Invited Commentary

Overnight Extubation in Patients With Mechanical Ventilation
Is It Harmful?

Peter K. Moore, MD; Michael A. Matthay, MD

The timing of extubation in patients with mechanical ventilation is confronted by intensivists and physicians in the United States on a daily basis. Theoretically, earlier extubation has the potential to prevent ventilator-associated complications and decrease the length of intensive care unit (ICU) and hospital stays. However, overnight extubation may be riskier, in part because fewer and less experienced physicians, nurses, and respiratory therapists are available. Although the clinically important question of when to extubate arises daily in the ICU, current research on the optimal timing for extubation is insufficient.

Related article

In this issue of *JAMA Internal Medicine*, Gershengorn et al[1] report the results of a retrospective cohort study of 97 844 adults who received mechanical ventilation in 165 US hospitals to determine the frequency of overnight extubation and to investigate whether nighttime extubation was associated with differences in outcomes. The primary results show that overnight extubation occurred in 20.1% of patients in this registry. Using propensity-matched analysis, overnight extubation was associated with higher odds of ICU mortality (5.6% vs 4.6% for intubation <12 hours and 11.2% vs 6.1% for intubation ≥12 hours) and hospital mortality (8.3% vs 7.0% for intubation <12 hours and 16.0% vs 11.1% for intubation ≥12 hours) compared with extubation during the day. In addition, patients who had received mechanical ventilation at least 12 hours before extubation had an increased odds of reintubation if extubated overnight.

This study is the first to report an association between increased mortality and extubation at night. In contrast, only 1 prior study by Tischenkel et al[2] addressed this question and reported that patients who were extubated overnight had lower rates of reintubation, with a statistically insignificant decrease in mortality. Several important differences between these 2 studies should be emphasized. The study by Tischenkel et al[2] was performed at 2 hospitals within a single medical center with strict, standardized ventilator weaning and extubation criteria. Furthermore, most of the participants were cardiac surgical patients (52% overall and 82% of the night extubation group). In fact, the lower rate of reintubation and the decrease in mortality, although insignificant, in the group extubated at night was lost when the cardiac surgical ICU patients were removed from the analysis. By contrast, only 2.4% of the patients included by Gershengorn et al were treated in a cardiac surgical ICU. Analysis of the findings from these 2 studies raises the possibility that overnight extubation may be beneficial for certain populations and harmful for others.

The study by Gershengorn et al[1] has many strengths. The study population was derived from a large national database that includes academic and private ICUs of multiple sizes and varied geographic location, which improved the generalizability of the findings. Given the large number of participants, propensity-matched pairs could be used in the analysis to reduce bias. Last, multiple sensitivity analyses were performed in which the associations between poor outcomes and nighttime extubation were still significant.

However, the use of this large database resulted in limitations related to incomplete information regarding the circumstances surrounding extubations. For example, compassionate extubations for patients at the end of life were not captured by the data set. Conceivably, compassionate extubation may occur more frequently at night when more family members are able to be present. The authors anticipated this problem and incorporated several steps to limit this bias, which could have skewed the association with higher mortality. First, the authors excluded patients who had limitations on their care before the first extubation attempt to eliminate patients with a preference to avoid reintubation. Second, the authors performed 2 sensitivity analyses in which they restricted their analysis to patients who survived more than 24 hours or to hospital discharge. Although mortality was no longer increased in those patients extubated overnight, reintubation remained significantly higher in these analyses, suggesting that these patients were at higher risk for worse outcomes.

Previous investigations have suggested that unplanned extubations occur more frequently at night.[3] This potential bias was not accounted for in the study by Gershengorn et al.[1] However, multiple evaluations of outcomes in this area have shown that although patients who have unplanned extubations have higher rates of reintubation, there seems to be no effect or even a decrease in mortality among patients who have unplanned extubation.[4] Thus, although inability to control for unplanned extubation may have influenced the rates of reintubation, it seems unlikely to explain the mortality difference observed in overnight extubations. Also, the decision to extubate at night for many of the patients in this registry may not have been executed by a board-certified critical care physician, a potentially important variable in reducing harm from nocturnal extubations.

It should be appreciated that the data set used for this analysis was relatively old (collected from 2000-2009). Advances in predictors of extubation success and postextubation care have changed clinical practice since 2000. For example, in 1 study,[5] unplanned noninvasive positive-pressure ventilation for respiratory failure after extubation increased mortality, and high-flow oxygen delivery after extubation reduced the risk for reintubation in other studies.[6,7] Reassuringly, the authors performed an additional analysis using a more recent database (APACHE Outcomes, 2010-2013), and extubation overnight was still associated with an increase in mortality.

This investigation is the first national, multicenter study to address the important questions surrounding the risks of overnight extubation. The association between nighttime extubation and increased mortality has the potential to affect the care of patients with mechanical ventilation. However, causation cannot be drawn from a retrospective study; although propensity matching and sensitivity analyses strengthen the associations in this study, they are imperfect statistical methods that cannot completely eliminate bias and confounding. Future prospective studies should be undertaken to confirm these findings, to assess for underlying mechanisms (**Table**), and to elucidate which patient populations are most likely to benefit from or be harmed by extubation at night. The risk factors for extubation failure have been described and emphasize that extubation failure can worsen clinical outcomes independent of the underlying severity of illness.[8]

Table. Theoretical Benefits of Nighttime Extubation and Reasons That Nighttime Extubation Might Be Riskier

Potential Benefits of Nocturnal Extubation	Potential Risks of Nocturnal Extubation
↓ Risk of ventilator-associated complications	Fewer and less experienced staff
↓ Pneumonia	•Physicians
↓ Weakness	•Respiratory therapists
↓ Delirium	•Nurses
↓ Stress ulcers	Often no intensivist in hospital
↓ ICU length of stay	Staff tired, less attentive
↓ Hospital length of stay	Diurnal variation in rapid response team outcomes
↓ Sedatives	
Normalize sleep-wake cycle	
Improve communication	

Abbreviations: ICU, intensive care unit; ↓, decrease.

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JAMA Internal Medicine | Original Investigation

Association Between Overnight Extubations and Outcomes in the Intensive Care Unit

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IMPORTANCE Little is known about the timing of extubations for patients in the intensive care unit (ICU) who undergo mechanical ventilation (MV) or whether overnight extubation is safe.

OBJECTIVES To describe the frequency of overnight extubations and assess the association between overnight extubations and clinical outcomes.

DESIGN, SETTING, AND PARTICIPANTS This retrospective cohort study included adults (aged ≥18 years) undergoing MV performed in US ICUs as part of the Project IMPACT database from October 1, 2000, to March 29, 2009. Data were analyzed from January 1, 2015, to July 5, 2016.

EXPOSURE Overnight extubation defined as occurring from 7 PM to 6:59 AM.

MAIN OUTCOMES AND MEASURES Multilevel multivariable regression analyses (clustered by individual ICU) were used to identify factors associated with overnight extubation. Propensity-matched pairs were created of patients undergoing overnight vs daytime extubation (separately for patients with MV duration <12 and ≥12 hours). Outcomes, including frequency of reintubation in the ICU, ICU and hospital mortality, and ICU and hospital length of stay (LOS), were assessed using χ^2 and Mann-Whitney tests.

RESULTS The cohort consisted of 97 844 patients (40.8% men; 59.2% women; mean [SD] age, 58.3 [17.9] years) across 165 ICUs. Of these, 20.1% of patients underwent overnight extubation and the percentage decreased over time (23.3% in 2000-2001 vs 18.8% in 2009; *P* = .001). After multivariable adjustment, duration of MV of less than 12 hours had the greatest association with overnight extubation (compared with 12 hours to <1 day: adjusted odds ratio [AOR], 0.20 [95% CI, 0.19-0.21]; 1 to <2 days: AOR, 0.26 [95% CI, 0.24-0.28]; 2 to <7 days: AOR, 0.22 [95% CI, 0.21-0.24]; and ≥7 days: AOR, 0.24 [95% CI, 0.22-0.26]). In all, 4518 propensity-matched pairs had MV duration of less than 12 hours and 5761 had MV duration of at least 12 hours. For MV duration of less than 12 hours, reintubation rates were similar for overnight and daytime extubations (5.9% and 5.6%, respectively; *P* = .50), but mortality was increased for patients undergoing overnight extubation (ICU, 5.6% vs 4.6%, *P* = .03; hospital, 8.3% vs 7.0%, *P* = .01). The ICU LOS was shorter for overnight vs daytime extubations (median [interquartile range], 1.1 [0.8-2.3] vs 1.4 [0.9-2.5] days; *P* < .001), and hospital LOS was similar (median [interquartile range], 7.0 [4.0-12.0] vs 7.0 [3.0-12.0] days; *P* = .03). Patients with MV duration of at least 12 hours who underwent overnight extubation had more frequent reintubation in the ICU (14.6% vs 12.4%; *P* < .001) and higher mortality in the ICU (11.2% vs 6.1%; *P* < .001) and in the hospital (16.0% vs 11.1%; *P* < .001), with no differences in LOS.

CONCLUSIONS AND RELEVANCE Approximately one-fifth of patients with MV in US ICUs undergo overnight extubation. These patients have higher rates of ICU and hospital mortality than patients undergoing extubation during the daytime. Further studies are needed to understand why overnight extubation results in poorer outcomes.

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Invited Commentary
Supplemental content

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Mechanical ventilation (MV) for acute respiratory failure is frequent in US intensive care units (ICUs).[1] Mechanical ventilation is associated with significant morbidity—pneumonia, weakness, and delirium—that increases with MV duration. Therefore, extubation as soon as patients are clinically ready may be beneficial, regardless of the time of day. However, major planned events in the ICU, such as elective extubations, traditionally have taken place during the day, when staffing is optimal.

Very little is known about the frequency, safety, or effectiveness of overnight extubations. With the addition of in-house intensivists 24 hours per day in some ICUs and expanded telemedicine coverage, ICU physician staffing overnight has increased.[2-6] Whether overnight extubations have increased over time and may now be commonplace is unknown. A single-center study[7] assessing reintubation and mortality rates associated with overnight extubations found no difference in outcomes for patients undergoing overnight compared with daytime extubations. However, four-fifths of the nocturnal extubations in that study occurred in patients who underwent cardiothoracic surgery; whether these findings generalize to other patient types or hospitals is unknown.

To address this uncertainty, we conducted a retrospective cohort study of adults with MV admitted to US ICUs. We hypothesized that (1) extubations are currently performed primarily during daytime hours across most US ICUs and (2) overnight extubations are associated with worse clinical outcomes.

Key Points

Questions How common are overnight extubations in the intensive care unit and are they associated with worse outcomes for critically ill patients?

Findings In this cohort study of 97 844 patients in US intensive care units who have undergone mechanical ventilation (MV), 20.1% underwent overnight extubation. Overnight extubation was associated with significantly higher hospital mortality compared with daytime extubation.

Meaning Overnight extubation is not common and is associated with worse outcomes for critically ill patients.

Methods

Study Design

We conducted a retrospective cohort study of patients in US ICUs using the Project IMPACT database from October 1, 2000, to March 29, 2009.[8] The institutional review board of Albert Einstein College of Medicine exempted this retrospective review from ethical approval and informed consent.

Hospitals participating in Project IMPACT were diverse in size and location but tended to be larger and more urban than general-population hospitals. Participation was voluntary and the ICUs paid for the service. Information was collected by on-site data collectors who were trained and certified to ensure standardization in data definitions and entry. Data were collected from all consecutive admissions to each ICU or from a random sample of admissions. Sites using the latter method collected information on 50% or 75% of all patients; the percentage was determined quarterly before data collection commenced.

Our cohort consisted of adults (≥18 years of age) undergoing MV who were admitted to an ICU participating in Project IMPACT. Only the first episode of MV during the first ICU stay was included for each patient. Patients were excluded if they died, received a tracheostomy, or had any limitations placed on their care (eg, orders for no cardiopulmonary resuscitation and/or to withhold or withdraw therapy) before a first extubation attempt. Data on the timing of the initiation and cessation of MV were available by hour and minute.

We defined an *extubation* as the discontinuation of MV in the absence of death. For our primary analysis, *overnight extubation* was defined as occurring from 7 PM to 6:59 AM.[7] *Reintubation* was defined as the resumption of MV after an extubation event.

For our analysis assessing the association of overnight extubation with outcomes, our primary outcome was reintubation occurring at any point during the initial ICU stay and further classified as occurring within the first 24, 48, or 96 hours after extubation. As secondary outcomes, we assessed ICU and hospital mortality and ICU and hospital lengths of stay (LOSs).

Statistical Methods

Data were analyzed from January 1, 2015, to July 5, 2016. We used standard summary statistics to describe the rates of extubation by hour of day across all patients in the cohort and in subgroups stratified by ICU type (medical, surgical, mixed medical-surgical, and other), admission type (medical, elective surgical, and emergent surgical), location before ICU arrival (emergency department, operating room or postanesthesia care unit, ward, stepdown or telemetry, and other), and duration of MV before an extubation attempt. We compared the characteristics of patients undergoing daytime and overnight extubations using unpaired, 2-tailed t tests and χ^2 tests as appropriate. Finally, we constructed a multilevel multivariable logistic regression model (clustered by individual ICU) to identify factors independently associated with overnight extubation; all available patient and ICU or hospital characteristics were included as independent variables. Factors of specific interest in this analysis included year of ICU admission and on-site overnight coverage (intensivist vs other clinician vs none). Restricted cubic splines with 4 knots (placed using the Harrell recommended percentiles) were used to model age and illness severity (mortality probability model at ICU admission [MPM_0-III])[9]; ICU bed number and duration of MV were stratified into relevant categories.

Given our observation that patients with MV duration of less than 12 hours had a significantly higher frequency of overnight extubations than patients with all other durations of MV, we performed post hoc stratification of all analyses evaluating time of extubation and outcomes by duration of MV; to do so, we created the following 2 subcohorts: (1) patients with MV duration of less than 12 hours and (2) patients with MV duration of at least 12 hours. We compared the patient and ICU or hospital characteristics of both subcohorts using unpaired, 2-tailed *t* tests and χ^2 tests as appropriate.

To evaluate the association of overnight extubations and outcomes, we used a propensity score–matching strategy to create pairs of patients (one with a daytime extubation and one with an overnight extubation) with similar propensity to receive overnight extubation. A propensity score is a probabilistic measure that reflects the propensity of a patient, based on other characteristics, in this instance to undergo extubation overnight. This score is not a marker of whether particular patients underwent overnight extubation but rather whether they were likely to have undergone overnight extubation given their characteristics. To create the propensity score for overnight extubation (dependent variable), we used a multivariable logistic regression that included all available patient-level data (the same patient characteristic variables as in the above multilevel model except that duration of MV was modeled using restricted cubic splines, with 4 knots using the Harrell recommended percentiles)[10-12]; the individual ICU to which each patient was admitted was included as a fixed effect.[13,14] The success of the propensity score was determined by its ability to balance independent covariates between the patients who underwent overnight extubation and those who did not. This covariate balance was assessed using standard mean differences.[15] One-to-one nearest neighbor–matching restricting pairs to have similar propensities to be extubated overnight were then used to create quasi-cases (those who underwent overnight extubation) and quasi-controls (those who underwent daytime extubation); matching was performed without replacement (controls could only be used once). The ICUs with fewer than 50 patients with, separately, MV duration of less than 12 and at least 12 hours, were excluded.

Rates of reintubation (the primary outcome) and each of our secondary outcomes were compared between the groups of matched pairs using χ^2 tests, unpaired, 2-tailed *t* tests, and Wilcoxon rank sum tests as appropriate. We also assessed LOS using the time to ICU or hospital discharge method to account for the competing risk for ICU or hospital death. All analyses were repeated for patient subgroups stratified by patient type, ICU type, and overnight on-site clinician.

Finally, we performed 4 types of sensitivity analyses. First, we conducted a sensitivity analysis in which we redefined *overnight extubation* as occurring from midnight to 4:59 AM (the definition for daytime extubation remained 7 AM to 6:59 PM). Second, we conducted a pair of analyses aimed at minimizing confounding from palliative extubations (those performed for the purpose of comfort and without expectation for patient survival); to do so, we restricted each subcohort to patients who survived (1) to hospital discharge and, separately, (2) at least 24 hours after extubation. Third, we conducted an analysis intended to minimize confounding from unplanned extubations; to do so, we excluded patients who underwent reintubation within the first hour after extubation (assuming that this would occur more commonly with unplanned extubations). Fourth, we used a separate clinical data set, APACHE (Acute Physiology and Chronic Health Evaluation) Outcomes, which contains data from more than 1 million US ICU admissions.[16] This data set is more current (January 7, 2010, to March 26, 2013), yet was not chosen for our primary cohort because it does not contain information on tracheostomies or limitations in care.

We compared characteristics and outcomes within APACHE Outcomes between patients undergoing overnight and daytime extubations using χ^2 tests, unpaired, 2-tailed *t* tests, and Wilcoxon rank sum tests as appropriate. The association of outcome with overnight extubation was then assessed using the same propensity-matching strategy as previously used for Project IMPACT. All statistical analyses were performed using STATA software (version 13; StataCorp), Microsoft Excel (Microsoft Corp), and SAS (version 9.4; SAS Institute Inc).

Results

After exclusions (eFigure 1 in the Supplement), the primary cohort consisted of 97 844 adults with MV (40.8% men; 59.2% women; mean [SD] age, 58.3 [17.9] years) admitted to one of 165 US ICUs (eTable 1 in the Supplement). Cohort ICUs varied by type (84 mixed medical-surgical [50.9%], 30 medical [18.2%], and 40 surgical [24.2%], 7 other [4.2%], and 4 unknown [2.4%]), size, and geographic region. On-site intensivists were present overnight in 44 ICUs (26.7%).

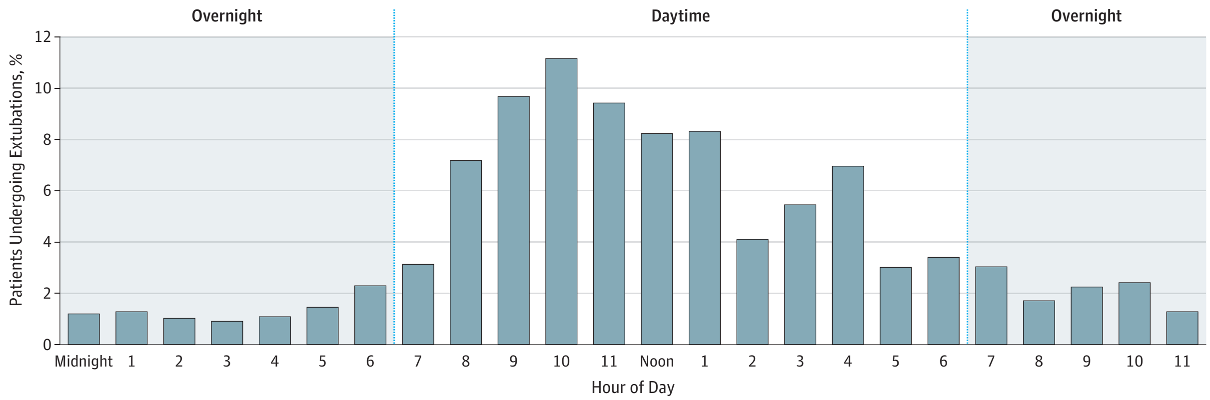
Factors Associated With Overnight Extubation

Approximately one-fifth (20.1%) of the cohort underwent overnight extubation (from 7 PM to 6:59 AM) (**Figure 1**). Compared with patients undergoing daytime extubations, those undergoing overnight extubation had more commonly undergone elective surgery (46.8% vs 24.8%; *P* < .001), were admitted to the ICU from the operating room or postanesthesia care unit (63.5% vs 40.2%; *P* < .001), and had a duration of MV of less than 12 hours (57.1% vs 19.8%; *P* < .001) (**Table 1**). Patients undergoing overnight extubation more commonly had a cardiovascular diagnosis at admission (51.8% vs 25.4%; *P* < .001) and less commonly had a respiratory or thoracic diagnosis at admission (16.2% vs 30.1%; *P* < .001). Overnight extubations decreased over time, with 23.3% of patients undergoing overnight extubation in 2000 to 2001 compared with 18.8% in 2009 (*P* = .001) (eFigure 2 in the Supplement).

Among patients with MV duration of less than 12 hours, 42.1% underwent overnight extubation vs only 11.9% of patients with MV duration of at least 12 hours (eFigure 3 in the Supplement). Daytime extubations were more common for patients from all locations before ICU admission, for all patient types, and for those admitted to all ICU types (eFigure 4 in the Supplement).

After multivariable adjustment, the factor with the greatest association with overnight extubation was duration of MV (adjusted odds ratio [AOR] for 12 hours to less than 1 day, 0.20 [95% CI, 0.19-0.21]; AOR for 1 to less than 2 days, 0.26 [95% CI, 0.24-0.28]; AOR for 2 to less than 7 days, 0.22 [95% CI, 0.21-0.24]; and AOR for 7 or more days, 0.24 [95% CI, 0.22-0.26]) compared with the reference MV duration of less than 12 hours (*P* < .001) (eTable 2 in the Supplement). The odds of over-

Figure 1. Distribution of Time-of-Day of Extubations



Overnight extubation was defined as occurring from 7 PM to 6:59 AM. Of the primary cohort of 97 844, in total, 79.9% of extubations occurred during the daytime and 20.1% occurred overnight.

night extubation decreased with year of ICU admission (AOR for 2004, 0.87 [95% CI, 0.78-0.96]; AOR for 2005, 0.86 [95% CI, 0.77-0.96]; AOR for 2006, 0.79 [95% CI, 0.71-0.88]; AOR for 2007, 0.78 [95% CI, 0.69-0.87]; AOR for 2008, 0.65 [95% CI, 0.57-0.74]; and AOR for 2009, 0.68 [95% CI, 0.48-0.96]) compared with reference year 2000 to 2001 ($P \le .03$) and was lower when a clinician other than an intensivist was on-site overnight (AOR, 0.81; 95% CI, 0.72-0.91; $P = .001$).

Association of Overnight Extubation With Outcomes

We compared patients who were and were not eligible for propensity matching based on data completeness (eTable 3 in the Supplement). Of 26 679 patients (27.3%) who had MV duration of less than 12 hours (eTable 4 in the Supplement), we created 4518 propensity-matched pairs (one patient with overnight extubation and the other with daytime extubation). Patients were well matched on all patient- and ICU-level characteristics (eTable 5 in the Supplement). Rates of reintubation were similar whether patients underwent overnight or daytime extubation ($P \ge .48$) (**Table 2**); for patients with overnight extubation, ICU mortality (5.6% vs 4.6%; $P = .03$) and hospital mortality (8.3% vs 7.0%; $P = .01$) were increased. The ICU LOS was slightly shorter for patients undergoing overnight vs daytime extubation (median [interquartile range], 1.1 [0.8-2.3] vs 1.4 [0.9-2.5] days; $P < .001$) and hospital LOS was similar (median [interquartile range], 7.0 [4.0-12.0] vs 7.0 [3.0-12.0] days; $P = .03$) (Table 2 and eFigure 5 in the Supplement).

From 71 165 patients (72.7%) with MV duration of at least 12 hours, we created 5761 propensity-matched pairs, also well matched on characteristics (eTable 5 in the Supplement). Rates of reintubation were higher for patients undergoing overnight extubation (14.6% vs 12.4%; $P < .001$) (Table 2). Mortality was also significantly higher for patients undergoing overnight vs daytime extubation in the ICU (11.2% vs 6.1%; $P < .001$) and in the hospital (16.0% vs 11.1%; $P < .001$). Length of ICU and hospital stays did not differ (Table 2 and eFigure 5 in the Supplement).

No patient subgroup was evaluated in which overnight extubation was associated with a reduction in the rates of reintubation or mortality (**Figure 2**). Length of ICU stay was shorter for surgical patients undergoing overnight extubation with short MV duration (<12 hours), but no different for patients with longer MV duration (≥12 hours) (**Table 3**).

Our results were robust to several sensitivity analyses (eFigure 6 and eTable 6 in the Supplement give APACHE Outcomes cohort details). Specifically, overnight extubation was associated with higher mortality for all patients (and higher rates of reintubation for patients with MV duration ≥12 hours) when the overnight cohort was limited to extubations that occurred only from midnight to 4:59 AM (eFigure 7 in the Supplement). Similarly, in the APACHE Outcomes cohort, mortality was significantly higher in patients with MV duration of at least 12 hours who underwent overnight extubation. Notably, in survivor cohorts—designed to limit confounding by palliative extubation—rates of reintubation were significantly higher in patients with MV duration of at least 12 hours who underwent overnight extubation. In patients remaining extubated for at least 1 hour (ie, patients less likely to have had unplanned extubations), ICU and hospital mortality but not reintubation rates were higher for patients with all MV durations. Length of stay in the ICU but not the hospital was reduced in the APACHE Outcomes cohort for surgical patients with short durations of MV (eTable 7 in the Supplement).

Discussion

Only one-fifth of patients with MV underwent overnight extubation in US ICUs, and the frequency of this practice decreased over time. As anticipated, no clear benefits were associated with overnight extubation. Although ICU LOS (but not hospital LOS) was reduced for surgical patients with short durations of MV (<12 hours), LOS reductions may be affected by the competing risk for mortality. Overnight extubations were associated with worse outcomes, that is, higher rates of ICU and hospital mortality. Moreover, for patients with longer MV durations (≥12 hours), overnight extubation was also clearly

Table 1. Baseline Characteristics of Cohort Stratified by Hour of Extubation

Characteristic[a]	Extubation, % Daytime[b] (n = 78 178)	Extubation, % Overnight[c] (n = 19 666)	*P* Value[d]
All patients	79.9	20.1	
Age, mean (SD), y	58.0 (18.1)	59.5 (17.1)	<.001
Race			
White	78.8	81.6	<.001
Black	14.2	11.3	
Other	7.0	7.1	
Female sex	41.7	37.1	<.001
Admission type			
Elective surgical	24.8	46.8	<.001
Emergent surgical	20.6	20.8	
Medical	54.6	32.3	
Insurance			
Private insurance	30.2	33.4	<.001
Medicare	46.1	47.0	
Medicaid	9.6	8.1	
Self-pay	10.5	8.6	
Other	3.5	2.8	
Location before ICU			
Emergency department	37.6	23.1	<.001
OR or PACU	40.2	63.5	
Ward	7.1	3.9	
SDU or telemetry	4.6	2.6	
Other	10.4	6.9	
Diagnostic group			
Respiratory or thoracic	30.1	16.2	<.001
Cardiovascular	25.4	51.8	
Sepsis	6.6	3.5	
Trauma	12.9	9.5	
Neurologic	9.7	7.0	
Metabolic or renal	5.7	4.1	
Gastrointestinal tract	9.7	8.0	
MPM_0-III, mean (SD), %	17.2 (16.3)	16.4 (17.1)	<.001
Comorbidities			
Gastrointestinal tract system	2.7	2.6	.38
Cardiovascular system	7.4	16.8	<.001
Respiratory system	8.2	4.5	<.001
Renal system			
Creatinine level >2 mg/dL	6.3	4.9	<.001
Dialysis	3.4	2.7	<.001
Immunocompromise present			
AIDS	0.5	0.4	.07
Corticiosteroids used	1.3	0.7	<.001
Nonsteroidal medications used	1.5	1.3	.012
Leukemia, lymphoma, myeloma	0.4	0.4	.31
Other	0.4	0.4	.09
Malignant disease			
Chemoradiotherapy for 1 y	2.4	1.9	<.001
Chemoradiotherapy anytime for HD/lymphoma	0.4	0.3	.13
Hematologic (5 y)	0.4	0.3	.07

(continued)

Table 1. Baseline Characteristics of Cohort Stratified by Hour of Extubation (continued)

Characteristic[a]	Extubation, % Daytime[b] (n = 78 178)	Overnight[c] (n = 19 666)	*P* Value[d]
Lymphoma (5 y)	0.5	0.4	.12
Solid organ (5 y)	6.2	5.2	<.001
Metastases (5 y)	3.1	2.7	.003
MV on ICU admission	80.1	87.0	<.001
MV duration			
<12 h	19.8	57.1	<.001
12 h to <1 d	23.3	16.8	
1 to <2 d	17.3	8.9	
2 to <7 d	26.0	10.8	
≥7 d	13.7	6.3	

Abbreviations: HD, Hodgkin disease; ICU, intensive care unit; MPM_O-III, mortality probability model; MV, mechanical ventilation; OR, operating room; PACU, postanesthesia care unit; SDU, stepdown unit.

SI unit conversion factor: To convert creatinine level to micromoles per liter, multiply by 88.4.

[a] Data were missing for race (1944 patients), sex (17 patients), insurance (1009 patients), location before the ICU (7 patients), and diagnostic group (1 patient). The MPM_O-III was not applicable to and, thus, not calculated for 22 389 patients with cardiac admission or transplant or admitted with an acute myocardial infarction.

[b] Indicates 7 AM to 6 PM.

[c] Indicates 7 PM to 6 AM.

[d] Calculated using the unpaired 2-tailed *t* test for continuous variables and χ^2 for categorical variables.

Table 2. Outcomes of Propensity-Matched Pairs[a]

Outcome	MV Duration <12 h Daytime Extubation[b]	MV Duration <12 h Overnight Extubation[c]	MV Duration <12 h *P* Value[d]	MV Duration ≥12 h Daytime Extubation[b]	MV Duration ≥12 h Overnight Extubation[c]	MV Duration ≥12 h *P* Value[d]
No. of matched patients	4518	4518	NA	5761	5761	NA
Reintubation, %						
Ever	5.6	5.9	.50	12.4	14.6	<.001
Within 24 h	3.5	3.7	.65	7.6	9.8	<.001
Within 48 h	4.5	4.5	.96	9.5	11.9	<.001
Within 96 h	5.2	5.5	.48	11.3	13.6	<.001
Mortality, %						
ICU	4.6	5.6	.03	6.1	11.2	<.001
Hospital[e]	7.0	8.3	.01	11.1	16.0	<.001
LOS, median (IQR), d						
ICU[f]	1.4 (0.9-2.5)	1.1 (0.8-2.3)	<.001	4.9 (2.6-10.1)	4.9 (2.5-10.1)	.086
Hospital[g]	7.0 (3.0-12.0)	7.0 (4.0-12.0)	.03	13.0 (7.0-23.0)	13.0 (7.0-23.5)	.51

Abbreviations: ICU, intensive care unit; IQR, interquartile range; LOS, length of stay; MV, mechanical ventilation; NA, not applicable.

[b] Matching was available for 5761 of 5763 patients with overnight extubation and MV of at least 0.5 day (>99.9%) and for 4518 of 4522 patients with overnight extubation and MV of less than 0.5 day (99.9%).

[b] Indicates 7 AM to 6 PM.

[c] Indicates 7 PM to 6 AM.

[d] Calculated using the unpaired 2-tailed *t* test for continuous variables and χ^2 for categorical variables.

[e] Not available for 2 patients with daytime extubation and 3 patients with overnight extubation for pairs with MV of less than 12 hours and for 3 patients with daytime extubation and 4 patients with overnight extubation for pairs with MV of at least 12 hours.

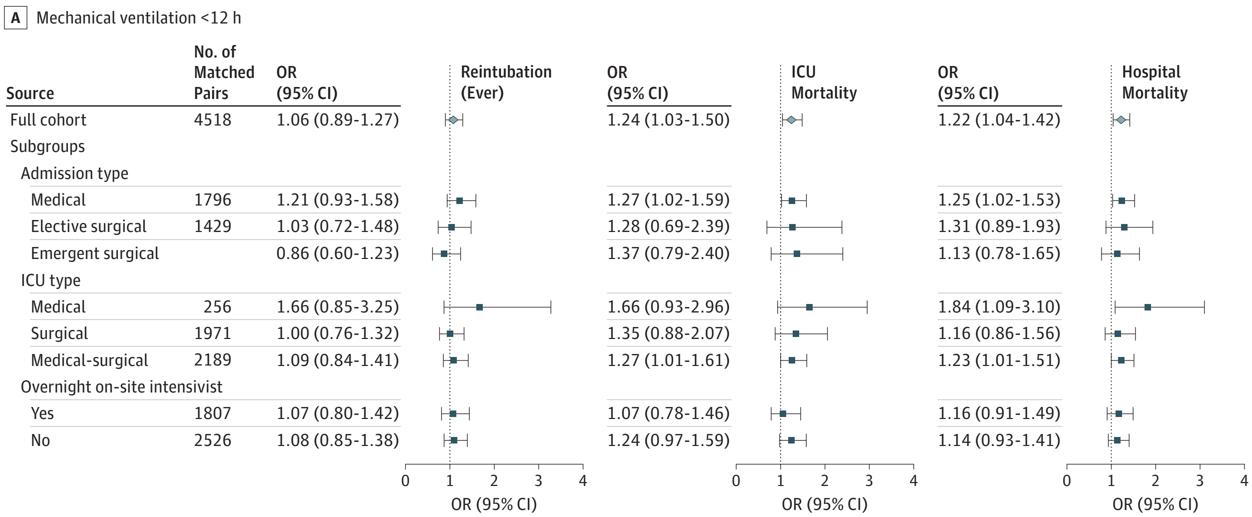
[f] Not available for 10 patients with daytime extubation and 11 patients with overnight extubation for pairs with MV of less than 12 hours and 29 patients with daytime extubation and 22 patients with overnight extubation for pairs with MV of at least 12 hours.

[g] Not available for 1 patient with overnight extubation for pairs with MV of less than 12 hours and 1 patient with overnight extubation for pairs with MV of at least 12 hours.

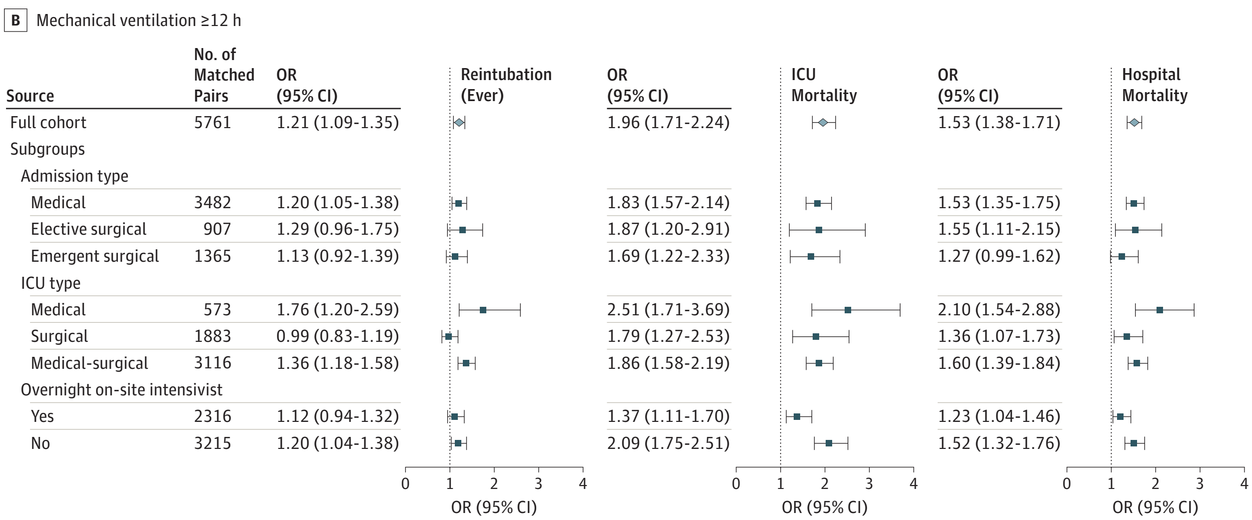
associated with increased odds of reintubation. These results are robust across different definitions of *overnight* and are consistent across many patient subgroups.

In nearly every cohort analyzed, the ORs associated with overnight extubation for ICU and hospital mortality were larger than those for reintubation; in many instances, the odds of reintubation were not even statistically significantly increased for patients undergoing overnight extubation, whereas their odds of mortality were significantly higher. This phenomenon of dying without reintubation has more than 1 possible explanation. First, patients may have a cardiopulmonary arrest while extubated and die before reintubation. However, the incidence of in-hospital cardiopulmonary arrest in the United States is low (2.85 per 1000 hospital admissions)[17]; thus, the

Figure 2. Odds of Reintubation and Mortality Associated With Overnight Extubation for Propensity-Matched Pairs Stratified by Patient Subgroup



Source	No. of Matched Pairs	Reintubation (Ever) OR (95% CI)	ICU Mortality OR (95% CI)	Hospital Mortality OR (95% CI)
Full cohort	4518	1.06 (0.89-1.27)	1.24 (1.03-1.50)	1.22 (1.04-1.42)
Subgroups				
Admission type				
Medical	1796	1.21 (0.93-1.58)	1.27 (1.02-1.59)	1.25 (1.02-1.53)
Elective surgical	1429	1.03 (0.72-1.48)	1.28 (0.69-2.39)	1.31 (0.89-1.93)
Emergent surgical		0.86 (0.60-1.23)	1.37 (0.79-2.40)	1.13 (0.78-1.65)
ICU type				
Medical	256	1.66 (0.85-3.25)	1.66 (0.93-2.96)	1.84 (1.09-3.10)
Surgical	1971	1.00 (0.76-1.32)	1.35 (0.88-2.07)	1.16 (0.86-1.56)
Medical-surgical	2189	1.09 (0.84-1.41)	1.27 (1.01-1.61)	1.23 (1.01-1.51)
Overnight on-site intensivist				
Yes	1807	1.07 (0.80-1.42)	1.07 (0.78-1.46)	1.16 (0.91-1.49)
No	2526	1.08 (0.85-1.38)	1.24 (0.97-1.59)	1.14 (0.93-1.41)



Source	No. of Matched Pairs	Reintubation (Ever) OR (95% CI)	ICU Mortality OR (95% CI)	Hospital Mortality OR (95% CI)
Full cohort	5761	1.21 (1.09-1.35)	1.96 (1.71-2.24)	1.53 (1.38-1.71)
Subgroups				
Admission type				
Medical	3482	1.20 (1.05-1.38)	1.83 (1.57-2.14)	1.53 (1.35-1.75)
Elective surgical	907	1.29 (0.96-1.75)	1.87 (1.20-2.91)	1.55 (1.11-2.15)
Emergent surgical	1365	1.13 (0.92-1.39)	1.69 (1.22-2.33)	1.27 (0.99-1.62)
ICU type				
Medical	573	1.76 (1.20-2.59)	2.51 (1.71-3.69)	2.10 (1.54-2.88)
Surgical	1883	0.99 (0.83-1.19)	1.79 (1.27-2.53)	1.36 (1.07-1.73)
Medical-surgical	3116	1.36 (1.18-1.58)	1.86 (1.58-2.19)	1.60 (1.39-1.84)
Overnight on-site intensivist				
Yes	2316	1.12 (0.94-1.32)	1.37 (1.11-1.70)	1.23 (1.04-1.46)
No	3215	1.20 (1.04-1.38)	2.09 (1.75-2.51)	1.52 (1.32-1.76)

Tests for interaction between overnight extubation and subgroups depicted for each outcome were assessed using the primary propensity-matched cohorts (all patients with mechanical ventilation [MV] duration <12 h and, separately, all patients with MV duration ≥12 h). No significant interaction ($P < .05$) was found between overnight extubation and any subgroup examined for any outcome. A, The full cohort included 4518 of 4522 patients undergoing overnight extubations (99.9%); 1796 of 1800 patients with medical admission undergoing overnight extubations (99.8%); 1429 of 1645 patients undergoing elective surgery and overnight extubations (86.9%); 1064 of 1077 patients undergoing emergent surgery and overnight extubations (98.8%); 256 of 263 patients in the medical ICU undergoing overnight extubations (97.3%); 1971 of 1990 patients in the surgical intensive care unit (ICU) undergoing overnight extubations (99.0%); 2189 of 2191 patients in the medical-surgical ICU undergoing overnight extubations (99.0%); 1807 of 1843 patients with an intensivist on-site undergoing overnight extubations (98.0%); and 2526 of 2532 patients without an intensivist on-site undergoing overnight extubations (99.8%). B, The full cohort included 5761 of 5763 patients undergoing overnight extubations (99.9%); 3482 of 3485 patients with medical admissions undergoing overnight extubations (99.9%); 907 of 910 patients undergoing elective surgery and overnight extubations (99.7%); 1365 of 1368 patients undergoing emergent surgery and overnight extubations (99.8%); 573 of 573 patients in the medical ICU undergoing overnight extubations (100%); 1883 of 1883 patients in the surgical ICU undergoing overnight extubations (100%); 3116 of 3118 patients in the medical-surgical ICU undergoing overnight extubations (99.9%); 2316 of 2318 patients with an intensivist on-site undergoing overnight extubations (99.9%); and 3125 of 3125 patients without an intensivist on-site undergoing overnight extubations (100%). OR indicates odds ratio.

contribution of patients who died as a result of cardiopulmonary arrest without reintubation is likely to be quite small. Second, patients may have goals of care limitations put in place after their initial extubation that preclude reintubation at the time of recurrent respiratory failure and resultant death. Our sensitivity analysis using APACHE Outcomes by necessity included more patients receiving potentially palliative extubations (because we could not identify them in this cohort), and we saw a greater magnitude of association between overnight extubations and mortality in this group, lending support to this theory. To our knowledge, no published study has evaluated the time of day of palliative extubations, yet these extubations might occur more commonly overnight when family and friends may be more able to be at the bedside (because family and caregivers are known to value being present at the time of death of patients in the

Table 3. LOS for Propensity-Matched Pairs Stratified by Patient Subgroup

	LOS, Median (IQR), d					
	ICU			Hospital		
Patient Group	Daytime Extubation[a]	Overnight Extubation[b]	*P* Value[c]	Daytime Extubation[a]	Overnight Extubation[b]	*P* Value[c]
MV <12 h[d]						
Full cohort	1.4 (0.9-2.5)	1.1 (0.8-2.3)	<.001	7.0 (3.0-12.0)	7.0 (4.0-12.0)	.03
Subgroup						
Admission type						
Medical	1.3 (0.7-2.2)	1.0 (0.7-2.1)	.08	4.0 (2.0-8.0)	4.0 (2.0-8.0)	.46
Elective surgical	1.5 (1.0-2.6)	1.2 (0.9-2.5)	<.001	8.0 (5.0-13.0)	9.0 (6.0-14.0)	.01
Emergent surgical	1.5 (1.0-2.6)	1.3 (0.8-2.4)	<.001	9.0 (6.0-14.0)	9.0 (5.0-14.0)	.55
ICU type						
Medical	1.3 (0.8-1.9)	1.0 (0.7-1.9)	.21	4.0 (2.0-8.0)	4.0 (2.0-9.0)	.85
Surgical	1.4 (0.9-2.5)	1.1 (0.8-2.2)	<.001	7.0 (4.0-12.0)	7.0 (4.0-13.0)	.11
Medical-surgical	1.4 (1.0-2.5)	1.2 (0.8-2.5)	<.001	6.0 (3.0-11.0)	6.0 (3.0-12.0)	.35
Overnight on-site intensivist						
Yes	1.4 (0.9-2.4)	1.1 (0.8-2.2)	<.001	7.0 (3.0-12.0)	7.0 (3.0-12.0)	.62
No	1.4 (0.9-2.4)	1.1 (0.8-2.2)	<.001	7.0 (3.0-12.0)	7.0 (4.0-12.0)	.02
MV ≥12 h[e]						
Full cohort	4.9 (2.6-10.1)	4.9 (2.5-10.1)	.09	13.0 (7.0-23.0)	13.0 (7.0-23.5)	.51
Subgroup						
Admission type						
Medical	4.9 (2.7-9.8)	4.9 (2.5-10.1)	.22	12.0 (6.0-22.0)	12.0 (6.0-22.0)	.36
Elective surgical	3.6 (2.0-7.0)	3.3 (1.9-7.8)	.82	13.0 (8.0-21.0)	14.0 (8.0-24.0)	.10
Emergent surgical	5.9 (3.0-12.4)	5.9 (2.8-11.8)	.31	17.0 (10.0-27.0)	16.0 (9.0-28.0)	.40
ICU type						
Medical	4.6 (2.7-9.4)	4.6 (2.3-9.8)	.52	11.0 (6.0-20.0)	11.0 (6.0-20.0)	.65
Surgical	5.0 (2.7-10.5)	4.8 (2.5-10.5)	.28	15.0 (8.0-25.0)	15.0 (8.0-25.0)	.58
Medical-surgical	5.0 (2.6-9.5)	5.0 (2.5-10.1)	.55	12.0 (7.0-21.0)	12.0 (7.0-23.0)	.17
Overnight on-site intensivist						
Yes	5.0 (2.6-9.9)	5.0 (2.5-10.1)	.51	14.0 (7.0-23.0)	14.0 (7.0-25.0)	.24
No	4.6 (2.6-9.5)	4.8 (2.4-10.1)	.79	13.0 (7.0-22.0)	12.0 (7.0-22.0)	.21

Abbreviations; ICU, intensive care unit; IQR, interquartile range; LOS, length of stay; MV, mechanical ventilation.

[a] Indicates 7 AM to 6 PM.

[b] Indicates 7 PM to 6 AM.

[c] Calculated using the unpaired 2-tailed *t* test for continuous variables and χ^2 for categorical variables.

[d] The full cohort included 4518 of 4522 patients undergoing overnight extubations (99.9%); 1796 of 1800 patients with medical admission (99.8%); 1429 of 1645 patients undergoing elective surgery (86.9%); 1064 of 1077 patients undergoing emergent surgery (98.8%); 256 of 263 patients in the medical ICU (97.3%); 1971 of 1990 patients in the surgical ICU (99.0%); 2189 of 2191 patients in the medical-surgical ICU (99.0%); 1807 of 1843 patients with an intensivist on-site (98.0%); and 2526 of 2532 patients without an intensivist on-site (99.8%).

[e] The full cohort included 5761 of 5763 patients undergoing overnight extubations (99.9%); 3482 of 3485 patients with medical admissions (99.9%); 907 of 910 patients undergoing elective surgery (99.7%); 1365 of 1368 patients undergoing emergent surgery (99.8%); 573 of 573 patients in the medical ICU (100%); 1883 of 1883 patients in the surgical ICU (100%); 3116 of 3118 patients in the medical-surgical ICU (99.9%); 2316 of 2318 patients with an intensivist on-site (99.9%); and 3125 of 3125 patients without an intensivist on-site (100%).

ICU[18]). In a retrospective study, we cannot clearly identify all patients in whom limitations on care were in place at the time of the need for reintubation. Residual confounding due to this issue, therefore, likely explains the differences we observe in the odds of reintubation and mortality associated with overnight extubation.

We had hypothesized that increases in overnight in-house intensivist staffing over time[2,3] would translate into a greater likelihood of overnight extubations occurring in the later years in our study. Although we found an increased likelihood of overnight extubation in ICUs with intensivists on-site overnight (compared with other clinicians), the likelihood of overnight extubation decreased with ICU admission year. In theory, the value added of in-house intensivists might be viewed as ensuring good care practices 24 hours a day in the ICU.[19,20] However, this drive for more active management overnight may be countered by a recognition that disruption of patients' sleep-wake cycles is likely harmful[21,22] and a move toward minimizing activities overnight that can wait until the morning.[23]

Our findings are not consistent with, what is to our knowledge, the only other published study[7] on the topic of timing of extubations in which rates of reintubation within 24 hours were lower (AOR, 0.5; 95% CI, 0.3-0.9; $P = .01$) and mortality rates were not statistically significantly different (AOR, 0.6; 95% CI, 0.3-1.0; $P = .06$) for patients undergoing overnight extubation. Several plausible reasons exist for these observed differences. First, the study by Tischenkel et al[7] included patients from a single academic medical center in which overnight extubations were more common than in other ICUs (30.1% of all extubations vs 20.1% in our cohort). Systems may be in place in that institution that are not present in others to make this practice safer. Second, more than half of the patients in the study by Tischenkel et al[7] were admitted to a cardiac surgical ICU, and those patients represented a significant proportion of patients undergoing overnight extubation (81.8%). In contrast, our cohort included only 4 cardiac surgical ICUs (2.4% of the 165 ICUs in the cohort). For postoperative patients in the cardiac surgical ICU for whom recommendations are to extubate early after surgery,[24] overnight extubation might be advantageous rather than waiting until the next morning. Finally, Tischenkel et al[7] excluded patients who had palliative extubations and adjusted for the extubation being unplanned. Our study is limited by the fact that we were unable to account for unplanned extubations.

Other limitations of our study include its retrospective nature, which restricts our ability to investigate why the time of day for extubation was chosen. More detail on this issue would help to better define our cohort and refine our analyses. Moreover, these data sets do not provide information on the reason for MV, thus limiting our ability to stratify patients based on indication. In addition, Project IMPACT—chosen as our primary data set because it has detailed information about care limitations, tracheostomy use, and staffing—ended data collection in 2009, and practices may have changed since then, which may mediate the association of overnight extubations and outcomes. However, the fact that our results are robust to sensitivity analyses using APACHE Outcomes (which is less detailed but contains data through 2013) alleviates much of this concern. In addition, patients were excluded from severity of illness (MPM_0-III) calculation and, thus, analyses of outcomes for patients who were extubated overnight who underwent cardiac surgery or transplant or were admitted with acute myocardial infarction could not be done; therefore, generalizability of our findings to these groups is limited. We also excluded patients with orders to limit care before extubation; however, this method for determining which patients would receive resuscitation if needed may be insensitive. Finally, we do not have information pertaining to reintubation events that occurred after the initial ICU stay. However, we expect that most reintubations related to a primary extubation failure likely occurred during the same ICU admission.

Conclusions

Our study presents, to our knowledge, the first multicenter evaluation of overnight extubations in the United States and the association of this practice with clinically meaningful outcomes. Our finding that overnight extubation is associated with higher mortality is of great potential clinical import. Although our study cannot prove causality, our findings raise serious concerns about the routine practice of overnight extubation for many patients in the ICU. We must be cautious as ICUs move to employ more high-level staff at night[2-6] and push for standardization of care throughout all hours of the day. Although overnight extubation may be safe (or even beneficial) to some patient subgroups not included in our analyses (eg, those who have had cardiac surgery), for many patients, this practice may confer harm.

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