Pilot Study on Pairing Sedation Strategies and Weaning Protocol

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1. SYNOPSIS:

Pilot studies are important initial step in exploring a new trial protocol. This is a pilot to assess feasibility of recruitment, randomization, retention, and assessment procedures of implementation of a three different sedation protocols in a randomized controlled trial (RCT) design. The purpose is to examine the feasibility of the protocol that is intended to be used in a larger scale study. This is not a hypothesis testing study. The future large RCT will compare the effect of three different validated ICU sedation strategies, each paired with a validated weaning protocol, on outcomes of mechanical ventilation.

2. LIST OF ABBREVIATIONS AND DEFINITION OF TERMS:

Abbreviation	Term
DI	Daily interruption
SAT	Spontaneous awakening trial
SBT	Spontaneous breathing trial
ICU	Intensive Care Unit
PDS	Protocol-directed sedation
MV	Mechanical ventilation
SAT-SBT	Paired SAT and SBT
NSD-SBT	Paired Analgesia first and SBT
PDS-SBT	Paired PDS and SBT
ABC	Awakening and breathing controlled trial

3. BACKGROUND AND SUMMARY:

A significant proportion of patients admitted to the intensive care unit (ICU) require mechanical ventilation (MV).[1] To maintain comfort and facilitate quality care, large quantities of sedatives and analgesics are often administered either by continuous infusion, with or without daily interruption (DI) of sedation, or as intermittent doses of analgesics.[2-7] The recently published SLEAP trial has shown that instituting protocol-directed sedation in patients requiring continuous infusion of sedatives and analgesics, when daily interruption (DI) of the sedative occurs, will improve MV outcomes, specifically the duration of MV.[8-13] Similarly, studies have shown that use of a weaning protocol for mechanically ventilated ICU patients reduces the time to mechanical ventilation liberation.[14-16]

The Consensus Conference on Intensive Care Medicine in 2007 recommended using weaning protocols with the spontaneous breathing trial (SBT) as the major diagnostic test to determine if a patient can be successfully extubated.[14, 16-18] Girard et al performed a randomized, multicenter, clinical trial (ABC- Awakening and Breathing Controlled trial) evaluating the pairing of a spontaneous awakening trial (SAT) with an SBT. The study did not require use of a specific protocol-directed sedation approach in the control arm. In the intervention group the authors conducted a spontaneous awakening trial (SAT) by holding sedatives, followed by a spontaneous breathing trial (SBT) to assess for weaning readiness. Subsequently,

this strategy of incorporating a daily interruption of sedation was challenged by Mehta et al who conducted a randomized controlled study comparing a PDS with DI and PDS without DI. Their findings suggested that there was no added value for incorporating a daily interruption of sedation among patients managed with a protocol-directed sedation approach. Most recently, a Danish study by Strøm et al. went a step further to investigate whether an analgesia-first approach to patient comfort that consisted of intermittent doses of intravenous opioids, and the initiation of IV sedation for short periods only when acute agitation was present, would be superior to a protocol similar to the ABC trial. The intervention arm received intermittent intravenous opioids for pain and sedation only if the analgesia-first approach fails. The intervention arm had significantly more days without ventilation (13.8 days ± 11.0 vs. 9.6 ± 10.0; p=0.0191) and fewer ICU days and hospital days. There was no difference was recorded in the occurrences of accidental extubations.

While the three above mentioned approaches are accepted and currently implemented in the critical care community the optimal time to conduct an SBT during each of these sedative approaches remains unknown. It is possible that a SAT strategy, where sedative and opioid infusions are interrupted, may lead to more agitation and anxiety than a strategy in patients managed with a sedation protocol where intravenous sedative and analgesic therapy is regularly titrated to maintain patients in a lightly sedated state. Moreover, it remains unclear whether there are advantages of an analgesia-first sedation strategy over either an SAT or sedation protocol strategy in terms of the time it takes to wean patients from MV. However, it is noteworthy to mention that the analgesia-first strategy was associated with more delirium episodes, which were attributed to the ability to assess for it in a more awake patient. However, comparing delirium occurrence in studies with different sedation goals and methodologies may be inaccurate.
We therefore propose a three-arm, randomized, pilot feasibility, study to assess the effect of these three (3) validated strategies for sedation and pain management on time to liberation of mechanical ventilation and other related outcomes.

Literature review

Protocol-directed sedation and daily interruption studies:

Brook AD et al. performed a randomized, single-center, clinical trial comparing protocol-directed sedation versus non-protocol-directed sedation in 321 mechanically ventilated patients. They included patients greater than the age of 17 who were admitted to the medical intensive care unit. 162 patients received protocol-directed sedation and 159 patients received the non-protocol-directed sedation. The primary outcome was the duration of mechanical ventilation and secondary outcomes included lengths of ICU and hospital stay. The results revealed a reduction in the mean duration of mechanical ventilation for the protocol-directed sedation group (89.1 ± 133.6 hrs. vs. 124.0 ± 153.6 hrs. p = 0.003); as well as a reduced length of stay in the ICU and hospital [5.7 ± 5.9 days vs. 7.5 ± 6.5 days (p = 0.013) and 14.0 ± 17.3 days vs. 19.9 ± 24.2 days (p < 0.001); respectively][1]. The intervention group had a reduced duration of

continuous intravenous sedation (3.5 ± 4.0 days vs. 5.6 ± 6.4 days; p = .003). Brook's study demonstrated the clinical benefits of having protocol-directed or nurse-directed sedation in the medical ICU. Since the study only involved patients in the medical ICU, it is uncertain if the results are applicable to surgical patients.

Kress JP, et al [11] performed a randomized, single-center, clinical trial to evaluate daily interruption of continuous infusions of sedation in 128 mechanically ventilated adult patients. Notable exclusion criteria were patients who were already receiving sedative agents upon transfer to the ICU and admission due to resuscitation from cardiac arrest. The primary end points of the study included: duration of MV, and lengths of stay in the ICU and hospital. Secondary outcomes included total doses of sedative (i.e. midazolam, propofol) and analgesic agents (i.e. morphine). Results from the study reveal a reduction in the median duration of mechanical ventilation for the daily interruption group (4.9 vs. 7.3 days, p=0.004). In addition, there was a reduction in the median length of stay in the ICU and hospital (6.4 vs. 9.9 days, p=0.02 and 13.3 vs. 16.9 days, p=0.19; respectively). The total dose of midazolam was lower in the daily interruption group (229.8 vs. 425.5 mg; p=0.05). The study found no difference in regards to the incidence of self-extubation. Kress' study showed positive clinical outcomes with DI in the medical ICU. The study was limited to a single-center and was only for patients that were admitted to the medical intensive care unit. It is not clear if the results can be reproduced in other centers or in critically ill surgical patients. In addition, there was no mention of the use of PDS-SBTs. These are some of the limitations of the study. In addition many clinicians are concerned about potential complications of sedation interruption (i.e. posttraumatic stress disorder, enhance catecholamine response leading to cardiac complications).

Does DI of sedative increase the risk of developing posttraumatic stress disorder (PTSD) or acute myocardial ischemia?

Kress et al addressed the concerns raised that daily interruption of sedation may precipitate PTSD or cardiac events in subsequent studies.[12, 19] One study evaluated the long-term psychological outcomes (minimal of 6 months after discharge), in 32 patients from the initial study (19 control 13 who received DI). The study did not find a statistical difference between the DI patients versus the patients who did not receive DI (0% vs. 32%, p = 0.06).[19] In a separate observational study, 74 patients with two established risks for CAD were evaluated for cardiac ischemia with continuous three-lead Holter monitoring, during a DI.[12] Of the 74 patients, 18 had an ischemic event. A comparison between periods of being awake versus sedation found no difference in the fraction of ischemic time between the two groups (0% vs. 0%, p=0.17). Further controlled studies are needed to identify and evaluate the risk of DI (i.e. sedative withdrawal, PTSD, CAD), especially studies to identify who is not eligible for DI.

Which patients should not receive DI of sedative?

Literature is not completely supportive of the implementation of DI of sedative in mechanically ventilated patients. de Wit et al. performed a randomized clinical study evaluating DI versus PDS.[20] The study was terminated prior to completion due to a higher incidence of hospital mortality in the DI group (13 patients vs. 7 patients, p=.04). The authors speculate that the high number of patients with drug and alcohol use disorders (39%) had an adverse impact on patient outcome. Further studies are warranted to evaluate the safety of DI in patients with a history of alcohol and other illicit drug abuse.

Pairing of DI with mechanical ventilator weaning protocol:

Girard TD, et al. performed a randomized, multicenter, clinical trial (ABC trial) evaluating the pairing of SAT with SBT.[9] The study involved 336 MV patients; one group was managed with a paired SAT and SBT and the other received usual care. The study included adult patients (≥18 years) who required MV beyond 12 hrs. Notable exclusion criteria included: admission due to cardiopulmonary arrest, continuous MV for ≥2 weeks, profound neurological deficit (i.e. stroke, dementia). The primary outcome was breathing without assistance. Other measured outcomes included: time to discharge from the ICU or hospital, total dose of sedative agents, and self-extubation. The result of the study revealed that the SAT-SBT group spent more days without breathing assistance (mean 14.7 vs. 11.6 days, p=0.02), and less time in the ICU and hospital (9.1 vs. 12.9 days, p=0.01 and 14.9 vs. 19.2, p=0.04; respectively). The intervention group received less total dose of benzodiazepine (20 vs. 39 mg, p=0.02). However, they had a higher incidence of self extubation (10 vs. 4%, p=0.03), but the incidence of self-extubation requiring reintubation was comparable (3 vs. 2 %, p=0.47). Girard's study revealed positive clinical outcomes with the pairing of SAT with SBTs, but it was not designed to evaluate whether patients actually need to be fully awake for initiation of ventilator weaning or whether it is safe to initiate weaning with a PDS while RASS is maintained at 0 to -3.

Can an analgesia-first approach effectively facilitate mechanical ventilation weaning for critically ill patients?

Strøm T et al evaluated an analgesia-first approach with avoidance of sedatives in critically ill patients requiring mechanical ventilation. In this randomized controlled trial, 140 patients were assigned in a 1:1 ratio to no sedation with analgesia (analgesia-first) group or to sedation with DI. The analgesia-first group or intervention arm received analgesics for pain control and sedation only if the analgesia first approach failed. The intervention arm had significantly more days without ventilation (13.8 days ± 11.0 vs. 9.6 ± 10.0; p=0.0191) and shorter ICU and hospital stays. No difference was recorded in accidental extubation, but delirium was significantly higher in the analgesia-first group (20% vs. 7%, p=0.04). The study questions if patients need to be manage with SAT with PDS during mechanical ventilation.

Is the pairing of SAT with PDS necessary?

Mehta S, et al. perform a randomized controlled trial, multicenter clinical trial of mechanically ventilated patients in the ICU. The study compared the use of PDS versus PDS plus SAT. The primary outcome measure was time to successful extubation and additional outcomes included duration of ICU and hospital stay, unintentional endotracheal tube removal, and incidence of delirium. The median time to extubation was comparable in PDS versus PDS plus SAT [7 vs. 7 days, respectively (p=0.52)]. In addition, the duration of ICU (10 vs. 10 days, respectively) and hospital stay (20 vs. 20 days, respectively) were not significantly different (p>0.05). Unintentional endotracheal tube removal was not significantly higher in the PDS group (12 vs. 10, p=0.064). The incidence of delirium was 54.1% in the PDS group and 53.3% in the PDS plus SAT group (p=0.83). In conclusion, when protocol-directed sedation for critically patients requiring mechanically ventilation is paired with daily interruption of sedatives, there is no additional benefit over the use of protocol-directed sedation alone but the patients in the DI group recived higher doses of sedatives and opioids and had a higher nurse workload

4. STUDY DESIGN

A prospective randomized, unblinded single-center clinical trial.
We will enroll patients admitted into the ICU at Long Beach Memorial Medical Center who require continuous intravenous administration of sedatives and/or opioids, and are anticipated to require MV for ≥ 48 hours.

Study Objectives: This pilot study is to compare the efficacy and safety between three (3) validated sedation strategies (i.e., ABC, SLEAP, or Analgesia-first protocol) paired with a SBT in mechanically ventilated adults.

a. **Trial interventions**
   i. SAT-SBT arm (Sedation infusion protocol with DI): Appendix A
   ii. PDS-SBT arm (sedation infusion protocol without DI): Appendix B
   iii. NSD-SBT arm (No sedation analgesia-first protocol): Appendix C

b. **Patient Population:**
   ICU patients in a mixed medical-surgical ICU will be evaluated to determine if they meet the inclusion and exclusion criteria. Informed consent (from the patient or substitute decision maker) will be required prior to enrollment.

c. **Inclusion criteria:**
   1. ≥ 18 years of age
   2. Mechanically ventilated with an expected duration of MV ≥ 48 hours
   3. ICU team has initiated continuous sedative and/or /analgesic infusions

d. **Exclusion criteria**:
   i. Admission after resuscitation from cardiac arrest

ii. Admission with traumatic brain injury or another acute neurologic event (e,g. stroke, uncontrolled seizures).
iii. History of severe dementia
iv. Admission because of acute alcohol withdrawal or acute drug intoxication
v. Administration of more than 24 hours of continuous sedation
vi. Allergy to fentanyl, midazolam, and/or propofol
vii. Lack of informed consent

e. Duration of treatment period: All specific study interventions will cease at 28 days following enrollment into the study, but Patients will continue to receive standard of care throughout their hospitalization.

f. Frequency and duration of follow-up: All study interventions will cease at 28 days, but data relevant to the study will be collected until the patient is discharged or dies.

g. Recruitment: The principle investigator and study coordinators will perform patient recruitment.

5. OUTCOMES

a. Outcomes measurement

i. Primary outcome

i. Protocol feasibility

1. Time to randomization
2. Proportion of time in target sedation in the first 48 hours (RASS 0 to -3)
3. Protocol compliance

ii. Days in deep sedation or coma: Number of days with RASS score of -4 or deeper
iii. Mechanical ventilation free days: This is the number of days where patients were breathing without assistance during the 28-day study period. This began at the time of enrolment. Patients who die during the study period will be assigned 0 ventilator-free days.

b. Secondary outcomes

i. Duration of weaning: Time from initiation of weaning until successful extubation
ii. ICU length of stay: The number of days from ICU admission to ICU discharge with admission day being ICU day 0
iii. Hospital length of stay: The number of days from hospital admission to hospital discharge with admission day being hospital day 0
iv. Mortality: 28 day hospital mortality
v. Total amount of sedatives and analgesics used: Total dosage in mcg (fentanyl) or mg (midazolam) administered
vi. Occurrence and duration of delirium. The occurrence of adverse events will be noted by the nurse on a case report form. Delirium assessment will be based on the CAM-ICU and will be done daily by the clinical managing team and/or study investigators.

vii. Time at the desired sedation goal: percent of time while on protocol at desired sedation goal.
viii. Time spent without pain: based on assessment by non-verbal pain scale (CPOT)
ix. Nursing assessment on perceived workload
x. Extubation failure: If patient required reintubation within 48 hours of extubation
xi. Self-extubation: Inadvertent removal of an endotracheal tube during the course of the study by the patient

6. RANDOMIZATION AND STRATIFICATION METHODS

The randomization numbers generated with a 1:1:1 ratio and put into sealed opaque, not re-sealable envelopes. Each subject will have a unique identification number and keep that number throughout the study.

This pilot study will assign 30 patients to each arm of the trial, based on a convenience of sample. No power analysis will be conducted at this phase. .

7. PATIENT SAFETY:

a. Serious Adverse Event Reporting: All adverse outcomes will be reported to the IRB according to guidelines. The principle investigator or managing ICU physician will determine if a serious adverse events (SAE) is study-related. A detailed submission of the event should be reported within 72 hours. Relevant progress notes from the nurses and physician will be reviewed as well as laboratory and diagnostic results, and procedure notes. Complete

documentation of these findings will be done by the principle investigator or managing ICU physician.

8. STATISTICS:

Continuous variables will be presented as the mean and median with standard deviation (SD). Discrete variables will be presented as frequencies and percentages. Student's t-test (adjusted for unequal variances when necessary) or Mann-Whitney U test will be used for continuous data where appropriate. Categorical data will be evaluated using the Pearson's chi-squared test or Fisher's exact test where appropriate. Time to extubation will be evaluated using the Kaplan-Meier survival estimate with censored data. In the matched-pair analysis, paired t-test or Wilcoxon signed-rank test will be used to evaluate continuous data where appropriate. Two-tailed statistical significance will be defined as a $p \leq 0.05$.

9. STUDY COMPLIANCE:

a. **Study Management:** Study compliance will be maintained with the following steps:

   i. Training session(s) for all health care providers involved in the care of the patient;
   ii. Project coordinators will provide all necessary training and study aids;
   iii. A telephone number will be made available at all times to answer questions and concerns;
   iv. Daily reminders form the project coordinators regarding compliance to all protocols;
   v. Audit of study compliance will be routinely performed.

b. Study coordinator: The study coordinator (HP) will be responsible for the day to day management of the study and will provide guidance and support to all participants.

c. Confidentiality and data storage

   i. The confidentiality of all patient identifiable information will be maintained throughout the research and thereafter. The research involves the collection or the study of existing data in such a manner that the patient cannot be identified directly or through identifiers. Only the patient's identification numbers will be used to classify patients as necessary for the study.

ii. The patient's identification numbers used in the study will be created with the separate keys. All data pertaining to the study will only be accessible to the investigators and will be stored in a locked room and cabinent.

d. **Principal investigator (PI):** The PI (MT) will oversee the entire study and will prepare and submit reports of SAE.

10. RELEVANCE AND VALUE:

The results of this study are clinically and economically relevant. The clinical data will provide information on what is the preferred sedation practice during mechanical ventilation weaning. In addition, the study will support a multi-disciplinary approach to managing mechanical ventilated patients. The measured outcomes from the study will generate further research to improve patient outcomes, specifically mechanically ventilated patients. The economic implications can be potentially derived from the length of ICU or hospital stay

11. CONSENT: The consent form will be prepared according to the MHS guidelines and the IRB approved version will be presented to the patient or surrogate decision maker and discussed by the study PI or representative.

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APPENDIX A

SAT-SBT ARM (SEDATION INFUSION PROTOCOL WITH DI FOLLOWED BY SBT)

1. **Start**
   Fentanyl 25 mcg/hr
   Midazolam 1 mg/hr
   Goal pain score: ≤ 3
   Goal sedation score: 0 to -3

2. **Titration**
   Fentanyl increase or decrease by 25 mcg/hr every 30 minutes
   Midazolam increase or decrease by 1 mg/hr every 60 minutes

   Fentanyl is titrated to goal pain score
   Midazolam is titrated to goal RASS score

   If RASS -4 to -5, DC midazolam. If RASS remains -4 to -5, then wean fentanyl and DC to achieve target RASS

   If RASS -4 to -5, yet patient shows an episode of agitation, bolus doses are used before increasing infusion:

   - Fentanyl 25 mcg Q 5 minutes
   - Midazolam 1 mg Q 5 minutes

3. **Daily interruption (SAT)**

   <u>Do not perform SAT if any of the following present:</u>
   a. Active seizures or increased ICP
   b. Use of continuous neuromuscular blockade (NMB)
   c. Active myocardial ischemia
   d. Refractory hypotension requiring ≥ 2 vasopressors
   e. Use of high frequency oscillatory ventilation
   f. Open chest or abdomen

   Perform SAT by stopping both fentanyl and midazolam (if acute pain is present or suspected, fentanyl may continue)

   Assess for wakefulness during sedative/analgesic interruption. If able to perform At least 3 out of 4 activities below, patient is awake:

   - Open eyes to voice
   - Use eyes to follow nurse upon request
   - Squeeze hand upon request

- Wiggle toes upon request

Leave them off if no agitation (RASS at 0 to -5) and proceed to SBT safety screen

Resume fentanyl and/or midazolam at ½ dose and titrate to goal pain score and goal RASS score, respectively, if agitated (RASS +1 to +4)

4. Spontaneous Breathing Trial (SBT)

Daily Screening

Respiratory Care Practitioners (RCP) conduct a daily screen every morning to assess readiness to wean:

- adequate oxygenation (SpO2 ≥90% on FIO2 ≤40% and PEEP ≤5)
- No evidence of myocardial ischemia in the previous 24 hours evidenced by **ST changes and elevated troponin**
- Hemodynamically stable (dopamine or dobutamine ≤ 5 mcg/kg/min, norepinephrine ≤ 2 mcg/min, or absence of vasopressin or milrinone at any dose)
- No evidence of increased intracranial pressure

If pass the screening, place on CPAP of 5 and PS of 6 for a 120-min trial

The patient's RN and RCP will observe the patient for failure criteria. Patients fail The SBT if they develop any of the following:

- RR > 35 or < 8 for ≥ 5 min
- SpO2 < 88% for ≥ 5 min
- Altered mental status
- Acute cardiac dysrhythmia
- HR > 130 or < 60
- Use of accessory muscles
- Abdominal paradox
- Diaphoresis
- Marked dyspnea

Patients who fail the SBT will be placed back on the ventilator settings used before The trial. If the SBT was successful, the patients' physicians will be notified to decide on extubation

APPENDIX B

PDS-SBT ARM (SEDATION INFUSION PROTOCOL WITHOUT DI FOLLOWED BY SBT)

1. **Start**
   Fentanyl 25 mcg/hr
   Midazolam 1 mg/hr
   Goal pain score: ≤ 3
   Goal sedation score: 0 to -3

2. **Titration**
   Fentanyl increase or decrease by 25 mcg/hr every 30 minutes
   Midazolam increase or decrease by 1 mg/hr every 60 minutes

   Fentanyl is titrated to goal pain score
   Midazolam is titrated to goal RASS score

   If RASS -4 to -5, DC midazolam. If RASS remains -4 to -5, then wean fentanyl and DC to achieve target RASS

   If RASS -4 to -5, yet patient shows an episode of agitation, bolus doses are used before increasing infusion:

   - Fentanyl 25 mcg Q 5 minutes
   - Midazolam 1 mg Q 5 minutes

3. **Do not perform daily interruption (SAT)**

4. **Spontaneous Breathing Trial (SBT)**

   Daily Screening
   Respiratory Care Practitioners (RCP) conduct a daily screen every morning to assess readiness to wean:

   - adequate oxygenation (SpO2 ≥90% on FIO2 ≤40% and PEEP ≤5)
   - No evidence of myocardial ischemia in the previous 24 hours
   - Hemodynamically stable (dopamine or dobutamine ≤ 5 mcg/kg/min, norepinephrine ≤ 2 mcg/min, or absence of vasopressin or milrinone at any dose)

- No evidence of increased intracranial pressure

If pass the screening, place on CPAP of 5 and PS of 6 for a 120-min trial

The patient's RN and RCP will observe the patient for failure criteria. Patients fail The SBT if they develop any of the following:

- RR > 35 or < 8 for ≥ 5 min
- SpO2 < 88% for ≥ 5 min
- Altered mental status
- Acute cardiac dysrhythmia
- HR > 130 or < 60
- Use of accessory muscles
- Abdominal paradox
- Diaphoresis
- Marked dyspnea

Patients who fail the SBT will be placed back on the ventilator settings used before The trial. If the SBT was successful, the patients' physicians will be notified to decide on extubation

APPENDIX C

NSP-SBT ARM (NO SEDATION PROTOCOL: ANALGESIA-FIRST SEDATION FOLLOWED BY SBT)

1. Fentanyl 25 mcg IVP Q 5 min PRN pain
   Goal pain score: ≤ 3
   Goal sedation score: 0 to -3

2. If fentanyl IVP cannot relieve pain after 4 doses, notify the study team for:
   - Fentanyl infusion (start at 25 mcg/hr and titrate every 30 minutes to goal pain score)
   - If fentanyl infusion was titrated up X2 and goal pain and sedation score not achieved, start propofol infusion (start at 5 mcg/kg/min and titrate to goal RASS score. Use propofol 6 hours only)

3. Spontaneous Breathing Trial (SBT)

   Daily Screening
   Respiratory Care Practitioners (RCP) conduct a daily screen every morning to assess readiness to wean:

   - adequate oxygenation (SpO2 ≥90% on FIO2 ≤40% and PEEP ≤5)
   - No evidence of myocardial ischemia in the previous 24 hours
   - Hemodynamically stable (dopamine or dobutamine ≤ 5 mcg/kg/min, norepinephrine ≤ 2 mcg/min, or absence of vasopressin or milrinone at any dose)
   - No evidence of increased intracranial pressure

   If pass the screening, place on CPAP of 5 and PS of 6 for a 120-min trial

   The patient's RN and RCP will observe the patient for failure criteria. Patients fail the SBT if they develop any of the following:

   - RR > 35 or < 8 for ≥ 5 min
   - SpO2 < 88% for ≥ 5 min
   - Altered mental status
   - Acute cardiac dysrhythmia
   - HR > 130 or < 60

- Use of accessory muscle
- Abdominal paradox
- Diaphoresis
- Marked dyspnea

Patients who fail the SBT will be placed back on the ventilator settings used before the trial. If the SBT was successful, the patients' physicians will be notified to decide on extubation

APPENDIX D

Richmond Agitation Sedation Scale (RASS)

+4	Combative	Overly combative, violent, immediate danger to staff
+3	Very agitated	Pulls or remove tube(s) or catheter(s); aggressive
+2	Agitated	Frequent non-purposeful movement, fights ventilator
+1	Restless	Anxious but movement not aggressive or vigorous
0	Alert and calm	
-1	Drowsy	Not fully alert but has sustained awakening (eye opening/eye contact to voice ≥ 10 seconds)
-2	Light sedation	Briefly awakens with eye contact to voice (< 10 seconds)
-3	Moderate sedation	Movement or eye opening to voice but no eye contact
-4	Deep sedation	No response to voice but movement or eye opening to physical stimulation
-5	Unarousable	No response to voice or physical stimulation

APPENDIX E

Critical-Care Pain Observation Tool (CPOT)

Facial expression	No mussular tension observed	Relaxed	0
	Presence of frowning, brow lowering, orbit tightening, & levator contraction	Tense	1
	All of the above facial movements plus eyelid tightly closed	Grimacing	2
Body movements	Does not move at all (does not necessarily mean absence of pain)	Absence of movement	0
	Slow, cautious movements, touching or rubbing the pain site, seeking attention through movements	Protection	1
	Pulling tubes, attempting to sit up, moving limbs/thrashing, not following commands, striking at staff, trying to climb out of bed	Restless	2
Muscle tension (passive flexion & extension of UE)	No resistance to passive movements	Relaxed	0
	Resistance to passive movements	Tense, rigid	1
	Strong resistance to passive movements, inability to complete them	Very tense or rigid	2
Compliance with ventilator (intubated) OR	Alarms not activated, easy ventilation	Tolerating vent	0
	Alarms stop spontaneously	Coughing but tolerating	1
	Asynchrony: Blocking ventilation, alarms frequently activated	Fighting ventilator	2
Vocalization (extubated)	Talking in normal tone or no sound		0
	Sighing, moaning		1
	Crying out, sobbing		2
Total, range			0-8