The agreement between emergency department and intensive care unit depth of sedation assessment

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Abstract

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RATIONALE: During mechanical ventilation, assessment and treatment of pain and agitation are important to ease patient discomfort, allow for ventilator synchrony, and decrease work of breathing. Despite this, it is uncommon for patients intubated in the emergency department(ED) to have level of sedation documented using a standardized scale. Studies focused on early depth of sedation frequently use first intensive care unit (ICU) sedation assessment as a proxy for ED depth of sedation; however, little evidence supports this practice. We sought to demonstrate the level of agreement between Richmond Agitation and Sedation Scale (RASS) measurements documented in the ED and the initial ICU RASS.

METHODS We performed a secondary analysis of LOTUS-FRUIT, a prospective cohort study of patients with acute respiratory failure requiring intubation at PETAL network institutions. Patients who were intubated in the prehospital or emergency setting and had a documented ED RASS were included. The period of analysis was from time of intubation to ICU admission. Weighted Cohen's Kappa was used to compare agreement between ED and initial ICU RASS. McNemar's test was used to compare documentation of deep sedation (RASS -3 to -5) in the ED and ICU.

RESULTS: Of the 784 patients who were intubated in the pre-hospital setting or ED, 180 had both an ED and initial ICU RASS documented. The most common indications for mechanical ventilation were respiratory failure (47.8%) and altered mental status (42.2%). The median time from intubation to ICU arrival was 4 hours (IQR 2.2-5.8). Most patients were admitted to a medical ICU (52.8%) followed by mixed (19.4%), surgical (14.4%), cardiac (8.9%) and neurological (4.4%) ICUs. Using a quadratic weighted kappa, ED and ICU RASS demonstrated substantial agreement (kappa=0.64). There was no statistically significant difference in the proportion with deep sedation between ED and ICU (p=0.51).

CONCLUSIONS: ED and ICU RASS measurements demonstrate substantial agreement. Although RASS assessments occurred uncommonly in the ED overall, when RASS in the ED was documented, patients were equally likely to be categorized as deeply sedated in the ED and on admission to the ICU. In settings where depth of sedation is not routinely measured in the ED, first ICU depth of sedation may serve as an appropriate proxy.

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Chapter 1. INTRODUCTION

Patients with respiratory failure frequently require analgesia and sedation in order to tolerate mechanical ventilation. Intensive care unit (ICU) based clinical guidelines recommend optimizing sedation through the routine assessment of depth of sedation, maintaining light sedation unless contraindicated, and avoiding continuous infusions of benzodiazepines[1]. While continuous infusion sedation is common[2], data suggest that daily interruptions[3,4] and protocol-based pain and agitation assessment paired with sedation weaning[5,6] is associated with fewer ventilator days, fewer nosocomial infections, and lower mortality. Despite this, the frequency of heavy sedation in the early post-intubation period is quite high[7].

There is little evidence to guide early sedation practices in the emergency department (ED), where mechanical ventilation is frequently initiated. My prior work shows that depth of sedation using validated measures of agitation and sedation[8] is infrequently measured in the ED. Observational data suggests that early deep sedation is common, and associated with increased duration of mechanical ventilation and mortality[7,9]. While these studies demonstrate that early deep sedation may be harmful, they frequently use initial ICU depth of sedation as a proxy for ED depth of sedation. Currently, there is no data demonstrating the agreement between ED and ICU depth of sedation for mechanically ventilated patients.

In order to place prior studies in context and inform future research in the field of early management of sedation and analgesia, it is important to understand the agreement between ED

and ICU depth of sedation. We sought to determine the degree of agreement between ED and initial ICU depth of sedation among mechanically ventilated patients cared for in PETAL (Prevention and Early Treatment of Acute Lung Injury) network hospitals.

Chapter 2. METHODS

We performed a secondary analysis of the Low Tidal Volume Universal Support: Feasibility of Recruitment for Interventional Trial (LOTUS-FRUIT)[10]. LOTUS-FRUIT is an observational cohort study of consecutive patients during the month of July 2016 with acute respiratory failure at PETAL-network hospitals aiming to determine whether default low tidal volume (6 ml/kg predicted body weight) improves outcomes as compared to usual care.

2.1 *PATIENT SELECTION*

Adult patients (≥18 years of age) who were intubated either in the ED or prehospital setting were included in our study. We excluded patients who did not have a documented Richmond Agitation and Sedation Scale (RASS)[8] score in both the ED and the intensive care unit. The RASS score is a validated tool to assess the depth of sedation for intensive care unit patients receiving mechanical ventilation. The ordinal 10-point scale ranges from +4 (combative) to -5 (unarousable).

2.2 *Statistical Analyses*

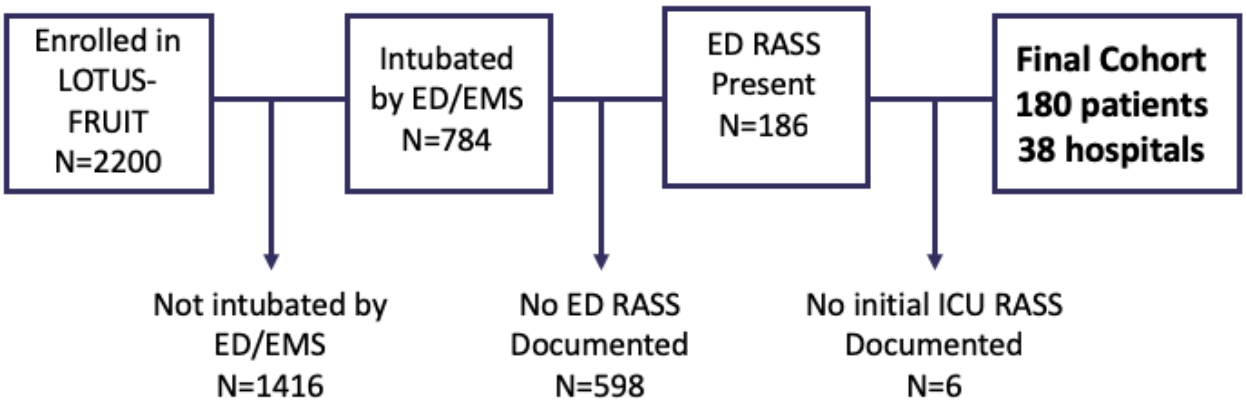
Baseline characteristics of the population were examined and descriptive statistics are reported. A Sankey plot was constructed to visualize flux between ED and ICU depth of sedation. To determine the agreement between ED and ICU depth of sedation, we used both an unweighted and a quadratic weighted Cohen's kappa[11]. A quadratic weight, defined as $1 - \{(i - j)/(k - 1)\}^2$ where i and j index the rows and columns of the scores in the ED and ICU and k is the maximum number of possible scores, was used in order to progressively penalize larger discrepancies between ED and ICU RASS scores. Kappa values of 0.8, 0.6, and 0.4 represent "almost perfect", "substantial", and "moderate" agreement, respectively[12]. We then examined the association between deep sedation (RASS -3 to -5) in the ED and in the ICU using McNemar's test. A sensitivity analysis was performed limited to those who were intubated for altered mental status. All analyses were performed in StataIC, version 15[13]. Bar graphs were made using Graphpad Prism 5 for MacOS, and Sankey Diagrams were made using SankeyMatic[14].

Chapter 3. RESULTS

3.1 *Patient Characteristics*

Two thousand two hundred patients were enrolled in LOTUS-FRUIT. 1,416 patients were excluded from our study as they were not intubated in the ED or by EMS prior to hospital arrival, 598 were excluded for not having a RASS documented in the ED, and 6 were excluded for not having a documented RASS on arrival to the ICU. Our final study cohort consisted of 180 patients from 38 hospitals (Figure 1).

Figure 1: Flow diagram



Mean age was 56±17.5 years and 139 (77.2%) were intubated in the emergency department. The most common reason for intubation was respiratory failure (47.8%) followed by altered mental status (42.2%). Patients were most frequently admitted to medical intensive care units (52.8%), followed by mixed (19.4%), surgical (14.4%), cardiac (8.9%), and neurological (4.4%) units. The median time from intubation to ICU arrival was 4 (IQR 2.2, 5.8) hours. The median RASS score was 3 (IQR -4, -1) in both the ED and ICU. See Table 1 for details. The distribution of RASS scores in the ED and ICU are presented in Figure 2. Flux from ED to ICU RASS is presented in the Sankey diagram in Figure 3.

Table 1: Baseline characteristics*

	Sedation Assessed in ED N=180
Age at admission, years	56.5+17.5
Intubation to ICU Admission Time, hours	4 [2.2-5.8]
Reason for Intubation	
Arrest/Shock	12 (6.7%)
Altered Mental Status/Airway	76 (42.2%)
Metabolic Abnormality	2 (1.1%)
Respiratory Failure	86 (47.8%)
Unknown	4 (2.2%)
Intubation Location	
EMS	41 (22.8%)

ED	139 (77.2%)
ARDS at Baseline	38 (21.1%)
Initial PaO2:FiO2	213 [126-352]
ICU Type	
Cardiac	16 (8.9%)
Medical	95 (52.8%)
Mixed	35 (19.4%)
Neuro	8 (4.4%)
Surgical	26 (14.4%)
Medications (Prior to ICU Admission)	
Any Vasopressor first 24 Hours	65 (36.1%)
Benzodiazepine Drip	32 (17.8%)
Benzodiazepine Bolus	43 (23.9%)
Opioid Drip	72 (40.0%)
Opioid Bolus	47 (26.1%)
Propofol	103 (57.2%)
Dexmedetomidine	9 (5.0%)
Ketamine	8 (4.4%)
Sequential Organ Failure Assessment Score$^{\alpha}$	4 [3-7]
28-Day Mortality	39 (21.7%)
Days alive free of mechanical ventilation	25 [12 – 27]
ICU Length of Stay, days	6 [3 – 9]

*Represented as mean±SD, median [IQR], or n (%)

$^{\alpha}$Excluding respiratory components of SOFA score

Figure 2: Distribution of RASS Scores in ED and ICU

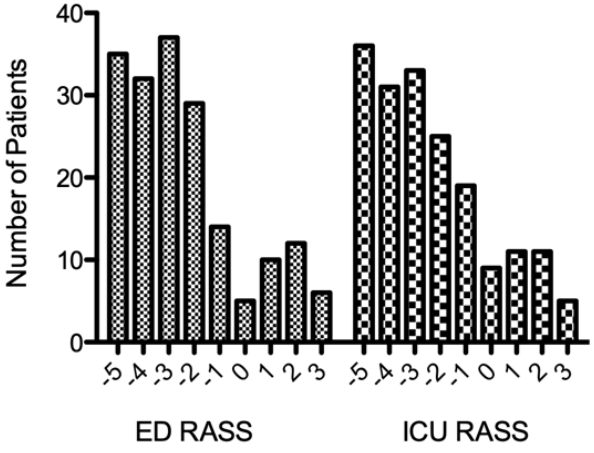
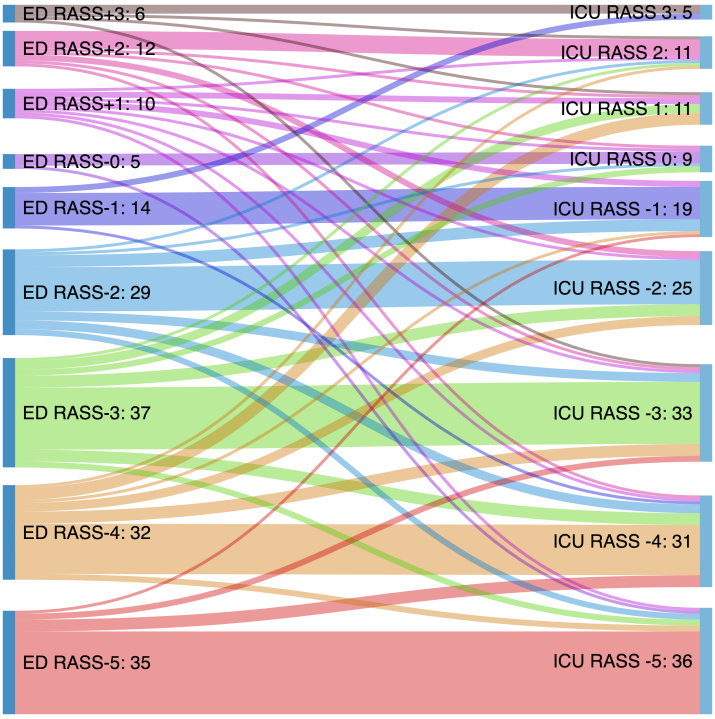


Figure 3: Flux between ED and ICU RASS Scores



3.2 *Agreement between ED and ICU depth of sedation*

The raw agreement between ED and ICU RASS scores was 59.4%. Using an unweighted kappa, ED and ICU RASS demonstrated moderate agreement (kappa=0.52, p<0.01,). ED and ICU RASS scores demonstrated substantial agreement using a quadratic weighted kappa (kappa=0.64, p<0.01). See Table 2 for details.

Table 2: Agreement between ED and ICU RASS

	Agreement	**Expected Agreement**	**Kappa**	**Std Error**	**P-value**
Unweighted Kappa	59.4%	14.8%	0.52	0.03	<0.01
Weighted Kappa*	94.3%	84.1%	0.64	0.07	<0.01

Using the dichotomized variable of deep sedation (RASS -3 to -5), there was no statistically significant difference between ED and ICU frequency of deep sedation (p=0.51) (table 3).

Table 3: Number of patients with deep sedation in ED and ICU

	Deep Sedation in ICU	**No Deep Sedation in ICU**
Deep Sedation in ED	84	20
No Deep Sedation in ED	16	60

In a sensitivity analysis restricting the population to only those who were intubated for altered mental status, ED and ICU RASS demonstrated moderate agreement (unweighted Kappa=0.47, $p<0.01$, quadratic weighted kappa=0.55, $p<0.01$). See Table 4 for details.

Table 4: Agreement between ED and ICU RASS among those intubated for altered mental status

	Agreement	**Expected Agreement**	**Kappa**	**Std Error**	**P-value**
Unweighted Kappa	54.0%	13.9%	0.47	0.04	<0.01
Weighted Kappa*	91.8%	81.6%	0.55	0.11	<0.01

*Quadratic weighted kappa

Using the dichotomized variable of deep sedation (RASS -3 to -5), there was no statistically significant difference between ED and ICU frequency of deep sedation (p=0.41) (table 5).

Table 5: Number of patients with deep sedation in ED and ICU (restricted to patients with altered mental status)

	Deep Sedation in ICU	**No Deep Sedation in ICU**
Deep Sedation in ED	35	5
No Deep Sedation in ED	8	28

Chapter 4. DISCUSSION

In our study of mechanically ventilated patients in PETAL network hospitals, documented depth of sedation in the ED had moderate to substantial agreement with documented depth of sedation in the intensive care unit. Additionally, there was no statistically significant difference in deep sedation in the ED as compared to the ICU. Presently, this is the first study to demonstrate the level of agreement between ED and ICU depth of sedation. This finding lends more credibility to prior literature examining the association between ED depth of sedation and patient outcomes, as they frequently used early ICU depth of sedation as a proxy for ED depth of sedation.

Numerous studies have sought to determine whether early deep sedation, including deep sedation in the emergency department where mechanical ventilation is frequently initiated, is associated with poorer patient outcomes. In an observational study of 251 patients at 25 hospitals in Australia and New Zealand, deep sedation (RASS -3 to -5) was associated with longer duration of mechanical ventilation (7.7 vs. 2.4 days) and higher mortality (adjusted HR=1.04)[7]. However, Shehabi, et al did not explicitly examine depth of sedation in the ED, but rather in the intensive care unit. Stephens, et al. performed a cohort study of adult mechanically ventilated patients at a single academic emergency department and found that a deeper (i.e. lower) ED RASS was associated with mortality. The same group subsequently performed a prospective, multi-center cohort study examining the association between emergency department depth of sedation and patient outcomes, however the results of this study are not yet published[15]. Both studies used first ICU RASS as a proxy for ED depth of sedation when ED RASS was not measured.

There are a number of implications to the finding that ED and initial ICU RASS demonstrate moderate to substantial agreement. Our group has previously demonstrated that depth of sedation is infrequently measured in the ED, and the variability in ED depth of sedation assessment is primarily driven by hospital site. While we would encourage emergency departments to check and document depth of sedation for all mechanically ventilated patients, the demonstrated agreement between ED and first ICU RASS may allow for interventions seeking to minimize deep sedation to be studied for both research and quality improvement purposes in centers that as of yet do not routinely document depth of sedation in the ED.

Our study has notable limitations. First, we are only able to compare depth of sedation measurements that were documented. Sedation may have changed between ED and first ICU measurements, however we are unable to capture that variability. Additionally, the range of time between intubation and ICU arrival (i.e. ED length of stay) is large (interquartile range 2.2-5.8 hours), and thus those with longer ED length of stay may be more likely to have divergent RASS scores. Lastly, we were only able to compare ED and ICU RASS scores when RASS was assessed in the ED. Our prior research shows ED sedation assessment is uncommon, and raises the question of whether there are patient-level or site-level factors that contribute to RASS assessment and contribute to other facets of sedation management that may impact the agreement between ED and ICU depth of sedation.

Chapter 5. CONCLUSION

Emergency department and first intensive care unit depth of sedation scores demonstrate moderate to substantial agreement. In settings where depth of sedation is not routinely measured in the ED, first ICU depth of sedation may serve as an appropriate proxy.

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