



Outcomes following nighttime extubation in a high-intensity medical intensive care unit

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1. Introduction

The optimal time to liberate patients from mechanical ventilation remains controversial. In most centers, extubation takes place during daytime hours due to less overnight physician coverage, hesitancy to disrupt the sleep-wake cycle, over-reliance on algorithmic weaning parameters [1], and a tendency to follow convention.

Multiple studies have shown that extubation failure is an independent risk factor for prolonged hospitalization and increased mortality through mechanisms such as ventilator associated pneumonia, weakness, and delirium [2,3]. Moreover, accidental extubation, self-extubation, and reintubation are risk factors for patient mortality in the intensive care unit (ICU) [4]. Thus, a fine balance exists between optimal sedation practices, overly aggressive extubation, and mindful delay.

A retrospective cohort study utilizing a large patient database from 2000 to 2009 cast significant doubts on the safety of overnight extubation [5]. In that study, Gershengorn et al. found that all-cause mortality increased significantly with nighttime extubation when compared to patients extubated during the day. However, two more recent publications have shown improved outcome measures with patients extubated at night in heterogeneous patient populations [6,7].

Overall, there is a paucity of literature on the safety of nocturnal extubation. The aim of the study is to explore variation in mortality and reintubation rates between nighttime and daytime extubations with a specific focus in the medical ICU patient population.

2. Materials and methods

This was a retrospective analysis of MICU patients who required mechanical ventilation between July 1, 2015 and June 30, 2017 at Advocate Christ Medical Center. The Institutional Review Board at Advocate Health Care Network in Downers Grove, IL approved this study via waiver of informed consent. Advocate Christ Medical Center is a 749-bed quaternary care center with 100 geographically distributed specialty-specific ICU beds, including a closed, 24-bed MICU. Two critical care board certified intensivists are present during the day (7 am to 7 pm) and one critical care board certified intensivist is available during the night (7 pm to 7 am). Staff intensivists are supported by a team of 8 to 10 daytime resident physicians, 3 nighttime resident physicians with consistent 1:2 nurse-to-patient and 1:12 respiratory therapist-to-patient coverage.

We first identified all patients who required mechanical ventilation in the MICU by searching our institution's APACHE clinical information system database (Cerner, Kansas City, MO). The database is prospectively generated for quality improvement and benchmarking purposes by trained nurse coordinators. Information on a multitude of variables is collected, including baseline patient characteristics, APACHE IV score, ICU length of stay (LOS), hospital LOS, ventilator days, ICU mortality, and hospital mortality.

Patients included in this study were intubated prior to or during their initial admission to the MICU and extubated during their index MICU stay. Exclusion criteria included: age <18 years-old, ventilator-dependence at baseline, tracheostomy tube in situ during index MICU stay, palliative extubation, and new DNR (do not resuscitate) order after extubation. Trained resident physicians, blinded to study

Abbreviations: AARC, American Association for Respiratory Care; AOR, Adjusted Odds Ratio; APACHE, Acute Physiologic Assessment and Chronic Health Evaluation; ARDS, Acute Respiratory Distress Syndrome; BMI, Body Mass Index; CI, Confidence Interval; cmH₂O, Centimeter of Water; DNR, Do Not Resuscitate; FiO₂, Fraction of Inspired Oxygen; ICU, Intensive Care Unit; IQR, Interquartile Ranges; LOS, Length of Stay; MICU, Medical Intensive Care Unit; mmHg, millimeter of mercury; OR, Odds Ratio; PaO₂, Partial Pressure of Oxygen; PS, Pressure Support; PEEP, Positive End Expiratory Pressure; SD, Standard Deviation.

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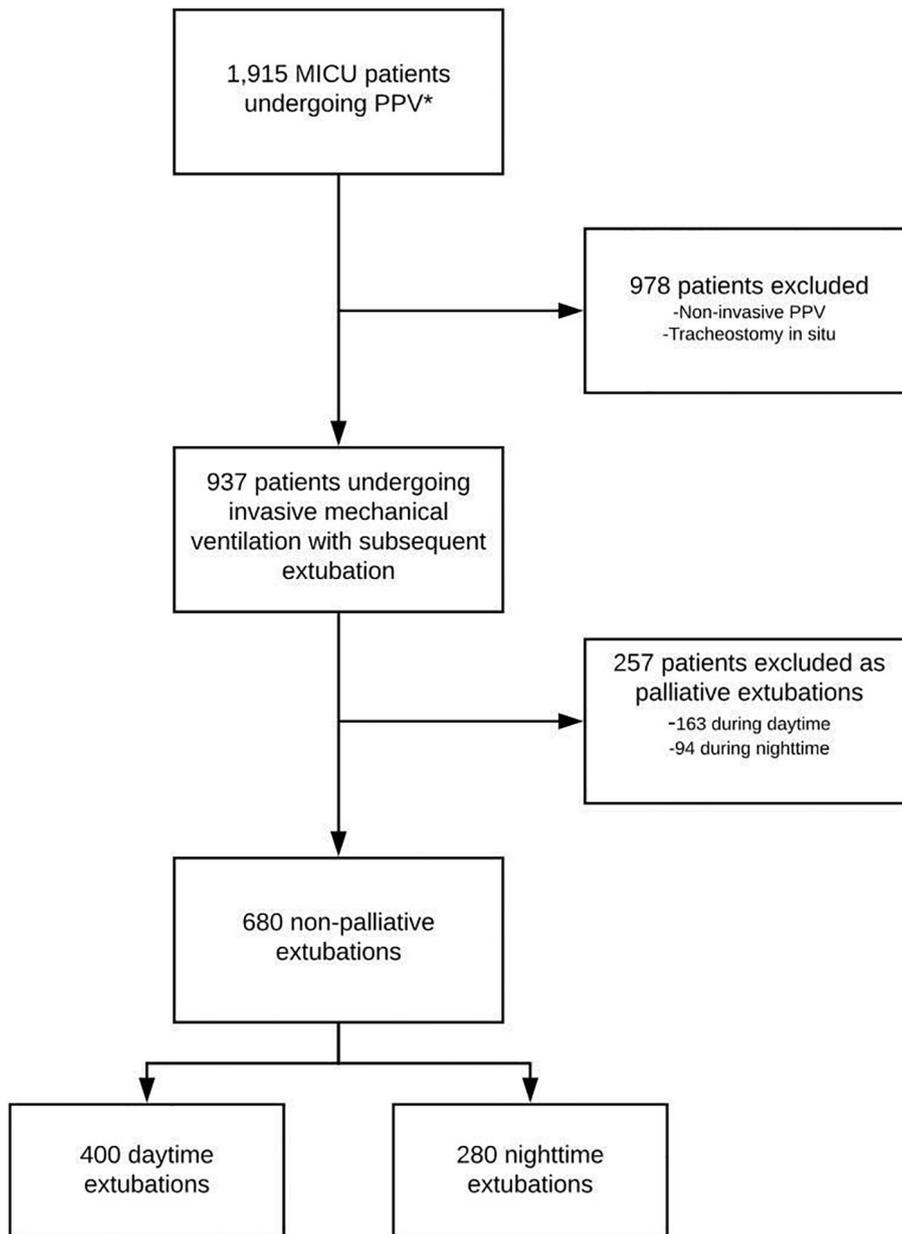
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outcomes, performed detailed chart review to determine study subject eligibility. For the purpose of this study, daytime extubation was defined as 7:00 AM to 6:59 PM and nighttime extubation was defined as 7:00 PM to 6:59 AM.

Extubation eligibility was assessed through scheduled mechanical ventilation weaning trials, and patients were extubated following physician approval. All patients who were intubated during their admission to the MICU underwent daily weaning from mechanical ventilation if they met the following criteria: stable hemodynamics, no acute delirium, normal intracranial pressure, and no paralytics. This process was initiated by a respiratory therapist if a weaning order was placed by a physician. A spontaneous awakening trial was subsequently performed with sedation titrated to a Richmond Agitation Sedation Scale of 0 to –1. The trial was considered successful if there was no agitation, oxygen saturation was above 92% and the PaO₂ was >65 mmHg on <50%

FiO₂. The trial was considered a failure if the patient was excessively anxious, agitated or had uncontrolled pain; there was respiratory distress with respirations above 35; the oxygen saturation was below 92% or PaO₂ was below 65 mmHg; or hemodynamic instability occurred.

If the patient passed the spontaneous awakening trial, they progressed to a spontaneous breathing trial. They were placed on pressure support ventilation (PS 7 cmH₂O, PEEP 5 cmH₂O, FiO₂ 0.5 or below) for 30–60 min. The trial was considered successful if the patient tolerated the above settings with no change in the clinical condition. The spontaneous breathing trial was considered a failure if any one of the following occurred: respiratory rate >30 or below 8; oxygen saturation below 92% or PaO₂ below 65 mmHg; respiratory distress; hemodynamic instability; or decline in mental status. If any of the above occurred, the patient was



*Positive Pressure Ventilation

Fig. 1. Patients Included in Study.

Table 1
Patient characteristics by time of extubation^d (N = 680).^c

Variable	Extubated during the day (N = 400)	Extubated at night (N = 280)	p-value
Age, mean (SD)	64.07 (15.97)	62.70 (17.07)	0.16 ^a
Gender, N (%)			0.61 ^b
Male	205 (51.25)	149 (53.21)	
Female	195 (48.75)	131 (46.79)	
Race, N (%)			0.18 ^b
Caucasian	226 (56.50)	156 (55.71)	
African American	144 (36.00)	112 (40.00)	
Hispanic and other	30 (7.50)	12 (4.29)	
BMI	30.34 (9.27)	31.56(10.32)	0.05 ^a
Admitting diagnosis, N (%)			0.40 ^b
Cardiac arrest	33 (8.25)	31 (11.07)	
Other cardiac ^e	47 (11.75)	40 (14.29)	
Pulmonary ^f	172 (43.00)	109 (38.93)	
Other	148 (37.00)	100 (35.71)	
APACHE	83.89 (28.32)	79.14 (27.48)	0.59 ^a

^a From Student's *t*-test,

^b From Pearson's Chi-square test of proportions,

^c From Mann-Whitney *U* test.

^d Values are presented as N (%) for categorical and mean (SD) for continuous.

^e Congestive heart failure, myocardial infarction, or cardiogenic shock.

^f COPD/asthma, airway obstruction, pneumonia.

returned to pre-trial ventilator settings with a Richmond Agitation Sedation Scale of 0 to −1.

Patients who met extubation criteria and had a rapid shallow breathing index <105 were extubated after an order was obtained from the physician. Physicians also had the discretion to extubate patients based on a focused bedside assessment outside of weaning parameters. All endotracheal intubations in the MICU were performed by the intensivist given 24 h in house availability. Absolute contraindications to nocturnal extubation were not delineated a priori. Timing of extubation was under the discretion of the intensivist.

A total of 680 subjects (400 extubated during the daytime and 280 extubated at night) were included in this retrospective study. Based on estimates of patients being extubated at this site from past years, with this sample size we have 80% power to detect a 4.1% difference in proportions between groups for the primary outcome of hospital mortality with an alpha of 0.05.

Descriptive statistics were calculated for all variables and presented overall and by group using median and interquartile ranges [IQR] for continuous variables as well as counts and percentages for categorical variables. The normality of the length of stay variables and mechanical ventilation duration was assessed with a Shapiro-Wilk test with a *p*-value less than or equal to 0.05 being considered non-normally distributed. For non-normally distributed continuous variables, a Mann-Whitney *U* test was utilized in the bivariate analysis. For dichotomous outcomes, comparisons were made between groups using Pearson's chi-squared test.

Multiple multivariate logistic regression models were constructed to assess the association between time of extubation and hospital mortality, time of extubation and intensive care unit mortality, and time of extubation and reintubation. Diagnosis and race were recategorized to allow for more robust cell sizes and mediators were omitted from the final models. Multiple multivariate linear regression models were created utilizing backwards stepwise regression for the outcomes of log-transformed hospital length of stay, intensive care unit length of stay, and hours on ventilator. Potentially confounding demographic and clinical variables that were identified a priori and adjusted for in the models included: age, gender, race, BMI, APACHE score, and admitting diagnosis. Finally, we performed sensitivity analysis in which the daytime group remained the same but the nighttime group was defined as 7:00 PM to 4:59 AM. All tests were two-tailed and a *p*-value of 0.05 or less was considered statistically significant in all analyses.

3. Results

A total of 1915 patients were identified as being admitted to the MICU and having positive pressure ventilation during their stay. Of these, 978 patients were excluded because they were solely on non-invasive positive pressure ventilation or had tracheostomy in situ and 257 were excluded because they were terminally extubated or expired. Therefore, the study cohort consisted of 680 patients, of which 400 (58.8%) underwent daytime extubation and 280 (41.2%) nighttime extubation (Fig. 1). The study cohort had mean age 63.5 (SD 16.4) years-old, mean BMI 30.3 (SD 9.3), mean APACHE IV score 81.5 (SD 31.5), and 354 (52.1%) were male. Characteristics of the study cohort by time of extubation are shown in Table 1. More specific admission characteristics with respect to intubation etiology are delineated in Fig. 2 and Fig. 3.

3.1. Mortality

A total of 34 (5.0%) patients died during their hospital stay, including 23 (5.8%) in the daytime extubation group and 11 (3.9%) in the nighttime extubation group (*p* = 0.26) (Table 2). Time of extubation was not significantly associated with ICU mortality (AOR = 1.00, 95%CI 0.35–2.84, *p* = 0.99) or in-hospital mortality (AOR = 0.76, 95% CI 0.34–1.70, *p* = 0.50), after adjusting for age, gender, race, BMI, APACHE IV score, and admitting diagnosis (Table 3).

3.2. Reintubation

A total of 43 (6.3%) patients were reintubated, including 26 (6.5%) in the daytime extubation group and 17 (6.1%) in the nighttime extubation group (*p* = 0.83). Of the reintubated patients, 26 (60.4%) were reintubated within 24 h, 8 (18.6%) were reintubated from 24 to 48 h, and 9 (20.9%) were reintubated from 48 to 72 h post-extubation. Specifics with respect to reintubation etiology are delineated in Fig. 5 and Fig. 6.

Nighttime extubation was not significantly associated with reintubation after adjusting for age, gender, race, BMI, APACHE score, and admitting diagnosis (AOR = 0.99, 95%CI 0.52–1.88, *p* = .97).

Of patients who were reintubated, there was no difference between daytime versus nighttime extubation with respect to ICU mortality (χ^2 0.02, *p* = 0.90) or hospital mortality (χ^2 0.10, *p* = 0.76; Table 3).

3.3. Length of stay and duration of mechanical ventilation

Patients extubated at nighttime had a shorter median ICU LOS (2.9 days [IQR 1.62–5.04]) when compared to patients extubated during daytime hours (3.8 days [IQR 2.03–6.43]) (*p* < 0.01). Median hospital LOS was also shorter in the nighttime extubation group (9.30 days [IQR 5.29–14.66]) versus the daytime extubation group (10.85 days [IQR: 6.78–17.32]) (*p* < 0.01). These findings persisted after adjustment for age, gender, race, BMI, APACHE score, and admitting diagnosis (*p* < 0.01; see Table 3).

Patients extubated at nighttime had a shorter median duration of mechanical ventilation (29.3 h [IQR 13.19–57.51]) compared to patients extubated during the daytime (46.3 h [IQR 22.20–95.04]) (*p* < 0.01).

3.4. Sensitivity Analysis

Our findings stood after sensitivity analyses in which nighttime was defined as 7:00 PM to 4:59 AM and the daytime remained 7:00 AM to 6:59 PM. For this analysis, the nighttime group consisted of 150 (27.3%) and the daytime group 400 (72.7%) subjects. We again adjusted for age, gender, race, BMI, APACHE IV score and admitting diagnosis. If extubated between 7:00 PM and 4:59 AM, there was an AOR 0.38 for hospital mortality (95%CI 0.11–1.32, *p* = 0.13), AOR 0.50 for ICU mortality (95%CI 0.12–2.27, *p* = 0.38), and AOR 0.88 for reintubation (95%CI 0.39–2.04, *p* = 0.78).

Daytime Admission Diagnosis

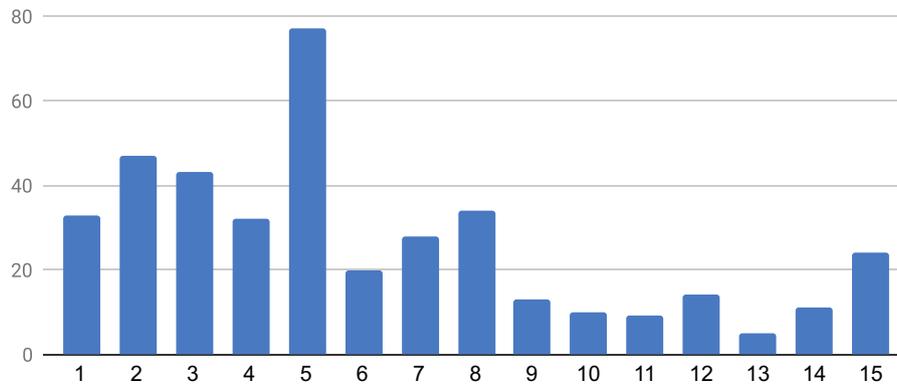


Fig. 2. Daytime Admission Diagnosis. 1 - Cardiac Arrest, 2 - Myocardial Infarction, Congestive Heart Failure, 3 - Respiratory Distress/Arrest, ARDS, 4 - Emphysema, Bronchitis, COPD, 5 - Pulmonary Sepsis, Bacterial Pneumonia, 6 - Airway Obstruction, Anaphylaxis/Angioedema, 7 - Overdose, Alcohol Withdrawal, 8 - Encephalopathy, Coma, CVA, Meningitis, 9 - Gastrointestinal Bleed, 10 - Gastrointestinal Other (including sepsis), 11 - Electrolyte Disturbance, Acute Kidney Injury, 12 - Post-Surgical, 13 - Malignancy, 14 - Sepsis, Renal, 15 - Other Sepsis, including cutaneous.

Nighttime Admission Diagnosis

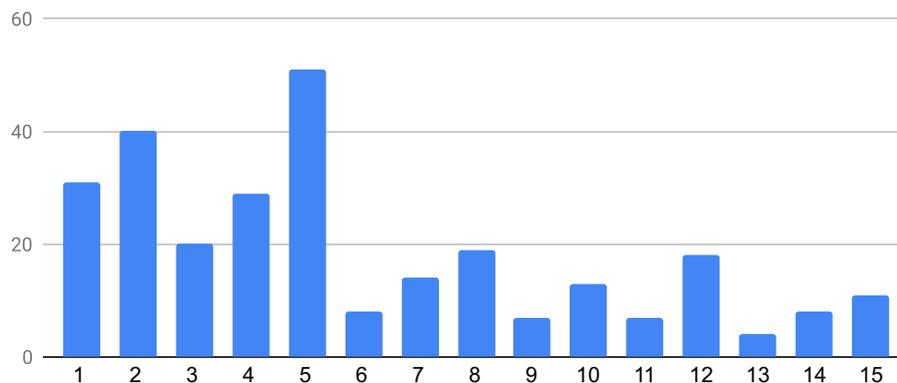


Fig. 3. Nighttime Admission Diagnosis. 1 - Cardiac Arrest, 2 - Myocardial Infarction, Congestive Heart Failure, 3 - Respiratory Distress/Arrest, ARDS, 4 - Emphysema, Bronchitis, COPD, 5 - Pulmonary Sepsis, Bacterial Pneumonia, 6 - Airway Obstruction, Anaphylaxis/Angioedema, 7 - Overdose, Alcohol Withdrawal, 8 - Encephalopathy, Coma, CVA, Meningitis, 9 - Gastrointestinal Bleed, 10 - Gastrointestinal Other (including sepsis), 11 - Electrolyte Disturbance, Acute Kidney Injury, 12 - Post-Surgical, 13 - Malignancy, 14 - Sepsis, Renal, 15 - Other Sepsis, including cutaneous.

Table 2
Unadjusted outcomes by time of extubation.^{a,d}

	Extubated during the day (N = 400)	Extubated at night (N = 280)	p-value
Hospital mortality	23 (5.8)	11 (3.9)	0.28 ^b
ICU mortality	11 (2.5)	7 (2.5)	0.84 ^b
Reintubation	26 (6.5)	17 (6.1)	0.82 ^b
ICU length of stay, days	3.78(2.03–6.43)	2.92(1.62–5.04)	<0.01 ^c
Hospital length of stay, days	10.85(6.78–17.32)	9.30(5.29–14.66)	<0.01 ^c
Mechanical ventilation, hours	46.27(22.20–95.04)	29.31(13.19–57.51)	<0.01 ^c

^a From Student's t-test,

^b From Pearson's Chi-square test of proportions,

^c From Mann-Whitney U test.

^d Values are presented as N(%) for categorical and mean (SD) for continuous.

4. Discussion

In this retrospective study of MICU patients undergoing extubation, we found no difference in mortality or the rate of reintubation between patients extubated at night or during the day. Patients extubated at night did have shorter hospital LOS, ICU LOS, and duration of mechanical ventilation.

Our results are consistent with two prior studies of adults undergoing nighttime extubation in mixed ICU populations. Tischenkel et al. [6] found no difference in the odds of in-hospital mortality (OR 0.6, 95%CI 0.3–1.0) or reintubation (OR 0.7, 95%CI 0.5–1.0) for nighttime extubation in a study of 2240 patients in one of five ICUs across two hospitals. Of note, 82% of their patients extubated at night were postoperative cardiothoracic patients, a population known to have improved outcomes with “fast track” extubation protocols [8–12]. In 2018, Everhart et al. [7] reported no difference in the odds of in-hospital mortality (OR 0.72, 95% CI 0.28–1.84, $p = 0.49$) or reintubation (OR 0.78, 95%CI 0.43–1.41, $p = 0.41$) for nighttime extubation in a study of 2241 patients in their center's ICUs.

However, medical patients made up a minority (<25%) of the population in both studies. The Tischenkel et al. study consisted of 433 MICU subjects, but only 54 (12.5%) nighttime extubations, while Everhart et al. reported on 553 medical patients, and only 49 (8.9%) nighttime extubations. This limits generalizability of the results of these studies to MICU patient populations. Our pure MICU cohort of 680 patients is larger than either of these two prior studies, with a higher percentage of patients extubated at night ($n = 280$, 41.2%). Our results suggest that MICU patients can be extubated at night without associated higher mortality or reintubation.

Table 3
Multivariate logistic regression models for hospital mortality, ICU mortality, and reintubation^a (N = 680).

Variable	Hospital mortality	ICU mortality	Reintubation
Extubation, night	0.76 (0.34–1.70); p = 0.50	1.00 (0.35–2.84); p = 0.99	0.99 (0.52–1.88); p = 0.97
Age	1.02 (0.99–1.04); p = 0.27	1.00 (0.97–1.04); p = 0.98	1.00 (0.98–1.02); p = 0.96
Gender	0.77 (0.36–1.67); p = 0.51	1.42 (0.49–4.06); p = 0.52	1.15 (0.61–2.16); p = 0.68
Race	0.99 (0.53–1.88); p = 0.98	1.22 (0.55–2.71); p = 0.63	1.06 (0.63–1.76); p = 0.84
BMI	0.98 (0.93–1.03); p = 0.34	0.96 (0.89–1.03); p = 0.22	0.97 (0.93–1.01); p = 0.11
Admitting diagnosis			
Cardiac arrest	2.98 (0.80–11.11); p = 0.11	5.65 (1.09–29.34); p = 0.04	0.84 (0.23–3.09); p = 0.80
Other cardiac ^b	3.65 (1.06–12.61); p = 0.04	6.87 (1.44–32.86); p = 0.02	1.39 (0.50–3.86); p = 0.53
Pulmonary ^c	1.91 (0.71–5.11); p = 0.20	1.52 (0.35–6.55); p = 0.58	1.51 (0.73–3.11); p = 0.27
APACHE	1.02 (1.01–1.04); p < 0.01	1.02 (1.00–1.04); p = 0.11	1.00 (0.99–1.02); p = 0.56
Reintubation	16.49 (7.05–38.59); p = 0.76	16.99 (5.74–50.37); p = 0.90	–

Abbreviations: CI, confidence interval; ICU, intensive care unit.

^a Values are presented as odds ratio (95% CI), p-value.

^b Congestive heart failure, myocardial infarction, or cardiogenic shock.

^c COPD/asthma, airway obstruction, pneumonia.

Our increased night extubation rate is likely multifactorial. Robust weaning protocols are adequate for low-risk patients but cannot substitute for decisions that fall outside of restrictive algorithmic parameters on high-risk patients [13–16]. Though physician behavior was not specifically measured, adherence to processes of care (SAT, SBT) has been shown to improve in the presence of available attending physician coverage [17,18]. We demonstrated that when a protocolized approach to a spontaneous awakening trial, followed by a spontaneous breathing trial is coupled with intensivist judgement nighttime extubation is equally as safe as daytime extubation and reduces the duration of ICU and hospital length of stay.

Patients extubated at night had a significantly lower duration of mechanical ventilation as well as a significantly shorter intensive care unit and hospital length of stay for several reasons (Table 2). Primarily, nighttime extubations allow more time for post-extubation observation prior to morning rounds. This gives the daytime intensivist a greater level of comfort in initiating transfers out of the ICU. Additionally, using the measure of clinical readiness for extubation as opposed to waiting for conventional daytime hours decreases sedation requirements, and reduces delirium in some patients, further decreasing length of stay.

In contrast, our results differ from Gershengorn et al.'s retrospective analysis of the project IMPACT database (Society of Critical Care Medicine, Mount Prospect, IL) [5]. In this study, the authors analyzed 97,844 patients extubated at one of 165 United States ICUs between October 2000 and March 2009. In a matched-pairs analysis, the authors found that patients who underwent nighttime extubation had higher mortality and a higher rate of reintubation if they had been on mechanical ventilation for longer than 12 h. There were several limitations to the study. First, the study showed no correlation between reintubation and mortality in either subgroup in the APACHE database and patients intubated for <12 h showed no difference in reintubation rates, but had increased risk of mortality. These findings largely discount the authors' primary mechanistic outcome of reintubation. Second, interim advances in critical care may have decreased the need for reintubation and mortality following planned extubation. Best practices in sedation choice and titration, as well as ARDS management have matured since Gershengorn et al.'s study [19–25].

Due to our sample size, we were able to exclude palliative extubations through detailed chart review and account for this possible confounder with respect to death. Despite Gershengorn et al.'s restrictive parameters to account for compassionate extubations in the survivor cohort, the odds ratio for mortality significantly outweighed the odds ratio for reintubation in most nocturnal subgroups. This suggests that more palliative extubations took place during evening hours. This was not accounted for in their propensity model and may have confounded their mortality results.

4.1. Limitations

Our study has limitations, including those inherent to a retrospective study design. A larger sample size could allow for further subgroup analyses. Additionally, this investigation was based in one academic MICU with 24-h intensivist coverage, which limits the generalizability of the results. Despite the observational nature of our study, the findings may still be pertinent to institutions with similar staffing models, patient volume, and acuity [6,7]. Furthermore, our aim was to evaluate outcomes in MICU patients since this population has been underrepresented in prior studies of nighttime extubation.

Our disproportionately high APACHE IV scores compared to overall low mortality rates necessitates mention. This is partly explained by the fact that we excluded 27% of the screened population due to palliative extubation while Everhart et al. and Tischenkel et al. excluded 17% and 3% respectively [6,7]. However, a direct comparison proves difficult given that our study utilized APACHE IV risk scoring as opposed to Elixhauser and Charlson comorbidity indices in the other studies [6,7]. Certainly, our limited sample size confounds our mortality metric and further subgroup analysis would have strengthened the study.

The discrepancy between duration of mechanical ventilation prior to extubation between groups may reflect a more cautious stance amongst night intensivists and may be substantiated when respiratory failure is secondary to deemed high risk features not accounted for with APACHE risk assessment. Given the retrospective analysis, specific details for extubating despite failed weaning trials and planned delay of extubation with successful SBT would have further clarified unintended selection bias between cohorts in high risk patients with obesity, upper airway obstruction or increased ICU LOS prior to extubation. Prospective analysis of these variables would be fertile ground for future research in night extubation safety.

We cannot exclude the possibility that our staffing pattern with respect to respiratory therapist patient ratio (1:12) may exceed other high intensity ICU's nationally. However, The American Association for Respiratory Care (AARC) position statement on Best Practices in Respiratory care provides no specific recommendations for staffing levels [26]. Regardless, we cannot eliminate that our RT staffing ratio may have confounded results.

Next, there appeared to be a bimodal distribution of extubation times peaking between 6:00 to 6:59 AM and 9:00 to 9:59 AM (Fig. 4). We maintained our definition of nighttime from 7:00 PM to 6:59 AM because it was decided upon a priori and our intensivist shifts change at 7:00 AM and 7:00 PM. Therefore, any extubation before 7:00 AM or after 7:00 PM is ordered by the nighttime intensivist. To test the robustness of our results, we performed a sensitivity analysis in which nighttime was limited to 7:00 PM - 04:59 AM to exclude early morning extubations that occurred between between 05:00 AM and 07:00 AM.

Extubations Plotted by Time

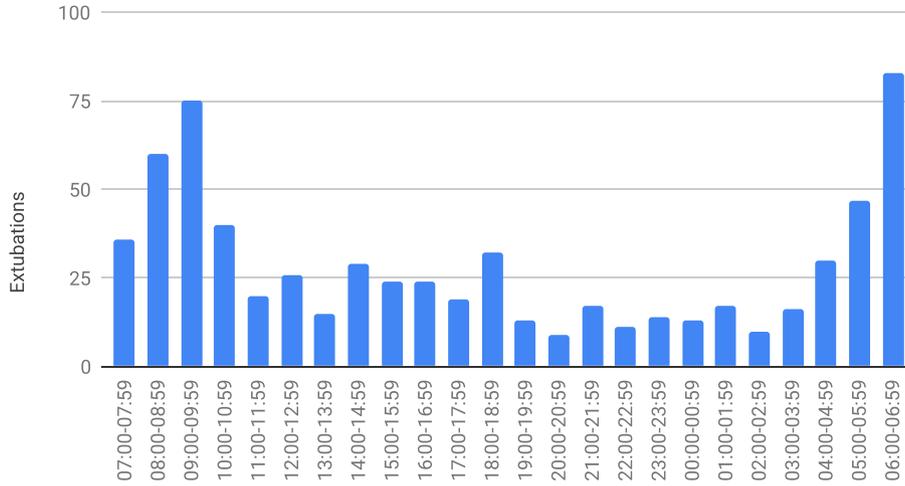


Fig. 4. Extubations Plotted by Time.

Causes for Reintubation-Daytime Extubations

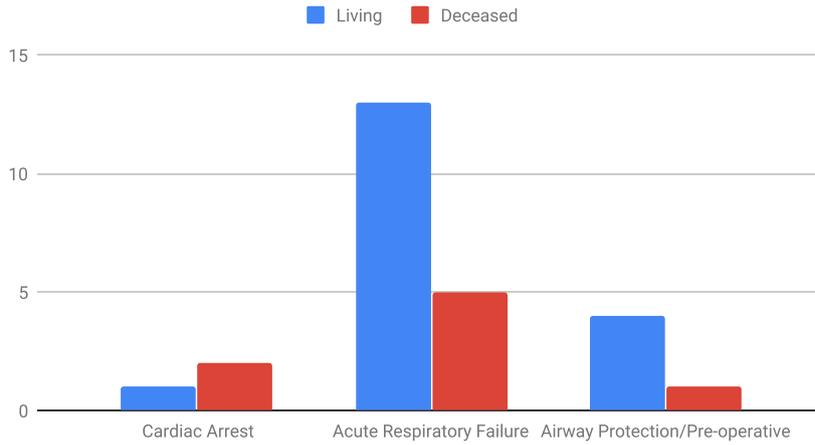


Fig. 5. Causes for Reintubation-Daytime Extubations.

Causes for Reintubation-Nighttime Extubations



Fig. 6. Causes for Reintubation-Nighttime Extubations.

Our findings remained consistent, which supports the safety of night extubation.

Due to the nature of the study, we could not track compliance with respect to weaning and sedation protocols. We also could not standardize the behavior or decision processes of intensivists or respiratory therapists. This cohort does, however, reflect real world practices in our MICU.

5. Conclusions

Patients extubated at night were not at increased odds of mortality or reintubation in our busy, urban, university-affiliated MICU with 24-h in-house intensivist coverage. Nighttime extubation was associated with shorter duration of mechanical ventilation, ICU length of stay, and hospital length of stay. Our results support the practice of extubating patients as soon as they are deemed ready for liberation from mechanical ventilation, regardless of the time of day.

Declarations of Competing Interest

No conflicts of interest exist for the authors of this manuscript.

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