The ED-SED Study: A Multicenter, Prospective Cohort Study of Practice Patterns and Clinical Outcomes Associated With Emergency Department SEDation for Mechanically Ventilated Patients

Brian M. Fuller, MD, MSCI[1,2]; Brian W. Roberts, MD[3]; Nicholas M. Mohr, MD, MS[4,5]; William A. Knight IV, MD[6,7,8]; Opeolu Adeoye, MD[6,8]; Ryan D. Pappal, BS, BA, NRP[9]; Stacy Marshall, MD[3]; Robert Alunday, MD[10]; Matthew Dettmer, MD[11]; Munish Goyal, MD[12]; Colin Gibson, MS[13]; Brian J. Levine, MD[14]; Jayna M. Gardner-Gray, MD[15,16]; Jarrod Mosier, MD[17,18]; James Dargin, MD[19]; Fraser Mackay, MD[19,20]; Nicholas J. Johnson, MD[21,22]; Sharukh Lokhandwala, MD[22]; Catherine L. Hough, MD, MS[22]; Joseph E. Tonna, MD[23,24]; Rachel Tsolinas, BA[25]; Frederick Lin, MD[26]; Zaffer A. Qasim, MBBS[26]; Carrie E. Harvey, MD[27]; Benjamin Bassin, MD[27]; Robert J. Stephens, MD, MSCI[2]; Yan Yan, MD, MA, MHS, PhD[28,29]; Christopher R. Carpenter, MD, MSc, FACEP, FAAEM[2]; Marin H. Kollef, MD[30]; Michael S. Avidan, MBBCh[31]

[1]Division of Critical Care, Department of Anesthesiology, Washington University School of Medicine in St. Louis, St. Louis, MO.

[2]Department of Emergency Medicine, Washington University School of Medicine in St. Louis, St. Louis, MO.

[3]Department of Emergency Medicine, Cooper University Hospital, Cooper Medical School of Rowan University, Camden, NJ.

[4]Department of Emergency Medicine, Roy J. and Lucille A. Carver College of Medicine, University of Iowa, Iowa City, IA.

[5]Division of Critical Care, Department of Anesthesiology, Roy J. and Lucille A. Carver College of Medicine, University of Iowa, Iowa City, IA.

[6]Division of Critical Care, Department of Emergency Medicine, University of Cincinnati Medical Center, Cincinnati, OH.

[7]Department of Neurology, University of Cincinnati Medical Center, Cincinnati, OH.

[8]Department of Neurosurgery, University of Cincinnati Medical Center, Cincinnati, OH.

[9]Washington University School of Medicine in St. Louis, St. Louis, MO.

[10]Division of Critical Care, Department of Emergency Medicine, University of New Mexico, Albuquerque, NM.

[11]Emergency Services and Respiratory Institutes, Cleveland Clinic Foundation, Cleveland, OH.

[12]Department of Emergency Medicine, MedStar Washington Hospital Center, Washington, DC.

[13]Georgetown University School of Medicine, Washington, DC.

[14]Department of Emergency Medicine, Christiana Care Health System, Newark, DE.

[15]Department of Emergency Medicine, Henry Ford Health System, Detroit, MI.

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[16]Division of Pulmonary and Critical Care Medicine, Department of Medicine, Henry Ford Health System, Detroit, MI.

[17]Department of Emergency Medicine, University of Arizona College of Medicine, Tucson, AZ.

[18]Division of Pulmonary, Allergy, Critical Care and Sleep, Department of Medicine, University of Arizona College of Medicine, Tucson, AZ.

[19]Pulmonary and Critical Care Medicine, Lahey Hospital & Medical Center, Burlington, MA.

[20]Emergency Medicine, Lahey Hospital & Medical Center, Burlington, MA.

[21]Department of Emergency Medicine, University of Washington/Harborview Medical Center, Seattle, WA.

[22]Division of Pulmonary, Critical Care, and Sleep Medicine, Department of Medicine, University of Washington/Harborview Medical Center, Seattle, WA.

[23]Division of Cardiothoracic Surgery, Department of Surgery, University of Utah Health, Salt Lake City, UT.

[24]Division of Emergency Medicine, Department of Surgery, University of Utah Health, Salt Lake City, UT.

[25]University of Utah School of Medicine, Salt Lake City, UT.

[26]Department of Emergency Medicine, University of Pennsylvania, Philadelphia, PA.

[27]Department of Emergency Medicine, University of Michigan Medical School, Ann Arbor, MI.

[28]Division of Public Health Sciences, Department of Surgery, Washington University School of Medicine, St. Louis, MO.

[29]Division of Biostatistics, Washington University School of Medicine, St. Louis, MO.

[30]Division of Pulmonary and Critical Care Medicine, Department of Medicine, Washington University School of Medicine in St. Louis, St. Louis, MO.

[31]Department of Anesthesiology, Washington University School of Medicine in St. Louis, St. Louis, MO.

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For information regarding this article, E-mail: fullerb@wustl.edu

Objectives: To characterize emergency department sedation practices in mechanically ventilated patients, and test the hypothesis that deep sedation in the emergency department is associated with worse outcomes.

Design: Multicenter, prospective cohort study.

Setting: The emergency department and ICUs of 15 medical centers.

Patients: Mechanically ventilated adult emergency department patients.

Interventions: None.

Measurements and Main Results: All data involving sedation (medications, monitoring) were recorded. Deep sedation was defined as Richmond Agitation-Sedation Scale of −3 to −5 or Sedation-Agitation Scale of 2 or 1. A total of 324 patients were studied. Emergency department deep sedation was observed in 171 patients (52.8%), and was associated with a higher frequency of deep sedation in the ICU on day 1 (53.8% vs 20.3%; $p < 0.001$) and day 2 (33.3% vs 16.9%; $p = 0.001$), when compared to light sedation. Mean (SD) ventilator-free days were 18.1 (10.8) in the emergency department deep sedation group compared to 20.0 (9.8) in the light sedation group (mean difference, 1.9; 95% CI, −0.40 to 4.13). Similar results according to emergency department sedation depth existed for ICU-free days (mean difference, 1.6; 95% CI, −0.54 to 3.83) and hospital-free days (mean difference, 2.3; 95% CI, 0.26–4.32). Mortality was 21.1% in the deep sedation group and 17.0% in the light sedation group (between-group difference, 4.1%; odds ratio, 1.30; 0.74–2.28). The occurrence rate of acute brain dysfunction (delirium and coma) was 68.4% in the deep sedation group and 55.6% in the light sedation group (between-group difference, 12.8%; odds ratio, 1.73; 1.10–2.73).

Conclusions: Early deep sedation in the emergency department is common, carries over into the ICU, and may be associated with worse outcomes. Sedation practice in the emergency department and its association with clinical outcomes is in need of further investigation. (*Crit Care Med* 2019; XX:00–00)

Key Words: emergency department; mechanical ventilation; sedation

The provision of sedation is almost universal in mechanically ventilated patients and is a modifiable variable related to clinical outcomes during critical illness. Evidence demonstrates that efforts to decrease sedation in the ICU improve outcome (1, 2). However, the majority of data come from randomized controlled trials which enrolled patients at 48–96 hours after intubation, or from observational data from an entire ICU stay (3–6). Recently, prospective, observational data showed that deep sedation during the first 48 hours of mechanical ventilation was associated with worse short- and long-term outcomes (7, 8). A systematic review and meta-analysis also showed harm associated with early deep sedation in the ICU (9). Despite this, up to 70% of ventilated patients arrive to the ICU deeply sedated, suggesting the pre-ICU environment could play a role in the genesis of deep sedation (8).

The initial management of mechanical ventilation and sedation occurs in the emergency department (ED) for approximately 250,000 patients annually in the United States (10). Despite this, the potential impact of ED-based sedation on clinical outcome has received little attention. In a prior investigation, ED sedation practices were discordant with guideline recommendations, including a high frequency of deep sedation and benzodiazepine use (11–13). Deep sedation in the ED was associated with increased mortality, longer ventilation duration, and longer lengths of stay (11). However, this was a single-center, retrospective study; it is therefore unknown if the results are generalizable. As a result, a knowledge gap persists regarding ED sedation practices and potential impact on outcome.

Given the outcome data associated with early sedation in the ICU, and the initial ED-based data that exists, the ED SEDation (ED-SED) study was conducted to 1) further characterize ED sedation practices across multiple centers and 2) test the hypothesis that deep sedation in the ED is associated with worse clinical outcomes.

MATERIALS AND METHODS

Study Design

This was a multicenter ($n = 15$), prospective cohort study, and reported in accordance with the Strengthening Reporting of Observational Studies in Epidemiology statement. (**Supplemental Table 1**, Supplemental Digital Content 1, http://links.lww.com/CCM/E814). The original design called for each of 18 sites to enroll for a 30-day period. Protocol initiation varied between institutions resulting in an enrollment period between June 1, 2018, and August 31, 2018. When three centers could not participate, enrollment was extended beyond 1 month in three sites to achieve the desired sample size and mirror accrual which would have occurred had the three original centers participated.

The study was conducted with waiver of consent. Approval from the Human Research Protection Office was obtained at each center prior to data collection. A detailed description of the study has been published (14).

Participants

All consecutive mechanically ventilated adult ED patients were screened. Inclusion criterion: receipt of mechanical ventilation via an endotracheal tube in the ED. Exclusion criteria: 1) death or discontinuation of mechanical ventilation within 24 hours; 2) transfer to another hospital; 3) neurologic injury (i.e., acute cerebrovascular accident, traumatic brain injury, status epilepticus, sudden cardiac arrest); and 4) chronic/home ventilation.

Assessments and Outcome Measures

Baseline data included demographics, comorbidities, vital signs, and laboratory variables. ED processes of care included length of stay, transfusion, antibiotic administration, central venous catheter placement, and vasopressor infusion.

Sedation-related data in the ED included neuromuscular blockers and induction agents for intubation. Subsequent medications related to ED analgesia and sedation included opiates, benzodiazepines, propofol, ketamine, dexmedetomidine, etomidate, haloperidol, quetiapine, and neuromuscular blockers.

Sedation depth in the ED was recorded. Given the pragmatic intent of the study and equivalence between scales, sedation depth was monitored according to standard operating procedures at each site (15). This included the Richmond Agitation-Sedation Scale (RASS; deep sedation defined as score of –3 to –5), or the Riker Sedation-Agitation Scale (SAS; deep sedation defined as score of 2 or 1) (15). When more than one sedation depth per patient was documented, the median value was used. In patients for whom no ED sedation depth was documented, the first ICU sedation depth was used as a surrogate, congruent with prior approach (11). We anticipated that some EDs may not routinely monitor sedation depth for mechanically ventilated patients, as ED-based sedation has not received clinical or research focus. In that situation, a documented Glasgow Coma Scale (GCS) was used as a surrogate for sedation depth (≤ 9 defined as deep sedation) (16).

Agents administered for analgesia and sedation during the first 48 hours of ICU admission were collected. Patients were followed until hospital day 28 or death. The primary outcome was ventilator-free days. Secondary outcomes included acute brain dysfunction during the first 48 hours after admission, mortality, ICU-, and hospital-free days. Acute brain dysfunction is a composite of delirium and coma (17). Delirium was assessed with the Confusion Assessment Method for the ICU per institutional protocols. Coma was defined as being unresponsive or responsive only to physical stimulus (i.e., RASS –4 or –5) with every measurement of sedation depth (17, 18).

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.

The primary analysis examined ventilator-free days as a function of ED sedation depth. A multivariable linear regression model was constructed to adjust for potentially confounding variables using backward elimination. A priori baseline characteristics with known prognostic significance for mortality in ED mechanically ventilated patients were purposefully selected for model inclusion (age, indication for mechanical ventilation, tidal volume, illness severity). Other clinically relevant and biologically plausible variables significant in univariate analysis at a p value of less than 0.10 level were also included in the model. 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.

From prior work regarding early deep sedation in the ICU and ED, we assumed a difference in mean ventilator-free days of 2.5 between groups. For 80% power and α of 0.05, we estimated a sample size of 324 patients (162 per group) would be required (8, 9, 11, 14).

RESULTS

Study Population

A total of 15 centers participated, and details regarding each are in **Supplemental Table 2** (Supplemental Digital Content 2, http://links.lww.com/CCM/E815). One-thousand ninety-four patients were assessed for inclusion and 324 comprised the final population (**Fig. 1**). Baseline characteristics are in **Table 1**.

Medications Administered

Medications used for intubation were recorded separately from post-intubation sedation (**Supplemental Table 3**, Supplemental Digital Content 3, http://links.lww.com/CCM/E816).

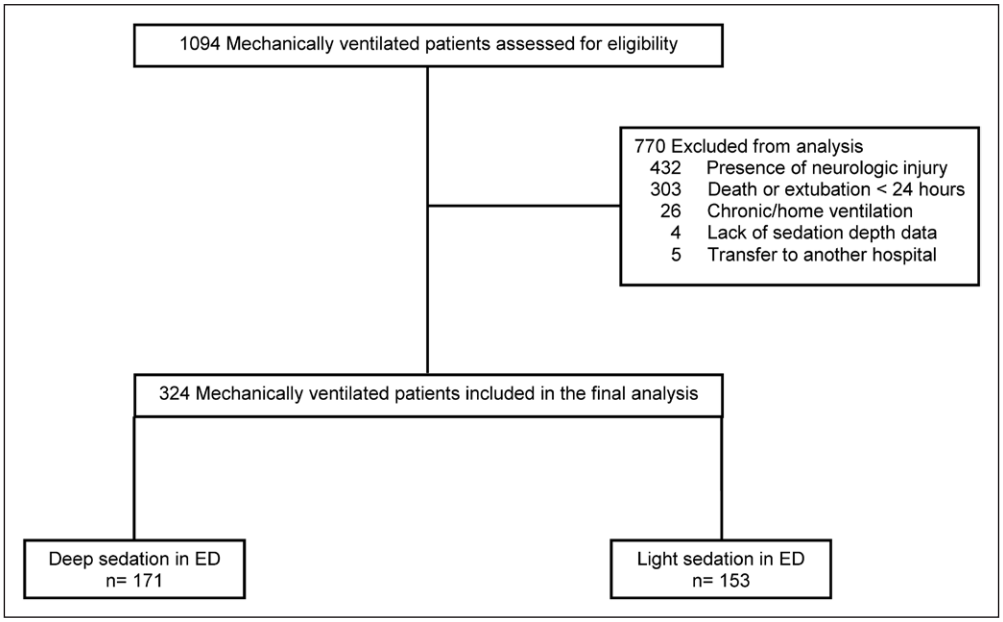

Figure 1. Flow diagram of patients in the study. ED = emergency department.

Sedation-related variables are in **Table 2**. The most commonly used agents were fentanyl (64.5%), propofol (65.7%), and midazolam (23.8%). Variability existed in dosing and frequency of use at each site (e.g., midazolam use ranged from 0% to 64.3%). Ninety-two patients (28.4%) were given no analgesia, 69 (21.3%) received no sedation, and 35 (10.8%) received neither sedation nor analgesia in the ED. Two patients receiving no analgesia or sedation were given long-acting neuromuscular blockade after intubation (RASS of 1 and –4, respectively). Self-extubation occurred in two patients (0.62%).

Sedation variables in the ICU during the first 48 hours of admission are presented in **Supplemental Table 4** (Supplemental Digital Content 4, http://links.lww.com/CCM/E817).

Depth of Sedation

The occurrence rate of deep sedation in the ED was 52.8% ($n = 171$), and there were significant differences ($p < 0.001$) in sedation levels between the two groups (deep sedation: RASS –4 [–5 to –3] and SAS 1 [1–2]; light sedation: RASS –1 [–2 to 1] and SAS 3 [3–4]) (Table 2). Deeply sedated patients received higher cumulative doses of fentanyl, propofol, and midazolam, with statistically significant differences existing for propofol.

In the deep sedation group, 92 (75%) and 54 (69%) patients were deeply sedated on ICU day 1 and 2, respectively. In contrast, in the light sedation group, 31 (20.3%) and 24 (16.9%) patients were deeply sedated on ICU day 1 and 2, respectively. Overall, patients exposed to deep sedation in the ED had higher frequency of deep sedation on ICU day 1 (53.8% ED-deep sedation vs 20.3% ED-light sedation; $p < 0.001$) and day 2 (33.3% ED-deep sedation vs 16.9% ED-light sedation; $p = 0.001$) (Supplemental Table 4, Supplemental Digital Content 4, http://links.lww.com/CCM/E817). The median RASS during the first 24 hours in the ICU was –3 (–4 to –2) in deeply sedated ED patients compared with –1 (–2 to –1) in those lightly sedated in the ED ($p < 0.001$). When compared with light sedation, deep sedation in the ED persisted such that significant differences in sedation depth existed for almost every hour during the first ICU day (**Fig. 2**). The median RASS during the second 24 hours in the ICU was –2 (–4 to 0) in deeply sedated ED patients compared with –1 (–2 to 0) in those lightly sedated ($p = 0.02$).

Clinical Outcomes

Clinical outcomes according to ED sedation depth are in **Table 3**. There was an unadjusted mean difference in ventilator-free days of 1.9 (95% CI, –0.40 to 4.13; $p = 0.11$) between groups. After adjusting for confounders, multivariable linear regression analysis demonstrated illness severity (Sequential Organ Failure Assessment [SOFA] score) was associated with fewer ventilator-free days (**Supplemental Table 5**, Supplemental Digital Content 5, http://links.lww.com/CCM/E818).

Similar results according to ED sedation depth existed for ICU-free days (unadjusted mean difference, 1.6; 95% CI, –0.54 to 3.83; $p = 0.14$) and hospital-free days (unadjusted mean difference, 2.3; 95% CI, 0.26–4.32; $p = 0.03$). Mortality was 21.1% in the deep sedation group and 17.0% in the light sedation group (between-group difference, 4.1%; odds ratio [OR], 1.30; 0.74–2.28; $p = 0.35$).

The occurrence rate of acute brain dysfunction was 68.4% in the deep sedation group and 55.6% in the light sedation group (between-group difference, 12.8%; OR, 1.73; 1.10–2.73; $p = 0.02$). Given this, a post hoc logistic regression model was conducted to examine the association between ED-deep sedation and acute brain dysfunction. The effect estimate (adjusted OR [95% CI]) of the association between ED-deep sedation and acute brain dysfunction during the first 48 hours in the ICU was 2.15 (1.18–3.92; $p = 0.01$) (**Supplemental Table 6**, Supplemental Digital Content 6, http://links.lww.com/CCM/E819).

DISCUSSION

Key Findings

Prior work demonstrated a high frequency of deep sedation in the ED, which was negatively associated with outcomes (11). Given the lack of ED-based sedation data, we conducted a multicenter, prospective cohort study to further characterize ED sedation practices and assess relationships between ED sedation depth and outcomes across multiple centers. We found that deep sedation was delivered to over half of mechanically

TABLE 1. Characteristics of Mechanically Ventilated Emergency Department Patients

	ED Sedation Depth Status			
Baseline Characteristics	**All Subjects (*n* = 324)**	**Deep Sedation (*n* = 171)**	**Light Sedation (*n* = 153)**	***p***
Age (yr)	56.1 (18.2)	56.2 (17.7)	56.2 (19.4)	0.99
Male, *n* (%)	197 (60.8)	106 (62.0)	91 (59.5)	0.64
Race, *n* (%)				
White	188 (58.0)	92 (53.8)	96 (62.7)	0.08
African-American	93 (28.7)	54 (31.6)	39 (25.5)	0.23
Hispanic	22 (6.8)	13 (7.6)	9 (5.9)	0.54
Asian	5 (1.5)	3 (1.8)	2 (1.3)	0.74
Native American	5 (1.5)	1 (0.3)	4 (1.2)	0.14
Other	11 (3.4)	8 (4.7)	3 (2.0)	0.08
Comorbidities, *n* (%)				
Diabetes mellitus	80 (24.7)	51 (29.8)	29 (19.0)	0.02
Cirrhosis	18 (5.6)	11 (6.4)	7 (4.6)	0.47
CHF	52 (16.0)	22 (12.9)	30 (19.6)	0.10
COPD	77 (23.8)	32 (18.7)	45 (29.4)	0.02
Malignancy	42 (13.0)	19 (11.1)	23 (15.0)	0.29
Psychiatric[a]	86 (26.5)	41 (24.0)	45 (29.4)	0.27
Mean arterial pressure	96.0 (79.0–112.0)	95.7 (78.3–112.3)	96.7 (80.0–111.3)	0.76
Lactate (mmol/L), *n* = 283	2.6 (1.4–4.6)	2.8 (1.5–4.6)	2.5 (1.4–4.6)	0.24
Creatinine (mg/dL), *n* = 316	1.1 (0.8–1.6)	1.2 (0.9–1.7)	1.1 (0.8–1.4)	0.04
Platelet (10^9/L), *n* = 321	234 (105.9)	229 (102.1)	241 (110.0)	0.34
Sequential Organ Failure Assessment score[b]	4.2 (3.3)	4.5 (3.4)	3.8 (3.1)	0.07
Reason for mechanical ventilation, *n* (%)				
Sepsis	55 (17.0)	27 (15.8)	28 (18.3)	0.55
Trauma	65 (20.1)	36 (21.1)	29 (19.0)	0.64
COPD	31 (9.6)	12 (7.0)	19 (12.4)	0.10
Drug overdose	31 (9.6)	20 (11.7)	11 (7.2)	0.17
CHF/pulmonary edema	16 (4.9)	5 (1.5)	11 (3.4)	0.08
Asthma	6 (1.9)	2 (0.6)	4 (1.2)	0.34
Other	120 (37.0)	69 (40.4)	51 (33.3)	0.19
Tidal volume (mL/kg predicted body weight)	6.9 (6.2–7.8)	6.9 (6.2–7.9)	6.8 (6.1–7.8)	0.81
Positive end-expiratory pressure (cm H_2O)	5.0 (5.0–8.0)	5.0 (5.0–8.0)	5.0 (5.0–8.0)	0.50
Process of care variables				
ED length of stay (hr)	4.8 (2.8–7.4)	4.3 (2.9–7.7)	5.1 (2.8–7.2)	0.34
Blood product transfusion, *n* (%)	41 (12.7)	20 (11.7)	21 (13.7)	0.58
Central venous catheter, *n* (%)	65 (20.1)	40 (23.4)	25 (16.3)	0.11
Antibiotics for infection, *n* (%)	152 (46.9)	73 (42.7)	79 (51.6)	0.09
Vasopressor infusion, *n* (%)	88 (27.2)	53 (31.0)	35 (22.9)	0.10

CHF = congestive heart failure, COPD = chronic obstructive pulmonary disease, ED = emergency department.

[a]Schizophrenia, bipolar disorder, major depression, anxiety.

[b]Modified score, which excludes Glasgow Coma Scale.

Continuous variables are reported as mean (SD) and median (interquartile range).

TABLE 2. Sedation Variables in the Emergency Department

	ED Sedation Depth Status			
Drug	**All Subjects *n* = 324**	**Deep sedation (*n* = 171)**	**Light sedation (*n* = 153)**	***p***
Fentanyl				
n (%)	209 (64.5)	105 (61.4)	104 (68.0)	0.22
Cumulative dose (μg)	200 (100–325.0)	200 (100–350.0)	188 (100–300.0)	0.64
Weight-based dose (μg/kg)	2.2 (1.1–4.6)	2.3 (1.2–4.7)	2.2 (1.1–4.5)	0.73
Dose (μg)/hr ED ventilation time	67.6 (39.0–113.5)	71.2 (39.8–112.1)	65.2 (33.9–119.4)	0.52
Propofol				
n (%)	213 (65.7)	108 (63.2)	105 (68.6)	0.30
Cumulative dose (mg)	315.0 (151.2–659.2)	334.5 (163.6–744.7)	252.0 (111.6–598.8)	0.04
Weight-based dose (mg/kg)	3.6 (1.8–8.1)	4.2 (2.4–8.4)	3.1 (1.2–6.7)	0.02
Dose (mg)/hr ED ventilation time	101.6 (55.2–195.6)	117.0 (67.8–215.0)	91.4 (41.3–151.6)	0.03
Midazolam				
n (%)	77 (23.8)	38 (22.2)	39 (25.5)	0.49
Cumulative dose (mg)	5.0 (2.0–7.0)	5.0 (2.0–8.0)	4.0 (2.0–6.0)	0.80
Weight-based dose (mg/kg)	0.05 (0.03–0.09)	0.06 (0.02–0.11)	0.05 (0.03–0.08)	0.88
Dose (mg)/hr ED ventilation time	1.3 (0.69–2.75)	1.2 (0.66–2.8)	1.4 (0.70–2.7)	0.99
Ketamine[a]				
n (%)	15 (4.6)	8 (4.7)	7 (4.6)	0.97
Cumulative dose (mg)	100 (50.0–100)	75 (40.0–175)	100 (85.0–100)	0.54
Weight-based dose (mg/kg)	1.1 (0.69–1.4)	0.70 (0.57–1.7)	1.2 (1.0–1.4)	0.40
Lorazepam				
n (%)	35 (10.8)	14 (8.2)	21 (13.7)	0.11
Cumulative dose (mg)	3.0 (2.0–6.0)	2.0 (2.0–4.0)	4.0 (1.0–9.5)	0.49
Weight-based dose (mg/kg)	0.03 (0.02–0.08)	0.03 (0.03–0.05)	0.04 (0.02–0.12)	0.63
Etomidate[a]				
n (%)	5 (1.5)	2 (1.2)	3 (2.0)	0.56
Cumulative dose (mg)	24.0 (20.0–36.0)	20.0 (20.0–NA)	30.0 (24.0–30.0)	0.20
Weight-based dose (mg/kg)	0.28 (0.17–0.36)	0.17 (0.17–NA)	0.34 (0.28–0.34)	0.20
Morphine				
n (%)	7 (2.2)	1 (0.6)	6 (3.9)	0.04
Cumulative dose (mg)	8.0 (4.0–8.0)	8.0 (NA)	6.0 (3.5–9.0)	1.0
Weight-based dose (mg/kg)	0.08 (0.05–0.12)	0.12 (NA)	0.07 (0.04–0.13)	0.57
Hydromorphone				
n (%)	21 (6.5)	9 (5.3)	12 (7.8)	0.35
Cumulative dose (mg)	2.0 (1.0–10.5)	2.0 (1.5–8.5)	3.0 (1.0–10.8)	0.86
Weight-based dose (mg/kg)	0.03 (0.02–0.15)	0.03 (0.02–0.18)	0.05 (0.02–0.16)	0.81

(*Continued*)

TABLE 2. (*Continued*). Sedation Variables in the Emergency Department

	ED Sedation Depth Status			
Drug	All Subjects *n* = 324	Deep sedation (*n* = 171)	Light sedation (*n* = 153)	*p*
Diazepam				
n (%)	1 (0.3)	0 (0.0)	1 (0.7)	0.29
Cumulative dose (mg)	30 (NA)	NA	30 (NA)	NA
Weight-based dose (mg/kg)	0.30 (NA)	NA	0.30 (NA)	NA
Haloperidol				
n (%)	6 (1.9)	4 (2.3)	2 (1.3)	0.49
Cumulative dose (mg)	5.0 (4.0–7.8)	5.0 (2.0–8.8)	6.0 (5.0–NA)	0.80
Weight-based dose (mg/kg)	0.06 (0.05–0.12)	0.06 (0.03–0.10)	0.09 (0.06–NA)	0.53
No analgesia in ED, *n* (%)	92 (28.4)	55 (32.2)	37 (24.2)	0.11
No sedation in ED, *n* (%)	69 (21.3)	39 (22.8)	30 (19.6)	0.48
No analgesia or sedation in ED, *n* (%)	35 (10.8)	20 (11.7)	15 (9.8)	0.58
Neuromuscular blocker, *n* (%)	29 (9.0)	17 (9.9)	12 (7.8)	0.51
Sedation tool used				
RASS, *n* (%)	253 (78.1)	138 (80.7)	115 (75.2)	0.23
ED RASS level	−3 (−4 to −1)	−4 (−5 to −3)	−1 (−2 to 1)	< 0.001
SAS, *n* (%)	50 (15.4)	19 (11.1)	31 (20.3)	0.03
ED SAS level	3 (2–3)	1 (1–2)	3 (3–4)	< 0.001
GCS, *n* (%)	21 (6.5)	14 (8.2)	7 (4.6)	0.19
ED GCS level	7 (4–13)	6 (3–7)	14 (11–15)	< 0.001

ED = emergency department, GCS = Glasgow Coma Scale, NA = not applicable, RASS = Richmond Agitation-Sedation Scale, SAS = Riker Sedation-Agitation Scale.

[a]These are doses separate from those given for intubation.

ventilated patients, with significant carryover of sedation depth into the early phase of ICU care. In addition, our descriptive data related to delivery of sedation in the ED suggest areas in need for quality improvement.

Comparison With Previous Investigations

The ED-SED study contributes novel data and addresses some weaknesses related to prior early sedation research. It is only the second investigation into sedation practices in the ED and the only ED-based sedation study to date that is prospective and multicenter (9, 11). It also highlights the influence that ED sedation depth may hold over early sedation depth in the ICU and its potential impact on outcome.

The majority of sedation research has ignored the most proximal time period of mechanical ventilation, allowing for pre-trial sedation depth and sedative delivery to go unchecked (19). Deep sedation during the first 48 hours of mechanical ventilation and its impact on outcome was recently demonstrated in a systematic review and meta-analysis which included two small randomized trials and seven cohort studies (9). The occurrence rate of early deep sedation was 34.7% (range, 19.6–80.6%) and was associated with higher mortality, ventilator duration, and lengths of stay. Distinct from that analysis, patients in the current study were followed prospectively from the time of intubation, allowing both an assessment of the impact of ED sedation depth on outcome and subsequent care. The ED was the origin of deep sedation in greater than 70% of the patients deeply sedated during the first 2 ICU days. In contrast, less than 20% of patients with light sedation in the ED were subsequently deeply sedated in the ICU. In addition to a higher frequency of deep sedation during the first 2 ICU days among patients deeply sedated in the ED, there was persistent separation in hourly ICU sedation depth between groups. These data suggest that carryover of sedation into the ICU is significant, and ED-based sedation could play a vital role in preventing iatrogenic coma and should receive increased attention clinically and in future research.

With respect to clinical outcomes, previous data have demonstrated negative consequences associated with deep sedation in the early ICU period and a single-center ED-based study (7–9, 11). The only statistically significant association between

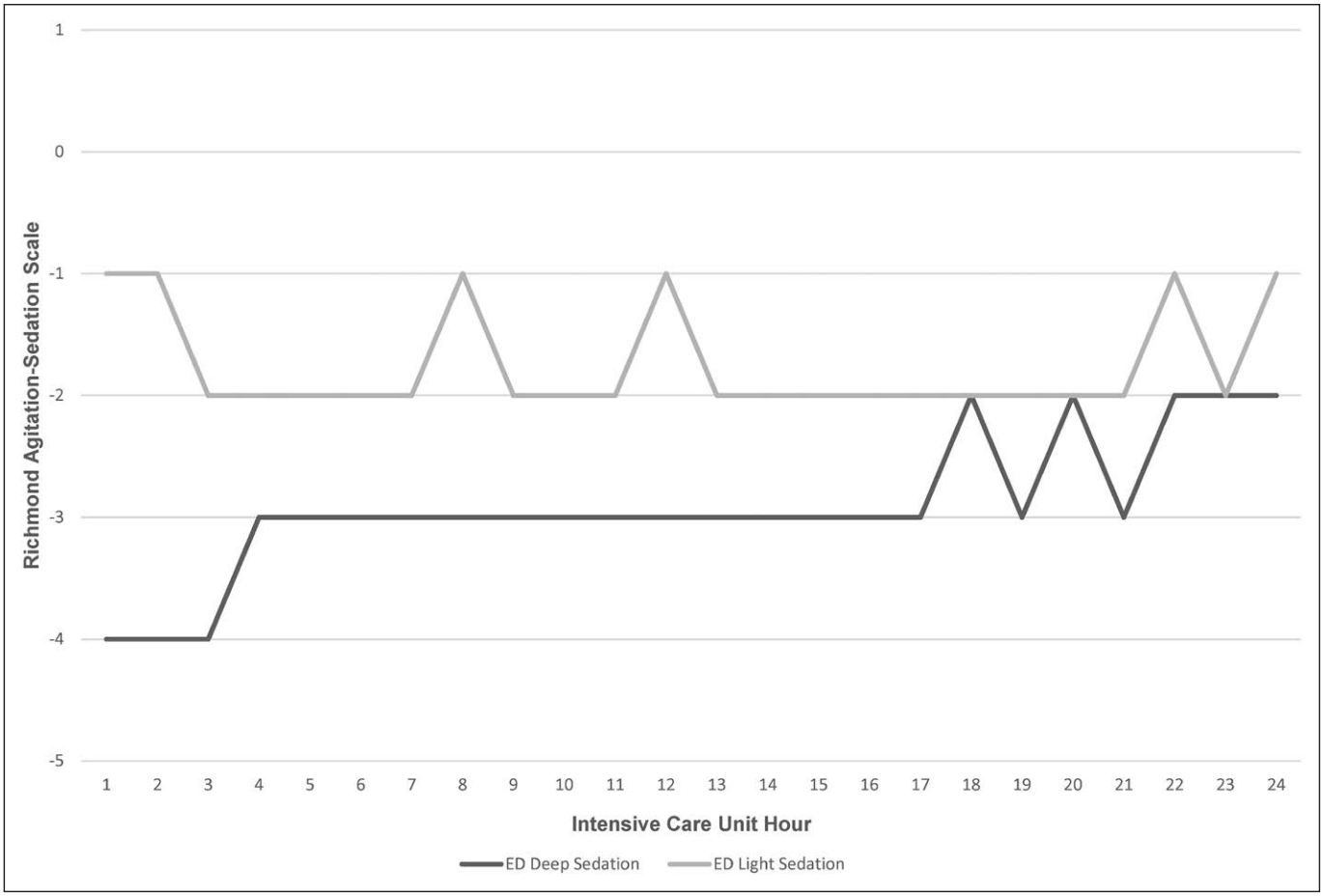

Figure 2. Hourly differences in Richmond Agitation-Sedation Scale during the first 24 hr in the ICU. When compared with light sedation, deep sedation in the emergency department persisted such that statistically significant differences in sedation depth existed for almost every hour during the first ICU day.

ED sedation depth and outcome was related to acute brain dysfunction. There was no difference between groups with respect to other clinical outcomes. However, clinically important effect sizes existed between groups and are congruent with prior research examining light versus deep sedation (4, 8, 16, 17, 20, 21). These effect estimates are imprecise and should be interpreted with caution at this time.

Mechanically ventilated ED patients were sedated primarily with fentanyl, propofol, and midazolam, consistent with prior single-center data and that from the ICU (8, 11, 15, 22). A protocol-driven approach to delivery of analgesia and sedation in the ICU is common and associated with a reduction in medication requirements, ventilator duration, and lengths of stay (12). In the current study, a higher propofol dose was observed in the deep sedation group and only six of 15 sites employed sedation protocols in the ED. There was wide practice variability with respect to medication use (i.e., midazolam in > 60% of patients in one site) and delivered doses across study sites. Further, no analgesia was given to 28.4% of patients, and 10.8% received no sedation or analgesia. Our descriptive data suggest areas for quality improvement related to sedation for mechanically ventilated ED patients, including protocolized assessments of pain and sedation depth, as well as sedation delivery, in order to reduce the unnecessary practice variability which seems to exist in the post-intubation sedation in the ED.

Taken as a whole, our data suggest that sedation practices in the ED: 1) influence sedation depth in the ICU; 2) have considerable practice variability (e.g., lack of goal-directed sedation or monitoring of sedation depth); and 3) may influence clinical outcome. Given the volume of patients receiving mechanical ventilation annually in the United States, even a small improvement in care could have great impact.

Limitations

The current study addresses some weaknesses related to prior ED-based sedation research, as it is prospective and multicenter. However, multiple limitations persist. The design allows us to only comment on associations and not causal effect. In calculating the sample size of 324 patients, we estimated a difference of 2.5 ventilator-free days between the two groups. After examining the impact of deep sedation in the ED across multiple centers for the first time, we saw an effect size difference of 1.9 ventilator-free days between the two groups, which did not achieve statistical significance. Therefore, our effect estimates were imprecise, yet the effect sizes were clinically meaningful and suggest this is an area in need of further work. Sedation depth was recorded with multiple sedation scales in the ED, and not at all for 24 patients. This required us to use GCS in these patients, which is an inconsistent surrogate for validated sedation scales. Although this may have

TABLE 3. Unadjusted Analysis of Clinical Outcomes According to Emergency Department Sedation Depth

Outcome	Deep Sedation ($n = 171$)	Light Sedation ($n = 153$)	Unadjusted OR or Between-Group Difference (95% CI)	*p*
Ventilator-free days	18.1 (10.8)	20.0 (9.8)	1.9 (−0.40 to 4.13)	0.107
ICU-free days	16.3 (10.5)	17.9 (9.4)	1.6 (−0.54 to 3.83)	0.139
Hospital-free days	11.8 (9.6)	14.1 (8.9)	2.3 (0.26–4.32)	0.027
Mortality, *n* (%)	36 (21.1)	26 (17.0)	1.30 (0.74–2.28)	0.354
Acute brain dysfunction, *n* (%)	117 (68.4)	85 (55.6)	1.73 (1.10–2.73)	0.017
Delirium	106 (62.0)	84 (54.9)	1.34 (0.86–2.09)	0.196
Coma	16 (9.4)	3 (2.0)	5.12 (1.47–18.08)	0.005

OR = odds ratio.

Ventilator-, ICU-, and hospital-free days are indexed to study day 28. Mortality refers to all cause in-hospital mortality, censured at day 28. Acute brain dysfunction is a composite outcome comprising delirium and coma and was assessed over the first 48 hr in the ICU. Delirium was assessed with the Confusion Assessment Method for the ICU, and coma was defined as being unresponsive or responsive to only physical stimulus (i.e., Richmond Agitation-Sedation Scale −4 or −5) with every measurement of sedation depth.

introduced heterogeneity, it reflects real-world practice and provides valuable information to tell the story regarding ED sedation. We did not assess the entire safety profile of light sedation in the ED and only tracked self-extubation. Based on these preliminary results, it seems that light sedation can be safely achieved in the ED, but future studies should assess for potential spikes in adverse events such as awareness, distress, device removal, etc. It is possible that ICU-based guidelines should not be applied to the ED, given the different models of practice between the two locations (e.g., staffing, nurse-to-patient ratios). Therefore, future studies should assess impact of ED-based goal-directed sedation on potential positive and negative outcomes, as well impact on staff. Finally, deep sedation may reflect illness severity, as there were observed differences between the two groups with respect to SOFA scores and vasopressor use.

CONCLUSIONS

Deep sedation in the ED is common in mechanically ventilated patients, carries over into the ICU, and may be associated with worse outcomes. Sedation practices in the ED and associated clinical outcomes are in need of further investigation.

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