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Association of early sedation level with patient outcomes in moderate-to-severe acute respiratory distress syndrome: Propensity-score matched analysis

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ABSTRACT

Purpose: Studies of early depth of sedation in mixed critically ill populations have suggested benefit to light sedation; however, the relationship of early depth of sedation with outcomes in patients with acute respiratory distress syndrome (ARDS) is unknown.

Materials and methods: We performed a propensity-score matched analysis of early light sedation (Richmond Agitation Sedation Scale Score, RASS 0 to -1 or equivalent) versus deep sedation (RASS -2 or lower) in patients enrolled in the non-intervention group of The Reevaluation of Systemic Early Neuromuscular Blockade trial. Primary outcome was 90 day mortality. Secondary outcomes included days free of mechanical ventilation, days not in ICU, days not in hospital at day 28.

Results: 137 of 486 participants (28.2%) received early light sedation. Vasopressor usage and Apache III scores significantly differed between groups. Prior to matching, 90-day mortality was higher in the early deep sedation (45.3%) compared to light sedation (34.2%) group. In the propensity score matched cohort, there was no difference in 90-day mortality (Odds Ratio (OR) 0.72, 95% CI 0.41, 1.27, $p = 0.26$) or secondary outcomes between the groups.

Conclusions: We did not find an association between early depth of sedation and clinical outcomes in this cohort of patients with moderate-to-severe ARDS.

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1. Introduction

Patients with acute respiratory distress syndrome (ARDS) often receive analgesia and sedation to improve ventilator tolerance, reduce discomfort, and, in some cases, to improve patient-ventilator synchrony. Current guidelines for managing analgesia and sedation in intensive

Abbreviations: ARDS, acute respiratory distress syndrome; ICU, intensive care unit; ROSE, Reevaluation of Systemic Early neuromuscular blockade; PS, propensity scores; RASS, Richmond Agitation Sedation Scale.

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care unit (ICU) patients recommend targeting a light level of sedation or a daily interruption of sedation to facilitate liberation from the ventilator [1,2]. Prior studies have reported that early, deep sedation in general populations of mechanically ventilated patients is associated with worse clinical outcomes including longer duration of mechanical ventilation, longer length of stay, subsequent delirium and increased mortality [3-8]. These studies, however, were not specific to patients with ARDS where there may be more of a theoretical benefit to deep early sedation given potential for severe dyspnea, high respiratory drive, acidosis, the importance of adherence to low tidal volume ventilation [9], frequent ventilator dyssynchrony, and need for prone positioning [10]. A recent expert panel stated that "patients with severe ARDS may be underrepresented in analgesia/sedation studies and currently recommended strategies

may not be feasible" [1]. Therefore, the optimal sedation target early in the disease course of moderate-to-severe ARDS is unknown.

The Reevaluation of Systemic Early neuromuscular blockade (ROSE) trial provides a platform to examine the relationship between early depth of sedation and clinical outcomes specifically in patients with moderate-to-severe ARDS. The trial also captured information on severity of illness and comorbidities that were not available in the majority of prior studies evaluating the relationship of early depth of sedation with clinical outcomes [8]. The primary objective of this study was to examine the association of early depth of sedation with 90-day in-hospital mortality in patients with moderate-to severe ARDS enrolled in the non-intervention arm of the ROSE trial using a propensity score matched analysis. As secondary objectives, we examined the relationship between early depth of sedation with days free of ventilation at day 28, days not in ICU at day 28, and days out of the hospital at day 28. We hypothesized that early light sedation would be associated with improved clinical outcomes in this cohort of patients with moderate-to-severe ARDS.

2. Material and methods

2.1. Study population

The Reevaluation of Systemic Early Neuromuscular Blockade (ROSE) trial was conducted by the National Heart, Lung, and Blood Institute Prevention and Early Treatment of Acute Lung Injury (NHLBI PETAL) Clinical Trials Network to determine the efficacy and safety of early continuous neuromuscular blockade combined with heavy sedation compared to a strategy of usual care with lighter sedation targets in participants with moderate-to-severe ARDS. The trial randomly assigned 1006 patients undergoing mechanical ventilation through an endotracheal tube 1:1 to receive 48 h of continuous neuromuscular blockade with concomitant deep sedation (intervention group) or usual care with lighter sedation targets (non-intervention group) as previously described [11,12]. Patients were eligible for inclusion into the ROSE study if they were 18 years of age or older and met the following criteria: (i) $\text{PaO}_2/\text{FiO}_2 < 150$ with $\text{PEEP} \geq 8$ cmH₂O (or if arterial blood gas was not available, an equivalent $\text{SpO}_2/\text{FiO}_2$ ratio) with confirmatory ratio between 1 and 6 h later, (ii) bilateral opacities not fully explained by lobar effusion, lobar/lung collapse, or nodules, and (iii) respiratory failure not fully explained by cardiac or fluid overload. Exclusion criteria have been previously described [11]. To be eligible for enrollment in the ROSE trial, patients met inclusion criteria for ≤ 48 h. For this sub-study, only the 506 participants in the non-intervention group were eligible for inclusion into the cohort. We did not include patients in the intervention arm as the protocol specified deep sedation for those receiving neuromuscular blockade.

2.2. ROSE trial design and oversight

The protocol of the ROSE Trial has been previously published [11]*. A central institutional review board and a data safety monitoring board provided oversight of trial procedures. Written informed consent for enrollment in ROSE was obtained from representatives of all patients. This propensity-score analysis was approved as a sub-study by the NHLBI PETAL Steering Committee. It was deemed exempt by the Wake Forest University Health Sciences IRB (IRB00060508).

2.3. Study design

We performed a propensity-score matched analysis of early light sedation versus early deep sedation in those patients enrolled in the non-intervention group. We chose a propensity score matched analysis to obtain an estimate of the effect of sedation adjusted for the impact of confounding factors in this cohort. A propensity score is well suited to deal with multiple mutually correlated variables. As Rosenbaum and

Rubin show, observed covariates are balanced at each value of the propensity score, meaning that patients in the two groups with equal propensity score have similar distributions of the modeled covariates [13].

2.4. Propensity score

In our primary analysis, we included in our propensity score variables that were hypothesized to be associated with early depth of sedation in patients enrolled in the ROSE trial: sex, history of prior stroke, history of dementia, history of chronic pulmonary disease, history of peripheral vascular disease, history of myocardial infarction, history of congestive heart failure. We also included the following variables related to the acute illness: vasopressors at time of enrollment, Apache III score, and baseline $\text{PaO}_2:\text{FiO}_2$ ratio. These variables were determined by the study team a priori. There is no consensus in the literature as to which variables to include in the propensity model (all baseline covariates, those associated with the exposure (early depth of sedation in our study), those associated with outcomes, or those associated with both) [14,15]. We chose to include variables that may be associated with the depth of sedation target chosen or achieved by the clinical team based on prior subject matter knowledge.

2.5. Exposure variable

In the ROSE trial protocol, light sedation was recommended in the non-intervention group (RASS of 0 to -1 , Riker 3 to 4, Ramsay 2–3). For the non-intervention participants that crossed over to receive neuromuscular blockade, deep sedation was recommended as in the intervention group. We defined our controls as "early deep sedation" to be a RASS score of -2 , -3 , -4 , or -5 , Riker score of 1 or 2, and Ramsay score of 4, 5, or 6. While previous studies have defined light sedation to include a RASS of -2 [4,16], we defined our cases as "early light sedation" as recommended in the protocol: RASS of 0 to -1 or the equivalent in the Riker or Ramsay scale. Indeed more recent guidelines have suggested that a RASS of -2 is deeper sedation than required for mechanical ventilation [1,2]. Participants were enrolled in ROSE within 48 h of initiation of mechanical ventilation and meeting criteria for ARDS. We used the sedation score closest and prior to randomization to describe early sedation level in our primary analysis. As a secondary analysis, we repeated the propensity analysis with sedation level recorded at 8 AM on day 1 of study enrollment as the exposure variable. For those patients in the non-intervention group, sedation was titrated per clinician discretion and sedation level was determined by the clinical team. Since previous studies have included a RASS of -2 as light sedation, we performed a sensitivity analysis in which we included RASS of -2 to be in the early light sedation group rather than the early deep sedation group.

2.6. Outcome variables

The primary outcome was in-hospital death from any cause at 90 days (in-hospital was defined as the time in the trial hospital plus transfer to another hospital, including the time in long-term acute care facilities). Participants still in a healthcare facility at Day 91 were considered alive. We examined the following as secondary outcomes: days free of ventilation at day 28, days not in ICU at day 28, and days not in hospital at day 28. Ventilator free days to day 28 are defined per the original study protocol as the number of days from the time of unassisted breathing to day 28 after randomization, assuming survival for at least two consecutive calendar days after initiating unassisted breathing and continued unassisted breathing to day 28. If a patient was receiving assisted breathing at day 27 or died prior to day 28, ventilator free days were counted as zero [11].

2.7. Statistical analyses

After reducing the dataset to those with complete case data, the groups were compared on the baseline characteristics of interest. To achieve a more precise estimation of treatment responses, propensity scores (PS) were utilized to create matching of 1:1 cases (early light sedation) to controls (early deep sedation) using a caliper size of 0.20 [17]. In a secondary analysis, we also matched again, using a ratio of 1:2 cases: controls. Independent *t*-tests and Fisher's Exact Tests were used to test for group differences in continuous and categorical variables, respectively, for demographic and treatment variables. Due to the skewness of the data, the Wilcoxon Two-Sample Test was used to test for differences in secondary outcomes. The balance achieved by the propensity score matching is measured by comparing the standardized mean difference of baseline variables before and after propensity score matching [18]. The standardized mean difference was calculated by subtracting the mean value of a variable in the deep sedation population from the mean value of the variable in the light sedation population, and then dividing this difference in values by the pooled standard deviation for continuous measures; correspondingly, for categorical data, the differences in proportions were divided by the pooled standard deviation. The early deep and early light sedation matched groups were then analyzed using conditional logistic regression for matched pairs data; this approach controls for the pairs created in the propensity score analysis and is used to test for differences in 90-day mortality between the early deep and light sedation groups. Secondary measures were compared using random effects models. Significance was assumed if observed *p*-values were < 0.05. All statistical analyses were performed using SAS, Version 9.4 (Cary, NC, USA).

3. Results

3.1. Study cohort and patient characteristics

Patient characteristics of the non-intervention group of the ROSE study have been previously described [12]. Baseline sedation score was missing in 19 of 505 patients in the non-intervention group and

thus those patients were excluded from our cohort. Our cohort for this sub-study included a total of 486 participants initially, which was reduced to 396 with complete-case data (Fig. 1). In this cohort, 285 (72.0%) were classified as receiving early deep sedation and 111 (28.0%) were classified as early light sedation (Fig. 2). Patient characteristics of this cohort are described in Table 1. Prior to propensity score matching, there were differences between the early light sedation and early deep sedation groups in vasopressor usage and Apache III scores.

3.2. Propensity matching

After removing those who were missing any of the covariates (Fig. 1), there were 285 controls (early deep sedation) and 111 cases (early light sedation) available for propensity matching. For our primary analysis using propensity score-matching with a caliper size of 0.20, the matched 1:1 cohorts achieved balance between groups on all pre-specified variables. There were no significant differences when compared using *t*-tests for continuous and Fisher's Exact Tests for categorical measures. The primary model matched 110 of the 111 cases to a corresponding control. The patient characteristics for those included in the primary matched analysis are included in Table 2. Presence of dementia shows an indication of imbalance between groups, with a standardized mean difference > 0.10, but the rates are very low in both groups (1.8% and 3.6% in early light sedation and early deep sedation, respectively). Additionally, a 1:2 match of cases to controls was created using propensity scoring; this model was unable to match 1:2 across all cases. Nine of the 110 previously-matched cases did not find a second match, reducing the sample size to 101 cases, effectively eliminating 8.2% of the cases from the regression model. In a sensitivity analysis, the mortality rate in the 90 patients who were excluded from the matching analysis due to missing covariates was examined relative to the PS-included subjects. The mortality rate in the early light sedation group in the 26 dropped subjects was 34.6% (9/26) and 33.6% (37/110) in those included in the PS dataset, *p* > 0.99; in the early deep sedation group, the rates were 43.8% (28/64) for those not included and 40.9% (45/110) for PS subjects in the early deep sedation group, with no difference in mortality (*p* = 0.88). If we expand this analysis to the original 486 subjects and

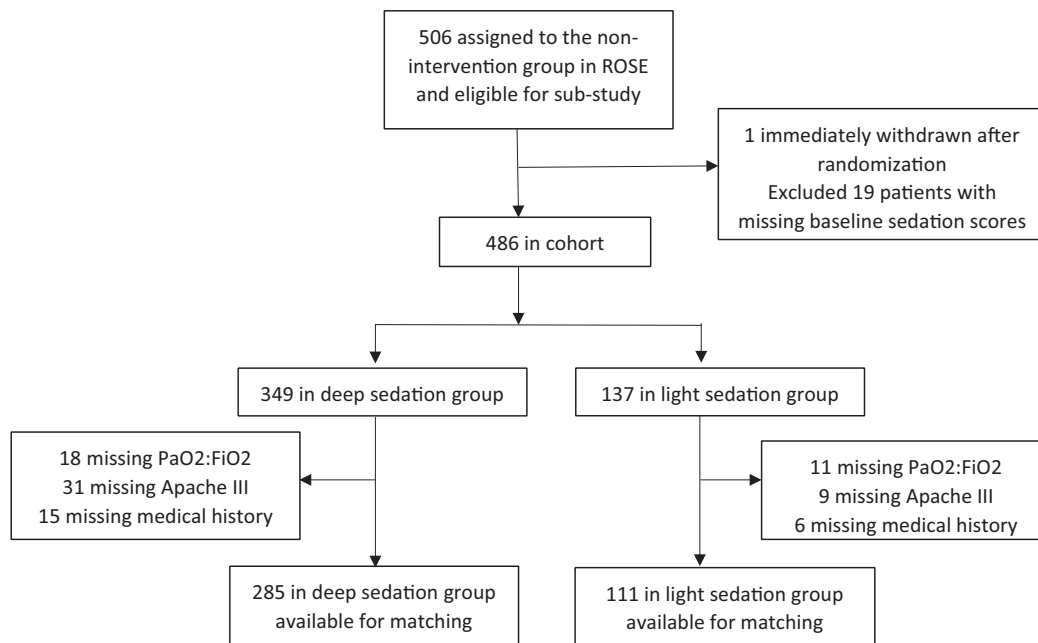
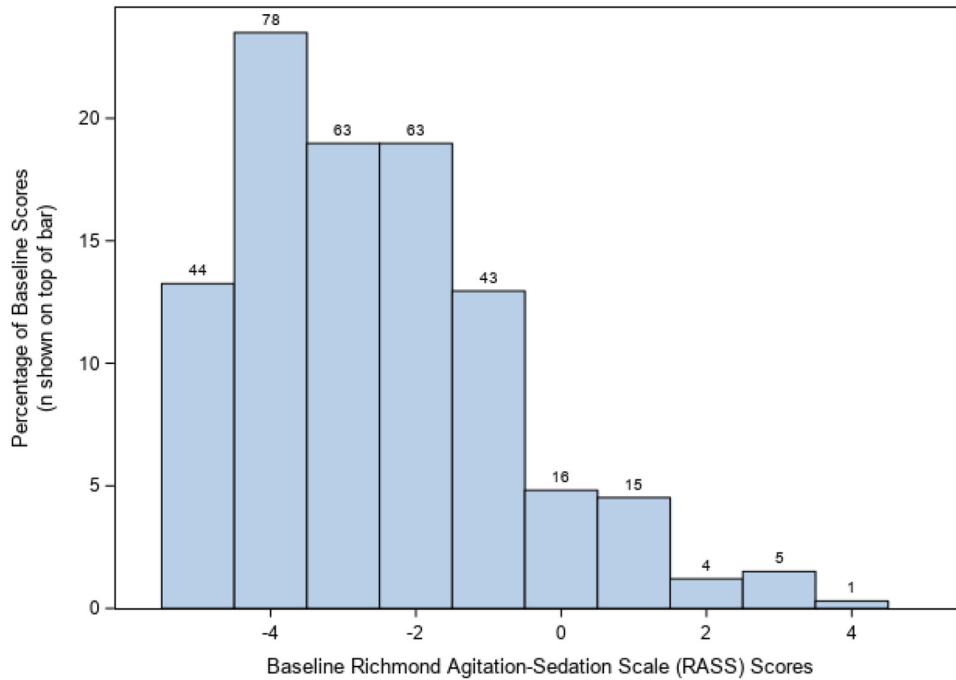


Fig. 1. Patient Enrollment and Group Assignment for Propensity Score Analysis.

Panel A:



Panel B:

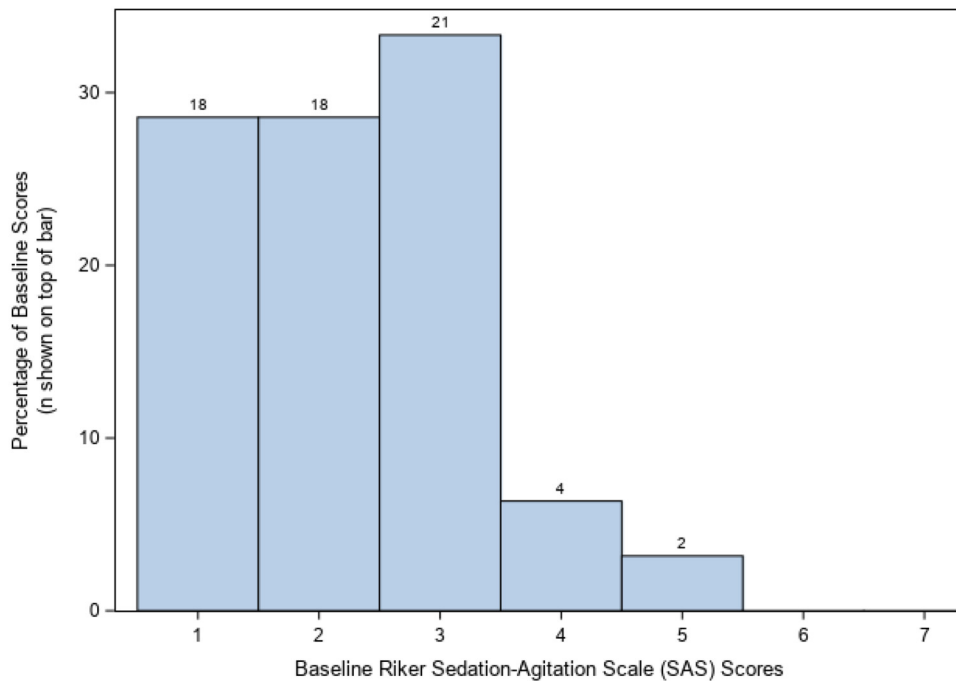


Fig. 2. Frequency of Baseline Sedation Scores in Non-Intervention Group (n = 396) by RASS (Panel A) and Riker Score (Panel B). Only 1 participant had a baseline Ramsay score recorded (score of 4).

compare the mortality rate of the 266 subjects not included in the PS analysis to those included, the rate of 37.0% (10/27) in the early light sedation group is not different from the PS subjects ($P = 0.82$); similarly, the mortality rate of 46.9% (112/239) in the early deep sedation group is not different from the PS subjects ($p = 0.35$).

3.3. Association of early depth of sedation with 90-day mortality

There was no association between early light sedation and 90-day mortality (Odds Ratio (OR) 0.72, 95% CI 0.41, 1.27, p -value = 0.26) in the primary propensity score matched conditional logistic regression

Table 1

Baseline characteristics and clinical outcomes between the two groups (early light sedation versus early deep sedation) in the entire cohort prior to propensity score matching (n = 396 potential participants).

	Early Light Sedation (n = 111)	Early Deep Sedation (n = 285)	Standardized Mean Difference	P-Value
Baseline Characteristics				
Age	Mean = 56.2 (SD = 15.9)	54.5 (15.7)	0.11	0.33
Sex: Female	55 (49.6%)	135 (47.4%)	0.04	0.74
History of stroke	5 (4.5%)	10 (3.5%)	0.05	0.77
History of dementia	2 (1.8%)	7 (2.5%)	-0.05	>0.99
History of chronic pulmonary disease	17 (15.3%)	57 (20.0%)	-0.12	0.32
History of congestive heart failure	8 (7.2%)	19 (6.7%)	0.02	0.83
History of peripheral vascular disease	6 (5.4%)	16 (5.6%)	-0.01	>0.99
History of myocardial infarction	5 (4.5%)	19 (6.7%)	-0.096	0.49
Acute Illness Characteristics				
Vasopressors at time of enrollment	59 (53.2%)	190 (66.7%)	-0.28	0.015
Apache III score	96.1 (27.2)	110.0 (29.7)	-0.49	<0.0001
Baseline PaO ₂ :FiO ₂	112.7 (32.9)	113.5 (42.0)	-0.02	0.83
Clinical Outcomes (mortality presented as n and %, days presented as median [P25, P75])				
90-day mortality	38 (34.2%)	129 (45.3%)	NA	0.054
Ventilator-free days	13 (0, 23)	0 (0, 22)	NA	0.20
ICU-free days	12 (0, 20)	4 (0, 19)	NA	0.069
Hospital-free days	3 (0, 14)	0 (0, 13)	NA	0.031

Values are in bold if the absolute standardized mean difference is >0.1, which can be a sign of imbalance [23].

model with 110 subjects in both groups; if we increase our matching to 1:2 cases: controls, the cases have 9 subjects who fail to find a satisfactory second match using the same caliper size (0.20) as in the 1:1 match. If the model is expanded to include those 9 subjects, the data become unbalanced in APACHE III score, so the caliper size was not changed for consistency. With those 9 subjects removed, the results are consistent with 101 cases and 202 controls (OR 0.67, 95% CI of 0.35, 1.26, p-value = 0.21). There is no indication of a relationship between early light sedation and mortality. Additionally, if the subjects with a RASS of -2 (approximately 19% of the sample) are included in the early light sedation group, there was no change in significance of the results nor in the directionality of the relationship (OR 0.79, 95% CI 0.36, 1.73, p-value = 0.55). Finally, when using day 1 sedation level as our exposure variable, the relationship between early slight sedation and mortality was similar (OR 0.62, 95% CI of 0.36, 1.06, p-value = 0.08) in 117 matched pairs.

3.4. Association of early depth of sedation with secondary outcomes

Prior to propensity matching, there was not a significant difference between days free of ventilation in the two study groups; the early light sedation group (median 13 days, 25th and 75th percentile 0, 23) was not different from the early deep sedation group (median 0 days, (0,22) p-value 0.20). While the early light sedation group had a higher number of days not in the ICU at 28 days (median 12 days, (0,20) versus median 4 days, (0, 19), this result was not significant (p-value = 0.07). One measure did indicate a difference between the groups; days not in the hospital at day 28 was higher in the early light sedation group (median 3 days (0, 14) compared to median of 0 days (0,13) in the deep sedation group, p = 0.03). When matched by propensity scores, however, the groups were no longer different. In the 1:1 propensity-score matched cohort, the early light sedation group had a median 13 days free of mechanical ventilation (0,23), 12 days out of the ICU (0, 20),

Table 2

Baseline characteristics and clinical outcomes between the two groups (early light sedation versus early deep sedation) in the primary propensity score matched cohort (n = 110 in each group).

	Early Light Sedation (n = 110)	Early Deep Sedation (n = 110)	Standardized Mean Difference*	P-Value
Baseline Characteristics				
Age	Mean = 56.0 (SD = 15.8)	55.3 (16.0)	0.04	0.74
Sex: Female	56 (50.9%)	51 (46.4%)	0.09	0.59
History of stroke	5 (4.5%)	5 (4.5%)	0	>0.99
History of dementia	2 (1.8%)	4 (3.6%)	-0.11	0.68
History of chronic pulmonary disease	17 (15.5%)	17 (15.5%)	0	>0.99
History of congestive heart failure	7 (6.4%)	6 (5.5%)	0.04	>0.99
History of peripheral vascular disease	6 (5.5%)	5 (4.5%)	0.05	>0.99
History of myocardial infarction	5 (4.5%)	5 (4.5%)	0	>0.99
Acute Illness Characteristics				
Vasopressors at time of enrollment	59 (53.6%)	61 (55.5%)	-0.04	
Apache III score	96.3 (27.2)	95.0 (30.3)	0.04	0.92
Baseline PaO ₂ :FiO ₂	112.6 (33.0)	113.9 (42.9)	-0.04	0.80
Clinical Outcomes (mortality presented as n and %, days presented as median [P25, P75])				
90-day mortality	37 (33.6%)	45 (40.9%)	NA	0.26
Ventilator-free days	13 (0, 23)	6.5 (0, 22)	NA	0.58
ICU-free days	12 (0, 20)	11 (0, 20)	NA	0.69
Hospital-free days	3.5 (0, 14)	0 (0, 15)	NA	0.47

* Values are in bold if the absolute standardized mean difference is >0.1.

and 3.5 days out of the hospital (0, 14). The early deep sedation group had median 6.5 days free of mechanical ventilation ((0, 23), $p = 0.58$ compared to light sedation), 11 days out of the ICU ((0, 20), $p = 0.69$), and 0 days out of the hospital ((0, 15), $p = 0.47$).

4. Discussion

In this sub-study of the ROSE trial, we did not find a statistically significant association between early depth of sedation and 90-day mortality using a propensity score matched analysis adjusting for baseline chronic conditions as well as severity of illness. We also found early depth of sedation did not have an association with days free of ventilation, days out of the ICU, or days out of the hospital at 28 days. We did find that early light sedation was not frequently achieved; 71.8% of the 486 participants in this sub-study still received early deep sedation (RASS of -2 , -3 , -4 , -5 or equivalent). Early deep sedation was more common in sicker patients (higher Apache III score, more vasopressor use) as expected but was otherwise not associated with specific patient factors (as shown in Table 1). This finding suggests the depth of sedation achieved early in a patient's disease course of ARDS likely depends on complex factors that are not patient-specific. For example, the implementation of ICU analgesia/sedation protocols, nurse and physician comfort and training, and local ICU culture all likely impact the sedation level achieved [1,19,20].

Understanding the impact of early sedation on patient outcomes in patients with moderate-to-severe ARDS is important and understudied. Early in a patient's ICU stay is when decisions about sedative agent and depth of sedation are made and when clinicians may be more likely to accept deeper sedation. Current guidelines for management of pain, agitation, and sedation in general ICU patients promote an analgesia first strategy, minimizing sedation and promoting wakefulness [2]. Experts in ARDS management also recommend targeting minimal or no sedation specifically in this patient population though no prospective analgesia/sedation studies have been conducted exclusively in ARDS patients [1]. It is possible the relationship between early sedation and patient outcomes is different in the ARDS population where adherence to low tidal volume ventilation is important, high respiratory drive can cause significant ventilator dyssynchrony, and prone positioning or neuromuscular blockade may be required.

Prior studies evaluating the relationship of early sedation and outcomes have enrolled mixed ICU populations. The results of these studies have generally supported early light sedation. A prospective, multicenter cohort study of a mixed ICU population in Australia and New Zealand (conducted in 2010) found that deep sedation within the first 48 h of ICU admission (defined as RASS of -3 to -5) was an independent predictor of death and time to extubation [4]. The study was replicated in Malaysian ICUs and again early deep sedation (RASS -3 to -5 in first 48 h after mechanical ventilation) was associated with increased time to extubation and mortality [5]. In each of these two studies the majority of the patients were ventilated for a reason other than primary respiratory failure. In a prospective cohort study conducted in Brazil (2011), early deep sedation (defined using the Glasgow Coma Scale) was again associated with increased time on mechanical ventilation, increased risk of tracheostomy, and higher mortality in a mixed ICU population [7]. Again only 15% of patients included in this study had moderate or severe ARDS. A meta-analysis by Stephens et al. that included 9 studies ($n = 4521$ patients) of mixed critically ill adults concluded that early deep sedation was associated with increased mortality and length of stay [8].

While the above studies support improved outcomes with early light sedation in the general population of patients receiving mechanical ventilation, the results may not be applicable to the sub-group of patients with moderate-to-severe ARDS. In the early period for patients with moderate-severe ARDS (first 48 h), the benefits of tightly controlled low tidal volume ventilation or prone positioning may outweigh the risks associated with increased sedation. It is also possible that the

results of prior studies may be at least partially explained by residual confounding by indication. The sicker patients may have received more sedation and were also more likely to have worse clinical outcomes. Our results suggest that the deep sedation group had worse clinical outcomes in unadjusted analysis, though this relationship was no longer present in the propensity matched models.

This study has several strengths. Only patients with moderate-to-severe ARDS ($\text{PaO}_2:\text{FiO}_2 < 150$ mmHg with a positive end expiratory pressure of ≥ 8 cm H_2O) were enrolled in the ROSE trial and thus included in this cohort study. Detailed information on baseline comorbidities and ARDS severity of illness were collected as part of the trial and allowed for matching based on these characteristics. We were able to evaluate sedation early in the disease course. To be eligible for the ROSE study, patients had moderate-severe ARDS for < 48 h and we used the sedation score prior to randomization in our analyses. All participants were treated with a strategy of low tidal volume ventilation within 2 h after randomization and a high PEEP strategy for up to 5 days after randomization per study protocol. Sedation data was complete on 96.2% of the participants. Finally, participants were enrolled from 48 hospitals across the United States, which supports the generalizability of our findings.

Our study also has several limitations. This study was a secondary analysis of a randomized control trial, and the findings may not be generalizable to a more general population that is not enrolled in a clinical trial. There is a risk of misclassification of depth of sedation over time in this secondary analysis. The sedation scores collected as part of the trial may not reflect the variability of sedation over time that occurs following initiation of mechanical ventilation. Patients may have crossed over from early light sedation to early deep sedation or early deep to early light sedation and this may not have been captured in the data collected. Despite this, our findings were robust when both baseline sedation level and day 1 sedation level were examined as the exposure variable. Subsequent studies designed to evaluate sedation should consider using the sedation index to better capture the fluctuation that may occur over time [3]. It is also important to note that the level of sedation captured by a sedation scale may reflect encephalopathy secondary to the disease process (i.e. septic encephalopathy) and not necessarily medications administered for the intent of sedation. It is possible that the relationship between early depth of sedation and patient outcomes is different for those patients with encephalopathy compared to those patients receiving sedative medications.

Finally, it is possible early light sedation has a small impact on clinical outcomes that this study was under-powered to detect. Patients with a baseline RASS of -2 made up 19% of the deep sedation group. While there was no change in our results when those patients were included in the light sedation group, it is possible there may be a different relationship between moderate sedation and clinical outcome in ARDS patients. There was missing data in several of the variables used to create our propensity score. The optimal approach for handling missing covariate data in propensity score based analyses is unknown, and there is no single method to handle missing values in covariates of a propensity score model which performs optimally in all situations [15,21,22]. Our analysis utilized a complete case analysis. Choi et al. argue that complete case analysis may be a good method for dealing with missing values in covariates when creating a propensity score; statistical efficiency may be lost but the interpretation is clear. We feel the results are still generalizable to a severe ARDS population though complete baseline data would allow for more certainty in that assumption.

5. Conclusion

In this secondary propensity score matched analysis of the ROSE trial we found that achieving the recommended goal of early light sedation was uncommon and was not associated with improved clinical outcomes compared to early deep sedation. Given prior research has shown that early deep sedation is associated with worse clinical

outcomes in a more general ICU population, further work is needed to understand this relationship early in the disease course of patients with moderate-to-severe ARDS.

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Credit author statement

Jessica Palakshappa: conceptualization, formal analysis, methodology, visualization, writing original draft, writing reviewing and editing
Gregory Russell: methodology, formal analysis, visualization, writing, reviewing and editing.

Kevin Gibbs: visualization, reviewing and editing.

Chad Kloefkorn: conceptualization, methodology, writing, reviewing and editing.

Douglas Hayden: conceptualization, formal analysis, methodology reviewing and editing.

Marc Moss: conceptualization, reviewing and editing.

Catherine L. Hough: conceptualization, methodology, writing, reviewing and editing.

Daniel Clark Files: conceptualization, methodology, writing, supervision.

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