Incidence and Risk Model Development for Severe Tachypnea Following Terminal Extubation

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BACKGROUND: Palliative ventilator withdrawal (PVW) in the ICU is a common occurrence.

RESEARCH QUESTION: The goal of this study was to measure the rate of severe tachypnea as a proxy for dyspnea and to identify characteristics associated with episodes of tachypnea.

STUDY DESIGN AND METHODS: This study assessed a retrospective cohort of ICU patients from 2008 to 2012 mechanically ventilated at a single academic medical center who underwent PVW. The primary outcome of at least one episode of severe tachypnea (respiratory rate > 30 breaths/min) within 6 h after PVW was measured by using detailed physiologic and medical record data. Multivariable logistic regression was used to examine the association between patient and treatment characteristics with the occurrence of a severe episode of tachypnea post extubation.

RESULTS: Among 822 patients undergoing PVW, 19% and 30% had an episode of severe tachypnea during the 1-h and 6-h postextubation period, respectively. Within 1 h postextubation, patients with the following characteristics were more likely to experience tachypnea: no pre-extubation opiates (adjusted OR [aOR], 2.08; 95% CI, 1.03-4.19), lung injury (aOR, 3.33; 95% CI, 2.19-5.04), Glasgow Coma Scale score > 8 (aOR, 2.21; 95% CI, 1.30-3.77), and no postextubation opiates (aOR, 1.90; 95% CI, 1.19-3.00).

INTERPRETATION: Up to one-third of ICU patients undergoing PVW experience severe tachypnea. Administration of pre-extubation opiates (anticipatory dosing) represents a key modifiable factor that may reduce poor symptom control.

KEY WORDS: dyspnea; end of life; palliative care; ventilator withdrawal

ABBREVIATIONS: aOR = adjusted OR; CMO = comfort measures only; GCS = Glasgow Coma Scale; IQR = interquartile range; MIMIC = Medical Information Mart for Intensive Care; PVW = palliative ventilator withdrawal; SOFA = Sequential Organ Failure Assessment

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Dr Fehnel and Mr de la Hoz served as co-first authors.

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Nearly 25% of deaths in the United States occur in ICUs.1,2 The majority of deaths in the ICU reflect a transition from curative to comfort-focused care through a process of palliative ventilator withdrawal (PVW).3 Numerous professional societies and patient groups have advocated for improved management of ventilated ICU patients transitioning to palliative care.4,10 Research conducted over the past 15 years has informed several aspects of palliative care in the ICU setting, particularly how to improve communication and family-centered care.10-27 In contrast, relatively little research has focused on the process of PVW. The practice therefore varies widely across ICUs28-34 and little is known about factors associated with better symptom control among terminally ill patients undergoing this procedure.

Patients undergoing PVW who are able to report symptoms describe the sensation of breathlessness or dyspnea as the most distressing symptom they experienced.10,35-37 Unfortunately, there are few data to guide the clinical approach to minimizing respiratory distress during PVW. Although evidence suggests lower rates of respiratory distress with gradual reduction of ventilator support (terminal weaning) vs immediate extubation,33 it is unknown whether administering analgesia/sedation pre-extubation (anticipatory dosing)38,39 relieves distress more effectively than giving these drugs only in response to observed symptoms.40,41 Assessing physical discomfort among patients undergoing PVW is challenging. A study of terminally ill ICU patients found that 50% were unable to communicate and 20% to 30% were comatose.42 Empirical evidence suggests that many patients deemed comatose retain the ability to experience the sensation of respiratory distress.33 Moreover, a study of 104 ICU patients, most with neurologic injuries, found that 40% of patients deemed comatose by highly trained physicians actually displayed clinical signs of consciousness.44

Taken together, the current report leverages the Medical Information Mart for Intensive Care III (MIMIC-III) database45 to better examine severe tachypnea in a cohort of ICU patients undergoing PVW. MIMIC is a rich dataset that collects detailed physiologic and clinical data from patients cared for in the seven ICUs at Beth Israel Deaconess Medical Center. The main objectives of the study were to describe the prevalence and identify modifiable factors associated with the occurrence of severe tachypnea among patients who underwent PVW through development of multivariable prediction models.

Patients and Methods

Data Source

Data were ascertained from the MIMIC-III,45 a publicly available dataset managed by the Laboratory for Computational Physiology at the Massachusetts Institute of Technology,46 which includes data from seven medical, surgical, and subspecialty ICUs at the Beth Israel Deaconess Medical Center. Data from January 1, 2008, to December 31, 2012, were used for this study. MIMIC-III contains de-identified, high-resolution physiologic and treatment data, including chart notes, continuous telemetry data and vital signs, nursing assessments, and the complete electronic health record.45 The study received exempt status by the Institutional Review Board at Beth Israel Deaconess Medical Center.

Study Population

Subjects who were mechanically ventilated and underwent PVW were identified from MIMIC-III based on the following eligibility criteria: (1) age ≥ 18 years; (2) mechanical ventilation followed by extubation; (3) comfort measures only (CMO) documented in an order or physician note prior to ventilator withdrawal (CMO order indicates all therapies are directed toward comfort but does not specify particular treatment approaches); and (4) death within 24 h of extubation. Sample size was determined by convenience sample of all data available for analysis.

Data Elements

Patient-level variables were extracted from the dataset as potentially associated with tachypnea or treatment of dyspnea based on prior literature26,28,32-35,40,47-58 and clinical experience. These variables included: demographic characteristics, insurance status, Glasgow Coma Scale (GCS) score (a score > 8 indicates lack of severe coma),59 the number of ventilator days (dichotomized at the median of 48 h), and Sequential Organ Failure Assessment (SOFA)60 score (dichotomized at the median > 8) and its components (eg, \( P_{aO_2}/F_{O_2} \) ratio most proximal to extubation).61 A binary variable was created indicating the presence of reduced diffusion capacity of lung \( P_{aO_2}/F_{O_2} < 200 \), a marker of ARDS. Anticipatory dosing with opioids was defined as the administration (by any route, bolus, or increase in continuous infusion rate) of morphine, fentanyl, or hydromorphone within 1 h pre-extubation.38,41,62 Fentanyl and hydromorphone were converted to morphine-equivalent doses, and a binary variable was created indicating whether opiates were administered within 60 min prior to extubation. Postextubation opiate administration was indicated by variables created in a similar fashion (morphine and morphine-equivalent doses of fentanyl and hydromorphone) at 1 h and 6 h postextubation, respectively. Variables indicating benzodiazepine (midazolam, lorazepam, and diazepam) and propofol administration were created at the time points of within 60 min prior to and 60 min following extubation. Primary and secondary ICU diagnoses were extracted from the electronic health record. Primary neurologic diagnosis was defined by the presence of any International Classification of Diseases, Tenth Revision, code for ischemic stroke, intracerebral hemorrhage, subarachnoid hemorrhage, status epilepticus, anoxic brain injury, cerebral edema, brain herniation/compression, hydrocephalus, or brain mass.63 Physiologic measures such as heart rate, respiratory rate, and other vital signs were obtained from telemetry data for up to 6 h post-
breathlessness in controlled settings. We used a respiratory rate dyspnea, it is a measurable objective sign that correlates with uniformly assessed, and although tachypnea is not equivalent to distinct sensations that vary in intensity.

The American Thoracic Society defines dyspnea as the “subjective experience of breathing discomfort that consists of qualitatively experience of breathing discomfort that consists of qualitatively experience of breathing discomfort that consists of qualitatively experience of breathing discomfort that consists of qualitatively

The primary outcome of interest was severe tachypnea following PVW. Among the 17,692 patients in the MIMIC-III database during the years 2008 to 2012, there were 1,251 patients undergoing PVW. The analytical sample consisted of 822 patients with complete CMO and postextubation respiratory rate data available for analysis; 248 of these patients (30%) experienced at least one episode of severe tachypnea following PVW. Median age was 73 years (interquartile range [IQR], 60-82 years) with 68% of patients aged > 65 years (Table 1). Of note, 50% of patients had a GCS score ≤ 8, indicating severe coma, and only 67% had a non-neurologic diagnosis. As shown in Figure 1, the highest proportion of patients experienced an episode of severe tachypnea within the first hour of extubation (19%). Only 20% received anticipatory dosing with opiates. The median morphine-equivalent bolus dose administered within 60 min prior to extubation was 4 mg (IQR, 2-5 mg), and the median change in continuous infusion rate was 5 mg/h (IQR, 3-10 mg/h). Postextubation, the majority of patients received opiates (58%), followed by benzodiazepines (30%) and propofol (8%).

In the unadjusted analysis, factors associated with having an episode of tachypnea within 1 h postextubation at the P < .20 level were: male sex, black race, GCS score > 8, SOFA score > 8, PaO2/FiO2 ratio < 200, no anticipatory dosing, no postextubation opiates, non-neurologic primary diagnosis, and ICU type. When these variables were entered into a multivariable model (Table 2), factors that remained independently associated with having a severe episode of tachypnea were: no anticipatory dosing (adjusted OR [aOR], 2.08; 95% CI, 1.03-4.19), no postextubation opiates (aOR, 1.90; 95% CI, 1.19-3.00), GCS score > 8 (aOR, 2.21; 95% CI, 1.30-3.77), and PaO2/FiO2 < 200 (aOR, 3.33; 95% CI, 2.19-5.04). The SOFA score was excluded from the final model to avoid collinearity with the PaO2/FiO2 ratio. To estimate the potential for synergistic effects for anticipatory dosing and postextubation opiate use, an interaction term (eg, the product of these effects) was included. We also explored the potential for interaction between sex and race but observed little evidence in favor of this; thus, the model assumes a sex effect consistent across categories of racial identification, and vice versa. The concordance statistic for the final model was 0.65 (95% CI, 0.60-0.70).

In the unadjusted analysis, factors associated with having an episode of tachypnea within 6 h following PVW at the P < .20 level were: male sex, black race, GCS score > 8, PaO2/FiO2 ratio < 200, no postextubation opiates up to 6 h, non-neurologic primary diagnosis, and ICU type. When these variables were entered into a multivariable model, factors that remained independently associated with having a severe episode of tachypnea were: male sex (aOR, 1.46; 95% CI, 1.03-2.09), GCS score > 8 (aOR, 2.25; 95% CI, 1.45-3.53), and PaO2/FiO2 ratio < 200 (aOR, 2.34; 95% CI, 1.60-3.41).

Cox proportional hazards modeling including the covariates of male sex, black race, GCS score > 8, PaO2/FiO2 ratio < 200, no anticipatory dosing, no postextubation opiates up to 6 h, non-neurologic primary diagnosis, and ICU type revealed only that...
### Table 1: Patient Characteristics and Their Unadjusted Association With Episodes of Severe Tachypnea Within 1 h and 6 h of Extubation (N = 822)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. (%) of Patients With Characteristic</th>
<th>No. (%) With Severe Tachypnea at 1 h (n = 153)</th>
<th>OR (95% CI)</th>
<th>No. (%) With Severe Tachypnea at 6 h (n = 248)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, y</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>18-40</td>
<td>31 (4)</td>
<td>8 (26)</td>
<td>1.54 (0.68-3.51)</td>
<td>10 (32)</td>
<td>1.00</td>
</tr>
<tr>
<td>41-60</td>
<td>156 (19)</td>
<td>32 (21)</td>
<td>1.15 (0.75-1.78)</td>
<td>49 (31)</td>
<td>0.93 (0.40-2.15)</td>
</tr>
<tr>
<td>61-80</td>
<td>381 (47)</td>
<td>66 (17)</td>
<td>0.84 (0.59-1.20)</td>
<td>114 (30)</td>
<td>0.86 (0.39-1.93)</td>
</tr>
<tr>
<td>81-100</td>
<td>250 (31)</td>
<td>47 (18)</td>
<td>1.00 (0.69-1.48)</td>
<td>73 (29)</td>
<td>0.83 (0.37-1.87)</td>
</tr>
<tr>
<td>Male sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>449 (55)</td>
<td>92 (60)</td>
<td>1.30 (0.92-1.84)</td>
<td>142 (57)</td>
<td>1.20 (0.89-1.62)</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>593 (85)</td>
<td>106 (17)</td>
<td>0.67 (0.41-1.10)</td>
<td>168 (28)</td>
<td>1.00</td>
</tr>
<tr>
<td>Black</td>
<td>41 (6)</td>
<td>16 (39)</td>
<td><strong>3.00 (1.55-5.80)</strong></td>
<td>18 (44)</td>
<td>1.83 (0.96-3.48)</td>
</tr>
<tr>
<td>Asian</td>
<td>23 (3)</td>
<td>3 (13)</td>
<td>0.90 (0.30-2.70)</td>
<td>9 (39)</td>
<td>1.50 (0.64-3.54)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>21 (3)</td>
<td>4 (19)</td>
<td>0.67 (0.41-1.10)</td>
<td>5 (23)</td>
<td>0.78 (0.28-2.18)</td>
</tr>
<tr>
<td>Other</td>
<td>22 (3)</td>
<td>3 (14)</td>
<td>0.64 (0.20-2.30)</td>
<td>7 (32)</td>
<td>1.09 (0.44-2.73)</td>
</tr>
<tr>
<td><strong>Insurance</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medicare</td>
<td>571 (70)</td>
<td>108 (19)</td>
<td>1.00</td>
<td>178 (31)</td>
<td>1.00</td>
</tr>
<tr>
<td>Medicaid</td>
<td>51 (6)</td>
<td>3 (18)</td>
<td>0.93 (0.44-1.95)</td>
<td>15 (29)</td>
<td>0.85 (0.45-1.59)</td>
</tr>
<tr>
<td>Private</td>
<td>180 (22)</td>
<td>34 (19)</td>
<td>1.01 (0.66-1.55)</td>
<td>49 (27)</td>
<td>0.81 (0.55-1.17)</td>
</tr>
<tr>
<td>Uninsured</td>
<td>16 (2)</td>
<td>2 (13)</td>
<td>0.62 (0.14-2.74)</td>
<td>4 (25)</td>
<td>0.68 (0.22-2.14)</td>
</tr>
<tr>
<td>GCS score &gt; 8</td>
<td>406 (50)</td>
<td>131 (85)</td>
<td><strong>1.65 (1.02-2.66)</strong></td>
<td>104 (26)</td>
<td><strong>1.47 (0.99-2.17)</strong></td>
</tr>
<tr>
<td>Ventilation &gt; 48 h</td>
<td>402 (51)</td>
<td>75 (52)</td>
<td>1.05 (0.73-1.50)</td>
<td>126 (31)</td>
<td>1.16 (0.85-1.58)</td>
</tr>
<tr>
<td>SOFA score &gt; 8</td>
<td>402 (49)</td>
<td>89 (58)</td>
<td><strong>1.56 (1.09-2.23)</strong></td>
<td>127 (52)</td>
<td>1.20 (0.88-1.62)</td>
</tr>
<tr>
<td>PaO2/FIO2 &lt; 200</td>
<td>268 (34)</td>
<td>76 (49)</td>
<td><strong>2.13 (1.50-3.05)</strong></td>
<td>100 (40)</td>
<td><strong>1.48 (1.09-2.03)</strong></td>
</tr>
<tr>
<td>Pre-extubation benzodiazepine</td>
<td>250 (30)</td>
<td>43 (28)</td>
<td>0.86 (0.59-1.27)</td>
<td>72 (29)</td>
<td>0.91 (0.66-1.27)</td>
</tr>
<tr>
<td>Pre-extubation propofol</td>
<td>94 (11)</td>
<td>15 (10)</td>
<td>0.80 (0.45-1.44)</td>
<td>28 (11)</td>
<td>0.99 (0.62-1.60)</td>
</tr>
<tr>
<td>No anticipatory dosing</td>
<td>652 (79)</td>
<td>128 (83)</td>
<td>1.35 (0.85-2.14)</td>
<td>128 (20)</td>
<td>1.34 (0.86-2.08)</td>
</tr>
<tr>
<td>Postextubation benzodiazepine</td>
<td>240 (29)</td>
<td>44 (29)</td>
<td>0.96 (0.65-1.41)</td>
<td>75 (30)</td>
<td>1.05 (0.76-1.47)</td>
</tr>
<tr>
<td>Postextubation propofol</td>
<td>64 (8)</td>
<td>8 (5)</td>
<td>0.57 (0.26-1.21)</td>
<td>19 (8)</td>
<td>0.91 (0.52-1.59)</td>
</tr>
<tr>
<td>No postextubation opiates at 1 h</td>
<td>374 (46)</td>
<td>57 (37)</td>
<td><strong>1.53 (1.07-2.20)</strong></td>
<td>105 (42)</td>
<td>1.23 (0.90-1.67)</td>
</tr>
<tr>
<td>No postextubation opiates at 6 h</td>
<td>304 (37)</td>
<td>71 (46)</td>
<td><strong>3.87 (2.58-5.82)</strong></td>
<td>93 (37)</td>
<td><strong>2.39 (1.65-3.46)</strong></td>
</tr>
<tr>
<td>Nonneurologic primary diagnosis</td>
<td>548 (67)</td>
<td>124 (81)</td>
<td><strong>2.39 (1.55-3.65)</strong></td>
<td>52 (21)</td>
<td><strong>1.76 (1.23-2.51)</strong></td>
</tr>
<tr>
<td><strong>ICU type</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgical</td>
<td>199 (24)</td>
<td>24 (16)</td>
<td>1.00</td>
<td>50 (26)</td>
<td>1.00</td>
</tr>
<tr>
<td>Medical</td>
<td>397 (48)</td>
<td>95 (62)</td>
<td><strong>2.29 (1.41-3.71)</strong></td>
<td>134 (36)</td>
<td><strong>1.61 (1.09-2.36)</strong></td>
</tr>
<tr>
<td>Trauma</td>
<td>104 (13)</td>
<td>14 (9)</td>
<td>1.13 (0.56-2.30)</td>
<td>25 (25)</td>
<td>0.97 (0.55-1.68)</td>
</tr>
<tr>
<td>Cardiac</td>
<td>81 (10)</td>
<td>14 (9)</td>
<td>1.52 (0.74-3.12)</td>
<td>27 (34)</td>
<td>1.51 (0.86-2.65)</td>
</tr>
<tr>
<td>Cardiac surgical</td>
<td>36 (4)</td>
<td>6 (4)</td>
<td>1.46 (0.55-3.87)</td>
<td>10 (32)</td>
<td>1.38 (0.61-3.13)</td>
</tr>
</tbody>
</table>

Bolded items indicate statistical significance at P < .05. GCS score > 8 indicates lack of severe coma. Anticipatory dosing indicates administration of opiates within 60 min prior to extubation. PaO2/FIO2 < 200 indicates substantial impairment in lung oxygen diffusion capacity and is a marker of ARDS. GCS = Glasgow Coma Scale; SOFA = Sequential Organ Failure Assessment.

*Reported proportions are by row and will not sum to 100.*
patients with a PaO2/FiO2 ratio < 200 were significantly associated with time to tachypnea episode (hazard ratio, 1.48; 1.11-1.97). Kaplan-Meier time-to-event curves comparing patients receiving and not receiving anticipatory dosing revealed no difference in time to death over the full 24 h postextubation period between groups (Fig 2). Log-rank test for equality of survivor functions ($P = .28$).

**Discussion**

We identified a 30% rate of severe tachypnea during PVW among a mixed population of critically ill patients. The highest incidence of severe tachypnea occurred in the first hour following extubation. A key finding of this analysis is that the odds of severe tachypnea following PVW are more than doubled without anticipatory dosing of opiates. Although a similar strength and direction of association were seen with postextubation opiate dosing, these findings lend empirical support to the theoretical rationale for anticipatory dosing of opiates pre-extubation to prevent uncontrolled symptoms during PVW. There was notably no difference in time to death between patients receiving anticipatory dosing and those who did not. Higher level of consciousness, no opiates given within 1 h of extubation, and lung injury (PaO2/FiO2 ratio < 200) were also associated with greater risk for severe tachypnea within 1 h of PVW.

Despite the immense resources devoted to the monitoring and care of ICU patients, the relatively high prevalence of this marker of distress during the transition to comfort measures is surprising but consistent with prior estimates. A small study of 32 terminally extubated patients in a neurologic ICU reported a 59% rate of labored breathing. Apart from the small sample size of the study, the assessment of labored breathing is not fully standardized and may have led to biased estimates. Others have estimated dyspnea rates of 34% among terminally extubated patients.

Previous evaluations of the use of anticipatory dosing of opiates in the setting of PVW have yielded unclear results. Two studies found that anticipatory dosing was not associated with earlier time to death, but the investigators did not examine symptom control or compare it with reactive dosing. A small study of 29 patients described anticipatory dosing as a treatment option for patients who were alert and at risk for poor postextubation symptom control, although characteristics of patients at risk were not delineated.

Finally, a study of 32 patients undergoing different PVW practices advised caution when using anticipatory dosing, particularly among comatose patients. Although reviews and guidelines treat the practice of dosing medications in anticipation of end-of-life symptoms as ethically and clinically acceptable, they also cite a lack of detailed empirical evidence.

There were differences in risk factors identified by the logistic regression and Cox proportional hazard models. These differences are in part attributable to logistic regression models estimating risk at the time points of 1 and 6 h postextubation, whereas the Cox proportional hazards model estimated risk at time of the tachypnea event. Taken together, interpretation of both models suggests that patients with a PaO2/FiO2 ratio < 200 are at highest risk for an episode of tachypnea. This characteristic is readily available in ICU patients prior to extubation and may be used to tailor approaches for reducing the risk of poorly controlled symptoms in the process of PVW. The mechanisms by which patients with higher levels of consciousness and male patients (in the 6-h model) seem to be at risk for higher rates of severe tachypnea are unclear, and they warrant further exploration in a carefully constructed prospective analysis. In the interim, particular attention should be paid to these risk groups during the process of PVW, with carefully titrated symptom-directed treatments.

A broader context at odds with our findings is studies reporting that the majority of family members of patients dying in the ICU perceive deaths to have occurred with comfort. However, the family members surveyed in this prospective study of 155 ICU patients undergoing terminal extubation in Canada identified 30% of families reporting that patients were “mostly comfortable,” and 9% of families reporting “slightly
TABLE 2 ] Independent Predictors of Severe Tachypnea 1 h and 6 h Following PVW (N = 822)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>1 h Post-PVW</th>
<th>6 h Post-PVW</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>1.47 (0.98-2.19)</td>
<td>1.46 (1.03-2.09)</td>
</tr>
<tr>
<td>Race</td>
<td>0.33 (0.065-6.29)</td>
<td>0.44 (0.03-7.64)</td>
</tr>
<tr>
<td>No anticipatory dosing</td>
<td>2.08 (1.03-4.19)</td>
<td>1.36 (0.91-1.99)</td>
</tr>
<tr>
<td>No postextubation opiates</td>
<td>1.90 (1.19-3.00)</td>
<td>1.35 (0.91-1.99)</td>
</tr>
<tr>
<td>ICU type</td>
<td>1.73 (0.51-5.91)</td>
<td>0.85 (0.03-2.17)</td>
</tr>
<tr>
<td>GCS score &gt; 8</td>
<td>2.21 (1.30-3.77)</td>
<td>2.25 (1.45-3.53)</td>
</tr>
<tr>
<td>PaO2/FIO2 &lt; 200</td>
<td>3.33 (2.19-5.04)</td>
<td>2.34 (1.60-3.41)</td>
</tr>
<tr>
<td>Nonneurologic primary diagnosis</td>
<td>3.81 (0.24-7.51)</td>
<td>2.76 (0.13-8.32)</td>
</tr>
<tr>
<td>No anticipatory dosing * no postextubation opiates</td>
<td>1.20 (0.16-4.34)</td>
<td>1.34 (0.21-5.56)</td>
</tr>
</tbody>
</table>

Data are presented as adjusted OR (95% CI). Bolded items indicate statistical significance at P < .05. PaO2/FIO2 < 200 indicates substantial impairment in lung oxygen diffusion capacity and is a marker of ARDS. Anticipatory dosing indicates administration of opiates within 60 min prior to extubation. No anticipatory dosing * no postextubation opiates indicates the interaction term for these covariates. Covariates listed in the table represent all variables included in the final models for the outcome at both time points. PVW = palliative ventilator withdrawal. See Table 1 legend for expansion of other abbreviation.

uncomfortable” or “very uncomfortable.” Although family perception of comfort and support during the dying process in the ICU is a core component of high-quality ICU care, the individual patient’s experience remains paramount. Studies using repeated measurement of objective markers of symptom control during PVW are rare in the medical literature.

Our study offers the advantage of precise calculation of the population at risk to provide robust estimates of episodes of severe tachypnea during PVW. To our knowledge, this study is the largest analysis of symptom control among PVW patients to date. This study is limited by the fact that tachypnea is not equivalent to the subjective experience of dyspnea among patients able to self-report. The respiratory distress observation scale is the only validated measure for dyspnea in this population, but it has yet to be universally adopted. The reporting rate of the respiratory distress observation scale was low in our population, which limited its use for this analysis. Other markers of respiratory distress, such as labored or obstructed patterns of breathing, are used as markers of comfort during the PVW process, but the integration of a validated, systematic approach to the identification and management of patients during PVW remains to be standardized in critical care practice. The use of observational data introduces the potential for uncontrolled confounding. However, analysis of the complete electronic health record, including free text documentation of each patient’s entire hospital course, renders the possibility of overlooking clinically relevant patient or ICU characteristics unlikely. Although ICU nurses validate all vital signs, some validation could occur erroneously. There were no major institutional changes in the process of PVW during the study period. The process of de-identification within the dataset, however, limits formal statistical tests for time period effects, which could alter the reported associations.

Conclusions

The prevalence of poorly controlled symptoms as measured by using severe tachypnea during PVW is common. The risk of severe tachypnea may be reduced with anticipatory dosing of opiates. Patients who are male, with higher levels of consciousness, or have more severe lung injury seem to be at greater risk for severe tachypnea. Further prospective study using standardized measurements of dyspnea, and interventions to improve symptom control during PVW, should be directed at these risk groups.
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References


