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Sedation/Delirium

μImpact of a nursing-driven sedation protocol with criteria for infusion initiation in the surgical intensive care unit

Justin B. Kaplan [a,1], Daniel S. Eiferman [b], Kyle Porter [c], Jennifer MacDermott [d,2], Jessica Brumbaugh [e], Claire V. Murphy [a,*]

[a] Department of Pharmacy, The Ohio State University Wexner Medical Center, 410 W. 10th Avenue, Columbus, OH 43210, USA
[b] Department of Surgery, Division of Critical Care, Trauma, and Burn, The Ohio State University Wexner Medical Center, 410 W. 10th Avenue, Columbus, OH 43210, USA
[c] Center for Biostatistics, Department of Biomedical Informatics, College of Medicine, The Ohio State University, 1800 Cannon Drive, Columbus, OH 432101, USA
[d] Center for Quality and Education, The Ohio State University Wexner Medical Center, 410 W. 10th Avenue, Columbus, OH 43210, USA
[e] The Ohio State University College of Pharmacy, 217 Lloyd M Parks Hall, 500 W. 12th Avenue, Columbus, OH 43210, USA

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ABSTRACT

Purpose: Analgesia and sedation protocols (ASPs) reduce duration of mechanical ventilation (MV) in the medical intensive care unit (ICU), but data in the surgical ICU (SICU) are limited. The objective of this study was to determine the impact of a nursing-driven ASP with criteria for infusion initiation in the SICU.
Materials and Methods: A single-center, retrospective study compared ventilator-free days at day 28 from start of MV (VFD28) before and after ASP implementation. Secondary endpoints included cumulative opioid and sedative requirements, level of sedation, incidence of delirium, SICU and hospital length of stay.
Results: One hundred thirty two patients were included (66 per group). The protocol group had greater VFD28 compared to the control group (21 vs. 14.5 days, $p = .04$). Lower rates of benzodiazepine (42.4% vs. 84.8%, $p < .001$) and opioid (24.2 vs. 78.8, $p < .001$) infusion use occurred in the protocol group, resulting in lower cumulative doses per ventilator-day through day 7. The protocol group had more documented sedation scores within target range. There were no differences in ICU delirium, SICU or hospital length of stay.
Conclusions: A nursing-driven ASP with criteria for infusion initiation in mechanically-ventilated SICU patients may increase ventilator-free time, maintain patients at the target sedation goal, and reduce opioid and benzodiazepine utilization.

1. Introduction

Sedation protocols have changed sedation practices in the intensive care unit (ICU) [1]. Several studies demonstrated that nursing-driven sedation protocols reduce duration of mechanical ventilation, ICU length of stay, hospital length of stay, and incidence of ventilator-associated pneumonia [2-4]. As a result, these protocols are recommended as standard of care for management of mechanically ventilated patients [5,6].

Despite widespread use, there may be challenges applying sedation protocols and daily spontaneous awakening trials in a surgical intensive care unit (SICU) population with pain and anxiety after trauma or surgery. Patients may require multiple surgical interventions, washouts, and dressing changes that preclude weaning sedation or decreasing the use of narcotic analgesics. Data supporting the use of sedation protocols were derived predominantly from medical ICU populations and limited data currently exist to support these practices in the SICU. Porhomayon and colleagues conducted a single center, observational study suggesting that a sedation protocol reduced duration of mechanical ventilation, opioid consumption, and sedative utilization in a 12-bed SICU. However, their protocol was entirely prescriber-driven, which may limit applicability to institutions using nursing-driven protocols [7]. The objective of this study was to assess the impact of a nursing-driven sedation protocol on duration of mechanical ventilation in a diverse SICU population.

2. Materials and methods

2.1. Study design

A single center, retrospective study was conducted in the 44-bed SICU at a large academic Level 1 Trauma Center to compare duration of mechanical ventilation before and after implementation of the

* Corresponding author at: The Ohio State University Wexner Medical Center, Doan Hall, Room 368, 410 West 10th Avenue, Columbus, OH 43210, USA.
E-mail address: Claire.Murphy@osumc.edu (C.V. Murphy).
[1] Permanent Address: Department of Pharmacy, Overlook Medical Center – Atlantic Health System, 99 Beauvoir Avenue, Summit, NJ 07901, USA.
[2] Permanent Address: Department of Surgery and Critical Care, Riverside Methodist Hospital, 3535 Olentangy River Road, Columbus, OH 43214, USA.

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nursing-driven sedation and analgesia protocol. A nursing-driven sedation protocol was implemented in the SICU at our institution in April 2011. Prior to protocol implementation ("control group"), all decisions related to sedation and pain management were made by the critical care team. Post-implementation ("protocol group"), the protocol enabled nurses to titrate analgesic and sedative medications to achieve adequate pain control (pain score < 5) and light levels of sedation (target Richmond-Agitation Sedation Scale (RASS) score of −1 to +1). Patients were assessed for level of pain and sedation at minimum every 4 h, with reassessment after any bolus administration or infusion

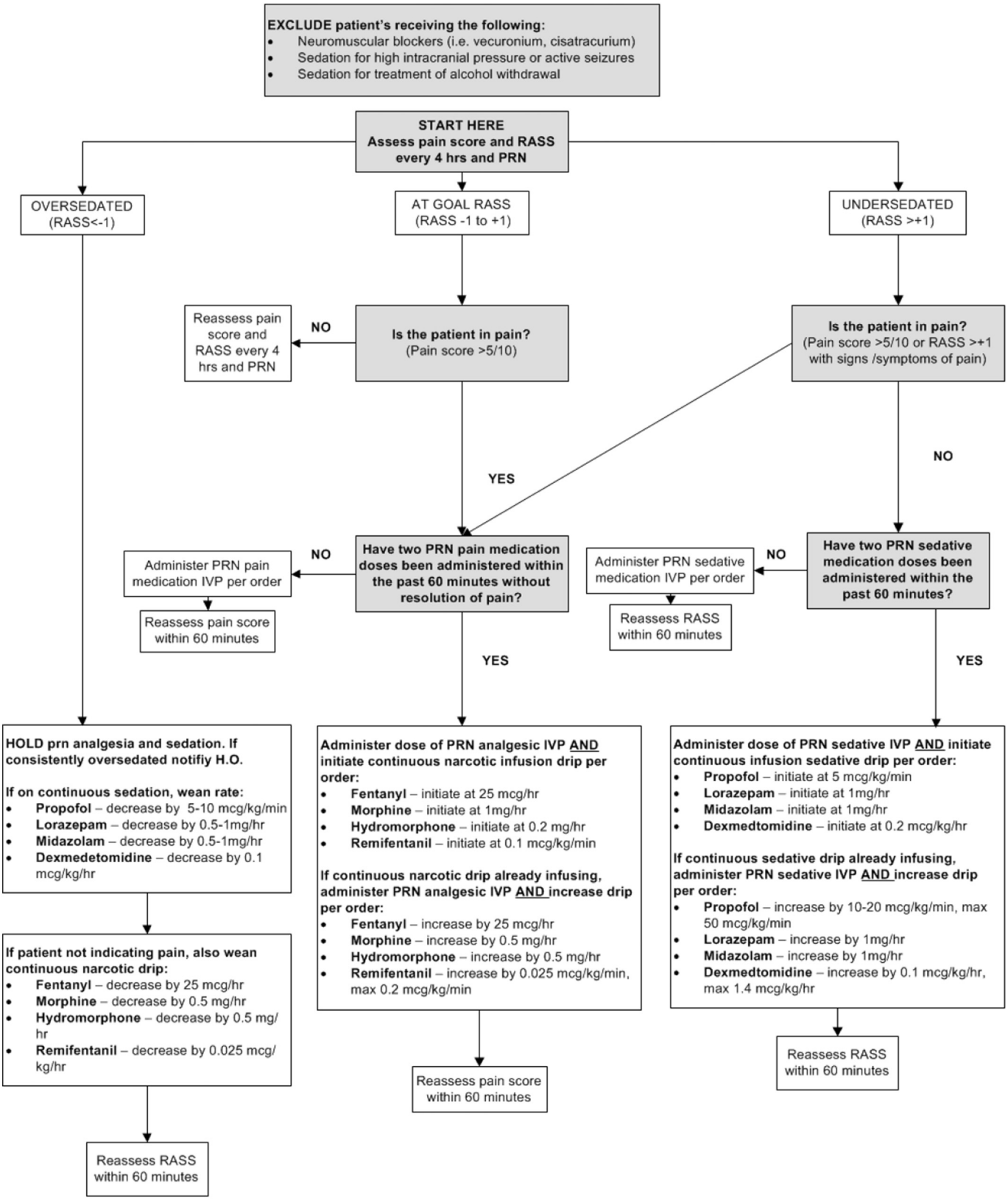

Fig. 1. The Ohio State University Wexner Medical Center sedation and analgesia algorithm for mechanically ventilated patients in the surgical intensive care unit.

dosing rate change at 60 min per nursing policy. More frequent assessment was conducted as needed based on the bedside nurse or provider's discretion. The protocol encouraged intermittent bolus administration of medications first with explicit criteria for initiation of continuous infusions (Fig. 1). Once continuous infusions of either analgesic or sedative medications were initiated, as needed analgesia or sedation was provided using the same drug (e.g., fentanyl bolus for patients on continuous infusion fentanyl, midazolam bolus for patients on continuous infusion midazolam, etc.). The dose for each as needed bolus is included in the institutional order-set for ICU sedation and corresponds with the current dosing rate of the continuous infusion (e.g. 100 μg IV push bolus fentanyl as needed for patient on continuous infusion fentanyl at 100 μg/h). Choice of sedative agent for as needed bolus administration with dexmedetomidine or propofol continuous infusions, and concomitant administration of enteral as needed analgesic or sedative agents were at the discretion of the treating team. This study was approved by the institutional review board.

Eligible patients were aged 18 to 89 years old admitted to the SICU who required at least 24 h of mechanical ventilation. Patients in the control group were admitted between November 1, 2009 and October 31, 2010 and patients in the protocol group between November 1, 2011 and October 31, 2012. A six-month washout period was included after protocol implementation to allow for nursing education and acclimation to the protocol. Patients were excluded for any of the following i) mechanical ventilation prior to hospital admission, ii) incarceration, iii) pregnancy, iv) transferred from another ICU, v) received continuous infusion neuromuscular blockade, inhaled prostacyclins, or deep sedation for the treatment of alcohol withdrawal or active seizures, or vi) transitioned to comfort care or terminally extubated within 7 days of SICU admission. Patients were also excluded if they sustained traumatic brain injury, were admitted to the neurosurgery, neurovascular, or burn services, or had surgical procedures performed by ear, nose, and throat, oral maxillofacial surgery, or plastic surgery for flap placement on the head or neck. These patients were excluded because they may have received mechanical ventilation solely for airway protection, and the nature of their injuries and/or procedures may preclude early extubation.

2.2. Baseline assessment and data collection

Data were collected retrospectively from the electronic medical records. Baseline demographics including age, sex, height, weight, and reason for ICU admission were recorded. Comorbidities were characterized using the Charlson Comorbidity Index, and severity of illness was captured with the Simplified Acute Physiology II (SAPS II) score [8,9]. Substance abuse history was assessed based on documentation in the admission history and physical note and the first SICU admission note. Patients with any active opioid medication on their prior to admission medication reconciliation list were considered opioid-tolerant. All other patients were considered to be opioid-naïve.

Richmond Agitation Sedation Scale (RASS) scores were recorded through day 7 from SICU admission [10]. RASS scores from −1 to +1 were considered to be within the target range. The percentage of patients who received continuous infusions of sedatives (benzodiazepines, propofol, dexmedetomidine) or opioid analgesics (fentanyl, hydromorphone, morphine) was collected. Cumulative doses were calculated for all sedative and opioid medications administered in the SICU through day 7. Cumulative values reflected all intravenous or enterally-administered opioids or sedatives including continuous infusions, scheduled, and as needed medications. These values did not account for any doses given in the operating room. Opioids were converted to intravenous (IV) morphine equivalents using the following conversions: IV morphine 10 mg equals hydromorphone 1.5 mg IV or 7.5 mg PO, oxycodone 20 mg PO, hydrocodone 30 mg PO, codeine 200 mg PO, methadone 3.75 mg IV or 7.5 mg PO [11]. Benzodiazepines were converted to midazolam equivalents using the following conversion: midazolam 0.5 mg equals alprazolam 0.5 mg, chlordiazepoxide 10 mg, diazepam 5 mg, lorazepam 1 mg, and clonazepam 0.25 mg [12]. Cumulative doses of propofol and dexmedetomidine were recorded from the medication administration record. Propofol was converted to micrograms per kilogram per ventilator-day. Dexmedetomidine was converted to micrograms per ventilator-day.

Confusion Assessment Method-Intensive Care Unit (CAM-ICU) results were collected for the first 7 days to assess the presence of delirium. Delirium was diagnosed when at least two consecutive nursing assessments were documented as CAM-ICU positive. Scores documented as “unable to assess” did not necessarily discount the diagnosis of delirium (e.g., if the patient had “delirium” followed by “unable to assess” followed by “delirium,” the patient was still considered to be delirious). Additionally, the initiation of an antipsychotic medication for delirium was collected. Administration of scheduled haloperidol, quetiapine, olanzapine, or risperidone to a patient who was not taking the medication prior to admission to the SICU was considered to be prescribed for treatment of delirium. “As needed” or one-time orders for these medications were not included in this definition. The incidence of self-extubation, time spent in restraints, ICU length of stay, hospital length of stay, and mortality at day 28 were also collected.

2.3. Study outcomes

The primary outcome was ventilator-free days at day 28 (VFD_{28}) from the start of mechanical ventilation. To be considered a VFD, patients had to be sustained without ventilator assistance for the 24-h period from midnight through midnight the following day. Patients who were mechanically ventilated for any amount of time from midnight through midnight the following day were deemed to be on the ventilator for that day. Secondary endpoints included the percentage of patients requiring continuous opioid or sedative infusions, cumulative opioid and sedative medication requirements through day 7, percentage of documented RASS scores within target sedation range through day 7, incidence of delirium, percentage of patients requiring a scheduled antipsychotic for delirium, incidence of self-extubation, restraint requirements, ICU length of stay, and hospital length of stay.

2.4. Statistics

Patient demographics and clinical characteristics were summarized for the control group and protocol group. Categorical variables were compared across study periods using Fisher's exact test. Continuous variables were presented as means and standard deviations (SD) or median and the interquartile range (IQR) depending on the distribution. Differences across time periods were compared using either two-sample *t*-test or Wilcoxon rank-sum test depending on the distribution. The primary outcome of VFD_{28} was compared by the Wilcoxon rank-sum test. We calculated that 66 patients per group would provide 80% power to detect a five-day difference in VFD_{28}. All analyses were run using SAS 9.4 (Cary, NC).

3. Results

Four hundred and eleven patients were screened for the study. After excluding 279 patients (99 admitted to neurosurgery or neurovascular services, 64 intubated for <24 h, 53 transferred from another ICU, 21 admitted to the burn service, 12 terminally extubated, 9 admitted to ENT/plastic surgery/oral maxillofacial surgery, 3 prisoners, and 18 for other reasons), 132 patients were included for evaluation (66 in the protocol group and 66 in the control group). Of the entire cohort, 42% were admitted to the SICU directly from the operating room, 16% were admitted for trauma that did not require surgery, and the remaining 42% were surgical patients readmitted to the SICU for medical complications (e.g., pneumonia, hypoxia). Baseline characteristics are summarized in Table 1. The two groups were similar with respect to age, height, weight, comorbidities, reason for ICU admission, and substance abuse. However,

Table 1
Baseline characteristics of patients in the control and protocol groups. Data are reported as median [25–75% interquartile range] unless otherwise noted.

Characteristic	Control Group (n = 66)	Protocol Group (n = 66)	p-Value
Age (years), mean (SD)	60.2 (17.3)	61.4 (16.6)	0.68
Male sex, n (%)	15 (34.1)	38 (73.1)	<0.001
Height (inches)	67 [64–69.5]	67 [66–70]	0.35
Weight (kg)	78.0 [68.4–103.7]	86.4 [71.9–103.0]	0.46
SAPS II score, mean (SD)*	55.2 (17.3)	48.6 (16.5)	0.03
Charlson Comorbidity Index	3 [2–4]	3 [2–4]	0.66
Reason for ICU admission, n (%)			0.16
Post-operative	31 (47.0)	24 (36.4)	
Trauma	13 (19.7)	9 (13.6)	
Other	22 (33.3)	33 (50)	
Primary service, n(%)			0.70
Acute care surgery	25 (37.9)	28 (42.4)	
Gastrointestinal surgery	14 (21.2)	9 (13.6)	
Thoracic surgery	8 (12.1)	10 (15.2)	
Other	19 (28.8)	19 (28.8)	
Medication history, n(%)			
Opioid-tolerant	18 (27.3)	31 (47.0)	0.03
Benzodiazepine-tolerant	9 (13.6)	7 (10.6)	0.79
Substance abuse	9 (13.6)	6 (9.1)	0.58

* SAPS II = Simplified Acute Physiology II.

the protocol group had a higher percentage of patients who were male and opioid-tolerant. The protocol group also had lower severity of illness per SAPS II score compared to the control group.

The SICU sedation protocol was associated with a greater median VFD_{28} compared to the control group (21 vs. 14.5 days, $p = .04$, Fig. 2). A lower percentage of patients in the protocol group received continuous infusion benzodiazepines (42.4% vs. 84.8%, $p < .001$) and continuous infusion opioids (24.2% vs 78.8%, $p < .001$) as compared with the control group. The protocol was also associated with significant reductions in median benzodiazepine use per ventilator-day, median opioid use per ventilator-day, and median dexmedetomidine use per ventilator-day through day 7. Propofol use per ventilator-day for the same time period did not differ significantly between groups (Table 2).

The protocol group had a greater percentage of documented RASS scores within the target sedation range of −1 to +1 compared to the control group ($p < .001$) and a lower percentage of documented RASS scores below −1 ($p < .001$), (Fig. 3). Very few documented scores in either group were above RASS of +1. The incidence of delirium captured with a positive CAM-ICU score was 25.8% in the protocol group compared to 30.3% in the control group ($p = .45$). A higher percentage of patients were treated with antipsychotics for delirium after protocol implementation although the difference was not statistically significant (33.3% vs. 25.8%, $p = .45$).

There were no differences in time spent in restraints per ventilator-day or number of self-extubations through day 7. Eight patients in the entire cohort self-extubated during the study period (6 in the protocol group, 2 in the control group). Three of the self-extubation patients in the protocol group required re-intubation within 24 h, while neither in the control group required re-intubation. The median ICU length of stay was 11 days in both groups ($p = .39$) and median hospital length of stay was 21.5 days compared to 22 days in the protocol and control groups, respectively ($p = .82$).

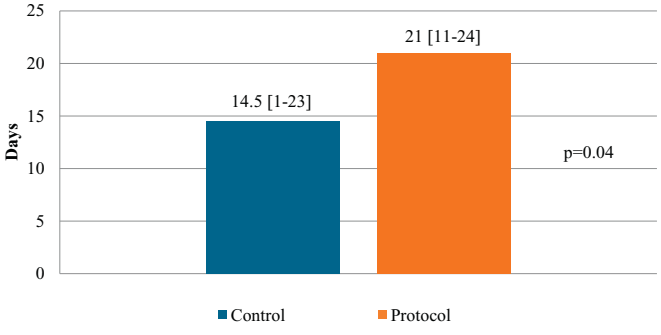

Fig. 2. Median ventilator-free days at day 28 from start of mechanical ventilation is shown. Data are represented as median [25–75% interquartile range].

4. Discussion

In this retrospective study of mechanically ventilated patients admitted to the SICU, a nursing-driven sedation protocol was associated with more ventilator-free days at day 28 by approximately 6.5 days. Benefits of the protocol also included fewer patients receiving continuous infusion opioids or sedatives, lower cumulative doses of opioids and benzodiazepines, and a greater number of documented RASS scores within the target sedation range.

Analgesia and sedation protocols have long been supported in medical ICU populations, but data are still limited for use in surgical ICU patients. In a mixed medical-surgical ICU population, Arias-Rivera and colleagues found that a nursing-driven sedation protocol did not have a significant impact on duration of mechanical ventilation or cumulative doses of sedatives and analgesics as compared to standard sedation practices [13]. In contrast, other studies suggest that protocolized pain and sedation in mechanically ventilated SICU patients may minimize ventilator time. Robinson and colleagues showed a reduction in duration of mechanical ventilation in trauma patients which translated into shorter hospital length of stay. Their study results, however, have limited generalizability to non-trauma SICU patients [14]. Porhomayon and colleagues demonstrated a shorter median duration of mechanical ventilation by two days with a sedation and analgesia protocol in a general SICU population [7]. However, the protocol used was exclusively prescriber-driven which may limit application of the findings to institutions using nursing-driven protocols [7]. The results of our study suggest that the benefit of increased ventilator-free time may also be applicable to a broader surgical population following a nursing-driven protocol.

To our knowledge, our study is the first to demonstrate that a purely nursing-driven sedation and analgesia protocol with criteria for infusion initiation may be beneficial in a diverse surgical population. The protocol aligns with the current Society of Critical Care Medicine Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption Guidelines which recommend the use of a validated tool for monitoring depth of sedation, an analgesia-first approach to sedation, and intermittent administration of analgesics and sedatives prior to continuous infusions [5]. The protocol used in this study almost entirely removed prescriber decision-making with respect to analgesic and sedative medications. The criteria-based protocol was intended to reduce the amount of sedation while minimizing use of continuous infusions. The clearly defined criteria required pain to be assessed and treated prior to administration of a sedative agent, and continuous analgesia and/or sedative infusions were only initiated if two bolus doses within a 60-min period failed to achieve the desired effect. Additionally, the protocol explicitly guided nurses in down-titrating and stopping analgesic and sedative infusions in response to oversedation. This component may be especially important in a surgical population to facilitate more rapid awakening and earlier assessment for extubation after surgical procedures. The combination of both the nursing-driven approach and a clearly defined starting and stopping criteria for infusions may be essential factors in increasing ventilator-free time in the critically-ill surgical population.

Beyond reducing ventilator time, our study corroborates previous findings that sedation protocols reduce the number of patients receiving continuous infusions of opioids and benzodiazepines and lowers cumulative sedative and pain medication requirements [2,3,7,14]. This held true in the protocol group despite having a greater number of patients who were opioid-tolerant at baseline. Utilization of non-benzodiazepine continuous infusion sedatives (e.g., propofol) did not

Table 2
Secondary endpoints related to analgesic and sedative utilization, ICU and hospital length of stay, and in-hospital mortality are shown. Data are reported as median [25–75% interquartile range] unless otherwise noted.

Endpoint	Control Group (n = 66)	Protocol Group (n = 66)	p-Value
Opioid use (IV morphine equivalents per ventilator-day)*	73.5 [20–136]	29.5 [17–52.5]	<0.001
Benzodiazepine use (midazolam equivalents per ventilator-day)*	10.4 [3.1–23.3]	2 [0.8–5.9], n = 63	<0.001
Propofol μg/kg/ventilator-day*	3563 [253–12,679], n = 14	2484 [82–8194], n = 17	0.32
Dexmedetomidine μg/kg/ventilator-day	376 [352–382], n = 5	183 [86–236], n = 7	0.03
Ventilator-days spent in restraints	4 [3–6]	4 [2–7]	0.81
Self-extubation events through day 7	2 (3.0%)	6 (9.1%)	0.27
ICU length of stay, days	11 [8–25]	11 [7–19]	0.39
Hospital length of stay, days	22 [12–39]	21.5 [14–35]	0.82
In-hospital mortality, n (%)	18 (27.3%)	11 (16.7%)	0.21

* Cumulative doses through day 7.

differ significantly between the protocol and control groups. This confirms that the reduction in benzodiazepine consumption was not simply offset by use of alternative agents. Judicious use of opioid and sedative medications in the protocol group translated into a greater percentage of RASS scores within target range and fewer RASS scores consistent with over-sedation.

The trend towards lower rates of ICU delirium in the protocol group may be related to lower cumulative exposure to benzodiazepines and that patients were less likely to be oversedated. Despite the positive trend, a statistically significant difference in ICU delirium was not found. A heightened awareness of ICU delirium and greater understanding of the CAM-ICU tool may have increased the likelihood of diagnosing ICU delirium in the protocol period as a result of provider and nursing education. It may also account for the observed increase in antipsychotics as a proactive intervention to treat ICU delirium in the protocol group. We hypothesize that these factors coupled with the lack of statistical power to detect a difference in ICU delirium as a secondary endpoint may explain these results.

One of the criticisms of our findings may be that ICU length of stay and hospital length of stay were unaffected despite increase in ventilator-free days in the protocol group. In a medical population, the primary factor keeping patients in the ICU is often acute respiratory failure requiring mechanical ventilation. In contrast, surgical patients may have additional factors precluding transfer out of the ICU after extubation such as management of indwelling catheters and drains or planned future trips to the operating room with anticipated need for ICU care post-operatively. While ICU length of stay was not reduced, there is undeniably a benefit to increasing ventilator-free days such as reducing incidence of ventilator-associated pneumonia and ICU acquired muscle weakness among others not evaluated in our study. Additionally, it may be notable that the frequency of self-extubations

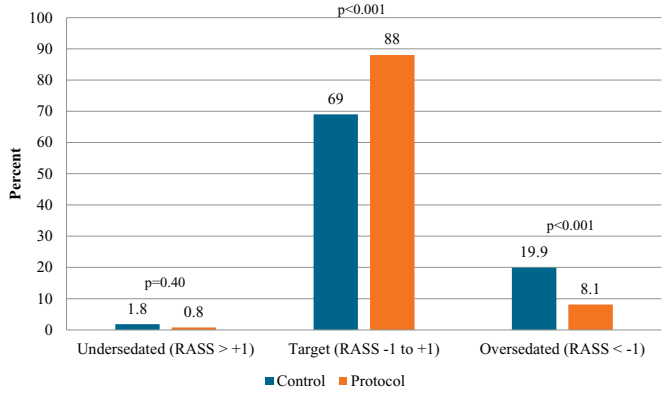

Fig. 3. Proportion of documented Richmond Agitation Sedation Scores (RASS) that met criteria for undersedated, target sedation, and oversedation within the first seven days from the start of mechanical ventilation for the control and protocol groups.

was higher in the protocol group compared to the control group. A plausible explanation may be that the deeper level of sedation in the control group precluded patients from pulling out their endotracheal tubes. Of the patients who self-extubated in the protocol group, only 50% required reintubation within 24 h suggesting that the others were ready to be liberated from the ventilator. While unintentional self-extubation may pose potential harm to patients, a reasonable number of self-extubations is expected with any strategy targeting a more awake patient. In our study, there was no significant harm to any patient that self-extubated.

There were several limitations to this study. First, it was a small, single-center, retrospective review and the quality of the data was limited by documentation in the electronic medical record. The electronic medical record system used by the institution changed in between the time periods of the study. Therefore, data for each group were recorded and collected from different systems, which may have impacted our results. Second, there were differences in baseline characteristics between the groups. Patients in the control group may have been sicker based on the SAPS II score. Given that the acuity of patients in the SICU should not have changed between the study time periods, we hypothesize that this finding is due to chance. Third, the institution did not utilize a validated tool for assessment of pain in non-verbal patients during the study period. Due to the limitations of using the self-reported numeric rating score pain scale in ICU patients and lack of objective assessment tool, we were unable to evaluate the impact of the protocol on pain control. Fourth, the protocol mandates that all patients with RASS scores outside the target range be treated accordingly and reassessed within 60 min. Assuming the nursing assessment was accurate, it would be expected that the "re-check" would find the patient back in the target range. Compared to the control group, this may have artificially increased the number of documented RASS scores within the target range. The ideal method for assessing level of sedation and pain control in retrospective studies remains unknown. Fifth, the severity of agitation (e.g., RASS +2 vs. RASS +4) may warrant a different response from the clinical team. A higher degree of agitation may require closer monitoring and earlier reassessment after administration of as needed analgesic or sedative agents. This issue is not addressed by the protocol, which still relies on the clinical judgment of the bedside nurse and treating team to address a severely agitated patient. Lastly, the retrospective nature of the study precluded investigators from assessing adherence to the protocol.

In summary, the nursing-driven sedation protocol for mechanically ventilated patients in the SICU was associated with more time free of mechanical ventilation. Lower benzodiazepine utilization and fewer pain and sedative continuous infusions may allow for more timely extubation and reduce incidence of ICU delirium. Larger randomized controlled trials utilizing a nursing-driven sedation and analgesia protocol should be performed in a SICU population to validate these findings.

Declarations of interest

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