

# Endotracheal Tube Size Is Associated With Mortality in Patients With Status Asthmaticus

Markos G Kashiouris, Christopher D Chou, Yub Raj Sedhai, Randy Bitrus, Matthew M Churpek, Casey Cable, Michael L'Heureux, Arjun Mohan, and Curtis N Sessler

**BACKGROUND:** There is limited evidence on the clinical importance of the endotracheal tube (ETT) size selection in patients with status asthmaticus who require invasive mechanical ventilation. We set out to explore the clinical outcomes of different ETT internal diameter sizes in subjects mechanically ventilated with status asthmaticus. **METHODS:** This was a retrospective study of intubated and non-intubated adults admitted for status asthmaticus between 2014–2021. We examined in-hospital mortality across subgroups with different ETT sizes, as well as non-intubated subjects, using logistic and generalized linear mixed-effects models. We adjusted for demographics, Charlson comorbidities, the first Sequential Organ Failure Assessment score, intubating personnel and setting, COVID-19, and the first  $P_{aCO_2}$ . Finally, we calculated the post-estimation predictions of mortality. **RESULTS:** We enrolled subjects from 964 status asthmaticus admissions. The average age was 46.9 (SD 14.5) y; 63.5% of the encounters were women and 80.6% were Black. Approximately 72% of subjects (690) were not intubated. Twenty-eight percent (275) required endotracheal intubation, of which 3.3% (32) had a 7.0 mm or smaller ETT (ETT  $\leq 7$  group), 16.5% (159) a 7.5 mm ETT (ETT  $\leq 7.5$  group), and 8.6% (83) an 8.0 mm or larger ETT (ETT  $\geq 8$  group). The adjusted mortality was 26.7% (95% CI 13.2–40.2) for the ETT  $\leq 7$  group versus 14.3% ([95% CI 6.9–21.7%],  $P = .04$ ) for ETT  $\leq 7.5$  group and 11.0% ([95% CI 4.4–17.5],  $P = .02$ ) for ETT  $\geq 8$  group, respectively. **CONCLUSIONS:** Intubated subjects with status asthmaticus had higher mortality than non-intubated subjects. Intubated subjects had incrementally higher observed mortality with smaller ETT sizes. Physiologic mechanisms can support this dose-response relationship *Key words:* status asthmaticus; endotracheal tube size; diameter; airway resistance; mortality; dynamic hyperinflation. [Respir Care 2022;67(3):283–290. © 2022 Daedalus Enterprises]

## Introduction

Globally, 21.6 million disability-adjusted life years are lost due to asthma and constitute 21% of years lost from all chronic respiratory diseases, which makes it 27th and 34th among the leading global causes of death and loss of

disability-adjusted life years, respectively.<sup>1</sup> In the United States of America alone, asthma has contributed to an increasing loss of disability-adjusted life years from as low as 861,178 years lost in 1997 up to 1,414,555 years lost in 2019.<sup>1</sup>

Severe asthma escalating to status asthmaticus can rapidly progress to respiratory failure, ICU admission, and endotracheal intubation. Existing literature suggests that 60%<sup>2</sup> of ICU patients require endotracheal intubation, and approximately

---

Drs Kashiouris, Cable, L'Heureux, Mohan, and Sessler are affiliated with Division of Pulmonary and Critical Care, Virginia Commonwealth University, Richmond, Virginia. Drs Chou and Bitrus are affiliated with Department of Internal Medicine, Virginia Commonwealth University, Richmond, Virginia. Dr Sedhai is affiliated with Department of Internal Medicine, Community Memorial Hospital, Virginia Commonwealth University, South Hill, Virginia. Dr Churpek is affiliated with Division of Allergy, Pulmonary and Critical Care, Department of Medicine, University of Wisconsin, Madison, Wisconsin.

---

The study was supported by a VCU Wright Center for Translational Science Award (UL1TR000058), Division of Pulmonary Disease and Critical Care Medicine, VCU School of Medicine.

Correspondence: Markos G Kashiouris MD MPH, Division of Pulmonary and Critical Care, Virginia Commonwealth University, PO Box 980509, Richmond, VA 23298. E-mail: mkashiouris@vcu.edu.

The authors have disclosed no conflicts of interest.

DOI: 10.4187/respcare.09609

10% eventually die.<sup>3</sup> Therefore, timely and optimal airway management in patients with status asthmaticus is critical.<sup>4</sup> Some experts suggest that clinicians should choose the largest

---

SEE THE RELATED EDITORIAL ON PAGE 373

---

endotracheal tube (ETT) possible.<sup>5</sup> The rationale for these recommendations is the optimization of suctioning, mucus plug removal, bronchoscopy, and airway resistance reduction.<sup>4,5</sup> However, it is unclear if clinicians strictly adhere to these recommendations given the lack of supporting evidence, positive or negative, since there is no published literature to explore the effect of differential ETT size in patient outcomes among subjects with status asthmaticus. In addition, other practical concerns may drive the selection of smaller ETTs, such as the concern for a lower intubation first-pass success rate<sup>6</sup> or higher risk of laryngeal and vocal cord injury.<sup>7,8</sup>

The present study explores the association of endotracheal intubation and the random variability in ETT internal diameter and all-cause hospital mortality among subjects admitted with status asthmaticus.

## Methods

### Study Design, Population, and Setting

We conducted a retrospective cohort study of subjects with status asthmaticus in an academic tertiary-care referral center in Richmond, Virginia, from 2014–2021. We included all subjects, intubated and non-intubated. The study was approved by the Virginia Commonwealth University Institutional Review Board, approval number HM20021447.

We enrolled adult participants of 18 y, or older, who presented to the hospital with status asthmaticus or asthma exacerbation. We identified the subject population with structured query language of subjects fulfilling the following criteria: (1) continuous albuterol nebulization, (2) International Classification of Diseases, Tenth Revision (ICD-10) charges of asthma, and (3) ETT size documentation. The standard of care in the study institution requires the ETT size to be documented daily by respiratory therapy. We followed up with the subjects until hospital discharge.

### Data Sources, Variables, and Measurements

We utilized the electronic health record and the administrative data. We obtained the following variables: subject demographics, that is, age (y), gender, race (Black vs other); height (cm); weight (kg); comorbidities; all underlying variables required for the calculation of the first Sequential Organ Failure Assessment (SOFA) score upon admission (points 0–24)<sup>9</sup>; the first arterial partial carbon-dioxide pressure upon admission ( $P_{aCO_2}$ , mm Hg). We calculated the

## QUICK LOOK

### Current knowledge

The time constant, that is, the time required to deflate 63% of the lung, has a linear relationship with the respiratory system's resistance and plays a critical role in dynamic hyperinflation. The endotracheal tube (ETT) resistor, whose key determinant is the ETT diameter, is in series with the respiratory system's resistance. Experts recommend the largest ETT size in patients with status asthmaticus.

### What this paper contributes to our knowledge

This study suggests that smaller ETT sizes were associated with higher mortality among invasively ventilated subjects with status asthmaticus.

first SOFA score from all its components upon hospital admission to adjust for the overall hospitalization severity of illness. Missing data were considered normal for the SOFA score calculations. We used  $S_{pO_2}/F_{IO_2}$  ratios to calculate missing  $P_{aO_2}/F_{IO_2}$  ratios. We calculated the Charlson comorbidity groups and index<sup>10</sup> from administrative ICD-10 code data only present on admission.<sup>11,12</sup> We also obtained the intubating personnel, setting and time, COVID-19 status, height, and body mass index (BMI). The study's primary outcome was in-hospital mortality by all causes, referred to simply as mortality in the manuscript.

### Bias

To mitigate the risk of selection bias, we did not exclude any subjects from the cohort. To address confounders, we adjusted for the severity of illness at hospital presentation (SOFA score) and the chronic comorbidity burden present on admission (Charlson). We further adjusted for the severity of hypercapnic respiratory failure upon presentation (first  $P_{aCO_2}$ ). Missing data were not imputed. To address chronic conditions that can interfere with liberation from mechanical ventilation, we adjusted for Charlson comorbidities. Finally, we followed the strengthening Standards of Reporting of Observational Studies in Epidemiology guidelines<sup>13</sup> for the scientific communication of the results.

### Study Groups and Quantitative Variables

We created groups based on ETT size: ETT  $\leq 7$  for 7.0 mm internal diameter, 7.5 mm (ETT  $\leq 7.5$ ), 8.0 mm or greater (ETT  $\geq 8$ ), and non-intubated subjects as separate group-cases. We selected status asthmaticus subjects who were not intubated to better understand the comparisons between each group and the non-intubated subjects. In

addition, we analyzed the quantitative variables age, SOFA score, Charlson index, height, BMI, and first  $P_{aCO_2}$  as continuous variables. The ETT internal diameter will be referred to as “diameter” or “size” in the manuscript.

### Statistical Methods

We selected all the subjects we could identify in our electronic health record. We used simple and generalized linear mixed-effects (GLME) models operating under the binomial distribution for in-hospital mortality as a binary outcome. We used the ETT status as categorical (factor) variables with 3 levels: zero ( $ETT \leq 7$ ), one ( $ETT \leq 7.5$ ), and 2 ( $ETT \geq 8$ ) and 4 (non-intubated). The coefficient of death for each ETT size is compared with the set base variable, zero, that is,  $ETT \leq 7$ . We employed each subject’s unique personal identifier to calculate the standard errors, which accounted for intergroup correlation. Finally, we calculated and graphed the adjusted model post-estimation mortality and marginal effects.<sup>14</sup>

We conducted 2 sensitivity analyses. The first was examining the ETT internal diameter (mm) as a continuous measure. The second examined the mortality effect modification of ETT size with the tertiles of the subject height to estimate the subjects’ overall size of the lungs and tracheas.

## Results

### Participants and Descriptive Data

We enrolled 964 status asthmaticus episodes of hospitalization (609 subjects). Of these, 28.4% (274 subjects) required endotracheal intubation. The average mortality for the entire cohort was 7.3%, which comprised 17.9% in the intubated and 2.5% in the non-intubated subgroups. The average hospital length of stay was 7.5 d, 10.6 d for the intubated group, and 6.3 d for the non-intubated group. Among the 274 intubated subjects, 3 (1%) had a 6.5 mm ETT, 29 (11.6%) had a 7.0 mm ETT, 159 (58%) had a 7.5 ETT, 78 (28.5%) had an 8.0 ETT, and 5 (1.8%) had an 8.5 ETT.

The entire cohort comprised 690 (71.6%) non-intubated subjects, 32 (3.3%) subjects in the  $ETT \leq 7$  group (ie,  $ETT \leq 7.0$  mm), 159 (16.5%) in the  $ETT \leq 7.5$  group (ie,  $ETT 7.5$  mm), and 83 (8.6%) in the  $ETT \geq 8$  group (ie,  $ETT \geq 8.0$  mm). Table 1 summarizes the cohort groups’ demographics, comorbidities, and severity.

### Outcome Data

The observed deaths were 10 (31.3%) for the  $ETT \leq 7$  group, 23 (14.5%) for the  $ETT \leq 7.5$  group, 16 (19.3%) for the  $ETT \geq 8$  group, and 17 (2.5%) for the non-intubated group.

The unadjusted death odds ratio for  $ETT \leq 7.5$  versus  $ETT \leq 7$  was 0.37 (95% CI 0.16–0.88,  $P = .02$ ) and for

$ETT \geq 8$  versus  $ETT \leq 7$  0.53 (95% CI 0.21–1.34,  $P = .18$ ). The unadjusted death odds ratio non-intubated versus  $ETT \leq 7$  was 0.06 (95% CI 0.02–0.14,  $P < .001$ ). The corresponding post-estimation marginal mortality predictions were 31.3% ( $ETT \leq 7$ ) versus 14.5% (95% CI 8.9–20.0,  $P = .01$ ) for the  $ETT \leq 7.5$ , and 19.3% (95% CI 10.7–27.8,  $P = .18$ ) for the  $ETT \geq 8$  group, respectively. The GLME post-estimated severity adjusted mortality was 26.7% (95% CI 13.2–40.2) for the  $ETT \leq 7$  group versus 14.3% (95% CI 6.8–21.7,  $P = .036$ ) for  $ETT \leq 7.5$  and 10.1% (95% CI 4.4–17.6,  $P = .02$ ) for the  $ETT \geq 8$  group, respectively.

Table 2 outlines the adjusted mortality coefficients from a GLME model, and Figure 1 illustrates the incremental statistically significant adjusted mortality decrease with incremental ETT size.

### Sensitivity Analyses

The sensitivity analysis of the statistical interaction of the height, classified in tertiles with the ETT size, disclosed that the taller subjects with the smallest ETT had the highest mortality (Fig. 2). Specifically, the top-height tertile subjects who had a 7.0 or smaller ETT had 1.8 times higher odds of death than the bottom-height tertile subjects who also had a 7.0 or smaller ETT ( $P = .02$ ), after adjusting for demographics and severity of illness and the interaction of height-tertiles with the ETT size.

In addition, when the ETT internal diameter was analyzed as a linear variable, it was found that every 1 mm increase in ETT size was associated with 0.23 times lower odds of death (95% CI 0.06–0.85,  $P = .03$ ), adjusted for demographics and severity of illness. The predicted mortalities are shown in Figure 3.

## Discussion

The present study reports that adult subjects with status asthmaticus were intubated with variable ETT diameters, ranging between 6.5–8.5 mm. Subjects intubated with a 7.0 mm or smaller ETT had double the hospital mortality compared to subjects with a larger ETT. In addition, there was a near-linear dose-effect relation of the ETT diameter with mortality (Figs. 1 and 2). These findings support the expert opinion of inserting the largest possible diameter ETT in patients with status asthmaticus who require endotracheal intubation. Furthermore, the sensitivity analysis (Fig. 3) suggested that for every mm decrease in ETT size was associated with higher odds of death.

Asthma exacerbations lead to half a million hospitalizations in the United States every year.<sup>15,16</sup> Approximately 10% of patients hospitalized for asthma require an ICU admission,<sup>17</sup> and around 2–4% of all hospitalized patients will require endotracheal intubation and invasive mechanical

# ETT SIZE AND MORTALITY IN STATUS ASTHMATICUS

Table 1. Baseline Characteristics of the Status Asthmaticus Cohort

	Endotracheal Tube Groups			
	ETT ≤ 7.0 mm <i>n</i> = 32 (3.3%)	ETT = 7.5 mm <i>n</i> = 159 (16.5%)	ETT ≥ 8.0 mm <i>n</i> = 83 (8.6%)	Non-Intubated <i>n</i> = 690 (71.6%)
Gender				
Female	26 (81.25%)	118 (74.21%)	27 (32.53%)	441 (63.91%)
Male	6 (18.75%)	41 (25.79%)	56 (67.47%)	249 (36.09%)
Race				
Non-Black	6 (18.75%)	30 (18.87%)	25 (30.12%)	126 (18.26%)
Black	26 (81.25%)	129 (81.13%)	58 (69.88%)	564 (81.74%)
Age at service	50.5 (17.92%)	47.7 (14.98%)	48.5 (15.14%)	50.6 (14.18%)
Diagnoses Present on Admission				
AMI	1 (3.45%)	15 (51.72%)	2 (6.90%)	11 (37.93%)
CHF	5 (3.23%)	27 (17.42%)	15 (9.68%)	108 (69.68%)
PVD	0	2 (25.00%)	1 (12.50%)	5 (62.50%)
Cerebrovascular disease	0	1 (25.00%)	0	3 (75.00%)
Dementia	0	1 (14.29%)	0	6 (85.71%)
COPD	23 (3.73%)	123 (19.94%)	57 (9.24%)	414 (67.10%)
Rheumatoid disease	1 (7.14%)	2 (14.29%)	2 (14.29%)	9 (64.29%)
PUD	0	0	1 (33.33%)	2 (66.67%)
Mild liver disease	0	4 (23.53%)	2 (11.76%)	11 (64.71%)
Hemiplegia or paraplegia	0	2 (50.00%)	1 (25.00%)	1 (25.00%)
Renal disease	4 (4.60%)	18 (20.69%)	9 (10.34%)	56 (64.37%)
Cancer	0	5 (22.73%)	3 (13.64%)	14 (63.64%)
Metastatic cancer	0	2 (28.57%)	0	5 (71.43%)
AIDS	0	0	1 (25.00%)	3 (75.00%)
COVID-19	2 (7.14%)	8 (28.57%)	2 (7.14%)	16 (57.14%)
Charlson comorbidity index	38 (3.32)	237 (20.68)	112 (9.77)	759 (66.23)
Intubation Personnel				
Anesthesia	4 (8.00%)	27 (54.00%)	19 (38.00%)	0
Pulmonary critical care	4 (12.90%)	15 (48.39%)	12 (38.71%)	0
Emergency medicine	16 (11.94%)	93 (69.40%)	25 (18.66%)	0
Paramedics	1 (10.00%)	5 (50.00%)	4 (40.00%)	0
Outside hospital	0	3 (100%)	0	0
Daytime intubation	14 (13.33%)	65 (61.90%)	26 (24.76%)	0
Nighttime intubation	11 (9.02%)	77 (63.11%)	34 (27.87%)	0
Height, cm	159.98 (20.15)	160.86 (18.66)	165.02 (24.70)	164.75 (16.38)
BMI	38.05 (25.40)	42.41 (44.36)	44.30 (46.51)	37.98 (31.39)
pH, ABG	7.16 (0.21)	7.22 (0.14)	7.23 (0.12)	7.32 (0.10)
P <sub>a</sub> CO <sub>2</sub> , mm Hg	77.93 (41.22)	70.37 (34.46)	74.69 (36.82)	51.23 (24.66)
SOFA neurological	3.03 (1.47)	3.21 (1.58)	2.81 (2.03)	0.85 (2.49)
SOFA respiratory	1.78 (1.39)	1.83 (1.27)	1.51 (1.33)	1.11 (0.92)
SOFA cardiovascular	3.75 (0.44)	3.84 (0.37)	3.76 (0.43)	3.98 (0.16)
SOFA renal	0.34 (0.48)	0.47 (0.79)	0.66 (0.90)	0.25 (0.57)
SOFA liver	0.06 (0.25)	0.06 (0.31)	0.10 (0.37)	0.03 (0.21)
SOFA hematological	0.19 (0.47)	0.14 (0.49)	0.13 (0.38)	0.09 (0.34)
SOFA total score	9.16 (2.58)	9.56 (2.46)	8.96 (2.80)	6.29 (2.79)

Data are presented as *n* (SD) unless otherwise noted.

ETT = endotracheal tube

AMI = acute myocardial infarction

CHF = congestive heart failure

PUD = peptic ulcer disease

PVD = peripheral vascular disease

AIDS = acquired immune deficiency syndrome

BMI = body mass index

ABG = arterial blood gas

SOFA = Sequential Organ Failure Assessment

## ETT SIZE AND MORTALITY IN STATUS ASTHMATICUS

Table 2. Adjusted Status Asthmaticus Mortality Analysis With Binomial Distribution Generalized Linear Mixed-Effects Model Regression

Parameter	Generalized Linear Mixed Model: Adjusted Mortality				
	Coefficient	Robust SE	z	P	95% CI
Comparison with $\leq 7.0$ mm ETT group					
ETT 7.5 mm vs $\leq 7.0$ mm group	-1.21	0.58	-2.09	.037	(-2.34 to -0.07)
ETT $\geq 8.0$ mm vs $\leq 7.0$ mm group	-1.63	0.72	-2.26	.02	(-3.05 to -0.21)
Non-intubated vs $\leq 7.0$ mm group	-3.35	0.78	-4.31	< .001	(-4.87 to -1.83)
Adjusted age at service, y	0.06	0.01	4.04	.001	(0.03-0.09)
Male vs female	-0.15	0.47	-0.32	.75	(-1.07 to 0.77)
Black vs other race	-1.15	0.44	-2.62	.009	(-2.01 to -0.29)
Height (each cm)	-0.02	0.02	-1.15	.25	(-0.05 to 0.01)
BMI (each unit)	-0.00	0.01	-0.31	.76	(-0.02 to 0.01)
SOFA (each unit)	0.21	0.06	3.84	< .001	(0.11-0.32)
P <sub>aCO<sub>2</sub></sub> , mm Hg	0.02	0.01	4.70	< .001	(0.01-0.03)
Charlson index, point	0.35	0.15	2.35	.02	(0.06-0.65)
COVID-19	1.11	0.76	1.45	.15	(-0.39 to 2.60)
COPD	-1.37	0.52	-2.64	.008	(-2.39 to -0.36)
Intubating personnel = anesthesia	-0.11	0.80	-0.13	.89	(-1.66 to 1.45)
Intubating personnel = pulmonary critical care	-1.45	1.52	-0.95	.34	(-4.42 to 1.53)
Intubating personnel = emergency medicine	-1.22	0.64	-1.89	.058	(-2.48 to 0.05)
Intubating personnel = paramedic/EMS	3.65	1.32	2.76	.006	(1.06-6.23)
Intubating personnel = outside hospital	0	0			
Daytime intubation	-0.28	0.57	-0.49	.62	(-1.39 to 0.83)
Nighttime intubation (6 PM to 7 AM)	0	0			
Intercept	-2.49	2.98	-0.83	.40	(-8.33 to 3.36)

SE = standard error  
 ETT = endotracheal tube  
 BMI = body mass index  
 SOFA = Sequential Organ Failure Assessment  
 EMS = emergency medical services

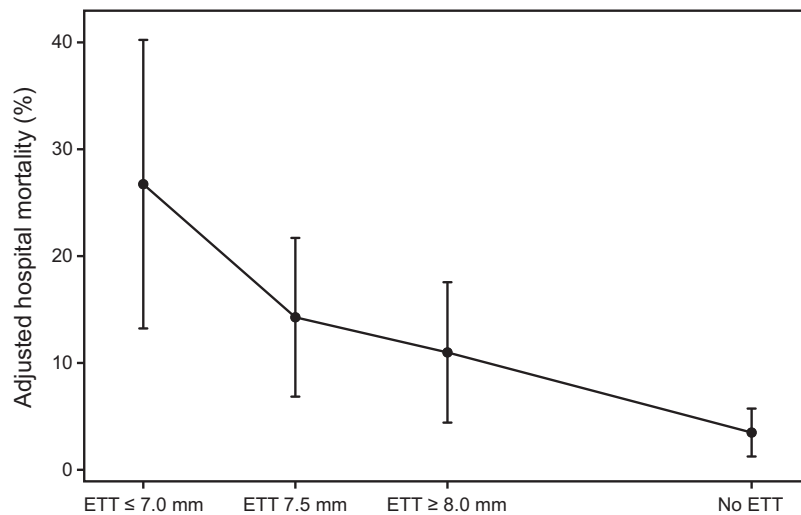


Fig. 1. Post generalized linear mixed-effects (GLME) marginal estimation status asthmaticus mortality predictions for each endotracheal tube (ETT) group.

ventilation.<sup>18,19</sup> The present study's findings are consistent with other studies that have reported higher mortality in mechanically ventilated subjects.<sup>17-19</sup>

The pathophysiological impact of differential ETT internal diameter on air flow dynamics has been previously reported in the literature. Flevari et al<sup>20</sup> reported that the

## ETT SIZE AND MORTALITY IN STATUS ASTHMATICUS

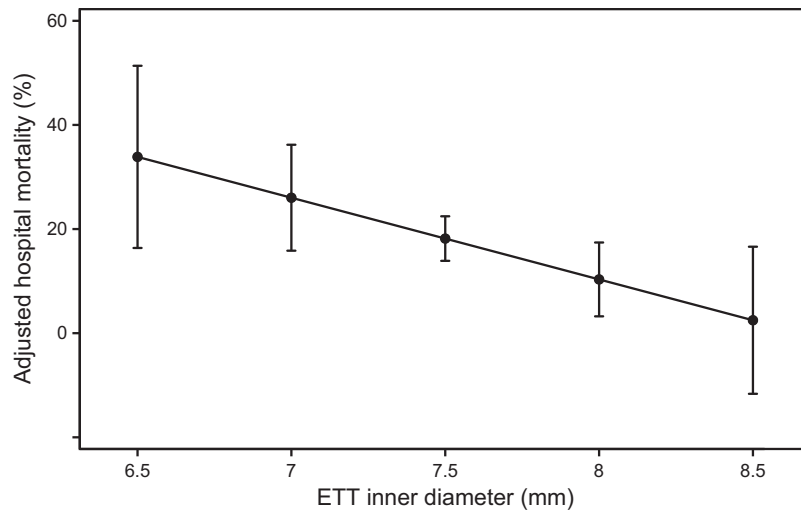


Fig. 2. Post generalized mixed-effects (GLME) liner model estimation of model-predicted mortality, with endotracheal tube (ETT) analyzed as a continuous variable.

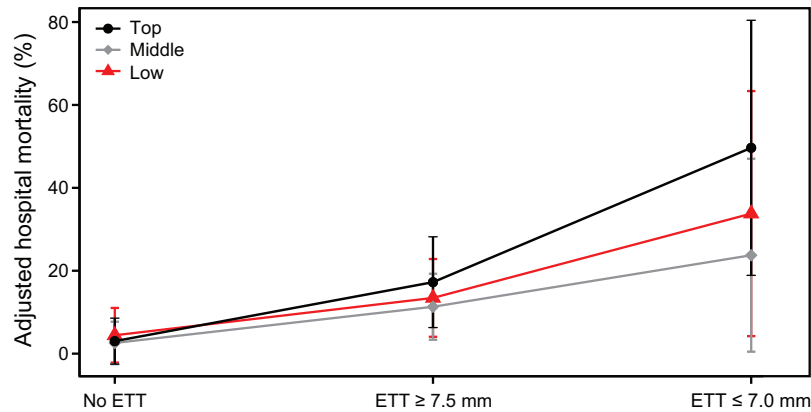


Fig. 3. Sensitivity analysis of differential height groups, expressed in tertiles (top, middle, low). Post generalized linear mixed-effects (GLME) marginal estimation status asthmaticus mortality predictions of endotracheal tube (ETT) groups in each subject-height tertile group.

resistance of ETT increased with increasing inspiratory flow and decreasing internal diameter of ETT. Similarly, Kim et al<sup>21</sup> observed an inverse linear relationship between peak inspiratory flow, peak airway pressure, and mean airway pressure with ETT diameter in a manikin-based cardiopulmonary resuscitation experiment.

Respiratory physiology, especially air flow dynamics, is an application in fluid dynamics. As a form of fluid, air travels through space in the same way as water through pipe or blood through a vessel. The mechanics of this movement is described via Poiseuille law:  $Q = P\pi r^4/8l\eta$ , where  $Q$  is flow,  $P$  is driving pressure,  $r$  is the lumen radius,  $l$  is lumen length, and  $\eta$  is fluid viscosity. The air flow is opposed by lumen resistance, and this can be described using Ohm law for resistance, which is that  $r = P/Q$ , where  $R$  is lumen resistance. In reconciling these formulae, we can determine  $r = 8l\eta/\pi r$ .<sup>4</sup> The ETT radius, that is, half of the internal

diameter, has an exponential effect on resistance; this is the critical determinant of airway resistance.

Mucus plugging is prominent in asthma, which can dramatically increase the resistance of an ETT. In fact, a landmark study identified that the airways of subjects who die of status asthmaticus have copious mucus plugs.<sup>22</sup> One study collected ETTs of extubated subjects and found that secretions could cause significant pressure drop with a given air flow, compared with a control ETT, and 50% of the ETTs with secretions had resistance equivalent to one tube size smaller.<sup>23</sup> A recent study by Yoshida et al<sup>24</sup> reported that “mucus plugs occluded more than 40% of the airways.” A tiny, 5 mm mucus plug on an 8.0 mm ETT would result in a 7.5 mm internal diameter and 3.75 mm radius, whereas the same mucus plug on a 7.0 mm ETT would result in a 6.5 mm diameter and a 3.25 mm radius. The calculated airway resistance is 177% higher in the second scenario given the

exponential contribution of the radius to the formula described above. The second, 7 mm ETT, will have around half (56%) of the flow in the first scenario, resulting in half-minute ventilation and double  $P_{aCO_2}$  and worsening hypercarbia.

Importantly, higher airway resistance prolongs the time constant and subsequently leads to worsening dynamic hyperinflation. The time constant ( $\tau$ ) is the product of resistance and compliance.  $\tau = R \times C$ . The time constant is defined as the time required inflating or deflating 63% of the lung volume.<sup>25</sup> The increased time constant and increased exhalation time will result in higher expiratory times, higher auto-PEEP,<sup>26</sup> and worsening dynamic hyperinflation. Dynamic hyperinflation will increase the positive pressure in the alveoli, requiring higher respiratory muscle work to create negative alveolar pressure in order to initiate a breath,<sup>27</sup> higher energy cost, higher respiratory muscle oxygen requirement,<sup>28</sup> and worsening dyspnea. Both lung and chest wall have lower compliance at hyperinflated volume states, which further exacerbates the work of breathing and the dyspnea.<sup>29</sup> In addition, the respiratory muscles' force-length relationship is altered, which further reduces the muscle-pump efficacy.<sup>27</sup> Air trapping and increased lung volumes force the diaphragm to flatten, which, according to Laplace law, creates a larger dome radius and less transdiaphragmatic pressure.<sup>30</sup> All the above create conditions that promote heavy sedation, paralysis, and all the adverse consequences of prolonged mechanical ventilation.<sup>31</sup> Finally, air trapping increases the risk of barotrauma, which can lead to tension pneumothorax and cardiac arrest.<sup>32</sup>

Air trapping from dynamic hyperinflation has detrimental hemodynamic consequences, leading to increased intrathoracic pressures, reduced venous return, and high transpulmonary pressure, increasing the right-heart afterload and reducing the overall cardiac output.<sup>33</sup>

In summary, the ETT airway resistance adds to the total airway resistance and contributes to worsening dynamic hyperinflation in an already strained physiological system of patients in status asthmaticus.

The present study sensitivity analysis suggested that taller subjects who received smaller ETT sizes had higher mortality than equivalent shorter subjects. In addition, the mortality difference among taller and shorter subjects was not significant when larger ETT sizes were used. There is a paucity of literature in adult subjects regarding ETT sizes. In pediatric patients, guidelines recommend the appropriate size of ETTs. Based on a patient's age, one can use either of 2 equations for cuffed tube size = (age/4) + 3 or uncuffed tube size = (age/4) + 4.<sup>34</sup> Height-based estimations exist in adult patients however, the choice of ETT based on height is not routinely used.<sup>35</sup> Mehta et al<sup>36</sup> studied subjects ready for extubation and showed that when compared to subjects with an 8.0 ETT those with 7.0 and 7.5 tubes had higher breathing frequency during all ventilator

modes and 15 min after extubation as well as lower tidal volumes during CPAP and pressure support ventilation (PSV). They also had a higher pressure-time product of the diaphragm during CPAP, PSV, and 15 min after extubation.

The present study has several limitations. First, as a single-center study, it may lack generalizability. Most of the cohort were Black, in terms of race, and the findings may not apply to different populations. In addition, in contrast to prior studies of ETT size in experimental models, the current study evaluated their clinical impact in a real-world clinical setting. We do not have ventilator pressure and waveform data for the intubated subjects. Missing data from SOFA scores were assumed to be missing randomly. Subjects in the study were treated in a diverse setting with distinct practice patterns, and the inclusion of subjects over a 7-y study period supports broad applicability and generalizability of the findings. Like all retrospective studies, association does not necessarily translate to causality.

## Conclusions

Experts recommend the largest ETT size in patients with status asthmaticus; however, its role in patient outcomes remains unclear. We set out to explore the association of ETT sizes with mortality in a large cohort of subjects with status asthmaticus. We report that subjects with status asthmaticus intubated with smaller size ETT sizes had disproportionately higher in-hospital mortality compared to subjects with larger ETT sizes, even after adjusting for multiple confounders. The mortality effect was more prominent in taller subjects who have larger total lung capacity. We hypothesize that higher mortality among subjects with smaller ETT could be attributed to higher overall airway resistance, thus higher time constant, contributing to worsening dynamic hyperinflation and hemodynamic consequences in an already hyperinflated chest from status asthmaticus. Future studies are required to externally validate these findings and uncover the exact pathophysiological mechanisms.

## REFERENCES

1. GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2020;396:1204-1222.
2. Peters JI, Stupka JE, Singh H, Rossrucker J, Angel LF, Melo J, et al. Status asthmaticus in the medical intensive care unit: a 30-year experience. *Respir Med* 2012;106(3):344-348.
3. Afessa B, Morales I, Cury JD. Clinical course and outcome of patients admitted to an ICU for status asthmaticus. *Chest* 2001;120(5):1616-1621.
4. McFadden ER. Acute severe asthma. *Am J Respir Crit Care Med* 2003;168(7):740-759.
5. Papiris S, Kotanidou A, Malagari K, Roussos C. Clinical review: severe asthma. *Crit Care* 2002;6(1):30-44.
6. Gandhi A, Sokhi J, Lockie C, Ward PA. Emergency tracheal intubation in patients with COVID-19: experience from a UK center. *Anesthesiol Res Pract* 2020;2020:1-9.

7. Colton House J, Noordzij JP, Murgia B, Langmore S. Laryngeal injury from prolonged intubation: a prospective analysis of contributing factors. *Laryngoscope* 2011;121(3):596-600.
8. Shinn JR, Kimura KS, Campbell BR, Sun Lowery A, Wootten CT, Garrett CG, et al. Incidence and outcomes of acute laryngeal injury after prolonged mechanical ventilation. *Crit Care Med* 2019;47:1699-1706.
9. Vincent JL, de Mendonça A, Cantraine F, Moreno R, Takala J, Suter PM, et al. Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multi-center, prospective study. Working group on "sepsis-related problems" of the European Society of Intensive Care Medicine. *Crit Care Med* 1998;26(11):1793-1800.
10. Sundararajan V, Henderson T, Perry C, Muggivan A, Quan H, Ghali WA. New ICD-10 version of the Charlson comorbidity index predicted in-hospital mortality. *J Clin Epidemiol* 2004;57(12):1288-1294.
11. Quan H, Sundararajan V, Halfon P, Fong A, Burnand B, Luthi J-C, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care* 2005;43(11):1130-1139.
12. Stagg V, Hilsden R, Quan ELIXHAUSER: H. Stata module to calculate Elixhauser index of comorbidity. *EconPapers* 2015. Available at: <https://econpapers.repec.org/software/bocbocode/s458077.htm>. Accessed May 14, 2021.
13. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The strengthening of reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *Ann Intern Med* 2007;147(8):573-577.
14. Williams R. Using the margins command to estimate and interpret adjusted predictions and marginal effects. *The Stata Journal* 2012;12(2):308-331.
15. Asthma Trends and Burden. American Lung Association. Available at: <https://www.lung.org/research/trends-in-lung-disease/asthma-trends-brief/trends-and-burden>. Accessed May 30, 2021
16. Akinbami LJ, Moorman JE, Bailey C, Zahran HS, King M, Johnson CA, et al. Trends in asthma prevalence, health care use, and mortality in the United States. *NCHS Data Brief* 2001;2012(2010):1-8.
17. Krishnan V, Diette GB, Rand CS, Bilderback AL, Merriman B, Hansel NN, et al. Mortality in patients hospitalized for asthma exacerbations in the United States. *Am J Respir Crit Care Med* 2006;174(6):633-638.
18. Leatherman J. Mechanical ventilation for severe asthma. *Chest* 2015;147(6):1671-1680.
19. Nanchal R, Kumar G, Majumdar T, Taneja A, Patel J, Dagar G, et al. Utilization of mechanical ventilation for asthma exacerbations: analysis of a national database. *Respir Care* 2014;59(5):644-653.
20. Flevari AG, Maniatis N, Kremiotis TE, Siempos I, Betrosian AP, Roussos C, et al. Rohrer's constant, K2, as a factor of determining inspiratory resistance of common adult endotracheal tubes. *Anaesth Intensive Care* 2011;39(3):410-417.
21. Kim JW, Lee JW, Ryu S, Park JS, Yoo I, Cho YC, et al. Changes in peak inspiratory flow rate and peak airway pressure with endotracheal tube size during chest compression. *World J Emerg Med* 2020;11(2):97-101.
22. Houston JC, Navasquez SD, Trounce JR. A clinical and pathological study of fatal cases of status asthmaticus. *Thorax* 1953;8(3):207-213.
23. Wilson AM, Gray DM, Thomas JG. Increases in endotracheal tube resistance are unpredictable relative to duration of intubation. *Chest* 2009;136(4):1006-1013.
24. Yoshida Y, Takaku Y, Nakamoto Y, Takayanagi N, Yanagisawa T, Takizawa H, et al. Changes in airway diameter and mucus plugs in patients with asthma exacerbation. *PLoS One* 2020;15(2):e0229238.
25. Al-Rawas N, Banner MJ, Euliano NR, Tams CG, Brown J, Martin AD, et al. Expiratory time constant for determinations of plateau pressure, respiratory system compliance, and total resistance. *Crit Care* 2013;17(1):R23.
26. Pepe PE, Marini JJ. Occult positive end-expiratory pressure in mechanically ventilated patients with airflow obstruction: the auto-PEEP effect. *Am Rev Respir Dis* 1982;126(1):166-170.
27. Soffler MI, Hayes MM, Schwartzstein RM. Respiratory sensations in dynamic hyperinflation: physiological and clinical applications. *Respir Care* 2017;62(9):1212-1223.
28. O'Donnell DE, Laveneziana P. Physiology and consequences of lung hyperinflation in COPD. *European Respiratory Review* 2006;15(100):61-67.
29. Takara LS, Cunha TM, Barbosa P, Rodrigues MK, Oliveira MF, Nery LE, Neder JA. Dynamics of chest wall volume regulation during constant work rate exercise in patients with chronic obstructive pulmonary disease. *Braz J Med Biol Res* 2012;45(12):1276-1283.
30. Kleinman BS, Frey K, VanDrunen M, Sheikh T, DiPinto D, Mason R, Smith T. Motion of the diaphragm in patients with chronic obstructive pulmonary disease while spontaneously breathing versus during positive pressure breathing after anesthesia and neuromuscular blockade. *Anesthesiology* 2002;97(2):298-305.
31. Shehabi Y, Chan L, Kadiman S, Alias A, Ismail WN, Tan MATI, et al; the Sedation Practice in Intensive Care Evaluation (SPICE) Study Group investigators. Sedation depth and long-term mortality in mechanically ventilated critically ill adults: a prospective longitudinal multi-center cohort study. *Intensive Care Med* 2013;39(5):910-918.
32. Jantz MA, Pierson DJ. Pneumothorax and barotrauma. *Clin Chest Med* 1994;15(1):75-91.
33. Teboul J-L, Monnet X, Chemla D, Michard F. Arterial pulse pressure variation with mechanical ventilation. *Am J Respir Crit Care Med* 2019;199(1):22-31.
34. Khine HH, Corrdry DH, Kettrick RG, Martin TM, McCloskey JJ, Rose JB, et al. Comparison of cuffed and uncuffed endotracheal tubes in young children during general anesthesia. *Anesthesiology* 1997;86(3):627-631; discussion 27A.
35. Cao AC, Rereddy S, Mirza N. Current practices in endotracheal tube size selection for adults. *Laryngoscope* 2020
36. Mehta S, Heffer MJ, Maham N, Nelson DL, Klinger JR, Levy MM. Impact of endotracheal tube size on preextubation respiratory variables. *J Crit Care* 2010;25(3):483-488.

This article is approved for Continuing Respiratory Care Education credit. For information and to obtain your CRCE (free to AARC members) visit [www.rcjournal.com](http://www.rcjournal.com)

