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The AIR-SED Study: A Multicenter Cohort Study of SEDation Practices, Deep Sedation, and Coma Among Mechanically Ventilated AIR Transport Patients

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OBJECTIVES: To characterize prehospital air medical transport sedation practices and test the hypothesis that modifiable variables related to the monitoring and delivery of analgesia and sedation are associated with prehospital deep sedation.

DESIGN: Multicenter, retrospective cohort study.

SETTING: A nationwide, multicenter (approximately 130 bases) air medical transport provider.

PATIENTS: Consecutive, adult mechanically ventilated air medical transport patients treated in the prehospital environment (January 2015 to December 2020).

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: All data involving sedation (medications, monitoring) were recorded. Deep sedation was defined as: 1) Richmond Agitation-Sedation Scale of −3 to −5; 2) Ramsay Sedation Scale of 5 or 6; or 3) Glasgow Coma Scale of less than or equal to 9. Coma was defined as being unresponsive and based on median sedation depth: 1) Richmond Agitation-Sedation Scale of −5; 2) Ramsay of 6; or 3) Glasgow Coma Scale of 3. A total of 72,148 patients were studied. Prehospital deep sedation was observed in 63,478 patients (88.0%), and coma occurred in 42,483 patients (58.9%). Deeply sedated patients received neuromuscular blockers more frequently and were less likely to have sedation depth documented with a validated sedation depth scale (i.e., Ramsay or Richmond Agitation-Sedation Scale). After adjusting for covariates, a multivariable logistic regression model demonstrated that the use of longer-acting neuromuscular blockers (i.e., rocuronium and vecuronium) was an independent predictor of deep sedation (adjusted odds ratio, 1.28; 95% CI, 1.22–1.35; $p < 0.001$), while use of a validated sedation scale was associated with a lower odds of deep sedation (adjusted odds ratio, 0.29; 95% CI, 0.27–0.30; $p < 0.001$).

CONCLUSIONS: Deep sedation (and coma) is very common in mechanically ventilated air transport patients and associated with modifiable variables related to the monitoring and delivery of analgesia and sedation. Sedation practices in the prehospital arena and associated clinical outcomes are in need of further investigation.

KEY WORDS: coma; deep sedation; mechanical ventilation; neuromuscular blockers; prehospital; sedation

The use of analgesia and sedation is near universal for mechanically ventilated patients. It has been known for almost 20 years that deep sedation and coma in critically ill patients is associated with increased risk of death (1). Efforts to decrease sedation depth improve outcome, and evidence-based guidelines suggest targeting light sedation for mechanically ventilated patients (2–7). Early deep sedation may be especially impactful, as it

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has been demonstrated that deep sedation during the first 48 hours of ICU care is independently associated with higher mortality (8–11). Similarly, deep sedation during an earlier period of respiratory failure, the emergency department (ED), is common (53–64%) and associated with worse clinical outcomes (12, 13). Due to therapeutic momentum, deep sedation in the ED has been shown to increase the frequency of early deep sedation in the ICU as well (12, 13). For these reasons, targeting sedation during the earliest periods of respiratory failure could be a high-yield intervention and positively impact outcome by reducing time that patients experience deep sedation and coma (14).

In the prehospital domain, over 640,000 critically ill patients required air medical transport annually in the United States (15). Similar to data from the early period in the ICU and ED, data suggest that prehospital sedation could be an important determinant of outcome. In a cohort study of air medical transport patients (n = 327), prehospital deep sedation was associated with increased hospital length of stay and fewer ventilator-free days (16). However, this was a single-center retrospective study, and we are unaware of other studies examining sedation for mechanically ventilated patients in the prehospital arena. It is therefore unknown if the results are generalizable and a knowledge gap persists. As a result, current prehospital sedation practices are incompletely understood, and a more comprehensive evaluation is warranted. Given the outcome data associated with early sedation depth, the objectives of this study were to: 1) characterize air medical transport analgosedation practices and sedation depth monitoring across a multicenter air medical transport provider and 2) assess predictors of prehospital deep sedation. We hypothesized that deep sedation would be common and associated with modifiable sedation-related variables.

MATERIALS AND METHODS

Study Design

This was a retrospective cohort study (January 2015 to December 2020) of consecutive, adult mechanically ventilated air medical transport patients treated in the prehospital environment. All patients were transported by the Community-Based Services (approximately 160 bases) of Air Methods, an air medical transport provider, dispersed across 48 states. The study is reported in accordance with the Strengthening Reporting of Observational Studies in Epidemiology statement (**Supplemental Digital Content 1**, http://links.lww.com/CCX/A873).

A data use agreement was signed between Air Methods and the study team prior to study initiation and prior to transfer of a de-identified dataset. The Human Research Protection Office (HRPO) at the primary study site determined that no consent was required for the study (HRPO Number 202006068).

Participants

All consecutive mechanically ventilated adult air medical transport patients were identified via electronic query of emsCharts, the electronic medical record system used by the Air Methods bases. Inclusion criterion: 1) age greater than or equal to 18 years and 2) receipt of mechanical ventilation via an endotracheal tube. Facility-to-facility transfers (e.g., ED-to-ICU), as well as scene flights (e.g., patients intubated in the field), were included. Exclusion criteria regarding subgroups of interest are described below.

Assessments and Outcome Measures

Baseline data including age, weight, gender, race, and vital signs were recorded. Laboratory variables included lactate, creatinine, hemoglobin, and arterial blood gases. These laboratory variables were those documented by the air medical crew and obtained prior arrival (e.g., in the ED to which the crew was dispatched). Process of care variables included endotracheal intubation (i.e., by air medical crew vs prior to arrival), vasopressor use, and duration of care. Duration of care (in hr) was calculated as the elapsed time from crew arrival and assumption of patient care to handoff of care at the receiving facility.

The indication for mechanical ventilation was extrapolated from the documented chief complaint and included sepsis, respiratory failure, cardiac (e.g., acute myocardial infarction, congestive heart failure), airway obstruction, sudden cardiac arrest, drug overdose, cerebrovascular accident, intracranial hemorrhage, seizure, traumatic brain injury, altered mental status, trauma, and other. A structured process for adjudication of the indication for mechanical ventilation was developed and followed.

Analgesia and sedation-related data included fentanyl, benzodiazepines (i.e., midazolam, lorazepam), propofol, ketamine, etomidate, and neuromuscular blockers

(i.e., succinylcholine, rocuronium, and vecuronium). Pertinent medications documented as given prior to air medical crew arrival were also recorded.

Sedation depth during air medical care was recorded and included the Ramsay Sedation Scale and the Richmond Agitation-Sedation Scale (RASS). We anticipated that many crews may not routinely monitor sedation depth for mechanically ventilated patients via a validated sedation scale, as prehospital sedation has not yet received any significant clinical or research attention. In situations where no Ramsay or RASS was documented, a documented Glasgow Coma Scale (GCS) was used as a surrogate for sedation depth (17). Deep sedation was defined as: 1) RASS of –3 to –5; 2) Ramsay of 5 or 6; or 3) GCS of less than or equal to 9 (17). Coma was defined as being unresponsive and based on median sedation depth: 1) RASS of –5; 2) Ramsay of 6; or 3) GCS of 3.

Statistical Analysis

Patient characteristics were assessed with descriptive statistics and frequency distributions. Categorical characteristics were compared using chi-square test or Fisher exact test. Continuous characteristics were compared using independent samples *t* test or Mann-Whitney *U* test. To further characterize prehospital sedation practices, two a priori subgroup analyses were conducted. To better assess for the influence of the indication for mechanical ventilation on documented sedation depth, patients with potential neurologic injuries were excluded. Since sedation depth could be influenced by medications received prior to the air medical crew's arrival, an analysis on only those patients intubated by the air medical crew was also conducted.

To assess for predictors of prehospital deep sedation, a multivariable logistic regression model was constructed to adjust for potentially confounding variables. Covariates (chosen a priori) were restricted to those without missing data and included baseline characteristics that could influence the occurrence of deep sedation (i.e., age, intubation location), as well as modifiable sedation-related variables, including use of a validated sedation scale to document depth (i.e., Ramsay or RASS vs GCS), and receipt of fentanyl, midazolam, ketamine, propofol, lorazepam, and neuromuscular blockers (i.e., succinylcholine vs longer-acting neuromuscular blockers [rocuronium, vecuronium]) (18). Collinearity was assessed and the model used variables that were independent of other variables. All tests were two-tailed, and a p value of less than 0.05 was considered statistically significant.

Given results of the primary multivariable model that showed that longer-acting neuromuscular blockers were associated with deep sedation, an exploratory post hoc sensitivity analysis was conducted, which adjusted for the total dose of analgesics and sedatives received. This was done to explore the possibility that patients receiving longer-acting neuromuscular blockers may receive higher sedative doses to prevent awareness with paralysis, leading to more deep sedation (i.e., in the causal pathway) (19, 20). Given the imbalance that was demonstrated with respect to indication for mechanical ventilation, a second post hoc sensitivity analysis was conducted, which adjusted for this covariate.

Regarding sample size, it was estimated a priori that approximately 15,000 patients per year would be included in the analysis. Therefore, while the sample size was fixed, we were confident that it would be sufficient in size to: 1) provide a descriptive analysis that had high external validity and 2) conduct analyses with adequate power, precision, and event per covariable ratio (21, 22).

RESULTS

Study Population

A total of 81,977 mechanically ventilated patients were in the dataset. After exclusion of 9,829 patients less than 18 years old, the final study population was 72,148 (**Supplemental Digital Content 2**, http://links.lww.com/CCX/A873). Baseline characteristics are in **Table 1**. The median duration of care was 1.2 hours (0.9–1.5 hr), and 45,038 patients (62.4%) were intubated by the air medical crew.

Medications Administered

Sedation-related variables are in **Table 2**. The most commonly used agents were fentanyl (50.8%), midazolam (38.8%), ketamine (38.6%), and propofol (13.0%). **Figure 1** demonstrates use of each agent according to year of presentation. There was significant increase in ketamine use over time, and significant decrease in midazolam ($p < 0.01$ for both, comparing first and second half of study). Neuromuscular blockers were given to 63.0% of the cohort. Rocuronium was given most frequently (32.7%), followed by succinylcholine (27.3%)

TABLE 1.
Characteristics of Mechanically Ventilated Air Medical Transport Patients

Baseline Characteristics	Prehospital Sedation Depth Status			
	All Subjects (*n* = 72,148)	Deep Sedation (*n* = 63,478)	Light Sedation (*n* = 8,670)	*p*
Age (yr)	56.4 (18.5)	56.2 (18.5)	58.1 (18.1)	< 0.01
Weight (kg), *n* = 71,548	82.0 (70.0–100.0)	82.0 (70.0–100.0)	84.0 (70.0–100.0)	0.26
Gender, *n* = 71,454				
Female, *n* (%)	28,274 (39.2)	24,844 (39.5)	3,217 (40.3)	0.16
Race, *n* = 4,104				
White, *n* (%)	2,937 (71.6)	2,534 (72.0)	378 (68.2)	0.08
African-American, *n* (%)	590 (14.4)	502 (14.3)	84 (15.2)	
Hispanic, *n* (%)	426 (10.4)	351 (10.0)	74 (13.4)	
Heart rate (beats/min), *n* = 72,046	92.5 (77.5–109.0)	92.0 (77.5–109.0)	92.5 (79.0–108.0)	0.18
Mean arterial pressure, *n* = 71, 816	89.0 (77.5–101.0)	89.0 (77.5–101.0)	89.0 (78.5–100.0)	0.82
Peripheral oxygen saturation (%), *n* = 70,911	96.3 (6.8)	96.3 (6.7)	96.4 (7.5)	0.15
Lactate (mmol/L), *n* = 9,851	3.7 (2.0–7.4)	3.8 (2.0–7.6)	3.3 (1.8–6.2)	< 0.01
Creatinine (mg/dL), *n* = 41,527	1.2 (0.9–1.8)	1.2 (0.9–1.8)	1.2 (0.8–1.9)	0.16
Hemoglobin (g/dL), *n* = 43,172	12.5 (3.0)	12.6 (3.0)	12.3 (3.2)	< 0.01
pH, *n* = 26,454	7.29 (7.18–7.38)	7.29 (7.18–7.38)	7.30 (7.19–7.39)	0.02
Pao_2, *n* = 25,962	105 (73–207)	108 (73–212)	95 (68–171)	< 0.01
$Paco_2$, *n* = 25,747	43 (35–54)	43 (35–54)	43 (35–55)	0.12
Indication for mechanical ventilation, *n* (%)				
Altered mental status	16,412 (22.7)	15,043 (23.7)	1,274 (15.8)	< 0.01
Respiratory failure	13,705 (19.0)	11,146 (17.6)	2,435 (30.1)	
Trauma	8,975 (12.4)	8.085 (12.7)	819 (10.1)	
Cardiac arrest	6,100 (8.5)	5,602 (8.8)	449 (5.6)	
Cardiac	3,593 (5.0)	2,994 (4.7)	563 (7.0)	
Intracranial hemorrhage	3,147 (4.4)	2,861 (4.0)	267 (3.3)	
Drug overdose	2,336 (3.2)	2,098 (3.3)	223 (2.8)	
Seizure	2,329 (3.2)	2,102 (3.3)	219 (2.7)	
Sepsis	1,974 (2.7)	1,702 (2.7)	246 (3.0)	
Traumatic brain injury	1,698 (2.4)	1,553 (2.4)	135 (1.7)	
Airway obstruction	392 (0.5)	347 (0.5)	41 (0.5)	
Other	11,487 (15.9)	9,945 (15.7)	1,406 (17.4)	
Process of care variables				
Duration of care (hr)	1.2 (0.9–1.5)	1.1 (0.9–1.5)	1.2 (0.9–1.7)	< 0.01
Intubation status, *n* = 72,056				
By air medical providers, *n* (%)	45,038 (62.4)	39,167 (61.8)	5,504 (68.2)	< 0.01
Before arrival, *n* (%)	27,018 (37.4)	24,227 (38.2)	2,566 (31.8)	
Vasopressors, *n* (%)	17,125 (23.7)	15,131 (23.8)	1,854 (23.0)	0.08

TABLE 2.
Sedation Variables for Mechanically Ventilated Air Medical Transport Patients

Drug	Prehospital Sedation Depth Status			p
	All Subjects (*n* = 72,148)	Deep Sedation (*n* = 63,478)	Light Sedation (*n* = 8,670)	
Fentanyl				
n (%)	36,648 (50.8)	32,276 (50.8)	4,077 (47.0)	0.53
Cumulative dose (μg)	100 (50–150.0)	100 (50–150.0)	100 (50–150.0)	0.47
Prearrival, *n* (%)	14,396 (20.1)	12,833 (20.2)	1,563 (19.4)	0.07
Midazolam				
n (%)	27,788 (38.8)	24,634 (38.8)	3,154 (39.0)	0.67
Cumulative dose (mg)	5.0 (2.5–6.0)	5.0 (2.5–6.0)	5.0 (2.5–6.0)	0.49
Prearrival, *n* (%)	2,255 (3.2)	2,033 (3.2)	222 (2.7)	0.03
Ketamine				
n (%)	27,647 (38.6)	24,547 (38.7)	3,100 (38.4)	0.62
Cumulative dose (mg)	225 (100–400)	225 (100–400)	207 (100–400)	0.91
Prearrival, *n* (%)	3,763 (5.3)	3,415 (5.4)	348 (4.3)	< 0.01
Propofol				
n (%)	9,331 (13.0)	8,229 (13.0)	1,102 (13.6)	0.09
Cumulative dose (mg)	138.6 (72.0–238.5)	138.0 (72.0–236.7)	144 (73.0–240.0)	0.21
Prearrival, *n* (%)	21,318 (29.8)	19,149 (30.2)	2,169 (26.9)	< 0.01
Etomidate				
n (%)	6,018 (8.4)	5,366 (8.5)	652 (7.5)	0.25
Cumulative dose (mg)	24.0 (20.0–30.0)	24.0 (20.0–30.0)	24.0 (20.0–30.0)	0.93
Prearrival, *n* (%)	18,866 (26.1)	17,044 (26.9)	1,622 (18.7)	< 0.01
Lorazepam				
n (%)	5,030 (7.0)	4,450 (7.0)	580 (7.2)	0.57
Cumulative dose (mg)	2.0 (1.0–2.0)	2.0 (1.0–2.0)	2.0 (1.0–2.0)	0.11
Prearrival, *n* (%)	7,451 (10.4)	6,644 (10.5)	807 (10.0)	0.19
Neuromuscular blockers, *n* (%)	45,479 (63.0)	41,113 (64.8)	4,366 (50.4)	< 0.01
Rocuronium, *n* (%)	23,562 (32.7)	21,175 (33.4)	2,387 (27.5)	< 0.01
Cumulative dose (mg)	80.0 (60.0–100.0)	80.0 (60.0–100.0)	85.0 (60.0–100.0)	0.26
Succinylcholine, *n* (%)	19,699 (27.3)	17,869 (28.1)	1,830 (21.1)	< 0.01
Cumulative dose (mg)	150.0 (110.0–200.0)	150.0 (110.0–200.0)	150.0 (110.0–200.0)	0.83
Vecuronium, *n* (%)	7,977 (11.1)	7,327 (11.5)	650 (7.5)	< 0.01
Cumulative dose (mg)	10.0 (7.5–10.0)	10.0 (7.5–10.0)	10.0 (8.0–10.0)	0.14
Sedation scale documented				
Ramsay Sedation Scale, *n* (%)	18,571 (25.7)	15,140 (23.9)	3,431 (39.6)	< 0.01
Ramsay level	5.5 (4.5–6)	6.0 (5.0–6.0)	1.0 (1.0–4.0)	< 0.01
RASS, *n* (%)	10,732 (14.9)	8,397 (13.2)	2,335 (26.9)	< 0.01
RASS level	-4 (-5 to -3)	-4 (-5 to -3)	-1 (-2 to 0)	< 0.01
GCS, *n* (%)	71,241 (98.7)	63,224 (99.6)	8,017 (92.5)	< 0.01
GCS level	4 (3 - 6)	3 (3–5)	7 (4–11)	< 0.01

GCS = Glasgow Coma Scale, RASS = Richmond Agitation-Sedation Scale.

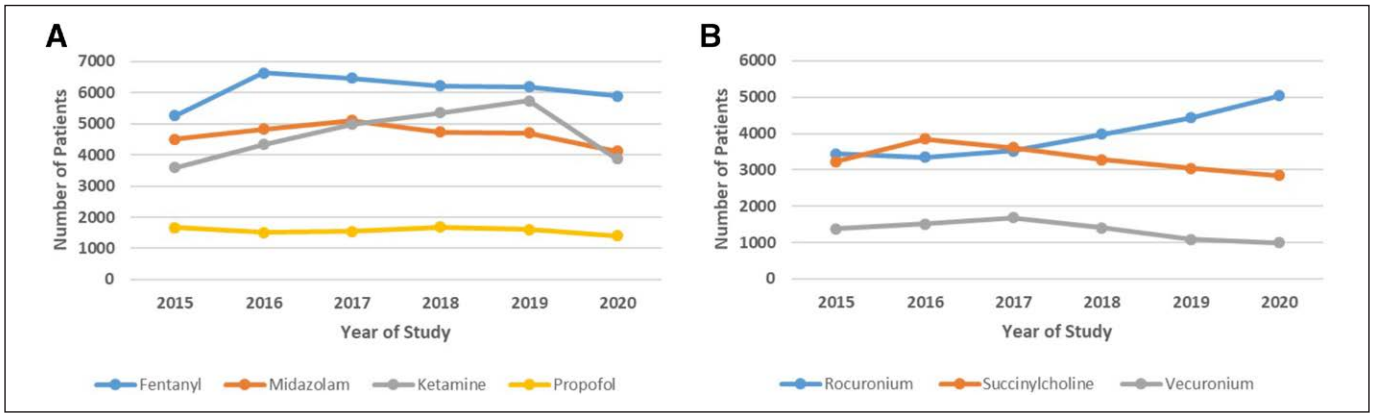

Figure 1. Trends in (**A**) sedation and (**B**) neuromuscular blocker use over time. There was a significant increase in ketamine and rocuronium use over time.

and vecuronium (11.1%). There was significant increase in rocuronium over time (Fig. 1); the use of succinylcholine and vecuronium decreased ($p < 0.01$ for all comparisons between the first and second half of the study).

Depth of Sedation

The Ramsay Sedation Scale was used to document sedation depth in 18,571 patients (25.7%) and RASS in 10,732 (14.9%). Overall, the frequency of deep sedation during air medical transport was 88.0% (n = 63,478), and there were significant differences ($p < 0.01$) in sedation levels between the groups (deep sedation, Ramsay 6 [5–6], RASS –4 [–5 to –3], GCS 3 [3–5]; light sedation, Ramsay 1 [1–4], RASS –1 [–2 to 0], GCS 7 [4–11]) (Table 2). Deeply sedated patients received neuromuscular blockers more frequently and were less likely to have sedation depth documented with validated sedation scales (i.e., Ramsay or RASS). Coma occurred in 42,483 patients (58.9%). **Figure 2** shows an increase in deep sedation and coma during the study period.

Subgroup Analyses

Baseline characteristics and sedation-related variables in the subgroup of patients: 1) after exclusion for potential neurologic injuries and 2) intubated by the air medical crew are in **Supplemental Digital Content 3–6** (http://links.lww.com/CCX/A873). With respect to analgesics, sedatives, neuromuscular blockers, and sedation depth, results for both subgroups were similar to the primary analysis. Overall, the frequency of deep sedation was 85.0% (n = 38,486) in the subgroup after exclusion for neurologic injuries and 87.7% (n = 39,167) in those intubated by the air medical crew.

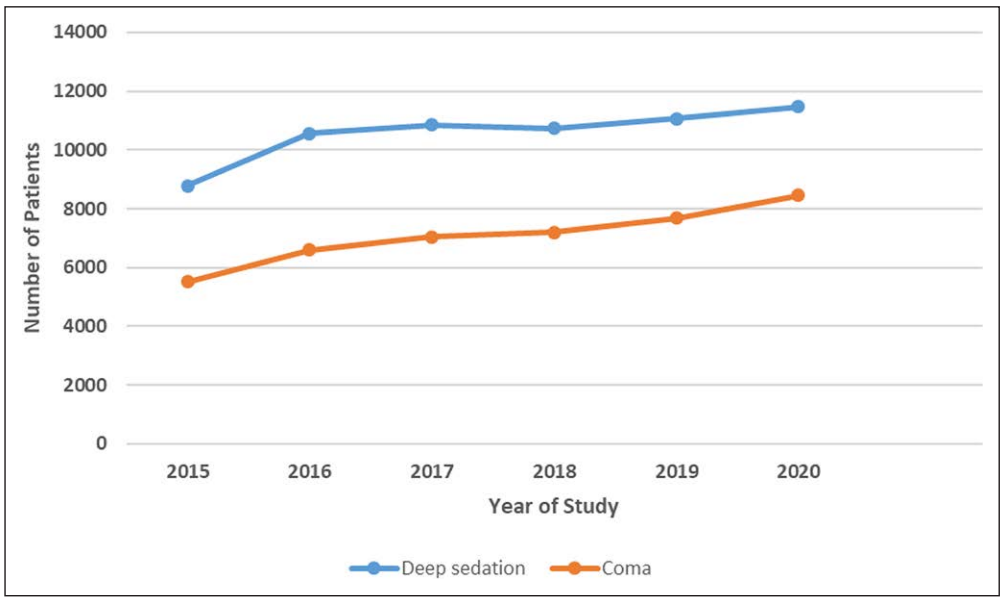

Figure 2. Trends in deep sedation and coma over time. There was a significant difference in deep sedation and coma ($p < 0.01$ for both) between the first and second half of the study period. The total number of patients transported according to year was: 2015 (n = 9,757), 2016 (n = 11,766), 2017 (n = 12,451), 2018 (n = 12,274), 2019 (n = 12,693), and 2020 (n = 13,207).

Predictors of Deep Sedation

Table 3 displays the multivariable logistic regression

TABLE 3.
Multivariable Logistic Regression Analysis With Deep Sedation As the Dependent Variable

Variables	Adjusted OR (95% CI)	SE	*p*
Age	0.99 (0.99–0.99)	0.001	< 0.001
Intubation by air medical crew	0.75 (0.71–0.79)	0.026	< 0.001
Use of validated sedation scale[a]	0.29 (0.27–0.30)	0.025	< 0.001
Longer-acting neuromuscular blocker[b]	1.28 (1.22–1.35)	0.025	< 0.001
Receipt (yes/no) of:			
Succinylcholine	0.98 (0.93–1.02)	0.045	0.574
Propofol	0.95 (0.88–1.01)	0.035	0.114
Fentanyl	0.97 (0.93–1.02)	0.024	0.277
Ketamine	1.01 (0.97–1.07)	0.025	0.592
Midazolam	0.99 (0.94–1.04)	0.026	0.665
Lorazepam	0.99 (0.90–1.08)	0.047	0.790

OR = odds ratio.
[a]Ramsay Sedation Scale or Richmond Agitation-Sedation Scale.
[b]Rocuronium or vecuronium.

model with deep sedation as the dependent variable. After adjusting for covariates, the use of longer-acting neuromuscular blockers (i.e., rocuronium and vecuronium) was an independent predictor of deep sedation (adjusted odds ratio [aOR], 1.28; 95% CI, 1.22–1.35; $p < 0.001$), while use of validated sedation scales was associated with lower odds of deep sedation (aOR, 0.29; 95% CI, 0.27–0.30; $p < 0.001$). These results remained consistent in sensitivity analyses which included: 1) medication dosing and 2) indication for mechanical ventilation in the multivariable model (**Supplemental Digital Content 7**, http://links.lww.com/CCX/A873).

DISCUSSION

Previous work has demonstrated that deep sedation during the most proximal period of acute respiratory failure (i.e., the ED and early ICU period) is common and associated with worse clinical outcomes (8–10, 12, 13). Given this impact, the sheer volume of mechanically ventilated patients treated in the prehospital air medical transport domain, and the lack of sedation-related data, we conducted a large, nationwide cohort study to characterize sedation practices and assess the frequency and predictors of deep sedation. There were several important findings.

Deep sedation (88.0%) was exceedingly common in air medical transport patients with very deep median sedation depth (coma frequency of 58.9%) for the vast majority of patients. Deep sedation and coma also increased over time. Light sedation (vs deep sedation) is recommended in critically ill, mechanically ventilated adults due to over 2 decades of evidence documenting the increased risk of morbidity and mortality associated with deep sedation (1, 7, 11, 23, 24). The earliest periods of respiratory failure may be the most impactful, given data showing: 1) early deep sedation is associated with harm and 2) deep sedation in the ED carries over into the ICU (8–13). Clinical outcome data regarding sedation depth in air medical transport patients is limited to one single-center study which demonstrated longer hospital lengths of stay associated with prehospital deep sedation (16). Recognizing the vast differences between the clinical settings of air medical transport and the hospital, clinical outcome data are urgently needed to assess if the prevailing practice pattern of prehospital deep sedation and coma can be justified.

Modifiable variables were associated with deep sedation in our cohort. To begin, a validated sedation scale (i.e., Ramsay Sedation Scale, RASS, Riker Sedation-Agitation Scale) was used to document sedation depth in a minority of patients, yet GCS was documented for almost the entire cohort. A protocol-driven, goal-oriented delivery of sedation and analgesia, with use of validated sedation scales, will reduce medication requirement and is recommended to achieve on-target

sedation and improve outcomes (7). Congruent with that, in our cohort, significantly more patients in the light sedation group were monitored with the RASS or Ramsay Sedation Scale, and their use was independently associated with a lower odds of deep sedation. This suggests that these scales can be effective prehospital to achieve target sedation goals. Overall though, our data demonstrate that clinical monitoring of sedation depth is uncommon in air medical transport patients.

This may be even more consequential when considering another important finding. Prehospital neuromuscular blockade use is common (63.0%), and significantly more patients that were documented as deeply sedated received neuromuscular blockers. Longer-acting neuromuscular blockers were also independently associated with deep sedation, and rocuronium use increased during the study period. Considering that these findings remained robust to sensitivity analyses, and similar analgesic and sedation doses existed between groups, this suggests that potentially paralyzed patients were being assessed as deeply sedated or comatose, with potential for underlying awareness with paralysis (19, 20). This further stresses the importance of goal-oriented sedation, with clinical monitoring of sedation depth.

Finally, air medical transport patients are sedated primarily with fentanyl, benzodiazepines, and ketamine. Compared with prior work from the ED and ICU, ketamine use was much higher in the prehospital domain, with much higher dosing than that observed in mechanically ventilated ED patients, despite a much shorter duration of care (i.e., approximately 1 vs 5 hr) (12, 13). There is some clinical rationale in support of ketamine, such as bronchodilation, analgesia, and hemodynamics. However, it is also associated with important cardiovascular (i.e., hypertension, hypotension, tachycardia) and neuropsychiatric (i.e., hallucinations, nightmares, delirium, agitation) adverse events (25, 26). There is also a paucity of patient-oriented outcome data regarding ketamine for mechanically ventilated patients, which questions its frequency of use in the prehospital arena, especially at the doses delivered in the current study (26). There was also a comparatively infrequent use of propofol, which has been almost uniformly associated, in over 2 decades of research, with improved outcomes when compared with benzodiazepines (7). These results suggest a need to reevaluate the delivery of analgesia and sedation, including any air medical sedation protocols that may be influencing these results.

Taken as a whole, our data suggest areas for quality improvement in air medical transport sedation practices, including protocol-driven assessments of sedation depth, as well as sedation delivery and neuromuscular blockade. Given the volume of patients receiving mechanical ventilation annually in this arena, even small improvements in this link in the chain of survival could have great impact.

To our knowledge, this is the largest and most robust assessment of prehospital sedation in mechanically ventilated patients to date. However, important limitations of the current study exist. First, we have no patient-centered clinical outcome data and therefore can make no reliable inferences regarding the potential harm of deep sedation in air medical transport patients. Given the volume of data regarding the negative effects of deep sedation in both the ED and ICU, we hypothesize that deep sedation in the prehospital environment is also associated with harm. However, this needs confirmed with further studies and the current work should be considered hypothesis-generating. Second, the study was retrospective and all data were obtained from routine clinical care (i.e., not during the conduct of a clinical trial or research protocol). Given this, along with the heterogeneous and inconsistent use of sedation scales, there is possibility of inaccuracies during routine clinical documentation. It is also difficult to assess if some medications were given exclusively for intubation or during the postintubation period. The fact that the data was consistent across subgroup analyses is reassuring, as is the fact that sedation scales have been shown to be highly reproducible during routine care. It is also important in that it reflects real-world care regarding this patient cohort. Third, while we followed a structured process regarding the adjudication of the cause of respiratory failure, it is likely that some patients were categorized incorrectly or could have satisfied multiple indications. This is important, as the indication for mechanical ventilation could have been the driver of deep sedation or depressed mental status, which is suggested by our sensitivity analysis, as opposed to medications delivered by the air medical crew. Fourth, it is possible that deep sedation was a marker of neurologic status/injury or driven by illness severity. Owing to the

high number of patients in the study, there were several statistical differences in Table 1 data, but clinically overall the two groups were well-matched in important surrogates for illness severity (e.g., vasopressors, vital signs, oxygenation). Finally, it is possible that ICU- and ED-based sedation practices and guidelines should not be applied in flight. Mechanically ventilated patients in the air medical environment pose unique challenges when compared with those in the hospital. This includes loud noises, limited space, and frequent bed-to-bed transfers during a comparatively brief encounter. Also, some transport mechanical ventilators are less responsiveness than those used in the hospital and may be more prone dyssynchrony. Given these factors, deep sedation (with or without paralysis) may be indicated for patient comfort and patient and crew safety while flying. Thus, while we hypothesize that reducing deep sedation and coma is beneficial, an alternative is that deep sedation while flying may be safest. Our current findings demonstrate the need to further evaluate prehospital sedation protocols, and are critically important to receiving clinicians in the ED or ICU so that they are aware that patients are very likely to arrive deeply sedated, and may require sedation interruption upon arrival. Given how impactful sedation is on outcome for mechanically ventilated patients, future studies will need to assess the most appropriate approach regarding sedation delivery in this most proximal period of respiratory failure.

CONCLUSIONS

Deep sedation (and coma) is very common in mechanically ventilated air transport patients and associated with modifiable variables related to the monitoring and delivery of analgesia and sedation. Sedation practices in the prehospital arena and associated clinical outcomes are in need of further investigation.

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