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Predictive models of prolonged mechanical ventilation yield moderate accuracy☆

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ABSTRACT

Purpose: To develop a model to predict prolonged mechanical ventilation within 48 hours of its initiation.
Materials and Methods: In 282 general intensive care unit patients, multiple variables from the first 2 days on mechanical ventilation and their total ventilation duration were prospectively collected. Three models accounting for early deaths were developed using different analyses: (*a*) multinomial logistic regression to predict duration > 7 days vs duration ≤ 7 days alive vs duration ≤ 7 days death; (*b*) binary logistic regression to predict duration > 7 days for the entire cohort and for survivors only, separately; and (*c*) Cox regression to predict time to being free of mechanical ventilation alive.
Results: Positive end-expiratory pressure, postoperative state (negatively), and Sequential Organ Failure Assessment score were independently associated with prolonged mechanical ventilation. The multinomial regression model yielded an accuracy (95% confidence interval) of 60% (53%-64%). The binary regression models yielded accuracies of 67% (61%-72%) and 69% (63%-75%) for the entire cohort and for survivors, respectively. The Cox regression model showed an equivalent to area under the curve of 0.67 (0.62-0.71).
Conclusions: Different predictive models of prolonged mechanical ventilation in general intensive care unit patients achieve a moderate level of overall accuracy, likely insufficient to assist in clinical decisions.

1. Introduction

Mechanical ventilation is commonly needed in critically ill patients for variable periods. Although most of these patients require ventilatory support for a short duration, approximately 30% of them need it for more than a week [1]. Predictions of duration of mechanical ventilation, particularly of a "prolonged" duration, are frequently performed by intensivists and influence important clinical decisions. Among these decisions, timing of tracheostomy [2,3] may be of special importance, but these can also involve initiation of nutrition [4], transfer to long-term ventilation facilities [5], and inclusion of patients in clinical trials. However, the limited accuracy of early predictions of prolonged mechanical ventilation by intensivists has become evident in recent studies [6–8]. An accurate objective tool to assist with this prediction would therefore be very useful but does not currently exist. Studies that aimed at developing such a tool have yielded models with low accuracy but have not accounted for early deaths [9–11]. Regarding this latter limitation, it is important to note that mechanical ventilation may be "not prolonged" when it is discontinued by means of clinical improvement and successful liberation, or alternatively by early death while it is still ongoing. Although type and severity of the illness are risk factors for a longer need of ventilatory support [9–13], those factors are also likely associated with early death and a resultant shorter duration of mechanical ventilation. Early death is then a competing event with prolonged duration of mechanical ventilation with shared risk factors.

The goal of this study was then to develop different models to predict prolonged duration of mechanical ventilation that could be applied early on its course. In order to account for the competing event early death and obtain a clinically useful tool, 3 different analyses for prediction model development were used. The primary aim was to develop a model to predict need of mechanical ventilation longer than 7 days within 48 hours of its initiation.

2. Materials and methods

2.1. Study design and setting

This was a prospective observational cohort study conducted in a general intensive care unit (ICU) of a university teaching hospital that admitted medical, surgical, and trauma patients from March 2012 to March 2014. During the study period, the ICU operated with a closed model where clinical teams led by intensivists had primary responsibility

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for patient care and used a respiratory therapist–driven weaning protocol applied every morning to all patients. The study was approved by the local institutional review board, which waived the need for informed consent given the nature of the study and the collection of data without identifiers. Part of this study was performed simultaneously with an evaluation of intensivists' clinical predictions previously reported [7].

2.2. Subjects

The subjects included were adult patients endotracheally intubated and undergoing mechanical ventilation for a minimum of 2 consecutive mornings in which a routine clinical, laboratory, and weaning evaluation was completed. Patients were excluded if they met any of the following criteria: admission on mechanical ventilation from home or other facility, plan for extubation after a successful weaning assessment on the second morning of ventilation, imminent withdrawal of care, and transfer to other facility on mechanical ventilation within 10 days of its initiation.

2.3. Data collection

Demographic, clinical, and laboratory variables, selected from those found to be associated with mechanical ventilation duration in prior studies, were collected from the time of intubation and from the time of the second morning rounds evaluation (hereafter called 2nd day). The selection of these time points was intended to include the data available to the intensivist at the time a patient is evaluated on mechanical ventilation for the second time in morning rounds. Respiratory variables (total respiratory frequency, minute ventilation, PaO_2/fraction of inspired oxygen [FIO_2], and positive end-expiratory pressure [PEEP]) were collected from the 2nd-day time point. The primary diagnosis responsible for the need of mechanical ventilation was classified into 5 categories: (*a*) head trauma with or without other trauma, (*b*) multiple trauma without head trauma, (*c*) pneumonia or acute respiratory distress syndrome, (*d*) vascular or neoplastic intracranial lesion, (*e*) postoperative, and (*f*) other medical diagnosis. For calculation of the Sequential Organ Failure Assessment (SOFA) score [14] Glasgow Coma Score was collected as recorded by ICU nurses without adjustment for sedation, and occasional missing values of bilirubin were estimated from values of adjacent days.

Subjects were followed up daily until successful discontinuation of mechanical ventilation (invasive and noninvasive) for 48 hours, death, or transfer to outside ventilator facility. The following data were collected during this follow-up period: insertion of tracheostomy, use of noninvasive ventilation or reintubation within 48 hours of extubation, death, and actual duration of mechanical ventilation. Actual duration of mechanical ventilation was defined as the number of days from initiation of invasive mechanical ventilation to successful discontinuation, ventilatory support withdrawal, or death. Passing midnight on mechanical ventilation was counted as 1 day. Actual duration of mechanical ventilation included any day with invasive ventilation via endotracheal tube or tracheostomy, and any day within 48 hours of attempted discontinuation with either noninvasive ventilation for more than 8 hours or reinitiation of invasive ventilation.

2.4. Data analysis and development of predictive models

Data were summarized with statistical measures according to the type and distribution of each variable. Predictive models were developed using 3 different analyses. (I) In the first analysis, subjects were classified into 3 categories according to mechanical ventilation duration and survival: ≤7 days died, ≤7 days survived, and >7 days survived or died. Multinomial logistic regression was used to develop a predictive model for this categorized duration. (II) In the second analysis, subjects were classified into 2 categories according to duration of mechanical ventilation (≤7 vs >7 days), and a multivariable binary logistic regression was used to develop predictive models for the entire cohort and for the subsample limited to ICU survivors, separately. (III) In the third analysis, time to being free from mechanical ventilation was modeled, instead of duration > 7 days, using Cox proportional hazards regression treating deaths as censored events. This analysis identifies variables predictive of duration of mechanical ventilation after adjusting for the probability of death. A negative coefficient estimate for this analysis indicates an increased risk of remaining longer on mechanical ventilation alive. For the development of each of these 3 prediction models, all collected variables were tested for their unadjusted association with the categories of duration or with time to being free from mechanical ventilation by using univariate multinomial logistic regression, univariate logistic regression, and univariate Cox regression, respectively. The variables found to be associated in each univariate analyses at the 0.15 significance level were then entered into the respective multivariate analysis to derive the prediction model. The multicollinearity, normality, and linearity assumptions were assessed for each model before developing the final model. The proportionality assumption was also assessed for the Cox regression model, without a significant departure being found. Results of regression analyses are reported using regression coefficients (RCs) with 95% confidence intervals (CIs) and *P* values. The predictive performance of the models was assessed using classification accuracy and the receiver operating characteristics area under the curve (AUC) for logistic regressions, and the Harrell *c* statistic for the Cox regression. These results are reported along with their 95% CI. Sensitivity and specificity for the binary regression models were calculated using standard formulae. All statistical analyses were carried out using STATA 12.1 (StataCorp LP, College Station, Tex).

3. Results

Of 282 subjects included, 229 (81%) survived the ICU stay to successful discontinuation of mechanical ventilation or transfer to a long-term ventilator facility. The remaining 53 subjects died while on mechanical ventilation or soon after its terminal withdrawal; 36 (68%) of them died at 7 days or less on mechanical ventilation. Categorized by duration on mechanical ventilation and ICU survival, 48% of subjects required 7 days or less and survived, 13% required 7 days or less and died, and

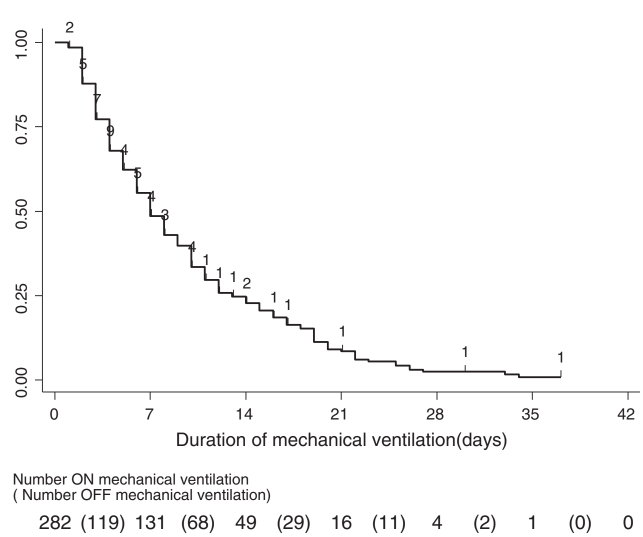

Figure. Probability of remaining on mechanical ventilation over time in the study cohort. The numbers on the curve indicate patients who died on mechanical ventilation over time. The numbers in parenthesis indicate patients successfully removed from the ventilator during each 7-day interval.