

# The Use of Continuous IV Sedation Is Associated With Prolongation of Mechanical Ventilation\*

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**Study objective:** To determine whether the use of continuous IV sedation is associated with prolongation of the duration of mechanical ventilation.

**Design:** Prospective observational cohort study.

**Setting:** The medical ICU of Barnes-Jewish Hospital, a university-affiliated urban teaching hospital.

**Patients:** Two hundred forty-two consecutive ICU patients requiring mechanical ventilation.

**Interventions:** Patient surveillance and data collection.

**Measurements and results:** The primary outcome measure was the duration of mechanical ventilation. Secondary outcome measures included ICU and hospital lengths of stay, hospital mortality, and acquired organ system derangements. A total of 93 (38.4%) mechanically ventilated patients received continuous IV sedation while 149 (61.6%) patients received either bolus administration of IV sedation (n=64) or no IV sedation (n=85) following intubation. The duration of mechanical ventilation was significantly longer for patients receiving continuous IV sedation compared with patients not receiving continuous IV sedation (185±190 h vs 55.6±75.6 h; p<0.001). Similarly, the lengths of intensive care (13.5±33.7 days vs 4.8±4.1 days; p<0.001) and hospitalization (21.0±25.1 days vs 12.8±14.1 days; p<0.001) were statistically longer among patients receiving continuous IV sedation. Multiple linear regression analysis, adjusting for age, gender, severity of illness, mortality, indication for mechanical ventilation, use of chemical paralysis, presence of a tracheostomy, and the number of acquired organ system derangements, found the adjusted duration of mechanical ventilation to be significantly longer for patients receiving continuous IV sedation compared with patients who did not receive continuous IV sedation (148 h [95% confidence interval: 121, 175 h] vs 78.7 h [95% confidence interval: 68.9, 88.6 h]; p<0.001).

**Conclusion:** We conclude from these preliminary observational data that the use of continuous IV sedation may be associated with the prolongation of mechanical ventilation. This study suggests that strategies targeted at reducing the use of continuous IV sedation could shorten the duration of mechanical ventilation for some patients. Prospective randomized clinical trials, using well-designed sedation guidelines and protocols, are required to determine whether patient-specific outcomes (eg, duration of mechanical ventilation, patient comfort) can be improved compared with conventional sedation practices. (CHEST 1998; 114:541-548)

**Key words:** critical care; intensive care unit; mechanical ventilation; outcomes; sedation

**Abbreviations:** ALI=acute lung injury; APACHE=acute physiology and chronic health evaluation; CI=confidence interval; FIO<sub>2</sub>=fraction of inspired oxygen; OR=odds ratio; SCC=Spearman correlation coefficient

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The presence of acute pain and anxiety are common among patients admitted to ICUs.<sup>1,2</sup> The most common reasons for such pain and anxiety include the patient's underlying disease process (eg,

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metastatic carcinoma, trauma), the performance of diagnostic or therapeutic procedures, patient interaction with life-sustaining interventions (eg, mechan-

ical ventilation, dialysis), and physical isolation from familiar surroundings and loved ones.<sup>2</sup> Narcotics are the most common class of drugs used for the management of acute pain in the ICU while benzodiazepines, major tranquilizers (*eg*, phenothiazines and butyrophenones), and propofol are the agents most commonly prescribed to achieve sedation.<sup>3,4</sup> To date, most clinical trials of analgesics and sedatives have been comparative studies with the goal of identifying the agent or agents associated with the best clinical efficacy and least toxic reactions.<sup>5-11</sup> Few studies have attempted to systematically evaluate the influence of analgesics and sedatives on the overall outcomes of critically ill patients.<sup>12,13</sup>

Based on the combined clinical experience of the multidisciplinary patient care team from our ICU, we hypothesized that the use of continuous IV sedation may be associated with prolongation of mechanical ventilation compared with other sedation practices (*eg*, bolus administration of sedatives and analgesics). This hypothesis was also supported by several clinical studies demonstrating that clinicians often prescribe analgesics and sedatives in an inconsistent manner without recognizing the full influence of these medications on patient outcomes.<sup>14,15</sup> Therefore, we performed a prospective observational cohort study that had two main goals. The first goal was to identify the various patterns of IV sedation administration within a medical ICU patient population. The second goal of this study was to compare patient outcomes according to the use of continuous IV sedation. It was our hope that such preliminary data could prove useful for the development of clinical protocols or guidelines outlining the optimal administration of these agents within the ICU setting. Additionally, these study results may serve as a foundation for the development of future randomized clinical trials examining different sedation practices.

## MATERIALS AND METHODS

### *Study Location and Patients*

The study was conducted at a university-affiliated urban teaching hospital: Barnes-Jewish Hospital (1,400 beds). During a 5-month period (August 1997 to December 1997), all patients receiving mechanical ventilation in the medical ICU (19 beds) were potentially eligible for this investigation. Patients were entered into the investigation if they were >17 years and excluded if they were temporarily admitted (*ie*, <24 h) to the medical ICU from a surgical service while awaiting a surgical ICU bed. The study was approved by the Washington University School of Medicine Human Studies Committee.

### *Study Design*

A prospective cohort study design was employed segregating patients according to whether they received continuous IV

sedation. The duration of mechanical ventilation was the main outcome variable compared between the two study groups. Secondary outcome variables evaluated included hospital mortality, lengths of intensive care and hospitalization, reintubation, the need for a tracheostomy, and the development of acquired organ system derangements. For purposes of this investigation, continuous IV sedation was considered to be present whenever a patient received an IV infusion of an analgesic or sedative class of agents (*eg*, narcotics, major tranquilizers, benzodiazepines, propofol). The bolus administration of these agents was also recorded. The use of these medications to facilitate endotracheal intubation was not recorded. This was purposely done in order to capture the pattern of IV sedation administration occurring during mechanical ventilation after the intubation procedure. Per our hospital's ICU nursing guidelines, the administration of IV sedation is usually titrated to achieve a targeted Ramsay level of 3.<sup>2,3</sup>

For all study patients, the following characteristics were recorded prospectively by one of the investigators: age, gender, ethnicity, the ratio of arterial blood oxygen tension to the concentration of inspired oxygen ( $\text{PaO}_2/\text{FIO}_2$ ), severity of illness based on APACHE II (acute physiology and chronic health evaluation) scores,<sup>16</sup> predicted mortality using APACHE II, the underlying indication for mechanical ventilation, the presence of COPD requiring treatment with corticosteroids or bronchodilators, underlying malignancy, and congestive heart failure requiring treatment with diuretics, vasodilators, or inotropes. One of the investigators made daily rounds on all study patients in the medical ICU to identify eligible patients. Patients entered into the study were prospectively followed up until they were successfully liberated from mechanical ventilation, discharged from the hospital, or died.

### *Definitions*

All definitions were selected prospectively as part of the original study design. We calculated APACHE II scores on the basis of clinical data available from the first 24-h period of intensive care.<sup>16</sup> The definitions for ARDS and acute lung injury (ALI) were taken from the American-European Consensus Statement.<sup>17</sup> For purposes of this investigation, pneumonia as an indication for mechanical ventilation included both community-acquired and hospital-acquired pneumonia. Pneumonia was determined to be present when a new or progressive infiltrate developed in conjunction with one of the following: radiographic evidence of pulmonary abscess formation; histologic evidence of pneumonia in lung tissue; a positive blood or pleural fluid culture; or two of the following: fever (temperature >38.3°C); leukocytosis (leukocyte count >10×10<sup>3</sup>/mm<sup>3</sup>); and purulent tracheal aspirate. Blood and pleural fluid cultures could not be related to another source and both had to be obtained within 48 h before or after the clinical suspicion of pneumonia. Microorganisms recovered from blood or pleural fluid cultures also had to be identical to the organisms recovered from cultures of respiratory secretions.

The organ system failure index was modified from that used by Rubin and coworkers.<sup>18</sup> One point was given for acquired dysfunction of each organ system as follows: renal, a twofold increase in baseline creatinine level or an absolute increase in baseline creatinine of 176.8 μmol/L (2.0 mg/dL); hepatic, an increase in total bilirubin level to >34.2 μmol/L (2.0 mg/dL); pulmonary: (1) a requirement for mechanical ventilation for a diagnosis of pneumonia, COPD, asthma, or pulmonary edema (cardiogenic or noncardiogenic), (2) a  $\text{PaO}_2$  of <60 mm Hg while receiving a fraction of inspired oxygen ( $\text{FIO}_2$ ) of ≥0.50, or (3) the use of at least 10 cm H<sub>2</sub>O of positive end-expiratory pressure; hematologic, the presence of disseminated intravascular coagu-

lation, a leukocyte count of  $<1,000$  cells/mm<sup>3</sup> ( $1.0 \times 10^9$ /L), or a platelet count of  $<75 \times 10^3$ /mm<sup>3</sup> ( $75 \times 10^9$ /L); neurologic, a new focal deficit (such as hemiparesis after cerebral infarction) or a new generalized process (for example, seizures or coma); GI, GI hemorrhage requiring blood transfusion, new ileus, or diarrhea lasting  $>24$  h and unrelated to previous bowel surgery; and cardiac, acute myocardial infarction, cardiac arrest (including significant acute arrhythmias requiring chemical or electrical cardioversion or defibrillation), or the new onset of congestive heart failure requiring medical therapy.

### Statistical Analysis

All comparisons were unpaired and all tests of significance were two tailed. Continuous variables were compared using the Student *t* test for normally distributed variables and the Wilcoxon rank-sum test for nonnormally distributed variables. The  $\chi^2$  test or Fisher's Exact Test were used to compare categorical variables. The primary data analysis compared two groups, patients receiving continuous IV sedation and patients who received either bolus IV sedation or no IV sedation following tracheal intubation. Values are expressed as the mean  $\pm$  SD (continuous variables) or as a percentage of the group from which they were derived (categorical variables). All *p* values were two tailed and *p* values  $\leq 0.05$  were considered to indicate statistical significance.

A linear regression model was used to test the null hypothesis that there was no difference in selected outcome variables between the patients receiving continuous IV sedation and those who did not.<sup>19</sup> This test controlled for age, gender, severity of illness using APACHE II, indication for mechanical ventilation, use of chemical paralysis, presence of a tracheostomy, the number of acquired organ system derangements, and mortality. Mortality was included because early death could artificially decrease lengths of stay. Linear least-squares regression techniques were then used to compare adjusted outcome measures between the groups of interest. Outcome measures were adjusted for the above-noted variables. Results were similar whether mortality was included in the model. Residual plots indicated the possibility of a nonnormal distribution of the data. Regressions were repeated after logarithmic transformation of outcome measures, with similar results. Therefore, the results of ordinary least-squares regression are presented. All adjusted means are predicted values evaluated at the means of the adjustment variables from the least-squares regression model. We have reported actual *p* values.

## RESULTS

### Patients

A total of 242 consecutive patients requiring mechanical ventilation were evaluated. The mean age of the patients was  $56.3 \pm 17.5$  years (range, 18 to 105 years). The mean APACHE II score was  $20.8 \pm 8.1$  (range, 1 to 59). One hundred twenty-one (50%) patients were men and 121 (50.0%) were women. The indications for mechanical ventilation included respiratory failure due to pneumonia (20.2%), drug overdose (8.3%), ARDS or ALI associated with sepsis or aspiration (13.6%), COPD or asthma (22.7%), pulmonary edema (11.2%), cardiac arrest (8.7%), pulmonary embolus (4.1%), and a miscellaneous category (mechanical ventilation following

neurologic dysfunction, for upper airway protection, following endoscopic procedures, or for an unclear etiology of respiratory failure) (11.2%).

### Continuous IV Sedation

Ninety-three (38.4%) patients received continuous IV sedation during their course of mechanical ventilation in the medical ICU. The main indication for the administration of continuous IV sedation was patient discomfort resulting from the application of mechanical ventilation. Patients receiving continuous IV sedation were statistically younger, had lower PaO<sub>2</sub>/FIO<sub>2</sub> ratios, and were more likely to have ARDS or ALI as an indication for mechanical ventilation compared with patients who did not receive continuous IV sedation (Table 1). Additionally, patients with underlying COPD and white patients were more likely to receive continuous IV sedation. However, these differences did not reach statistical significance. No statistically significant differences in the clinical characteristics shown in Table 1 were found between patients receiving bolus administration of IV sedation (*n*=64) and patients receiving no IV sedation (*n*=85) following tracheal intubation.

Lorazepam (72.0%) and fentanyl (71.0%) were the two most commonly prescribed agents for continuous IV sedation (Table 2). The overall duration of administration for continuous IV sedation was  $6.0 \pm 6.4$  days. Twelve (12.9%) of the patients receiving continuous IV sedation also received chemical paralysis while 66 (71.0%) of these patients also received bolus infusions of IV sedation. The number of patients receiving bolus infusions of IV sedation was statistically greater among patients who also received continuous IV sedation (Table 2).

### Clinical Outcomes

The outcome variables are shown in Table 3. The unadjusted mean duration of mechanical ventilation was statistically greater among patients receiving continuous IV sedation compared with patients who did not receive continuous IV sedation. The curves in Figure 1 demonstrate the duration of mechanical ventilation for patients with and without the administration of continuous IV sedation. These curves diverge primarily during the first 2 weeks of mechanical ventilation. Similarly, patients receiving continuous IV sedation had significantly longer lengths of intensive care and hospitalization, more acquired organ system derangements, and a greater incidence of reintubation (Table 3). No statistically significant difference in hospital mortality or the use of tracheostomy was observed according to the use of continuous IV sedation. No statistically significant differences were found comparing patients receiving only

**Table 1—Baseline Patient Characteristics and Indication for Mechanical Ventilation Stratified According to Method of IV Sedation\***

Variable	Continuous IV Sedation (n=93)	No Continuous IV Sedation (n=149)	p Value
<b>Baseline characteristics</b>			
Age, yr	48.8±16.8	60.9±16.3	<0.001
Gender, No. (%)			
Male	42 (45.2)	79 (53.0)	0.234
Female	51 (54.8)	70 (47.0)	
Race, No. (%)			
White	57 (61.3)	71 (47.7)	0.071
Black	34 (36.6)	76 (51.0)	
Other	2 (2.1)	2 (1.3)	
COPD, No. (%)	40 (43.0)	47 (31.5)	0.071
Congestive heart failure, No. (%)	5 (5.4)	7 (4.7)	0.813
Underlying malignancy, No. (%)	18 (19.4)	29 (19.5)	0.983
APACHE II score	20.2±6.5	21.2±8.9	0.702
Predicted mortality	35.8±22.1	38.9±28.3	0.702
PaO <sub>2</sub> /FIO <sub>2</sub>	175±107	232±152	0.005
<b>Indication for Mechanical Ventilation</b>			
Pneumonia, No. (%)	22 (23.7)	27 (18.1)	0.297
Drug overdose, No. (%)	5 (5.4)	15 (10.1)	0.197
ARDS or ALI, No. (%)	18 (19.4)	15 (10.1)	0.041
COPD/asthma, No. (%)	22 (23.7)	33 (22.2)	0.785
Pulmonary edema, No. (%)	11 (11.8)	16 (10.7)	0.793
Cardiac arrest, No. (%)	5 (5.4)	16 (10.7)	0.149
Pulmonary embolus, No. (%)	4 (4.3)	6 (4.0)	>0.999
Other, No. (%)	6 (6.4)	21 (14.1)	0.066

\*Means are expressed±SD.

bolus administration of IV sedation with patients receiving no IV sedation for the duration of mechanical ventilation (68.5±73.9 h vs 45.9±75.8 h; p=0.070) and the hospital length of stay (14.8±15.4 days vs 11.3±12.9 days; p=0.127). However, the ICU length of stay was statistically greater among

patients receiving bolus administration of IV sedation (5.7±4.2 days vs 4.1±3.9 days; p=0.017).

The duration of mechanical ventilation for the entire study group was found to be significantly correlated with APACHE II scores (Spearman correlation coefficient [SCC]=0.2527, p<0.001), pre-

**Table 2—Use of IV Sedation and Chemical Paralysis**

Variable	Continuous IV Sedation (n=93)	No Continuous IV Sedation (n=149)	p Value
<b>Continuous infusion agent, No. (%)</b>			
Lorazepam	25 (26.9)	—	
Fentanyl	24 (25.8)	—	
Propofol	2 (2.1)	—	
Lorazepam+fentanyl	42 (45.2)	—	
Duration of continuous infusion, d	6.0±6.4	—	
Bolus sedation, No. (%)	66 (71.0)	64 (42.9)	<0.001
<b>Bolus infusion agent, No. (%)</b>			
Lorazepam	16 (17.2)	14 (9.4)	0.073
Fentanyl	9 (9.7)	7 (4.7)	0.129
Midazolam	5 (5.4)	8 (5.4)	0.998
Morphine	3 (3.2)	1 (0.7)	0.160
Lorazepam+fentanyl	32 (34.4)	33 (22.2)	0.036
Haloperidol	1 (1.1)	1 (0.7)	>0.999
Duration of bolus sedation, d	2.3±3.6	1.6±0.7	0.389
Bolus doses administered	4.6±5.4	3.7±2.5	0.901
Chemical paralysis, No. (%)	12 (12.9)	0 (0.0)	<0.001
Duration of chemical paralysis, d	4.0±3.4	—	

**Table 3—Clinical Outcome Measures\***

Outcome	Continuous IV Sedation (n=93)	No Continuous IV Sedation (n=149)	p Value
Duration of mechanical ventilation, h	185±190	55.6±75.6	<0.001
Length of intensive care, d	13.5±33.7	4.8±4.1	<0.001
Length of hospital stay, d	21.0±25.1	12.8±14.1	<0.001
Acquired organ system derangements	3.1±2.2	2.5±1.4	0.018
Reintubation, No. (%)	14 (15.1)	7 (4.7)	0.005
Tracheostomy, No. (%)	15 (16.1)	13 (8.7)	0.080
Hospital mortality, No. (%)	28 (30.1)	50 (33.6)	0.576

\*Mean±SD.

dicted mortality using APACHE II (SCC=0.2539,  $p<0.001$ ), the number of acquired organ system derangements (SCC=0.3825,  $p<0.001$ ), and the duration of continuous IV sedation (SCC=0.7989,  $p<0.001$ ). Comparison of the mean length of stay variables with adjustment for age, gender, severity of illness, mortality, indication for mechanical ventilation, use of chemical paralysis, presence of a tracheostomy, and the number of acquired organ system derangements demonstrated significant differences according to the presence or absence of continuous IV sedation (Table 4). The unadjusted and adjusted distributions of the duration of mechanical ventilation according to the use of continuous IV sedation are shown in Figure 2.

### Hospital Mortality

Seventy-eight (32.2%) of the patients died during their hospitalization. APACHE II scores were significantly greater in hospital nonsurvivors compared with hospital survivors ( $26.1\pm 8.0$  vs  $18.3\pm 6.9$ ;  $p<0.001$ ). Multiple logistic regression analysis identified predicted mortality using APACHE II

(adjusted odds ratio [OR]=1.04; 95% confidence interval [CI]=1.03 to 1.05;  $p<0.001$ ), the number of acquired organ system derangements (adjusted OR=1.25; 95% CI=1.14 to 1.38;  $p=0.014$ ), and the presence of a tracheostomy (adjusted OR=2.69; 95% CI=1.64 to 4.39;  $p=0.044$ ) as being significantly related to hospital mortality while controlling for other potential confounding variables.

### DISCUSSION

We demonstrated a statistically significant association between the use of continuous IV sedation and the duration of mechanical ventilation. Even after adjusting for potential confounding variables, multiple linear regression analysis demonstrated that patients receiving continuous IV sedation had nearly twice the duration of mechanical ventilation compared with patients not receiving continuous IV sedation. Similarly, the adjusted ICU and hospital lengths of stay were statistically greater among patients receiving continuous IV sedation. These preliminary observations are important in identifying a potentially modifiable variable that could directly influence patient outcomes. Our data suggest that more prudent administration of continuous IV sedation may reduce the duration of mechanical ventilation among some patients admitted to the ICU setting. Although mechanical ventilation is often a life-sustaining intervention, shortening the duration of ventilatory support represents an important quality-of-life outcome due to patient discomfort and the inherent risks associated with endotracheal intubation and ventilatory support.<sup>20,21</sup> Prolonging the time spent receiving mechanical ventilation can increase a patient's likelihood for developing specific complications, including ventilator-associated pneumonia, barotrauma, airway complications (eg, tracheal stenosis and ulceration), and unanticipated extubation with resultant arterial oxygen desaturation.<sup>22-25</sup> Indeed, clinicians are frequently faced with the dilemma of trying to liberate patients from mechanical

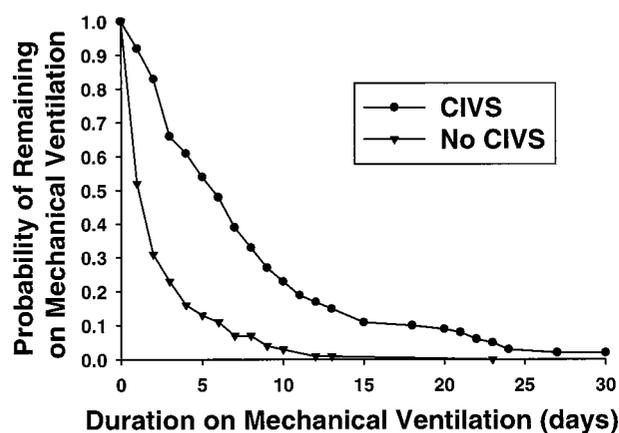


FIGURE 1. Kaplan-Meier curves for patients receiving continuous IV sedation (CIVS) (closed circles) and patients not receiving continuous IV sedation (closed triangles).

**Table 4—Adjusted Outcomes According to Administration of Continuous IV Sedation\***

Variable	Continuous IV Sedation (n=93)	No Continuous IV Sedation (n=149)	p Value
Duration of mechanical ventilation, h	148 (121, 175)	78.7 (68.9, 88.6)	<0.001
Length of intensive care, d	9.6 (8.4, 10.9)	7.2 (6.6, 7.7)	0.007
Length of hospital stay, d	19.4 (16.7, 22.1)	13.8 (12.8, 14.9)	<0.001

\*Values shown are means per patient and 95 percent CIs. Outcome variables have been adjusted for age, gender, severity of illness, mortality, indication for mechanical ventilation, use of chemical paralysis, presence of a tracheostomy, and the number of acquired organ system derangements.

ventilation as quickly as possible to avoid these complications vs continuing high levels of sedation so as to minimize patient discomfort associated with the application of ventilatory support.<sup>26</sup>

Our findings are consistent with the results of previous investigations demonstrating a relationship between specific sedation practices and the duration of mechanical ventilation. Barrientos-Vega and colleagues<sup>27</sup> found that the specific agent used for continuous IV sedation was an important determinant of the duration for weaning patients from mechanical ventilation. In a randomized clinical trial, patients receiving a midazolam infusion had statistically longer time intervals from the discontinuation of the drug infusion until extubation compared with patients receiving propofol ( $97.9 \pm 54.6$  h vs  $34.8 \pm 29.4$  h;  $p < 0.001$ ).<sup>27</sup> This difference was attributed to the more rapid reversal of the sedative properties of propofol compared with midazolam as has been suggested by other investigators as well.<sup>28</sup> However, contradictory studies suggest that midazo-

lam can be effectively used as a sedating agent when compared with propofol.<sup>5,29</sup>

More recently, there has been a refocusing of clinical interest away from the specific agent(s) used for achieving sedation toward the way in which sedating agents are employed. Devlin and colleagues<sup>30</sup> developed a guideline for the use of IV sedation among ICU patients requiring mechanical ventilation. Using a before-after study design, these investigators found that the implementation of their sedation guideline produced a nonsignificant trend toward shorter total ventilation times and a statistically significant savings in total sedation costs. However, the main focus of their study, to decrease the costs associated with providing sedation, and its lack of power precluded any definite conclusions regarding the overall effectiveness of sedation guidelines in the ICU setting. Similarly, Watling et al<sup>31</sup> showed that a simple to employ sedation protocol, based on a continuous infusion of a benzodiazepine or morphine to produce apnea or decreased respiratory efforts, could be successfully applied to patients requiring mechanical ventilation. However, these two studies did not set out to modify sedation practices in order to achieve a specific patient-related outcome (eg, decreased duration of mechanical ventilation). In contrast, Cheng and coworkers<sup>9</sup> demonstrated that modifying sedation practices for patients undergoing coronary artery bypass grafting could reduce the duration of mechanical ventilation following surgery without an increase in perioperative morbidity. These investigators found a strong relationship between the duration of mechanical ventilation and the specific sedation practices employed for this group of patients.

The findings of our investigation may provide some insights for improving current sedation practices. First, there appears to be a relationship between the duration of mechanical ventilation and the administration of continuous IV sedation. Reducing the unnecessary use of continuous IV sedation, or shortening the duration of its administration, may decrease the duration of mechanical ventilation for some patients. Second, the existing variability in

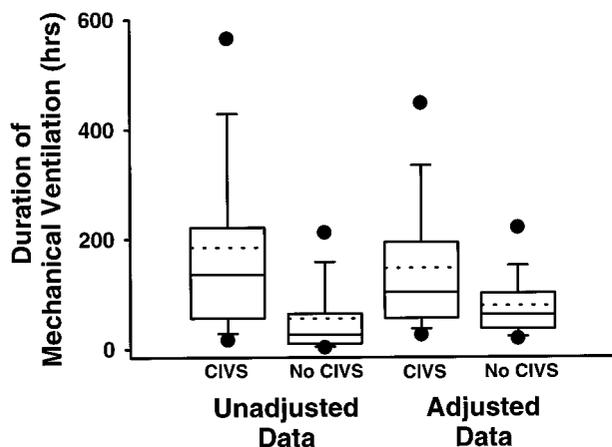


FIGURE 2. Box plots for the unadjusted and adjusted durations of mechanical ventilation for patients receiving and not receiving continuous IV sedation (CIVS). Boxes represent 25th to 75th percentiles with 50th percentile (solid line) and mean (broken line) values shown within or outside of the boxes. The 10th and 90th percentiles are shown as capped bars, and closed circles mark the fifth and 95th percentiles.

sedation practices, as suggested by our study and the available medical literature, indicates that the use of sedation guidelines or protocols may prove beneficial in achieving more uniform sedation practices. Diminishing this variability should also allow the impact of subsequent changes or modification of these practices to be investigated more objectively in order to identify optimal sedation practices. Our study results also suggest that sedation practices should be standardized, or at least evaluated as a confounding variable, in any investigation employing the duration of mechanical ventilation as an outcome variable. This represents a potentially important omission from the design of several recent investigations that have attempted to identify the optimal method for weaning patients from ventilatory support.<sup>32-34</sup>

Our study has several important limitations. First, it was an observational study that did not dictate how IV sedation was to be administered to patients receiving mechanical ventilation. Therefore, a direct causal relationship between the use of continuous IV sedation and the duration of mechanical ventilation is only suggested by our data. Future randomized clinical trials employing sedation strategies aimed at reducing the unnecessary use of continuous IV sedation are needed to establish this relationship. Second, this study was performed within a single ICU examining only adult medical patients. Therefore, these results may not be directly applicable to other ICUs caring for different groups of critically ill patients or utilizing different sedation practices. Third, we primarily employed benzodiazepines and narcotics for IV sedation. Greater use of alternative agents, such as propofol, may also have produced different results. Fourth, we did not assess the adequacy of sedation from the patients' perspective as a quality-of-life measure. This is a common omission in the critical care literature due to the difficulties encountered in making these measurements.<sup>35</sup> Lastly, we did not contact physicians to obtain their indications for the administration of continuous IV sedation. Therefore, we were not able to estimate the number of patients receiving continuous IV sedation who could have been treated without this mode of therapy. Despite these limitations, the large statistically significant difference observed between the adjusted durations of mechanical ventilation (Table 4) strongly suggests that the administration of continuous IV sedation contributed to the prolongation of mechanical ventilation for some patients.

In summary, this preliminary study demonstrates a relationship between the administration of continuous IV sedation and the duration of mechanical ventilation. These data suggest that measures aimed at reducing the use of continuous IV sedation could decrease the duration of mechanical ventilation for

some patients. Indeed, several studies already suggest that these types of improvements in clinical practice are possible.<sup>9,30</sup> The development and application of sedation guidelines or protocols offers one potential strategy for achieving more appropriate utilization of IV sedation.<sup>4,36</sup> Based, in large part, on this experience, we have undertaken a randomized controlled trial examining the efficacy and safety of a nursing-initiated sedation protocol aimed at avoiding the unnecessary use of IV sedation among patients requiring ventilatory support.

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