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CLINICAL INVESTIGATION

Association Between Noninvasive Positive Pressure Ventilation Use and Clinical Outcomes During a Severe Asthma Exacerbation: A Cohort Study

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OBJECTIVES: The evidence supporting the use of noninvasive positive pressure ventilation (NPPV) during severe asthma exacerbations is limited. We determined the annual trend in NPPV use, endotracheal intubations, and in-hospital mortality among all hospitalizations for an asthma exacerbation. We additionally evaluated the association between NPPV use and subsequent endotracheal intubation and in-hospital mortality.

DESIGN: Retrospective, propensity-score–matched cohort study.

SETTING: Administrative data from Healthcare Cost and Utilization Project's State Inpatient Databases for New York and Florida, 2006–2019.

PATIENTS: Patients 5–80 years old hospitalized with an asthma exacerbation.

INTERVENTIONS: Receipt of NPPV.

MEASUREMENTS AND MAIN RESULTS: Among 296,788 hospitalizations for an asthma exacerbation between 2006 and 2018, NPPV use for an asthma exacerbation increased from 1.2% to 7.4% (absolute difference, 6.1%; 95% CI, 5.6–6.7%) in adults and from 0.7% to 7.1% (absolute difference, 6.4%; 95% CI, 5.5–7.3%) in pediatric patients. Among 41,902 ICU encounters, we propensity-score matched 1,972 adult and 1,622 pediatric patients who received NPPV with 6,510 adults and 4,766 pediatric patients who did not receive NPPV. NPPV use was associated with a decreased risk of subsequent intubation (risk ratio [RR], 0.48; 95% CI, 0.40–0.57) and improved in-hospital mortality (RR, 0.33; 95% CI, 0.21–0.54) in adults. In pediatric patients, use of NPPV was associated with a decreased risk of intubation (RR, 0.50; 95% CI, 0.29–0.89), but not significant for an improvement in in-hospital mortality (RR, 0.41; 95% CI, 0.15–1.11).

CONCLUSIONS: NPPV use for asthma exacerbations has increased. In adult and pediatric patients, NPPV use for an asthma exacerbation was associated with a decreased risk of endotracheal intubation. Furthermore, NPPV use for an asthma exacerbation was associated with improved in-hospital mortality in adult patients.

KEYWORDS: asthma; asthma exacerbation; critical care; intensive care; noninvasive ventilation

Asthma is a common disease that affects approximately 5% of people worldwide (1–3). In the United States alone, approximately 25 million individuals are affected by asthma, wherein loss of control results in 1.5 million emergency department visits, 180,000 hospitalizations, and 3,500 deaths annually (4). Of those hospitalized for an asthma exacerbation, approximately

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KEY POINTS

Question: Does noninvasive positive pressure ventilation (NPPV) decrease the risk of subsequent endotracheal intubation and in-hospital mortality among adult and pediatric patients admitted to the ICU for an asthma exacerbation?

Findings: In this retrospective, propensity-score–matched cohort analysis, NPPV use for an asthma exacerbation was associated with a decreased likelihood of subsequent endotracheal intubation in adult and pediatric patients. Furthermore, NPPV use was associated with improved in-hospital mortality in adult patients.

Meaning: In this study, NPPV use decreases the risk of subsequent intubation. Furthermore, in this study, NPPV use improves in-hospital mortality in adults experiencing an asthma exacerbation.

10% are admitted to an ICU and approximately 2% are endotracheally intubated for invasive mechanical ventilation (IMV) (5). Notably, for patients with asthma who receive IMV, in-hospital mortality is approximately 100 times higher than for those who do not (5).

Noninvasive positive pressure ventilation (NPPV) improves clinical outcomes when used for used for certain (6–13), but not all (7, 14–17), etiologies of acute respiratory failure (ARF). For example, prior studies demonstrate that NPPV improves hospital length of stay (LOS) (18–21), and in-hospital mortality (6, 7, 9, 11, 18, 20–24) during ARF due to acute exacerbations of chronic obstructive pulmonary disease (COPD) and cardiogenic pulmonary edema, and, consequently, clinical practice guidelines from the European Respiratory Society (ERS) and American Thoracic Society (ATS) strongly recommend utilization of NPPV for ARF due to these etiologies (11).

In contrast, data regarding the use of NPPV in the treatment of severe asthma exacerbations in the ICU are limited (25, 26). One prior meta-analysis evaluating the use of NPPV for the treatment of asthma exacerbations in adults concluded that NPPV "may be beneficial" but "regular use of NPPV in status asthmaticus remains controversial" (25). In adults, some studies have demonstrated that NPPV use is associated with a decreased hospital LOS (27), decreased utilization of IMV (28), and improved in-hospital mortality (27, 28). However, other studies did not show an association between NPPV use and subsequent intubation rates or in-hospital mortality (29–31). Among pediatric patients, one prior meta-analysis evaluating NPPV use during asthma exacerbations found that NPPV use was associated with improved physiologic parameters and decreased hospital LOS, but did not evaluate the effect of NPPV use on subsequent receipt of IMV or in-hospital mortality (32). Given the limited, and conflicting, evidence supporting NPPV use in asthma exacerbations, the 2017 ERS/ATS clinical practice guidelines regarding NPPV utilization concluded that they were unable to give a recommendation regarding the utility of NPPV for the treatment of ARF from severe asthma exacerbations (11).

Despite these data, the use of NPPV among patients admitted to the hospital for asthma exacerbations has increased over the past 2 decades (27–29, 33, 34). Absent high-quality, randomized controlled trials supporting NPPV use for asthma exacerbations, large observational analyses evaluating the association between NPPV use and clinical outcomes are needed. In this study, we use administrative claims data to describe the trends in NPPV use, endotracheal intubation, and in-hospital mortality among adult and pediatric patients hospitalized for an asthma exacerbation. Then, using propensity-score matching analyses, we describe the association between NPPV use and subsequent receipt of endotracheal intubation and in-hospital mortality among patients admitted to the ICU for an asthma exacerbation.

MATERIALS AND METHODS

Study Design and Data Sources

We performed an observational analysis of all patients hospitalized for an asthma exacerbation within the New York and Florida State Inpatient Databases (SID) using Healthcare Cost and Utilization Project (HCUP) data between 2006 and 2019 (35). This study has two parts. First, we described the annual rates and characteristics of "all" hospitalizations for asthma exacerbations in this cohort including NPPV use, endotracheal intubation, and in-hospital mortality. Second, among patients treated in the ICU, we evaluated the association of NPPV use with receipt of subsequent endotracheal intubation and in-hospital mortality using propensity-score matching. We constructed separate

models for the adult (18–80 yr) and pediatric populations (5–17 yr). We queried data between 2005 and 2018 and 2005–2019 for New York and Florida, respectively, given the completeness of data at the time of our analyses, and so as not to overlap with atypical trends during the subsequent COVID-19 pandemic. The SID include patient-level data for all inpatient discharges from nonfederal community (including teaching and nonteaching) hospitals. SID allows ascertainment of in-hospital outcomes irrespective of payor and linkage across multiple encounters. Notably, data on the occurrence of procedures within the emergency department is not available within the SID. We linked the SID with the American Hospital Association Annual Survey Database (36), which provided information on hospital characteristics. Our local institutional review board determined this study to be nonhuman subjects' research. Before data collection, our team received HCUP training and completed an HCUP data user agreement. We followed the Strengthening the Reporting of Observational Studies in Epidemiology reporting guideline for cohort studies (**eTable 1**, https://links.lww.com/CCM/H871) (37).

Study Population

To evaluate the trends in use of NPPV, endotracheal intubation, and in-hospital mortality for asthma exacerbations, we identified every encounter for an asthma exacerbation in patients 5–80 years old who were admitted to the hospital from 2006 to 2019, including encounters for which patients were transferred from another facility during their hospitalization. We defined an asthma exacerbation based on either a primary diagnosis of an asthma exacerbation or a primary diagnosis of respiratory failure with a secondary diagnosis of an asthma exacerbation using the *International Classification of Diseases*, 9th revision (ICD-9) or *International Classification of Diseases*, 10th revision (ICD-10) codes (**eTable 2**, https://links.lww.com/CCM/H871). A priori, we excluded patients with concomitant diagnoses of COPD, neuromuscular disease, obstructive sleep apnea (OSA), or asthma COPD overlap during the index hospitalization or the year before admission to limit confounding by indication (**Fig. 1**). This definition of asthma exacerbation is consistent with prior high-quality studies utilizing administrative data (27, 28). Due to limitations of the SID, asthma exacerbation severity based on therapeutic interventions, physiologic parameters, or laboratory data was not assessed.

To evaluate the outcomes of NPPV use specifically during ICU admissions, we selected only cases with an ICU indicator billing code (eTable 2, https://links.lww.com/CCM/H871) (38). We evaluated only patients admitted to an ICU as NPPV use in a non-ICU setting for an asthma exacerbation may be less common and potentially could be more reflective of an alternative indication for NPPV (e.g., OSA). Furthermore, we excluded patients admitted to a noncommunity hospital (e.g., rehabilitation and long-term acute care hospitals) and/or those with missing data for age, gender, and/or hospital identifier. Additionally, we excluded patients who did not report residence in New York or Florida due to concerns regarding the accuracy of longitudinal follow-up. Finally, after identifying all admissions, we randomly selected a single ICU encounter per patient across the study period for analyses to reduce computational complexity and yield model convergence.

Exposure and Outcomes

The exposure variable was receipt of NPPV. The individual co-primary outcomes were receipt of endotracheal intubation and in-hospital mortality. We used ICD-9 and ICD-10 procedure codes to determine NPPV use and endotracheal intubation during the ICU stay (eTable 2, https://links.lww.com/CCM/H871). The ICD codes used to identify NPPV encompass all forms of NPPV, including continuous and bilevel positive airway pressure (CPAP and BPAP, respectively). However, we were unable to distinguish between specific modes of support (i.e., CPAP vs. BPAP). Additionally, we did not formally define the use of alternative supportive modalities (e.g., supplemental oxygen) within the NPPV or non-NPPV groups. We used procedure dates for both NPPV and endotracheal intubation to ensure that post-extubation NPPV use was not counted as a positive exposure. Further, we evaluated the timing of NPPV and/or endotracheal intubation following hospital admission to help inform the likelihood that receipt of NPPV and/or intubation was related to the asthma exacerbation; however, we did not exclude any cases based on this evaluation.

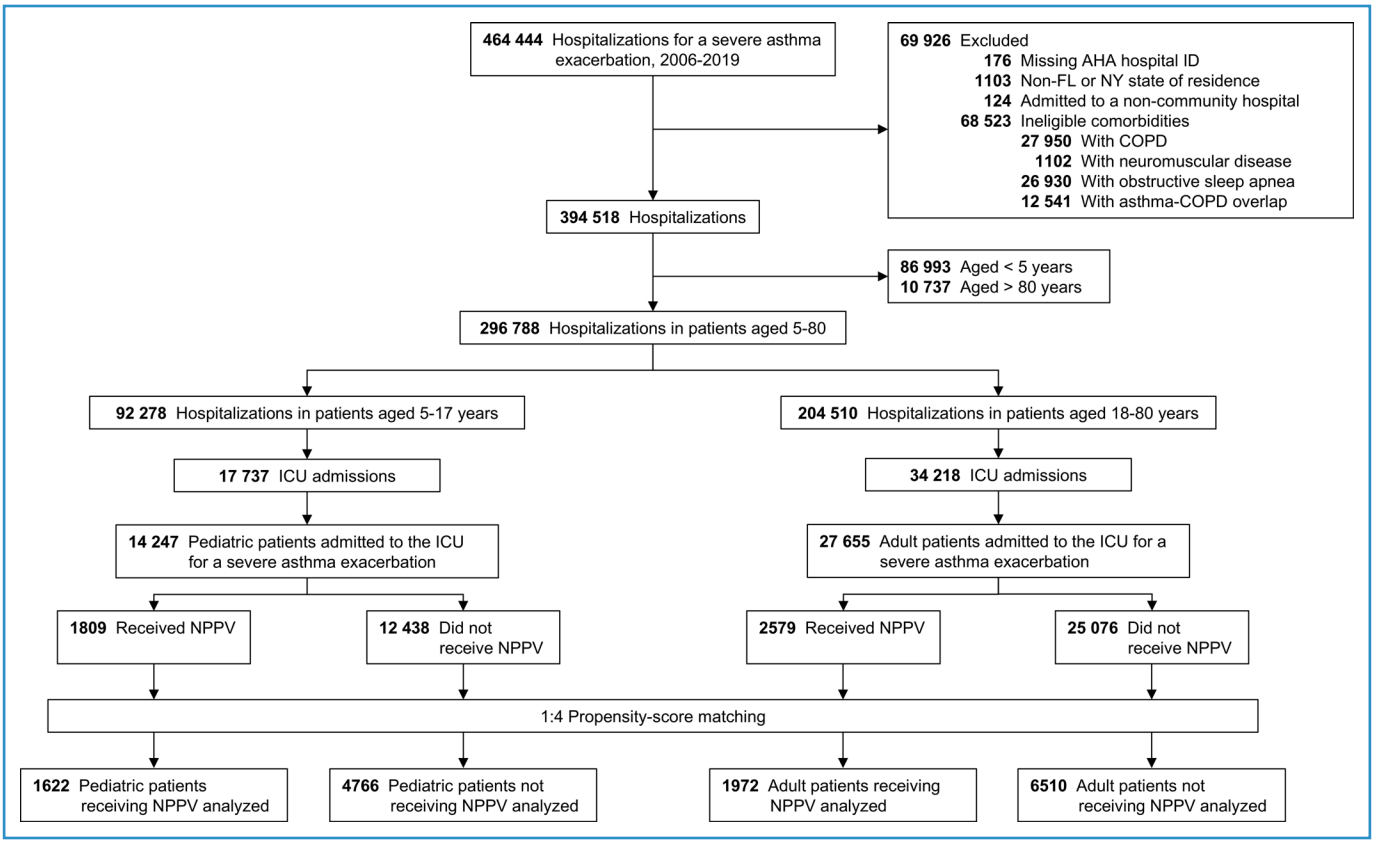

Figure 1. Flow diagram for the section of adult and pediatric propensity-score–matched cohorts by noninvasive positive pressure ventilation (NPPV) use. Patients 5–18 and 19–80 yr old admitted to the ICU for an asthma exacerbation were stratified into propensity-score–matched cohorts by NPPV use. Patients with missing data, non-Florida (FL) and non-New York (NY) state-of-residence, noncommunity hospitals, and diagnosed with ineligible comorbidities were excluded. AHA = American Hospital Association, COPD = chronic obstructive pulmonary disease, ID = identifier.

We determined in-hospital mortality using discharge status codes. Among patients who received ICU level care, we evaluated the association between NPPV use and in-hospital mortality, regardless of whether they were subsequently intubated.

Statistical Analysis

We determined the annual trend (and 95% CIs) in NPPV use, endotracheal intubations, and in-hospital mortality as a proportion of the total asthma hospitalizations (with the annualized number of asthma hospitalizations as the denominator). Next, we propensity-score–matched ICU cases receiving NPPV to those that did not receive NPPV to account for differences in the baseline characteristics between these groups (**Tables 1** and **2**; and **eTables 3–6**, https://links.lww.com/CCM/H871). We modeled propensity scores based on age at hospital admission, sex, race-ethnicity, primary insurance/payor, median income quartile for ZIP code of residence, admission year, discharge quarter, tobacco use, Elixhauser comorbidity indices (using data from the index hospitalization and 1 yr before the hospitalization using previously validated algorithms) (39), number of hospitalizations for asthma in the prior year, number of ICU admissions for asthma in the prior year, and number of endotracheal intubations for asthma in the prior year. Utilizing American Hospital Association data, we further matched cases based on hospital location, type of institution (teaching vs. nonteaching, trauma center), number of inpatient beds, and number of ICU beds.

We estimated propensity scores using nonparsimonious logistic regression modeling with NPPV as the dependent variable and every covariate as an independent variable. Matching used a 1:4 (1 NPPV: 4 no NPPV) protocol without replacement (greedy matching) and a caliper width equal to 0.25 SDs of the logit of the propensity score. We estimated absolute standardized mean differences to assess matching success,

TABLE 1.
Patient Characteristics of Adult Patients by Noninvasive Positive Pressure Ventilation Use, Before and After Propensity-Score Matching

Characteristics	Unmatched Patients			Propensity-Score–Matched Patients		
	NPPV (*n* = 2,579), *n* (%)	No NPPV (*n* = 25,076), *n* (%)	Standardized Mean Difference	NPPV (*n* = 1,972), *n* (%)	No NPPV (*n* = 6,510), *n* (%)	Standardized Mean Difference
Age, yr						
18–40	1,307 (50.7)	9,947 (39.7)	0.22	1,024 (51.9)	3,260 (50.1)	0.04
41–65	1,039 (40.4)	11,746 (46.8)	0.13	771 (39.1)	2,613 (40.1)	0.02
≥ 66	233 (9.0)	3,383 (13.5)	0.14	177 (9.0)	637 (9.8)	0.03
Sex, female	1,702 (66.0)	17,850 (71.2)	0.11	1,294 (65.6)	4,289 (65.9)	0.01
Race/ethnicity[a]						0.08
White	735 (28.6)	9,766 (39.1)	0.22	575 (29.1)	2,083 (32.0)	0.06
Black	953 (37.1)	7,914 (31.7)	0.11	724 (36.7)	2,327 (35.8)	0.02
Hispanic	568 (22.1)	5,707 (22.9)	0.02	429 (21.8)	1,437 (22.1)	0.01
Other or unknown	314 (12.2)	1,591 (6.4)	0.20	244 (12.4)	663 (10.2)	0.07
Primary payer						0.09
Medicare	404 (15.7)	5,440 (21.7)	0.16	302 (15.3)	1,062 (16.3)	0.03
Medicaid	962 (37.3)	6,253 (24.9)	0.27	695 (35.2)	2,056 (31.6)	0.08
Private	736 (28.5)	7,721 (30.8)	0.05	601 (30.5)	1,996 (30.7)	0.00
Other/self-pay	477 (18.5)	5,661 (22.6)	0.10	374 (19.0)	1,396 (21.4)	0.06
Median income for ZIP code, quartile						
First (lowest)	975 (41.2)	9,817 (40.6)	0.03	793 (40.2)	2,597 (39.9)	0.01
Second	567 (24.0)	6,882 (28.4)	0.13	451 (22.9)	1,568 (24.1)	0.03
Third	436 (18.4)	4,739 (19.6)	0.05	383 (19.4)	1,290 (19.8)	0.01
Fourth (highest)	388 (16.4)	2,764 (11.4)	0.12	345 (17.5)	1,055 (16.2)	0.03
Asthma-related outcomes occurring within 1 yr before the index ICU admission						
Hospitalization(s)						
0	2,057 (79.8)	21,689 (86.5)	0.18	1,573 (79.8)	5,370 (82.5)	0.07
1	328 (12.7)	2,418 (9.6)	0.10	252 (12.9)	771 (11.8)	0.03
2	99 (3.8)	617 (2.5)	0.08	77 (3.9)	207 (3.2)	0.04
3+	95 (3.7)	352 (1.4)	0.15	70 (3.6)	162 (2.5)	0.06
ICU admission(s)						
0	2,427 (94.1)	23,989 (95.7)	0.07	> 1,857 (> 94.2)[b]	6,184 (95.0)	0.03
1	120 (4.7)	900 (3.6)	0.05	89 (4.5)	265 (4.1)	0.02
2	21 (0.8)	137 (0.6)	0.03	14 (0.7)	42 (0.7)	0.01
3+	11 (0.4)	50 (0.2)	0.04	< 11 (< 0.6)[b]	19 (0.3)	0.01
Endotracheal intubation(s)						
0	2,516 (97.6)	24,839 (99.1)	0.12	> 1,923 (> 97.5)[b]	6,400 (98.3)	0.04
1	50 (2.0)	217 (0.9)	0.09	37 (1.9)	99 (1.5)	0.03
2	< 11 (< 0.4)[b]	< 11 (< 0.0)[b]	0.06	< 11 (< 0.6)[b]	< 11 (< 0.2)[b]	0.03
3+	< 11 (< 0.4)[b]	< 11 (< 0.0)[b]	0.05	< 11 (< 0.6)[b]	< 11 (< 0.2)[b]	0.02

NPPV = noninvasive positive pressure ventilation.

[a]"Other" race includes Asian, Pacific Islander, Native American, and other race designations.

[b]Cell values < 11 are not published in accordance with the Healthcare Cost and Utilization Project Data Use Agreement; accordingly, cells with ">" value are to account for columns where tabulated data may result in a value < 11.

Unmatched and propensity-score–matched patient characteristics are presented for adult patients admitted to the ICU for an asthma exacerbation.

TABLE 2.
Admission and Hospital Characteristics of Adult Patients by Noninvasive Positive Pressure Ventilation Use, Before and After Propensity-Score Matching

Characteristics	Unmatched Patients			Propensity-Score–Matched Patients		
	NPPV (*n* = 2,579), *n* (%)	No NPPV (*n* = 25,076), *n* (%)	Standardized Mean Difference	NPPV (*n* = 2,579), *n* (%)	No NPPV (*n* = 25,076), *n* (%)	Standardized Mean Difference
Admission characteristics						
Admission year						
2006	81 (3.1)	1,912 (7.6)	0.20	47 (2.4)	193 (3.0)	0.04
2007	67 (2.6)	1,821 (7.3)	0.22	40 (2.0)	164 (2.5)	0.03
2008	82 (3.2)	1,923 (7.7)	0.20	55 (2.8)	230 (3.5)	0.04
2009	127 (4.9)	2,085 (8.3)	0.14	85 (4.3)	324 (5.0)	0.03
2010	149 (5.8)	2,042 (8.1)	0.09	101 (5.1)	415 (6.4)	0.05
2011	160 (6.2)	1,956 (7.8)	0.06	106 (5.4)	424 (6.5)	0.05
2012	227 (8.8)	1,973 (7.9)	0.03	163 (8.3)	568 (8.7)	0.02
2013	246 (9.5)	1,941 (7.7)	0.06	180 (9.1)	582 (8.9)	0.01
2014	302 (11.7)	1,897 (7.6)	0.14	222 (11.3)	681 (10.5)	0.03
2015	285 (11.1)	1,743 (7.0)	0.14	232 (11.8)	675 (10.4)	0.05
2016	275 (10.7)	1,700 (6.8)	0.14	242 (12.3)	722 (11.1)	0.04
2017	307 (11.9)	1,704 (6.8)	0.18	271 (13.7)	745 (11.4)	0.07
2018	206 (8.0)	1,583 (6.3)	0.07	178 (9.0)	584 (9.0)	0.00
2019	65 (2.5)	796 (3.2)	0.04	50 (2.5)	203 (3.1)	0.04
Discharge quarter						
1–January–March	794 (30.8)	7,833 (31.2)	0.01	604 (30.6)	2,002 (30.8)	0.00
2–April–June	648 (25.1)	5,953 (23.7)	0.03	501 (25.4)	1,663 (25.6)	0.00
3–July–September	467 (18.1)	4,740 (18.9)	0.02	357 (18.1)	1,157 (17.8)	0.01
4–October–December	670 (26.0)	6,550 (26.1)	0.00	510 (25.9)	1,688 (25.9)	0.00
Hospital characteristics						
Hospital state						
Florida	933 (36.2)	18,517 (73.8)	0.82	712 (36.1)	2,890 (44.9)	0.17
New York	1,646 (63.9)	6,559 (26.2)	0.82	1,260 (63.9)	3,620 (55.6)	0.17
Hospital characteristics						
Hospital location, urban	2,519 (97.7)	24,469 (97.6)	0.01	1,924 (97.6)	6,332 (97.3)	0.02
Medical school affiliation	1,795 (69.6)	12,610 (50.3)	0.40	1,394 (70.7)	4,335 (66.6)	0.09
Certified trauma center	1,313 (60.3)	7,111 (36.7)	0.49	1,135 (57.6)	3,411 (52.4)	0.10
Number of hospital beds						
< 500 beds	1,429 (55.4)	16,696 (66.6)	0.23	1,002 (50.8)	3,624 (55.7)	0.10
500+ beds	1,150 (44.6)	8,380 (33.4)	0.23	970 (49.2)	2,886 (44.3)	0.10
Number of ICU beds						
< 50 ICU beds	1,727 (67.0)	17,354 (69.2)	0.05	1,142 (57.9)	3,835 (58.9)	0.02
50+ ICU beds	852 (33.0)	7,722 (30.8)	0.05	830 (42.1)	2,675 (41.1)	0.02

NPPV = noninvasive positive pressure ventilation.

Unmatched and propensity-score–matched admission and hospital characteristics are presented for adult patients admitted to the ICU for an asthma exacerbation.

with standardized differences less than 0.1 indicating acceptable balance.

In the matched cohort, we used a modified Poisson regression approach with robust SEs (40). This was implemented using generalized estimating equations and assuming an independent working correlation structure. Standard model checks (e.g., residual diagnostics) were conducted to ensure adequate model fit. After original propensity-score matching, only state of residence was unacceptably imbalanced (standardized mean difference: adult 0.17, pediatric 0.18); as such, we constructed one model including state of residence as a covariate and one excluding this variable. Last, we performed sensitivity analyses to evaluate our method of selecting a single random ICU encounter per patient for analysis (**Supplementary Methods** and **eTable 7**, https://links.lww.com/CCM/H871). We considered two-sided *p* values (not adjusted for multiple testing) to be significant at *p* value of less than or equal to 0.05. We performed all analyses using SAS v9.4 (SAS Institute, Cary, NC).

RESULTS

Study Population

Among 75,567,518 hospital admissions between 2005 and 2019, we identified 296,788 hospitalizations that met our definition for an asthma exacerbation (Fig. 1). From these encounters, we identified 27,655 unique adult and 14,247 unique pediatric patients admitted to the ICU for an asthma exacerbation after randomly selecting one ICU encounter per patient. Among these ICU admissions for asthma exacerbations, 2579 (9.3%) adult and 1809 (12.7%) pediatric patients received NPPV. Propensity-score matching yielded 8482 adult and 6388 pediatric matched patients, among whom 1972 (23.2%) adult and 1622 (25.4%) pediatric patients received NPPV (Fig. 1). Among those who received NPPV, 98.4% occurrences of NPPV and 98.0% of endotracheal intubations occurred within the first 3 days of hospitalization.

Baseline demographics, asthma history, comorbidity indices, and hospital characteristics are outlined for adult (Tables 1 and 2; and eTable 3, https://links.lww.com/CCM/H871) and pediatric patients (eTables 4–6, https://links.lww.com/CCM/H871). Adult patients who received NPPV were more likely to be younger (age 18–40 yr, 51% vs. 40%), male (34% vs. 29%), identify as Black/African American (37% vs. 32%), have Medicaid as their primary insurance (37% vs. 25%), and been admitted to the hospital for asthma greater than or equal to 3 times during the preceding year (3.7% vs. 1.4%). Furthermore, adults who received NPPV were more likely to be treated in a teaching facility (70% vs. 50%), a facility associated with a trauma center (60% vs. 37%), and within a hospital with greater than or equal to 500 beds (45% vs. 33%). Pediatric patients who received NPPV were more likely to be older (age 13–17 yr, 26% vs. 20%), female (45% vs. 40%), identify as other/unknown race (19% vs. 10%), and have Medicare/Medicaid as their primary payor/insurance (68% vs. 62%). Like adults, pediatric patients who received NPPV were more likely to be treated in a teaching hospital (94% vs. 86%), within a hospital with greater than or equal to 500 beds (83% vs. 71%), and within a hospital with greater than or equal to 50 ICU beds (70% vs. 61%).

Trend in NPPV Use, Endotracheal Intubations, and Mortality

Among all adult hospitalizations, NPPV use increased from 1.2% in 2006 to 7.4% in 2018 (difference, 6.1%; 95% CI, 5.6–6.7%; **Fig. 2*A***; and **eTable 8**, https://links.lww.com/CCM/H871). However, endotracheal intubation rates (3.7% vs. 4.0%; difference, 0.3%; 95% CI, –0.2% to 0.8%) and in-hospital mortality (0.3% vs. 0.4%; difference, 0.1%; 95% CI, –0.01% to 0.3%) remained stable. Following a similar trend as adults, among all pediatric hospitalizations, NPPV use increased from 0.7% in 2006 to 7.1% in 2018 (difference, 6.4%; 95% CI, 5.5–7.3%; **Fig. 2*B***; and eTable 8, https://links.lww.com/CCM/H871) but endotracheal intubation rates (1.0% vs. 0.8%; difference, –0.2%; 95% CI, –0.6% to 0.2%) and in-hospital mortality (0.1% vs. 0.1%; difference, –0.01%; 95% CI, –0.1% to 0.1%) remained stable.

NPPV Use and Endotracheal Intubation

In propensity-score–matched analyses of adult patients who did and did not receive NPPV, 2198 (25.9%) were subsequently endotracheally intubated. NPPV use was associated with a lower risk of subsequent endotracheal intubation as compared with those that did not receive NPPV (15.1% vs. 29.2%; risk ratio [RR], 0.48; 95% CI, 0.40–0.57; **Fig. 3**).

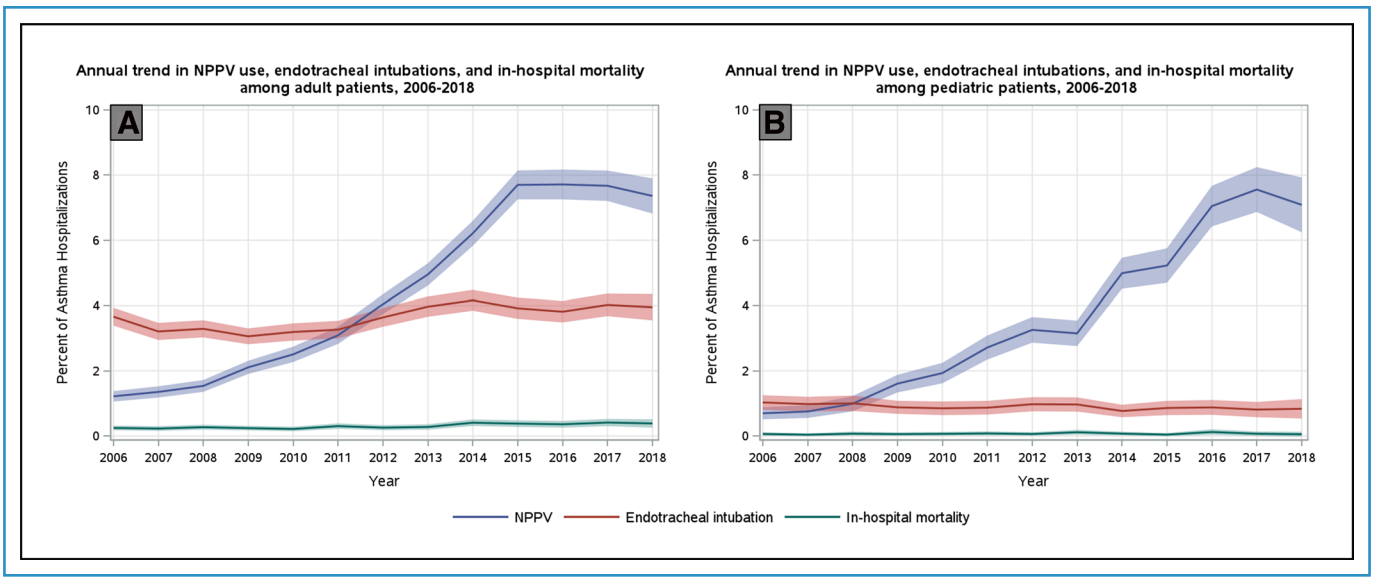

Figure 2. Annual trend in noninvasive positive pressure ventilation (NPPV) use, endotracheal intubations, and in-hospital mortality among adult and pediatric patients admitted for severe asthma exacerbations between 2006 and 2018. Among adult (**A**) and pediatric (**B**) patients hospitalized for an asthma exacerbation, NPPV use (*blue*) increased between 2006 and 2018, while endotracheal intubations (*red*) and in-hospital mortality (*green*) remained stable over the same period. *Shaded areas* represent the 95% CI.

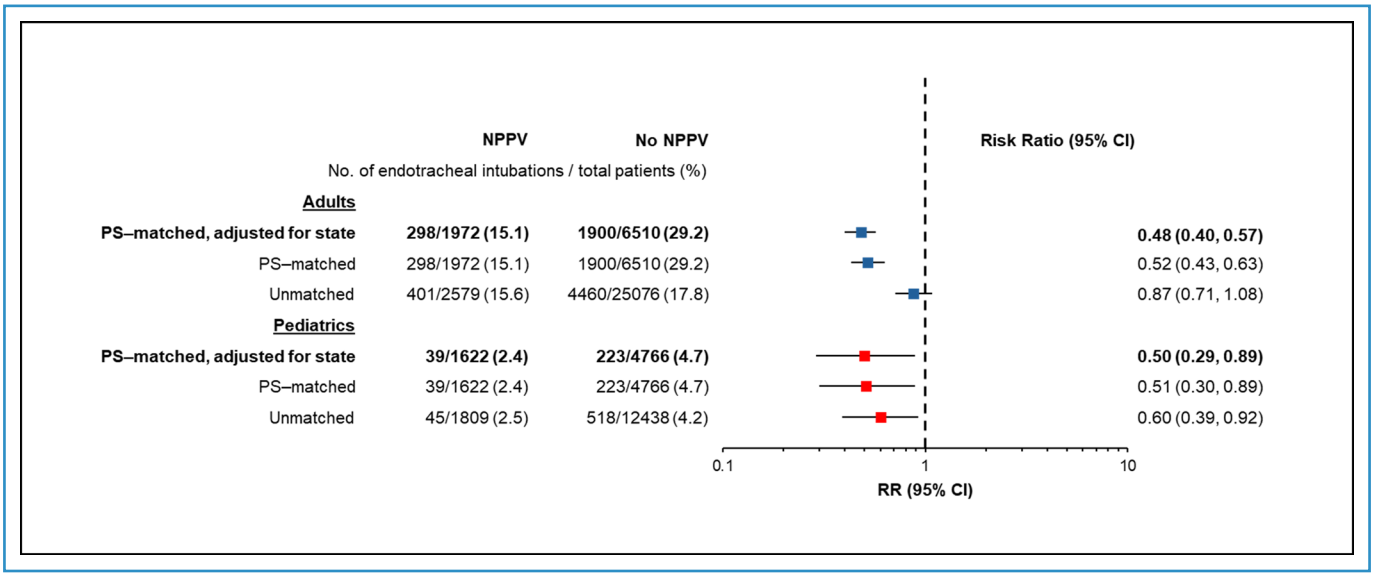

Figure 3. Associations between noninvasive positive pressure ventilation (NPPV) use and the risk of subsequent endotracheal intubation among adult and pediatric patients experiencing a severe asthma exacerbation. In propensity-score (PS)–matched analyses including adjustment for state of residence, NPPV use was associated with a lower risk of subsequent endotracheal intubation in adult (risk ratio [RR], 0.48; 95% CI, 0.40–0.57) and pediatric (RR, 0.50; 95% CI, 0.29–0.89) patients hospitalized for a severe asthma exacerbation.

In propensity-score–matched analyses of pediatric patients who did and did not receive NPPV, 262 (4.1%) were subsequent endotracheally intubated. Similar to adults, NPPV use was associated with a lower risk of subsequent endotracheal intubation as compared with those that did not receive NPPV (2.4% vs. 4.7%; RR, 0.50; 95% CI, 0.29–0.89; Fig. 3). Propensity-score–matched results were similar with and without adjustment for state (unbalanced covariate) in both adult and pediatric analyses. In unmatched analyses, NPPV use was associated with a lower risk of subsequent endotracheal intubation in pediatric patients (RR, 0.60; 95% CI, 0.39–0.92), but not in adult patients (RR, 0.87; 95% CI, 0.71–1.08).

NPPV Use and In-Hospital Mortality

In propensity-score–matched analyses of adult patients who did and did not receive NPPV, 223 died (2.6%) during the hospitalization. NPPV use was associated with a lower risk of in-hospital mortality as compared with those that did not receive NPPV (1.2% vs. 3.1%; RR, 0.34; 95% CI, 0.21–0.54; **Fig. 4**). In propensity-score–matched analyses of pediatric patients who did and did not receive NPPV, less than 0.5% died during the hospitalization. The risk of in-hospital mortality was not significantly different for those who received NPPV compared with those who did not (0.2% vs. 0.5%; RR, 0.41; 95% CI, 0.15–1.11; Fig. 4). Propensity-score–matched results were similar with and without adjustment for state (unbalanced covariate) in both adult and pediatric analyses. In unmatched analyses, NPPV use was associated with a similar risk of in-hospital mortality in both adult (1.1% vs. 1.6%; RR, 0.69; 95% CI, 0.46–1.04) and pediatric patients.

DISCUSSION

We found that the use of NPPV has significantly increased among adult and pediatric patients hospitalized for asthma exacerbations. Despite this increase, rates of endotracheal intubations and in-hospital mortality associated with asthma exacerbations have remained stable and low. In our propensity-score–matched analyses, NPPV use was associated with a decreased risk of endotracheal intubation and improved in-hospital mortality for adults admitted to the ICU for asthma. Similarly, among pediatric patients experiencing an asthma exacerbation, NPPV use was associated with a decreased risk of subsequent endotracheal intubation, but not a statistically significant difference in hospital mortality. While a large, randomized trial would better evaluate the risks and benefits of NPPV use during severe asthma exacerbations, such a trial may be unlikely given the increasing use of NPPV and potential concerns about clinical equipoise. Absent such a trial, our findings contribute to the growing body of observational data supporting the use of NPPV in both adult and pediatric patients admitted to the ICU experiencing an asthma exacerbation.

In a recent study evaluating NPPV use in adult asthma exacerbations using administrative data, receipt of NPPV was associated with less endotracheal intubations and improved in-hospital mortality (28). Our work validates these findings utilizing an all-payer administrative data from two different states; furthermore, our work extends these findings to the pediatric population, among whom we found that NPPV use

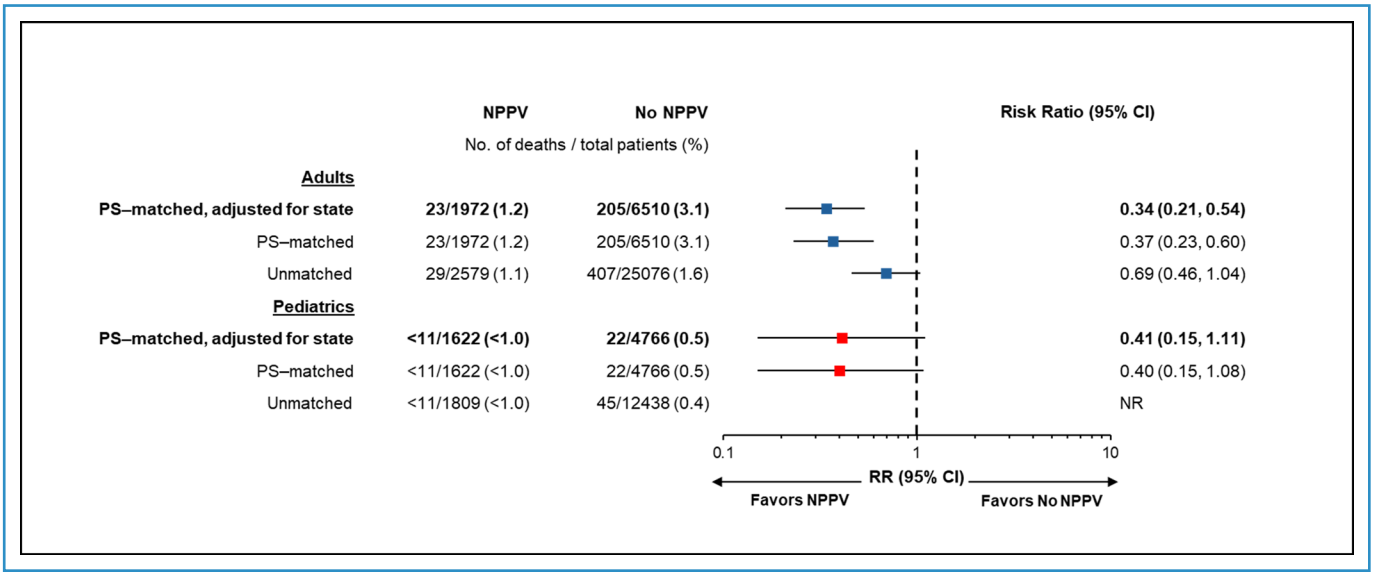

Figure 4. Associations between noninvasive positive pressure ventilation (NPPV) use and the risk of in-hospital mortality among adult and pediatric patients experiencing a severe asthma exacerbation. In propensity-score (PS)–matched analyses including adjustment for state of residence, NPPV use was associated with a lower risk of in-hospital mortality among adults (risk ratio [RR], 0.34; 95% CI, 0.21–0.54) but not pediatric (RR, 0.41; 95% CI, 0.15–1.11) patients hospitalized for a severe asthma exacerbation. [a]Cell values less than 11 are not published in accordance with the Healthcare Cost and Utilization Project Data Use Agreement. NR = not reported.

was associated with a decreased risk of endotracheal intubation. To our knowledge, this study is the first to evaluate the association between NPPV use and subsequent endotracheal intubation rates and in-hospital mortality in pediatric patients experiencing a severe asthma exacerbation.

Like other studies, we found that NPPV use during asthma exacerbations has significantly increased over time, which has occurred despite the current ERS/ATS clinical practice guideline that does not explicitly recommend NPPV use for severe asthma exacerbations (27–29, 33, 34). Despite increased NPPV use over the study period, we observed no significant change in the rates of endotracheal intubations or in-hospital mortality among critically ill patients with asthma exacerbations. While on the surface these observations may not appear compatible with NPPV improving patient outcomes, it is possible that some accrued benefits from NPPV have been negated by the previously described increase in acuity and comorbidity burden among patients experiencing asthma exacerbations (27, 28, 41–45). Furthermore, it is possible that some patients receive NPPV despite being at low risk for intubation or in-hospital mortality, either because of other hypothetical benefits (e.g., decreased ICU LOS), overuse of NPPV in unnecessary situations, or both. Taken together, these reasons may explain how NPPV use is increasing, intubation rates and mortality rates are stable, and, yet NPPV use is still associated with improvement in these outcomes during asthma exacerbations.

Despite recent evidence, some experts have cautioned against routine use of NPPV for severe asthma exacerbations until large, high-quality, randomized controlled trials demonstrate efficacy (46, 47). However, as evidenced by the trends found in this study, many clinicians are already (and increasingly) utilizing NPPV for asthma exacerbations. Importantly, our findings were restricted to patients admitted to an ICU, where familiarity with NPPV and clinical vigilance are likely higher than in less acute settings. Furthermore, NPPV is undoubtedly not appropriate in all cases. For instance, delaying IMV may pose a risk of peri-intubation complications for some patients due to decreased physiologic reserve, respiratory acidosis, and hemodynamic instability secondary to dynamic hyperinflation and insensible losses (48, 49).

This study has several limitations. First, all observations are limited by the retrospective cohort design and patients in this study were nonrandomly assigned to receipt of NPPV. Although propensity-score–matched analyses can mitigate this limitation to some degree, this strategy may not completely resolve confounding by indication. Further, propensity-score matching does not address the effect of unmeasured confounders on outcomes. Although alternative propensity-score methods (e.g., inverse probability of treatment weighting) could have been chosen, our strategy intuitively replicated a randomized controlled trial design and most cases receiving NPPV were successfully matched. Second, this study used administrative claims and ICD codes, which are primarily designed for reimbursement. However, ICD codes used in this study are consistent with prior studies evaluating clinical outcomes in patients with asthma in the ICU (27, 28, 50). Third, due to limitations of the SID databases, we were not able to reliably ascertain certain clinical details including physiologic or laboratory parameters, pertinent asthma therapeutic interventions, or treatment allocation in the emergency department. Further, we did not attempt to identify patients with contraindications to NPPV (e.g., facial trauma or cardiac arrest) or account for specific post-admission diagnoses (e.g., pneumonia or venous thromboembolism), which could limit the robustness of our findings. We did, however, attempt to collect relevant historical markers of asthma severity, including history of prior hospitalization, ICU admission, and endotracheal intubation in the preceding year due to asthma. Fourth, to ensure model convergence in our propensity-score–matched analysis, we included only one ICU encounter per patient, rather than all ICU encounters. While this approach may limit the generalizability of our findings, it is notable that 85% of patients included in our analysis had only a single ICU encounter. Strengths of our study include the use of a large cohort of patients, representing 97% of hospital admissions in Florida and New York over 14 years. Furthermore, this cohort encompasses a diverse population, including adult and pediatric patients, those with government-sponsored insurance or no insurance, and those hospitalized across various types of ICUs.

CONCLUSIONS

In this large retrospective study, NPPV use for an asthma exacerbation was associated with a decreased

risk of endotracheal intubation and improved in-hospital mortality in adults. Similarly, in pediatric patients, NPPV use was associated with a decreased risk of endotracheal intubation, but not a statistically significant difference in hospital mortality. These findings contribute to growing evidence supporting careful NPPV use during severe asthma exacerbations.

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Dr. Krings is the guarantor of the article, taking responsibility for the integrity of the work from inception to publication. Dr. Krings conceived of and designed the study in its entirety. Dr. Abbott, Dr. Razi, Dr. Goss, Ms. Buss, and Mr. Keller were responsible for the analysis and analytical plan. Dr. Abbott, Ms. Carpenter, and Dr. Krings together prepared the first draft of the article. All authors provided approval of the final article version.

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