5	
Level 4	12.2	16.8	11.5	14.8	
Other†	2.7	2.1	2.7	2.2	
Elixhauser comorbidity score, mean (SD)‡	4.8 (6.5)	4.7 (6.7)	4.8 (6.9)	5.0 (6.8)	0.01
Shock POA, %	2.2	2.2	2.1	2.5	0.20
Acute respiratory failure POA, %	12.5	11.8	12.9	14.8	<0.0001
Acute renal failure POA, %	6.6	6.0	7.2	7.2	0.009
Acute neurologic failure POA, %	2.4	2.0	2.6	2.4	0.56
Acute hematologic failure POA, %	2.9	3.1	3.4	3.5	0.01
Acute hepatic failure POA, %	0.4	0.2	0.3	0.2	0.02
Acute metabolic failure POA, %	4.2	4.0	4.4	5.2	0.0003

Definition of abbreviations: AECOPD = acute exacerbation of chronic obstructive pulmonary disease; NA = not applicable; NIV = noninvasive ventilation; POA = present on admission.

*Mantel-Haenszel chi-square and Cochran-Armitage tests for trends were used for categorical variables, and linear regression to test for trends across quartiles was used for continuous variables.

†Includes patients with missing data.

‡Calculated without cardiac arrhythmia comorbidity per Healthcare Cost and Utilization Project software (44).

hospital was not significantly associated with the odds of receiving IMV during AECOPD (quartile 4 vs. quartile 1 aOR, 0.87; 95% CI, 0.64–1.18) or the odds of hospital death (quartile 4 vs. quartile 1 aOR, 0.76; 95% CI, 0.57–1.02).

Sensitivity Analysis

Multiple sensitivity analyses yielded results similar to those of our primary analyses. Please refer to Tables E4–E7 in the online supplement for results of individual sensitivity analyses.

Discussion

We examined the association between hospital NIV case volume and NIV failure among patients with AECOPD. We hypothesized that patients with AECOPD would be the most likely to demonstrate improved outcomes with greater hospital NIV case volume ("practice makes perfect"). However, we observed that higher NIV case volume was associated with higher rates of NIV failure and no significant improvement in mortality, contrary to our hypothesis and the results of prior studies of case-volume relationships in critical care that have demonstrated improved outcomes with higher case volume (15, 16, 19). Our findings suggest that improving processes of care and/or patient selection in implementing NIV may reduce NIV failure rates and improve real-world effectiveness of NIV for reducing mortality from AECOPD.

Our findings both replicate and extend results of prior studies of the use of NIV during COPD. Similarly to previous studies demonstrating changing ventilatory practices for AECOPD in the United States (10, 11), we observed that use of NIV for AECOPD is now greater than IMV. Our findings of increased mortality for patients in whom NIV fails compared with those initially treated with initial IMV were also similar to prior studies (11, 28, 33–35, 45). In addition, associations of greater burden of comorbidities and acute organ failures with higher risk of NIV failure are consistent with prior work (46–50). Taken together, evidence to date shows that NIV has been robustly implemented in clinical practice for AECOPD following clinical efficacy trials (6–8). However, high rates of NIV failure identified at some hospitals suggest that further work is needed to maximize the real world effectiveness of

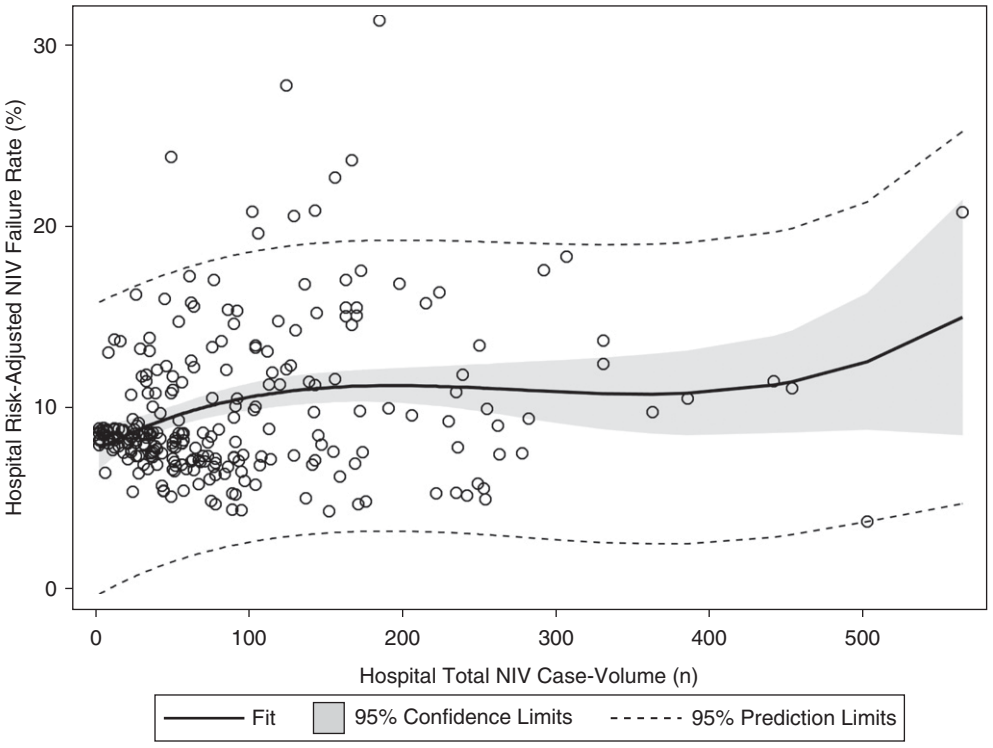

Figure 2. Association of hospital total NIV case volume and hospital risk-adjusted NIV failure rate for acute exacerbations of chronic obstructive pulmonary disease. Cubic spline regression is depicted for visualization purposes. Spearman's correlation $r = 0.13$; $P = 0.03$. NIV = noninvasive ventilation.

NIV even for an indication (AECOPD) with strong evidence (6–8).

While Kahn and colleagues (16, 17) and Cooke and coworkers (18) previously described mixed findings for case-volume–outcome relationships for IMV, we are unaware of descriptions of case-volume–outcome relationships for NIV. Our findings differ from improved outcomes seen with higher case volume observed in studies of other illnesses and procedures (15, 16, 19–21, 51). Our study may also be compared with one by Lindenauer and colleagues (52), who identified inverse associations between NIV use and IMV rates during COPD.

Methodological differences likely account for seemingly disparate results between studies. For example, our study included all AECOPD hospitalizations, whereas Lindenauer and colleagues included a cohort of patients who received NIV and/or IMV. A cohort including patients who received either NIV or IMV is more likely to result in the negative correlation between rates of NIV and IMV within a hospital than the cohort including all patients with AECOPD included in our analysis. In addition, we excluded patients with admission DNR orders. Patients with DNR orders are more likely to receive NIV than IMV (53), are ineligible for "NIV failure," and are more likely to die (54), a combination of factors that may influence associations between NIV rate and NIV failure, as well as associations between NIV rates and death. Clustering of patients with DNR orders within hospitals may also affect evaluation of hospital-level practices and NIV-associated events (55).

Why might higher NIV case volume be associated with greater risk for NIV failure? We found that hospitals with higher total NIV case volume tended to use NIV in patients with more comorbidities and acute organ failures, suggesting potential overuse among patients at higher risk of NIV failure. Selecting patients with high risk of NIV failure appears to increase mortality risks associated with NIV, without proportional gain in benefits, and may partially explain why hospitals with high rates of using an evidence-based intervention (NIV) (4, 6–9) did not achieve significant mortality benefits.

In addition to patient selection, we identified that a large degree of between-hospital variation in NIV failure rates was attributable to unmeasured hospital factors. We speculate that unmeasured hospital factors may also play a role in NIV failure rates, such as site of NIV use (ward, intermediate care, ICU); nurse (12), respiratory therapist (13), and physician (14) staffing ratios; and intensity of surveillance of patients (e.g., frequency of blood gas monitoring) or use of multidisciplinary NIV teams (56).

Prior studies of critical strain have shown that when critical care bed availability and monitoring capabilities were strained, patients awaiting ICU care experienced worse outcomes (22, 23). Thus, hospitals with high NIV case volume may have increased strain on resources and/or use NIV in higher-risk patients, an interaction that may result in higher NIV failure rates. Further studies are needed to investigate associations between patient selection, hospital structural factors, resource strain, and NIV case volume to inform potential mechanisms for the association between high NIV case volume and increased rates of NIV failure.

Clinical trials demonstrate reduced risk of death for patients with AECOPD and respiratory distress treated with NIV as compared with conventional treatment

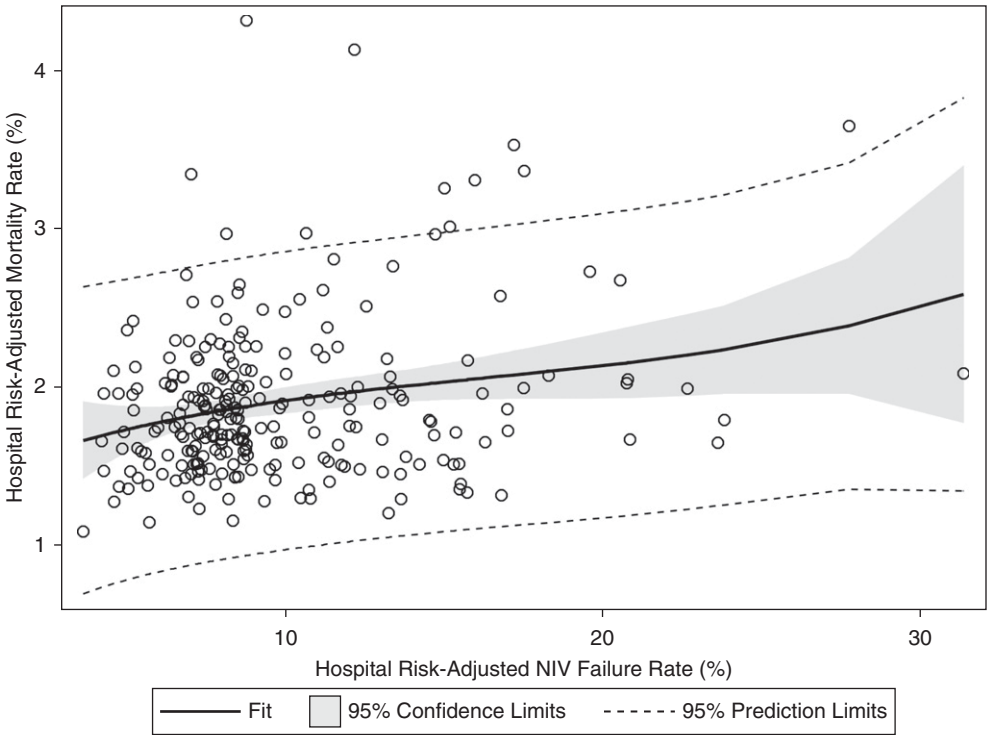

Figure 3. Association of hospital risk-adjusted NIV failure rates and hospital risk-adjusted mortality rates for acute exacerbation of chronic obstructive pulmonary disease. Cubic spline regression is depicted for visualization purposes. Spearman's correlation $r = 0.15$, $P = 0.02$. NIV = noninvasive ventilation.

(4, 6–9). Contrary to our hypothesis, we did not observe significantly lower COPD mortality among hospitals with high NIV case volume likely related to the associations between NIV case volume, NIV failure, and mortality. We speculate that potential mortality benefits achieved by greater use of NIV among patients with AECOPD may be counteracted by harms from increased NIV failure rates, reducing the net effectiveness of NIV for AECOPD for patients admitted to high-NIV case-volume hospitals.

Limitations

Our study has several limitations. We included only hospitals in California and did not have detailed hospital characteristics, which may limit the generalizability of our results. However, the California State Inpatient Database provided us with the unique ability to identify patients with early DNR orders in a large and diverse cohort.

We studied administrative data that relies on ICD-9-CM diagnosis and procedure codes with associated procedure days to identify diseases and procedures, which could be subject to misclassification. Specifically, the use of a principal diagnosis of acute respiratory failure with a secondary diagnosis of AECOPD present on admission raises the possibility that patients with additional causes of respiratory failure were included in our cohort.

We used validated algorithms to identify COPD and forms of mechanical ventilation used in multiple previous studies with high specificity and positive predictive value (11, 27, 28, 34), though other data sources that allow abstraction of respiratory therapist charges may provide increased sensitivity for identifying NIV (28). A more granular database with laboratory, vital sign, or other physiologic data may have attenuated risk for unmeasured confounding and better allowed distinction between patient selection and hospital structural factors as potential mechanisms of increased NIV failure rates in hospitals with higher case volume (51).

We were also unable to account for correlated data for patients with multiple hospitalizations in our analysis. Furthermore, we defined all patients who had an IMV start date on or after an NIV

Table 2. Hospital-level associations of noninvasive ventilation case volume and outcomes for acute exacerbations of chronic obstructive pulmonary disease

	Spearman's Correlation (*r*)	*P* Value
Hospital total NIV case volume and hospital risk-adjusted NIV failure rates	0.13	0.03
Hospital total NIV case volume and hospital risk-adjusted IMV rates	−0.05	0.43
Hospital total NIV case volume and hospital risk-adjusted mortality rates	−0.11	0.08
Hospital risk-adjusted NIV failure rates and hospital risk-adjusted mortality rates	0.15	0.02

Definition of abbreviations: IMV = invasive mechanical ventilation; NIV = noninvasive ventilation.

Table 3. Patient-level outcomes for acute exacerbations of chronic obstructive pulmonary disease

	Hospital NIV Quartile 1	Hospital NIV Quartile 2	Hospital NIV Quartile 3	Hospital NIV Quartile 4	aOR for Q4 vs. Q1 (95% CI)
NIV failure, %	7.2	7.2	11.4	12.0	1.95 (1.12–3.40)
IMV rate, %	6.6	6.7	7.3	6.8	0.87 (0.64–1.18)
Hospital mortality rate, %	1.9	1.7	2.0	1.6	0.76 (0.57–1.02)
Hospital mortality rate for patients treated with NIV, %	5.8	5.3	5.1	4.5	0.79 (0.43–1.47)
Hospital mortality rate for NIV failure, %	23.1	31.3	29.4	22.3	0.67 (0.21–2.11)

Definition of abbreviations: aOR = adjusted odds ratio; CI = confidence interval; IMV = invasive mechanical ventilation; NIV = noninvasive ventilation; Q1 = quartile 1; Q4 = quartile 4.

start as NIV failure (11, 34, 35, 52); it is possible that some of these patients transitioned from NIV to IMV for other reasons (e.g., invasive procedures) that do not represent NIV failure. Although the strength of correlations between case volume and hospital-level associations was weak, we found a similar direction of effects for hospital-level and patient-level analyses. In addition, hierarchical regression models used estimation techniques (57) that likely resulted in conservative estimates of hospital-level correlations.

Conclusions

Despite the benefits of NIV for AECOPD clearly demonstrated in efficacy trials and strong evidence of positive case volume–outcome associations shown in other conditions, hospitals using more NIV did not show better outcomes for patients with AECOPD. Our observation of possibly increased risk of NIV failure in high-volume hospitals may suggest suboptimal patient selection, hospital processes, or care structures at hospitals using the most NIV. Further research is needed to identify factors that achieve appropriate use of NIV, balance under- and overuse, and maximize benefits of NIV during AECOPD. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

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