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Predictors of Agitation in the Adult Critically Ill

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Abstract

Background—Agitation in critically ill adults is a frequent complication of hospitalization resulting in multiple adverse outcomes. Potential causes of agitation in critically ill patients are numerous; however, data about factors that predict agitation are limited.

Objectives—The purpose of this study is to identify predictors of agitation by investigating demographic and clinical characteristics of critically ill patients.

Methods—A medical record review was performed identifying agitation using the Richmond Agitation-Sedation Scale or the use of an “agitation” keyword. A total of 200 patients were studied from a medical and surgical ICU. Two models were examined: 1) on admission and 2) 24 hours prior to the first agitation event. Data pertaining to baseline demographics and preadmission risk factors as well as clinical data were collected and evaluated by logistic multivariable regression to determine predictors of agitation.

Results—Predictors of agitation on admission to the ICU were: past medical history of illicit substance use, height, both the Sequential Organ Failure Assessment (SOFA) respiratory and central nervous system subscores, and use of restraints. Predictors of agitation identified from data gathered within 24 hours prior to agitation were: past medical history of psychiatric diagnosis, height, SOFA score, P/F<200mmHg, serum pH, percent of hours using restraints, percent of hours using mechanical ventilation, pain, and presence of genitourinary catheters.

Conclusions—In this study predictors of agitation on admission and within 24 hours prior to agitation onset were primarily clinical variables. This allows considerable opportunity for intervention to ameliorate or prevent agitation.

Keywords

agitation predictors; agitation; psychomotor agitation; hyperactive delirium; ICU

One of the more frequent complications in the intensive care unit (ICU) is agitation. Agitation is associated with adverse clinical outcomes: longer ICU stay, longer duration of mechanical ventilation, a higher rate of self-extubation, unplanned catheter removal, excessive sedation, increased utilization of resources, and increased ICU costs.^{1–3} Studies show that from 42–71% of critically ill patients experience agitation.^{2–5} Recognizing the impact of agitation, The Society of Critical Care Medicine's (SCCM) recently updated sedation and analgesia guidelines now also include agitation, emphasizing the need for prompt identification.⁶

Potential causes of agitation in critically ill patients are numerous; however, data about factors that predict agitation are limited. As agitation is often identified after overtly agitated behavior is observed, a critical barrier to progress in the field has been the lack of identification of the precursors of agitation. Empirically based information would therefore assist care providers to identify those at risk as well as predict agitation providing an opportunity to implement preventative strategies. Therefore the purpose of this study was to examine the relationship of demographic and clinical characteristics of critically ill patients in the development of agitation.

METHODS

Subjects and Setting

The study was conducted in an 865-bed academic, Level I Trauma Center, using two adult ICU units (medical-respiratory ICU [MRICU] and surgical trauma ICU [STICU]). All adult patients, 18 years of age and older, consecutively admitted to the MRICU and STICU over a two month period, were evaluated for inclusion using a medical record review. Approval was obtained from the University Institutional Review Board. Patient exclusion criteria were an ICU length of stay (LOS) less than 24 hours, those with medical records that were not available, and patients previously admitted during the study. Other exclusion criteria were conditions interfering with sedation scale scoring: administration of paralytics; patients with chronic neuromuscular disorders; and patients with head trauma or stroke.

Measures

Agitation—Agitation was identified using documentation of the Richmond Agitation-Sedation Scale (RASS), a 10 point scale from +4 (combative) to –5 (unarousable).⁷ The RASS has demonstrated excellent interrater reliability and criterion, construct, and face validity in critical care settings.^{7–11} The RASS was the standard sedation-agitation tool used in both of the target ICUs and routinely obtained every 4 hours in the units. A RASS of +1 (restless) through +4 (combative) were used to identify agitation. The +1 RASS was accepted as an indicator for agitation as use of positive numbers in the RASS have been documented as an agitation scale.⁷

Agitation was also identified using the keyword “agitation” (i.e. “agitated”, “agitation”, “agit”) recorded from the medical record using physicians’ and nurses’ notes in the nursing bedside flowsheet, emergency department documentation, operating room notes, and circle-the-item for reporting agitation in flowsheets.

Predictors of Agitation

Demographics and Preadmission Risk Factors: Risk factors previously associated with agitation in the critically ill were identified from the literature. Data collection included demographic characteristics (age, gender, ethnicity, race), marital status, weight, height, Body Mass Index, hospital admission source (clinic, emergency department [ED], home, long term care, or outside hospital), ICU admission source (operating room, general hospital floor, ED, outside hospital), admitting diagnosis category, and severity of illness data for the Acute Physiology And Chronic Health Evaluation III (APACHE III),¹² the Sequential Organ Failure Assessment (SOFA),¹³ as well as the Charlson Age-Comorbidity Index.¹⁴ SOFA scores were collected daily; the APACHE III was also collected on the day of the first agitation event. Additional data collected were a history of diabetes, alcohol abuse, illicit substance use, tobacco use, psychiatric diagnosis, as well as overuse/abuse and prescribed use of psychiatric medications.

Clinical Risk Factors: Measurable clinical factors were also identified from the literature. Clinical data collected on admission and 24 hours prior to the first agitation event were worst daily values (defined as most extreme or farthest from the normal laboratory mean value) for: creatinine, blood urea nitrogen, daily urine output, bilirubin, hematocrit, and glucose, as well as Glasgow Coma Score (GCS), PaO₂, heart rate, mean arterial pressure, respiration rate, FiO₂, and temperature. Data collected hourly included: pain rating (Numerical Rating Scale), RASS score, use of restraints and type of restraints, use of mechanical ventilation (MV), total number of all catheters as well as number and specific category of invasive lines and catheters (peripherally inserted, centrally inserted, genitourinary [GU], and gastrointestinal [GI]), use of dialysis, presence of sepsis (using Criteria of Bone¹⁵), hospital-acquired pneumonia (by documentation), and community-acquired pneumonia (by documentation). For variables that occurred continuously (e.g. mechanical ventilation, restraints), use was calculated by hourly percent of time used. For acute renal failure, the RIFLE¹⁶ classification system rating was recorded. All laboratory values for the 5 study days for the following blood tests were obtained on the reporting hour: pH, sodium, potassium, albumin, magnesium, white blood count (WBC), and hemoglobin.

Clinical Outcomes—To fully describe the sample, data were collected related to ICU and hospital length of stay (LOS), discharge destination or outcome (long term care or other facility, home/prior living arrangement, or death), and adverse events.

Procedure

All data were collected from the medical record by a single investigator (RSB). A pilot study was performed using subjects not part of the study cohort. Data audits used convenience sampling on approximately 10% of all subjects. The error rate was less than 0.03%.

The goal was to obtain an equal number of subjects in each of the two study units spanning the majority of a two month period. Data were collected during the first 5 days of ICU stay as agitation onset is highest in the first 3 to 5 days.^{2,4}

The hour was used as the documentation epoch for all recurrent data collection. The hour was considered an agitation hour only if the RASS was +1 or above, or the keyword agitation was found in the medical record during that hour. If any agitation or multiple agitation episodes were documented within the hour, it was considered to be one agitation hour. Data collection included ICU location and the ICU hour from admission.

DATA ANALYSIS

Descriptive statistics were computed on patients' baseline demographic and clinical variables. Categorical data was described as number (%), normally distributed continuous data was described as mean $\pm$ SD, and non-normal continuous data was described as the median with interquartile range (25th – 75th percentile). Only the first reported occurrence of agitation during the study period was examined for every subject. Any report of agitation during the five study days was used to identify two study groups (agitated versus non-agitated subjects).

Two separate models were examined to identify predictors of agitation. The first model focused on factors on admission to the ICU that might predict agitation. The second model primarily considered factors within 24 hours prior to the first episode of agitation. The time period of 24 hours was chosen to capture slower-responding physiologic changes (i.e. renal or hematologic indices).

For both scenarios (factors on admission and factors within 24 hours of first agitation), each potential risk factor was examined univariately in simple logistic models to determine its relationship to agitation. Here, the response variable was agitated or not agitated. As a screening tool for risk factors, the alpha level for significance was set to 0.10. Next, logistic regression models were constructed using all significant variables of the univariate analysis and subsets of the significant variables from the univariate analysis. Subsets reduced multicollinearity generated by constructing models including more than one measure of severity of illness (i.e. only total SOFA, or only SOFA subscores, only total APACHE, or only APACHE subscores). For each subset considered, backward elimination was used to select the significant predictors of agitation. In these models, the alpha level was changed to a 0.05 level of significance. Testing was conducted using the Likelihood Ratio. Alternative models were compared in terms of statistical significance of each predictor, goodness-of-fit statistics (AICc, BIC and R^2 values), and predictive power (e.g. area under the curve [AUC] of the ROC curve and percent correct classification) in order to determine the best model. Statistical analysis was performed using SAS 9.3 and SAS JMP v Pro10.0 (Cary, NC).

RESULTS

Subjects

Three hundred and eighty three patients sequentially admitted into the ICUs were screened, 179 from the MRICU and 204 from the STICU. There were 79 MRICU subjects and 104 STICU subjects not meeting inclusion criteria. In all, 200 subjects, 100 from each ICU, were included in the final analyses. A full report of the sample was described in a companion paper that included agitation onset, frequency, and associated temporal factors.¹⁷

Overall the sample subjects had a mean age of 55 years and were primarily men, non-Hispanic, and white or African-American (Table 1). Approximately one quarter (28.5 %) of the agitation documentation was based on the RASS with the balance using an agitation keyword. Of the 200 subjects, 118 (59%) were agitated at some point over the 5 day study period and comprised the agitated group for this analysis; 102 (86%) had agitation on day 1.

Predictors of agitation on ICU admission—For the univariate analysis, factors found significantly associated with agitation on ICU admission are listed in Table 2. Logistic regression analysis showed that the majority of variables remaining in the final model were clinical factors. The model was statistically significant, indicating that the predictors as a set reliably distinguished between subjects with and without agitation (chi square = 68.071, $p < .0001$ with $df = 5$). The AUC for the receiver operating characteristic (ROC) was 0.85. Prediction success overall was 75% (79.3% for subjects with agitation and 69.1% for subjects without agitation). Predictors of agitation were identified as past medical history of illicit substance use, height, both the SOFA respiratory and CNS subscores, and use of restraints (Table 3).

Predictors of agitation within 24 hours prior to agitation—In the univariate analysis, factors present within 24 hours prior to first agitation were generally the same as the on-admission group (Table 2). The majority of the variables predicting agitation on this model were also clinical factors. The model was statistically significant, (chi square = 94.4, $p < .0001$ with $df = 9$) and its associated AUC for the ROC was 0.92. Prediction success overall was 83% (85% for subjects with agitation and 79% for subjects without agitation). Predictors of agitation were identified as height, past medical history of psychiatric diagnosis, SOFA score, P/F < 200, serum pH, percent of hours using restraints, percent of hours using mechanical ventilation, pain rating, and presence of GU catheters (Table 3). Predictors of agitation similar for on-admission and within 24 hours to agitation models were height and restraint use.

Clinical Outcomes

Patient outcomes (length of stay, discharge status and mortality) were also compared between agitated and non-agitated subjects. There was no difference with respect to number of hospital days prior to ICU admission ($p=0.21$), ICU length of stay ($p=0.12$), number of hospital days after ICU discharge ($p=0.89$), total hospital length of stay ($p=0.56$) or in-hospital mortality (19%) ($p=0.11$). Discharge destination was different ($p=.02$); non-agitated subjects were more likely to be discharged to home/prior living arrangement.

All adverse events were analyzed. In the total sample (n=200), 33 experienced 50 adverse events. Of agitated subjects (n=118), 32 (27%) had 49 adverse events compared to 1 (1%) in nonagitated subjects (p<.0001). Of the 49 adverse events in agitated subjects, 45 (90%) were reported concurrent with agitation during the hour, 3 were reported within 2 hours of documented agitation, and 1 within 4 hours of intermittent agitation. There were 28 adverse events in the MRICU and 22 in the STICU. Of all subjects with adverse events, 5 (15%) self-extubated, 3 (9%) pulled out critical catheters or tubes (central line, epidural catheter, NG tube sutured to nare), 1 (3%) fell out of bed, 1 (3%) tore off restraints, and 30 (91%) pulled out non-critical catheters/tubes/leads.

DISCUSSION

In this study predictors of agitation on admission and within 24 hours prior to agitation were primarily clinical variables and may represent the severity of the disease process. Agitation was not associated with a longer ICU or hospital stay but was associated with multiple clinically significant adverse events.

Predictors of agitation on ICU admission

Demographics and Preadmission Risk Factors—Of the preadmission risk factors only past medical history of illicit drug use and height were predictive of agitation. A record of illicit drug use increased the odds of having agitation almost 2.5 times. Woods¹ reported a univariate association with agitation based on marijuana use; Gardner et al.⁴ evaluated drug abuse but did not find them to be a significant predictor.

Height predicted agitation but no other study has reported similar results. This was true for both models – the explanation for this relationship is unclear. This result is further confounded as factors associated with height were not predictors, such as weight or body mass index.

Severity of Illness—Although none of the total severity of illness measures predicted agitation, SOFA respiratory and CNS subscores did. The odds of having agitation increased over 1½ times for every point increase in the SOFA respiratory subscore. The odds of having agitation increased almost two-fold for every point increase in the SOFA CNS subscore. Oxygenation level and neurologic condition have been shown to be associated with agitation.^{1,4} Impaired oxygenation may result in neurologic deterioration, and the converse can also be true, in cases where neurologic deterioration leads to inadequate ventilation. Pulmonary and neurologic subscores of the Multiple Organ Dysfunction Score¹⁸ (MODS) have been found associated with agitation;⁴ the MODS subscores use the same factors as the SOFA. Therefore patients who have respiratory or neurologic compromise may be at most risk for agitation on admission.

Clinical Risk Factors—Only use of restraints at admission was predictive of agitation increasing the odds of having agitation over 3.5 times. Restraint use has been reported in 34% of agitated subjects and 50% of episodes of agitation.² Although it is difficult to determine whether restraint use precedes or follows agitation, the association of restraints and agitation is clear. In an observational study by Werner et al.,¹⁹ nursing home residents

exhibited either the same or more agitated behaviors when they were restrained, suggesting that the act of restraining may contribute to agitation. Werner and colleagues suggest that restriction of movement using physical restraints produces an increase in stress which may increase agitation.

Predictors of agitation within 24 hours prior to agitation

Other investigators have examined risk factors for agitation at varying times before the event, including use of daily data with time-varying covariates¹ and data collected within 48 hours prior to agitation.^{1,2} Risk factors similar to those in ours included 1 preadmission risk factor, 1 severity of illness factor, and 3 clinical factors. It is possible that the large number of first-day agitation could have influenced our findings in this model.

Demographics and Preadmission Risk Factors—Past medical history of psychiatric diagnosis was identified as a risk factor in this model increasing the risk of agitation 6 times. Jaber et al.² also described a correlation between psychiatric history and agitation using data collected on regular use of antipsychotic medications. They reported regular use of psychoactive drugs increased the risk of agitation five times.

Severity of Illness—Increasing severity of illness was a predictor of agitation using the total SOFA score. An increase in one point on the SOFA score was associated with more than a two-fold increase in the risk of agitation. Gardner et al.⁴ also reported this relationship with greater APACHE II scores (23.8 versus 17.5; $p=0.002$) as well as MODS (8.2 versus 6.8; $p=0.002$) on days with reported agitation. Jaber et al.² described a similar relationship only in the univariate analysis using the Simplified Acute Physiology Score II.²⁰

Clinical Risk Factors—Use of restraints was associated with agitation both on admission and within 24 hours prior to the first agitation event. The odds ratio (OR) reflected a 1%-of-the-time use of restraints. Calculating for hourly use, restraints for 4 hours almost doubled the risk of having agitation; using them for 6 hours increased the risk of agitation over 2.5 times. Use of physical restraints may lead to stress, further aggravating existing neuropathology, which may increase stress and agitation even more.²¹ Patient safety is an important consideration when limiting restraint use and all factors should be weighed carefully before making restraint decisions.

Indicators of oxygenation were risk factors for the onset of agitation on admission and within 24 hours prior to agitation. A $P/F<200$ increased the risk of agitation over 4.5 times. The amount of time of mechanical ventilation (MV) also predicted agitation. Calculating for hourly use, MV for 6 hours almost doubled the risk for agitation; using them for 12 hours increased the risk over 3.5 times, 18 hours over 16 times, and 24 hours over 41 times. Although guidelines suggest weaning as soon as feasible, MV duration (to support respiration/oxygenation) is not usually just a few hours. Presence of MV in a critically ill patient should be considered seriously with respect to agitation.

As discussed earlier with the on-admission model, use of MV may be another marker of oxygenation and neurologic dysfunction, although it is not clear why one of these variables is a prediction in the first model and not in the second. Use of MV was not identified in

other studies as a predictor of agitation but is related to other types of respiratory measures that have been shown to be predictive.^{1;4} Similar to others,¹ acidemia was a risk factor for agitation, which may reflect respiratory dysfunction and/or a greater level of illness. Not all investigators have evaluated pH with respect to the onset of agitation.^{2;4}

The increasing number and types of catheters in the critically ill may certainly lead to discomfort and agitation. The presence of a GU catheter increased the likelihood of agitation over 3.5 times. Yu et al.²² studied postoperative agitation in 2,000 subjects. Logistic regression analysis identified presence of a GU catheter to be a predictor of agitation ($p=0.022$). GU catheters can be painful;²³ it is possible that pain or discomfort may have been the source for these findings.

Lower pain ratings were associated with agitation – no other study has similar results. The explanation for this relationship is unclear as the reverse relationship would be expected. Pain has been shown to be correlated with agitation;^{24;25} however, measurement of pain, especially in a population that is often nonverbal, is difficult and valid evaluation is often elusive.

Clinical Outcomes

Our overall mean ICU stay (3.9 days) was much shorter than the ICU length of stay reported by others (6 days^{1;4}). Agitation has also been associated with a prolonged ICU stay.^{1;2} Different findings can be attributed to differences in populations, agitation measurement, or differences in clinical trends. Of agitated ICU patients, we did not find increased in-hospital mortality. Our mortality rate (19%) was generally similar to others.^{1–3}

Adverse events and rates were similar to other studies. Our unplanned or self-extubation rate (15%) was similar to Jaber² (17%); however, Woods¹ (26%) was higher; differences in the sample population and agitation determination could account for this.

Overall the majority of predictors of agitation on admission as well as 24 hours prior to agitation were clinical in nature. This allows considerable opportunity for intervention. Current efforts to evaluate need for GU catheters daily and to remove GU catheters as soon as feasible are recommended to reduce catheter-associated urinary tract infection risk. There may be an added benefit of reducing agitation. Limiting restraint use for patients when feasible, considered a nurse-sensitive quality indicator by the National Quality Forum,²⁸ may improve patient safety outcomes and may minimize agitation. Using lighter levels of sedation results in improved clinical outcomes (shorter MV, shorter ICU stay, less PTSD, less depression, more accurate assessment of patient issues) and may also reduce agitation. Current practice initiatives to facilitate early weaning and shorten ventilator time may also result in mitigating agitation.

Limitations of the study: findings are dependent on data completeness and quality, and the data were not originally recorded for research purposes. However, medical record reviews monitor in real time and integrate multiple data sources. In an effort to mitigate some disadvantages, we used a stringent definition of agitation and used a larger sample size with good general population representation.

CONCLUSIONS

Agitation is recognized as a serious problem in ICUs. Primarily clinical factors were implicated in the onset of agitation. Agitation was not associated with a longer ICU stay or hospital stay but was associated with multiple significant adverse events.

This study contributes new knowledge to the identification of agitation in the medical and surgical ICU patient populations allowing a better understanding of risk factors of agitation. Identification of patients at particularly high risk for developing agitation provides an opportunity to implement preventative strategies. Additional research is needed to identify the cause(s) of agitation, interventional therapies for prevention, and treatment once agitation has occurred.

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Summary of Key Points

- Overall the majority of predictors of agitation on admission as well as 24 hours prior to agitation were clinical in nature allowing considerable opportunity for intervention.
- Knowledge of predictors may facilitate early and prompt intervention.
- Currently guidelines exist to remove GU catheters as soon as possible, limit restraint use for patients when feasible, use lighter levels of sedation, and facilitate extubation. In light of predictors found in this study, adherence to current guidelines may also prevent/reduce agitation.
- Agitation is associated with multiple significant adverse events.

Table 1

Demographics and other descriptors for entire sample and by presence of agitation (at least one observation of agitation during the study time).

Variable	Entire sample n = 200	Non-agitated Pts n = 82 (41%)	Agitated Pts n = 118 (59%)
Gender			
Male	113 (56.5)	42 (51)	73 (62)
Female	87 (43.5)	40 (49)	45 (38)
Ethnicity			
Hispanic or Latino	6 (3)	5 (6)	1 (1)
Not Hispanic or Latino	194 (97)	77 (94)	117 (99)
Race			
Asian	3 (1.5)	2 (2)	1 (1)
Black or African-American	94 (47)	39 (48)	55 (47)
White	103 (51.5)	41 (50)	62 (53)
ICU Type			
Medical Respiratory ICU	100 (50)	36 (44)	64 (54)
Surgical Trauma ICU	100 (50)	46 (56)	54 (46)
Admission Source			
Long term care	3 (1.5)	2 (1)	1 (0.5)
Home	16 (8)	4 (2)	12 (6)
Clinic	20 (10)	7 (3.5)	13 (6.5)
Outside hospital	60 (30)	23 (11.5)	37 (18.5)
ED	101 (50.5)	46 (23)	55 (27.5)
Admitting Diagnosis			
Trauma	36 (18)	18 (22)	18 (15)
Sepsis	35 (17.5)	17 (21)	18 (15)
Respiratory failure	27 (13.5)	6 (7)	21 (18)
Hematologic/oncologic problem	27 (13.5)	8 (10)	20 (17)
Other	22 (11)	9 (11)	12 (10)
Renal/GI problem/DKA	28 (14)	15 (19)	13 (11)
Hepatic problem	13 (6.5)	4 (5)	9 (8)
Cardiovascular problem	8 (4)	4 (5)	4 (3)
Drug overdose/poisoning	4 (2)	1 (1)	3 (3)
Age (years)	55.5 (+/- 16.4)	56 (+/- 16.4)	55.1 (+/- 16.5)
Total ICU length of stay (days)	3.9 (2.5–8)	2.7 (2–8)	4.8 (3–9.4)
Total hospital length of stay (days)	11.1 (6.3–21.6)	9.1 (6–19.4)	12.8 (6.9–21.8)
APACHE III score	68 (+/- 31.9)	57.7 (+/- 34.3)	74.7 (+/- 28.2)
SOFA	6.625 (+/- 3.8)	5.39 (+/- 3.7)	7.48 (+/- 3.7)
Charlson Comorbidity Index	4.69 (+/- 3.3)	4.8 (+/- 3.3)	4.6 (+/- 3.4)

Abbreviations: patients (pts); intensive care unit (ICU); emergency department (ED); gastrointestinal (GI); Diabetic ketoacidosis(DKA); Acute Physiology And Chronic Health Evaluation (APACHE III); Sequential Organ Failure Assessment (SOFA) Data are presented as number (%), mean +/- SD, or median (25th – 75th percentiles)

Table 2

Demographic, preadmission and clinical risk factors with univariate significance

Demographic and Preadmission Risk Factors				
Variable	At admission		24 hrs prior to onset of Agitation	
	Non-agitated	Agitated ^a	Non-agitated	Agitated ^a
Gender				
Male	42 (51)	73 (62) [*]	—	—
Female	40 (49)	45 (38) [*]	—	—
Height in cm	167.3 (10.3)	172.1 (10.7) ^{**}	—	—
Weight in kg	77.1 (22.5)	83.9 (26.1) [*]	—	—
Subject PMH				
Illicit substance use	26 (32)	55 (47) ^{**}	—	—
Psychiatric diagnosis	10 (12)	28 (24) ^{**}	—	—
Severity of Illness Scores				
Variable	At admission		24 hrs. prior to onset of Agitation	
	Non-agitated	Agitated ^a	Non-agitated	Agitated ^a
Total SOFA score	6.6 (3.8)	5.4 (3.7) ^{**}	5.9 (4.1)	7.4 (3.7) ^{**}
Respiratory subscore	0.8 (0.9)	1.3 (1.1) ^{**}	0.9 (1)	1.2 (1.1) [*]
CNS subscore	1.2 (1.3)	2.5 (1.2) ^{**}	1.3 (1.3)	2.5 (1.1) [*]
GCS	12.3 (3.8)	8.6 (3.6) ^{**}	12.3 (3.8)	8.6 (3.6) ^{**}
APACHE III score	57.7 (34.3)	74.7 (28.2) ^{**}	57.7 (34.3)	73.7 (29.3) ^{**}
Clinical Risk Factors				
Variable	At admission		24 hrs. prior to onset of Agitation	
	Non-agitated	Agitated ^a	Non-agitated	Agitated ^a
P/F < 200 mmHg	1 (1)	12 (10) ^{**}	8 (4)	23 (11.5) [*]
FiO ₂	0.36 (0.21–0.53)	0.5 (0.4–0.7) ^{**}	0.36 (0.21–0.53)	0.5 (0.4–0.7) ^{**}
Serum pH	7.39 (+/- 0.07)	7.36 (+/- 0.095) ^{**}	7.39 (+/- 0.09)	7.36 (+/- 0.09) ^{**}
Serum magnesium	1.89 (+/- 0.32)	1.99 (+/- 0.47) [*]	1.85 (+/- 0.39)	1.98 (+/- 0.45) [*]
Serum hemoglobin	10.3 (+/- 2.5)	10.3 (+/- 2.2)	9.1 (+/- 2.3)	10.1 (+/- 2.2) ^{**}
Serum glucose	146 (+/- 66)	168 (+/- 84) [*]	146 (+/- 66)	165 (+/- 84) [*]
Abnormal Temp ≥38	12 (15)	35 (30) ^{**}	12 (15)	37 (31) ^{**}
Abnormal Temp ≥38, <36	19 (23)	47 (40) ^{**}	19 (23)	49 (42) ^{**}
Use of restraints (and percent of time)	6 (7)	40 (34) ^{**}	12 (15)	63 (53) ^{**}
Use of MV (and percent of time)	15 (8)	70 (35) ^{**}	18 (9)	80 (40) ^{**}
Highest pain rating	0 (0–5.25)	0 (0–2.25) ^{**}	6 (2–8.25)	0 (0–4) ^{**}

Demographic and Preadmission Risk Factors				
Variable	At admission		24 hrs prior to onset of Agitation	
	Non-agitated	Agitated ^a	Non-agitated	Agitated ^a
Total number of catheters	3.2 (+/- 1.8)	4.1 (+/- 2.1) **	4.1 (+/- 1.9)	4.5 (+/- 2)
Presence of GU catheter	44 (54)	90 (76) **	52 (63)	97 (82) **
GI & other catheters	0 (0-1)	1 (0-1) **	1 (0-1)	1 (0-1.25)

Data are presented as number (%), mean +/- SD, or median (25th – 75th percentiles)

Abbreviations: centimeter (cm); kilogram (kg); MRICU (Medical Respiratory ICU); STICU (Surgical Trauma ICU); past medical history (PMH); Sequential Organ Failure Assessment (SOFA); central nervous system (CNS); Acute Physiology And Chronic Health Evaluation (APACHE III); PaO₂/FiO₂ (P/F); mechanically ventilated (MV); Glasgow Coma Score (GCS); Genitourinary (GU); Gastrointestinal (GI)

^a At least one documented observation of agitation during the 5-day study time

* p 0.05<.01;

** p 0.05

Table 3Predictors of agitation^a

Variable:	Odds ratios	95% CI	LR <i>p</i> -value
On admission to the ICU			
Past medical history of illicit substance use	2.43	1.18 – 5.15	0.015
Height	1.04	1.01 – 1.08	0.016
SOFA respiratory subscore	1.58	1.11 – 2.28	0.0097
SOFA CNS subscore	1.90	1.45 – 2.54	<.0001
Use of restraints	3.77	1.39 – 11.53	0.008
24 hrs prior to onset of first agitation event			
Past medical history of psychiatric diagnosis	6.24	1.4 – 32.4	0.015
Height	1.06	1.01 – 1.12	0.015
SOFA score	2.3	2.1 – 2.6	0.012
P/F <200 mmHg	4.7	1.4 – 17.9	0.011
Serum pH	1.3 ^b	1.02 ^b – 1.75 ^b	0.026
Restraints (1% of time)	1.04	1.01 – 1.08	0.0003
Mechanical ventilation (1% of time)	1.03	1.01 – 1.04	0.0004
Pain	1.2	1.05 – 1.4	0.0059
Presence of GU catheter	3.8	1.2 – 12.98	0.0264

^a At least one observation of agitation during the study timeAbbr: Sequential Organ Failure Assessment (SOFA); central nervous system (CNS); PaO₂/FiO₂ (P/F); Likelihood Ratio (LR)^b for each 0.05 increase in pH