Determinants of Time-To-Weaning in a Specialized Respiratory Care Unit*

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Background: As the decision-making process in long-term respiratory care units often depends on time-based outcomes, we sought to identify independent predictors of time-to-weaning (TTW) in a hospital-based specialized respiratory care unit.

Methods: Characteristics that were identified in previous studies as predictors of weaning success in ICUs and long-term ventilator units were prospectively collected on 113 consecutive admissions to our unit. TTW analyses were performed with Kaplan-Meier curves, log rank test, and Cox proportional regression.

Results: The TTW was shorter in patients with static lung compliance (Cst) of > 20 mL/cm H2O, a normal creatinine level (0.6 to 1.4 mg/dL), a rapid shallow breathing index (RSBI) of < 105, intact skin, and in those patients from a surgical referral source. We found an interaction between RSBI and Cst (p = 0.02) such that patients with an RSBI of < 105, regardless of Cst, had a median TTW of 11 days, those with an RSBI of > 105 and a Cst of > 20 had a median TTW of 31 days, and those with an RSBI of > 105 and a Cst of ≤ 20 mL/cm H2O had not reached a median TTW by 60 days (p = 0.007 [log rank for linear trend]). In a Cox-proportional hazard model, both this categorization model of RSBI and Cst, and renal function had a significant impact on TTW.

Conclusions: In a multivariate model incorporating the variables reviewed, only the lung parameters (RSBI combined with Cst) and renal function remained independently associated with TTW.

Key words: acute physiology and chronic health evaluation; creatinine; lung compliance; respiratory insufficiency; respiratory mechanics; ventilator weaning

Abbreviations: APACHE = acute physiology and chronic health evaluation; CI = confidence interval; Cst = static lung compliance; LTAC = long-term acute care; PCU = Pulmonary Care Unit; ROC = receiver operating characteristic; RSBI = rapid shallow breathing index; TTW = time-to-weaning

The increasing acuity of medical illness has resulted in a shortage of ICU beds available to ventilator-dependent patients. Moreover, there are mounting challenges on hospitals to recover the costs of care for such patients. As a partial solution, many individuals whose need for ventilator support extends beyond their need for acute care are now managed in settings other than ICUs, including specialized respiratory care units, and intermediate-term and long-term care facilities.

Limited resources and bed availability in such hospital-based units have encouraged more optimal management in order to accelerate liberation from mechanical ventilation, accommodate incoming patients, and facilitate the transfer of patients with a poor weaning prospect to long-term acute care (LTAC) units that have a more favorable reimbursement structure. However, such management decisions depend not only on estimates of the likelihood of liberation from mechanical ventilation but also on the time frame for such an outcome. Moreover, while certain ventilator modalities and therapist-implemented protocols have been proposed to accelerate weaning, further progress in that regard depends on the accurate identification of independent predictors of delayed weaning in some individuals. Although many previous studies have identified predictors of weaning outcome, they usually have not addressed the time required to achieve weaning, did not always accommodate all potential confounders, or may have been developed in the ICU setting as predictors of rapid wean potential (eg, the rapid shallow breathing index [RSBI]) with uncertain applicability to the longer term ventilator units.

Therefore, we sought to prospectively assess the
performance in a hospital-based specialized respiratory care unit of variables that were identified in previous studies as predictors of wean success. Since time from hospital admission to successful weaning represents time-to-event data, we adopted a survival analysis model to simultaneously incorporate all relevant variables and to identify independent predictors of time-to-weaning (TTW).

**Materials and Methods**

**Patients**

The Pulmonary Care Unit (PCU) at Harper University Hospital in Detroit, MI, is a specialized respiratory care unit for the care of patients with intensive pulmonary needs. The unit consists of nine beds, and provides noninvasive cardiac and respiratory monitoring. All patients who received ventilation via a tracheostomy who had been admitted to the PCU from its inception in June 2001 until August 2003 were included in the study. We excluded four patients who were admitted to the PCU through that period for a planned intervention with known disposition after completion of the intervention (e.g., transfers from long-term care facilities for specialized procedures, transfers under hospice care, or for comfort measures). The PCU admission criteria included the following: the presence of an inner diameter of at least 7 mm; hemodynamic stability; positive end-expiratory pressure of ≤ 8 cm H₂O; fraction of inspired oxygen of < 60%; the failure of weaning attempts in the ICU; the absence of potentially lethal dysrhythmias; the absence of titratable drips; and the lack of need for neuromuscular blockade or continuous sedatives with the exception of patient-controlled anesthesia (PCA) pumps and epidural therapy. Additionally, though poor rehabilitation potential and mental status were not absolute contraindications, the potential ability to wean was favored for admission to the unit.

**Potential Determinants of Wean Outcome**

The following potential determinants, based on a review of the literature, were prospectively collected on the day of admission to the PCU: the location of the patient before admission to the PCU (medical vs surgical unit); age and race; acute physiology and chronic health evaluation (APACHE II) score; creatinine level; skin integrity; respiratory parameters, including static lung compliance (Cst); and the RSBI, and whether the patient had emphysema. Other variables collected included the albumin level within 1 week of admission to the PCU and ejection fraction, if it was available from a cardiac echocardiography report within 2 months of admission to the PCU. We also recorded the number of days from admission to the PCU to placement of a tracheostomy, the number of hospital days before admission to the PCU, and the use of the following medications on admission to the PCU: systemic steroids; benzodiazepines; opiates; β-blockers; and the use of nebulated or inhaled steroids or bronchodilators. The disposition of patients at hospital discharge was recorded as follows: home (including home ventilator); rehabilitation facility; nursing home; LTAC unit; hospice (including home hospice); and dead.

**Weaning Protocol**

A therapist-driven protocol, which was modeled after the available comparative studies of wean modalities, was implemented to optimize the time required to achieve wean weaning. The respiratory therapists who were in charge of the weaning protocol were blinded to the Cst and RSBI, which were separately obtained by the investigators. In each case, an attempt was made to identify and address the impediments to weaning in weekly multidisciplinary meetings that included a nutritionist, respiratory therapist, speech pathologist, physical therapist, social worker, pharmacist, physician (LSA), unit manager, and members of the nursing staff. Impediments to weaning were included only in as much as they were deemed to contribute to the respiratory failure, and were classified as neurologic (including central, spinal, or neuromuscular causes), cardiac (including coronary artery disease and congestive heart failure), infections (any cause including pneumonia), or pulmonary (including COPD, asthma/bronchitis, obesity hypoventilation, ARDS, and interstitial lung disease). Patients were placed on assist-control ventilation on arrival in the PCU and were considered ready for a weaning trial if systolic BP was between 90 and 180 mm Hg, heart rate was between 50 and 130 beats/min, temperature was < 101°F (< 38.3°C), and minute ventilation was < 15 L/min. On each of the first 2 days following admission to the PCU, patients who considered to be ready for weaning underwent spontaneous breathing trials, and a successful trial was followed by use of a tracheostomy mask with oxygen supplementation to maintain a pulse oximetry saturation of ≥ 94%. Those failing the spontaneous breathing trials on the first 2 days were rested using assist-control ventilation for the remainder of the day and spent subsequent days receiving pressure support ventilation at a level sufficient to maintain a respiratory rate of < 30 breaths/min. For patients who tolerated the trials, pressure support was decreased by 2 cm H₂O at least twice daily. The tolerance of pressure support at 5 cm H₂O for at least 2 h was followed by use of a tracheostomy mask. Patients undergoing a spontaneous breathing trial or a pressure support trial were returned to therapy with assist-control ventilation if they had a respiratory rate of > 30 breaths/min, and an increase in heart rate by 20 beats/min, a decrease in systolic BP by ≥ 20 mm Hg, or a decrease in oxygen saturation by ≥ 5%. The TTW was calculated as the number of days from admission to the PCU to the first day of the last successful 48-h weaning trial regardless of ultimate outcome.

**Definitions and Measurements**

The term wean as used in this study conforms to its use in general practice as reflecting the process of liberation from mechanical ventilation without implying a protracted process. Although the majority of patients originated from the different ICUs of Harper Hospital, < 10% were directly admitted from LTAC facilities and were considered for the purpose of our analysis to have originated from a medical (as opposed to surgical) unit regardless of their location prior to the LTAC facility admission. A diagnosis of emphysema was not based on a chart report but rather on a review of chest radiographs, confirmed history, or prior documentation by a pulmonologist. A decubitus ulcer was considered to be present for any stage skin breakdown of the sacrum. Renal function on admission to the PCU was categorized based on the creatinine level as normal (0.6 to 1.4 mg/dL) or abnormal (including creatinine values of < 0.6 or > 1.4 mg/dL, and dialysis). Cst was measured by dividing the delivered tidal volume (in milliliters) by the difference between plateau and positive end-expiratory pressures (in centimeters of water). To obtain a plateau pressure, we used the inspiratory hold plateau by visual inspection of the pressure-time curve on the ventilator display. The RSBI was obtained by dividing the respiratory frequency (in breaths per minute) by the tidal volume (in liters). Tidal volume and respiratory rate were obtained from...
a hand-held spirometer (Boehringer Laboratories: Norristown, PA) over a minute of spontaneous unassisted breathing with the patient disconnected from the ventilator circuit.

Statistical Analysis

Time-to-event analyses were used to model TTW. Kaplan-Meier estimates were used to determine the cumulative probability of successful weaning within the hospital stay, log-rank tests for comparison of the TTW between groups, and Cox proportional regression to calculate hazard ratios. We also dichotomized some of the continuous variables based on consensus, a review of the receiver operating characteristic (ROC) curve coordinates, or a review of the literature. For instance, an RSBI cutoff of 105, an albumin level cutoff of 2 g/dL, and a Cst cutoff of 20 mL/cm H2O were based on a review of the ROC coordinates cutoff of 15, an albumin level cutoff of 2 g/dL, and a Cst cutoff of 70 years were used based on data from previous studies that used those cutoffs. An APACHE score cutoff of 15, an albumin level cutoff of 2 g/dL, and a Cst cutoff of 20 mL/cm H2O were based on a review of the ROC coordinates of those variables for the optimal sensitivity and specificity for weaning success. An ejection fraction of 50% was used as a cutoff that separates normal heart function from abnormal heart function.

Cox proportional hazard regression was used in a backward stepwise algorithm that incorporated all variables that were significantly associated with TTW in the univariate analyses. We tested the proportionality of the hazards assumption underlying this test by introducing a time-dependent covariate in the Cox model. Collinearity diagnostics were performed using tolerance estimates for individual variables in a linear regression model.

Cox proportional hazard regression was also used to examine interactions among potential covariates. For instance, having identified an interaction between Cst and RSBI in their effect on TTW, we attempted to characterize this interaction by ranking these two variables into four ordinal categories, from the expected most favorable impact to the expected least favorable impact. An ejection fraction of 50% was used as a cutoff that separates normal heart function from abnormal heart function.

Table 1—Characteristics of Patients on Admission to the PCU*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>60.5 ± 16.2 (15–85)</td>
</tr>
<tr>
<td>Cst, mL/cm H2O</td>
<td>29.1 ± 9.5 (13–52)</td>
</tr>
<tr>
<td>RSBI</td>
<td>151.9 ± 97.5 (42–551)</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>51.5 ± 15.8 (15–75)</td>
</tr>
<tr>
<td>APACHE II score</td>
<td>13.5 ± 6.2 (5–27)</td>
</tr>
<tr>
<td>Serum albumin, g/dL</td>
<td>2.2 ± 0.6 (1.0–4.4)</td>
</tr>
<tr>
<td>Time from PCU admission to tracheostomy placement, d</td>
<td>17 (0–93)</td>
</tr>
<tr>
<td>Time in hospital before transfer to the PCU, d</td>
<td>19 (0–164)</td>
</tr>
<tr>
<td>Referral origin, %</td>
<td></td>
</tr>
<tr>
<td>Medical ICU</td>
<td>54</td>
</tr>
<tr>
<td>LTAC facility</td>
<td>10</td>
</tr>
<tr>
<td>General surgical ICU</td>
<td>11</td>
</tr>
<tr>
<td>Cardiothoracic ICU</td>
<td>19</td>
</tr>
<tr>
<td>Neurosurgical ICU</td>
<td>6</td>
</tr>
</tbody>
</table>

*Values given as mean ± SD (range), unless otherwise indicated.
†Values given as median (range).

Results

General

Accrual was as projected, with 113 admissions to the PCU over a period of 26 months. The proportion of female patients was 51% (58 of 113 patients). The proportion of patients dying during their hospital stay was 27% (31 of 113 patients). Sixty-four percent of patients were transferred from a medical service, and 36% of patients were transferred from a surgical service (Table 1). The proportion of patients who weaned during their hospital stay was 56% (63 of 113 patients). Other characteristics are shown in Table 1. Table 2 shows that the most commonly identified impediment to weaning was infection (73% of patients), with multiple impediments identified in several patients, and that the general disease categories identified as specific impediments to weaning did not differentiate between ultimate weaning success and weaning failure. Table 3 shows the distribution of patients per category that was considered as a potential determinant of TTW. Note that our racial distribution was unequal, with 75% of patients (85 of 113 patients) being African-American, closely matching the population of downtown Detroit served by Harper University Hospital (Table 3). The median number of days spent in the hospital before transfer to the PCU was 19 days in patients who successfully weaned, and was also 19 days in those who did not (p = 0.57 [Wilcoxon rank sum test]). Similarly, the median number of days from hospital admission to the placement of a tracheostomy was 16 and 18 days, respectively, in those who were successfully weaned vs those who did not (p = 0.34 [Wil-
Information on the use of different medications on admission to the PCU was available in 47% of our patients. The use of the medications reviewed did not have a significant impact on weaning success rates (data not shown).

Most patients were alert, with 71% of patients having a normal Glasgow coma score of 15 on admission to the PCU (mean ± SD score: 13.2 ± 3.5). However, 15% of patients had severe impairment of consciousness with a Glasgow coma score of 8. Of the 79 patients who had available blood gas measurements on admission to the PCU, 78% had a PaO₂/fraction of inspired oxygen ratio of > 140. Overall, patients who were successfully weaned were more likely to be discharged home (16% vs 2%, respectively; p = 0.001), to a rehabilitation unit (34% vs 0%, respectively; p < 0.001), or to a nursing home (12% vs 2%, respectively; p = 0.03) [Fig 1]. Alternatively, those who failed to wean were more likely to be discharged to a LTAC facility (47% vs 28%, respectively; p = 0.03) or to have died (47% vs 7%, respectively; p < 0.001) [Fig 1]. The most common factors contributing to death were infection (30%), malignancy (30%), and CNS event (ie, stroke or hemorrhage, 17%).

### Individual Predictors of TTW

Factors associated with a significantly shorter time from admission to the PCU to successful weaning, listed in order of decreasing hazard ratio for weaning success, were as follows: Cst, > 20 vs ≤ 20 mL/cm H₂O; a normal creatinine level (0.6 to 1.4 mg/dL) vs an abnormally low creatinine level (< 0.6) or an abnormally high creatinine level (> 1.4 mg/dL or ≥ 1.4 mg/dL). Table 2 and Table 3 provide further details.

### Table 2—Proportion of Patients With Different Identified Impediments to Weaning Stratified by Weaning Outcome

<table>
<thead>
<tr>
<th>Impediment to Weaning</th>
<th>Group Not Weaned, %</th>
<th>Group Weaned, %</th>
<th>Total, %</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurologic disease</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>0.98</td>
</tr>
<tr>
<td>Cardiac disease</td>
<td>33</td>
<td>35</td>
<td>34</td>
<td>0.79</td>
</tr>
<tr>
<td>Infection</td>
<td>74</td>
<td>72</td>
<td>73</td>
<td>0.85</td>
</tr>
<tr>
<td>Lung disease</td>
<td>33</td>
<td>35</td>
<td>34</td>
<td>0.84</td>
</tr>
</tbody>
</table>

*Total exceeds 100% because of multiple identified impediments in several patients.

### Table 3—TTW Analysis Based on Characteristics on Admission to the PCU

| Characteristic: Category1/2† | Category 1 | Category 2 | Distribution of Patients per Category | Median TTW, d | Hazard Ratio for Category1/2‡§ | p Value||
|------------------------------|------------|------------|--------------------------------------|--------------|-------------------------------|---------|
| Cst ≤ 20/20 mL/cm H₂O        | 21 (21)    | 81 (80)    |                                      | > 177        | 2.3 (1.1–5.0)                 | 0.02    |
| Creatinine < 0.6 or > 1.4/0.6–1.4 mg/dL | 45 (45) | 54 (55) |                                  | 35           | 2.2 (1.3–2.8)                 | 0.002   |
| RSBI > 105/105               | 47 (59)    | 33 (41)    |                                      | 35           | 1.9 (1.1–3.5)                 | 0.02    |
| Decubitus ulcer present/absent | 41 (40) | 61 (60) |                                    | 31           | 1.8 (1.0–3.1)                 | 0.03    |
| Referral origin medical/surgical | 61 (54) | 52 (46) |                                     | 26           | 1.7 (1.0–2.7)                 | 0.04    |
| APACHE score > 15/15         | 34 (33)    | 68 (67)    |                                      | 26           | 1.7 (0.97–3.1)                | 0.06    |
| Ethnicity African-American/other | 85 (75) | 25 (25) |                                             | 21           | 1.3 (0.7–2.3)                 | 0.39    |
| Age ≥ 70/≤ 70 yr             | 40 (35)    | 73 (65)    |                                      | 20           | 1.1 (0.7–1.9)                 | 0.60    |
| Ejection fraction < 50%/≥ 50% | 28 (31)    | 62 (69)    |                                      | 26           | 1.0 (0.6–1.8)                 | 0.99    |
| Emphysema present/absent     | 21 (19)    | 92 (81)    |                                      | 21           | 0.9 (0.5–1.7)                 | 0.77    |
| Albumin ≤ 2/2 g/dL           | 38 (38)    | 62 (62)    |                                      | 16           | 0.8 (0.5–1.4)                 | 0.46    |

*Values are given as the No. (% of available total).
†From admission to the PCU to successful weaning.
‡Category 1 comprises patients with an expected worse prognosis compared to those in category 2; the hazard ratio for TTW therefore uses category 2 as the reference category.
§Values in parentheses are 95% CI.
||Log-rank p value for equality of TTW distribution.
dialysis); an RSBI of ≤ 105 vs > 105; the absence vs the presence of a decubitus ulcer; and a surgical vs a medical referral origin (Table 3, Fig 2). APACHE II score, Emphysema, race, age, albumin level, and ejection fraction were not associated with weaning success or TTW (Table 3).

Multivariable Analyses

There was a significant interaction between Cst and the RSBI on TTW (p = 0.02), indicating that the effect of RSBI on weaning success rate was not equivalent at different levels of Cst. To characterize this interaction, we ranked the RSBI and Cst data into the following four categories, from expected most favorable to expected least favorable impact on the prospect of weaning: (1) RSBI of ≤ 105 and a Cst of > 20 mL/cm H₂O (27 subjects); (2) RSBI of ≤ 105 and Cst of ≤ 20 mL/cm H₂O (5 subjects); (3) RSBI of > 105 and Cst of > 20 mL/cm H₂O (36 subjects); and (4) RSBI of > 105 and Cst of ≤ 20 mL/cm H₂O (9 subjects).

There was no significant difference in TTW between patients in category 1 (RSBI of ≤ 105 with Cst of > 20 mL/cm H₂O) and those in category 2 (RSBI of ≤ 105 and Cst of ≤ 20 mL/cm H₂O; p = 0.93), and these two categories were combined in subsequent analyses. There was a significant linear trend of increased TTW from combined category 1 and 2 (median TTW, 11 days), to category 3 (median TTW, 31 days), and to category 4 (median TTW not reached after > 60 days) with a log rank p value for the trend of 0.007. Using patients with an RSBI of ≤ 105 as the reference group, the hazard ratio for TTW in patients with an RSBI of ≤ 105 and a Cst of > 20 mL/cm H₂O was 1.6 (95% confidence interval [CI], 0.9 to 3.0; p = 0.14), and the hazard ratio for TTW in patients with an RSBI of > 105 and a Cst of ≤ 20 mL/cm H₂O was 5.4 (95% CI, 1.3 to 23.3; p = 0.02).

A Cox proportional regression was used to adjust for the following potential categoric covariates: abnormally low creatinine level (< 0.6 mg/dL) or abnormally high creatinine level (> 1.4 mg/dL) vs normal creatinine level (0.6 to 1.4 mg/dL); medical vs surgical referral source; presence vs absence of decubitus ulcers; and the three-way categorization of RSBI and Cst (categories 1/2, 3, and 4). In that model, only the three-way categorization of RSBI and Cst remained an independent predictor of TTW, with renal function approaching significance (three-way categorization, p = 0.02; significance for scores for creatinine, p = 0.07; medical vs surgical referral source, p = 0.17; and presence of decubitus ulcers p = 0.24).

Analysis of Impact of Emphysema

Given the importance of the RSBI and Cst in our model and recognizing that neither of these parameters is an ideal predictor of the prospect for weaning in patients with emphysema, we scrutinized the potential impact of emphysema on our results. The area under the ROC curve of Cst as a predictor of emphysema was 0.66 (test of null hypothesis that true area is 0.5, p = 0.03), indicating that a higher Cst on admission to the PCU was of some predictive value for patients with a prior diagnosis of emphysema. For instance, 29% of patients with a Cst of ≥ 30 mL/cm H₂O had emphysema compared to 9.4% of those with a Cst of < 30 mL/cm H₂O (p = 0.02 [Fisher exact test]). However, there was no interaction between Cst and emphysema on TTW (p = 0.46), and the presence of emphysema was not associated with delayed weaning (Table 3). Nevertheless, by excluding the 21 patients with emphysema from our data set, our results were actually reinforced with median TTWs in patients with an RSBI of ≤ 105, an RSBI of > 105 and a Cst of > 20, and an RSBI of > 105 and a Cst of ≤ 20 of 7, 26, and > 160 days, respectively (p < 0.001 [log rank test for linear trend]) [Fig 3]. Similarly, after the exclusion of patients with emphysema in our Cox proportional regression model, creatinine level and the three-way categorization of RSBI and Cst were both independent predictors of TTW (three-way categorization, p = 0.03; creatinine level, p = 0.02). In the group of patients without a diagnosis of emphysema, and using patients with an RSBI of ≤ 105 as the reference group, the hazard ratio for TTW in patients with an RSBI of ≤ 105 and a Cst of > 20 mL/cm H₂O was 1.6 (95% CI, 0.8 to 3.4; p = 0.22), and the hazard ratio for TTW in patients with an RSBI of > 105 and a Cst of ≤ 20 mL/cm H₂O was 12.5 (95% CI, 1.6 to 100; p = 0.02) [Fig 3]. Similarly, using patients with abnormal creatinine levels as a reference group, the hazard ratio for TTW in patients with a normal creatinine level was 2.6 (95% CI, 1.2 to 5.5; p = 0.02).

Discussion

Using a survival model of analysis, this study has identified several predictors of shorter TTW in a long-term ventilator unit including high Cst (> 20 cm H₂O), normal creatinine level, low RSBI (≤ 105), intact skin, and a surgical referral source. However, in a multivariable model, the RSBI combined with Cst, and the creatinine level remain independently associated with TTW, particularly in patients without emphysema.

While several previous studies have proposed de-
Figure 2. Kaplan-Meier curves of the time course from admission to the PCU to successful weaning.

Top left, A: Cst ≤ 20 mL/cm H₂O vs > 20 mL/cm H₂O. Top right, B: creatinine level of < 0.6 or > 1.4 vs 0.6 to 1.4 mg/dL. Middle left, C: RSBI > 105 vs ≤ 105. Middle right, D: decubitus ulcer vs intact skin. Bottom right, E: medical vs surgical referral origin.
terminants of weaning success in similar units, we have extended those reports by doing the following: (1) recognizing the importance of taking into account lung parameters such as the RSBI and Cst when assessing the potential impact of other variables; (2) showing the separate contribution of the Cst in patients with unfavorable RSBI; (3) identifying renal function as an additional independent determinant of TTW; (4) indicating that weaning success is an important determinant of disposition on hospital discharge; and (5) providing time-based data that may be more relevant to the needs of a long-term ventilator unit.

In addressing that latter point, the planning of resource allocation, selection criteria, and decision making concerning patient disposition all depend on time-based outcomes. For instance, the median TTW of 31 days in patients with high RSBI but high Cst is nearly equivalent to the geometric mean length of stay for such patients (Diagnosis-related Grouping code 483, 34 days) beyond which hospitals may not recover their costs of care.25 One potential implication could be to initiate early evaluations for transfer to LTACs for such patients, perhaps depending on the number of days already spent in the hospital prior to admission to the specialized respiratory care unit. While our hospital admission and discharge criteria were not based on the results of our study, the type of data generated here may be useful, for example, in anticipating the number of beds to allocate in similar units, in early planning for alternate dispositions of patients not expected to be liberated from mechanical ventilation within a certain time frame, and in refining selection criteria for admission to the unit to accommodate the expected inflow of incoming patients. A more detailed assessment of the proportion (by quartiles) of patients weaning within a certain number of days based on pulmonary and renal function on admission to our PCU is shown in Table 4. Table 4 indicates, for example, that 75% of patients with favorable lung and renal parameters will wean within 18 days. Important caveats in the interpretation of our data include the need to prospectively validate this model, and the relatively small group of patients with unfavorable RSBI and Cst.

We closely examined whether Cst and RSBI may be negatively correlated, and therefore whether the effect of these variables on weaning may be explained by one or the other but not necessarily by both. In that analysis, we found no evidence for collinearity by performing diagnostic testing in a linear regression model that included RSBI and Cst as independent variables, with weaning success as the dependent variable (tolerance collinearity statistic for both variables, 0.97). Further, there was no meaningful correlation between Cst and RSBI ($r = -0.19; p = 0.10$). Last, a two-by-two table cross-tabulation of Cst of $\geq 20$ mL/cm H2O vs $< 20$ mL/cm H2O against an RSBI of $\geq 105$ vs $> 105$ suggests that these two variables are independent ($p = 0.77$ [Fisher exact test]). Therefore, both RSBI and Cst are useful to our model.

There are potential limitations in the use of the RSBI and Cst as determinants of TTW in patients with emphysema. For instance, an elevated Cst due to emphysema may be more relevant to the needs of a long-term ventilator unit. In addressing that latter point, the planning of resource allocation, selection criteria, and decision making concerning patient disposition all depend on time-based outcomes. For instance, the median TTW of 31 days in patients with high RSBI but high Cst is nearly equivalent to the geometric mean length of stay for such patients (Diagnosis-related Grouping code 483, 34 days) beyond which hospitals may not recover their costs of care. One potential implication could be to initiate early evaluations for transfer to LTACs for such patients, perhaps depending on the number of days already spent in the hospital prior to admission to the specialized respiratory care unit. While our hospital admission and discharge criteria were not based on the results of our study, the type of data generated here may be useful, for example, in anticipating the number of beds to allocate in similar units, in early planning for alternate dispositions of patients not expected to be liberated from mechanical ventilation within a certain time frame, and in refining selection criteria for admission to the unit to accommodate the expected inflow of incoming patients. A more detailed assessment of the proportion (by quartiles) of patients weaning within a certain number of days based on pulmonary and renal function on admission to our PCU is shown in Table 4. Table 4 indicates, for example, that 75% of patients with favorable lung and renal parameters will wean within 18 days. Important caveats in the interpretation of our data include the need to prospectively validate this model, and the relatively small group of patients with unfavorable RSBI and Cst.

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There are potential limitations in the use of the RSBI and Cst as determinants of TTW in patients with emphysema. For instance, an elevated Cst due to emphysema may be associated with worse outcome instead of portending successful weaning. Our data did show that a prior diagnosis of emphysema was significantly more prevalent in individuals with higher Cst (ie, $\geq 30$ mL/cm H2O). Additionally, patients with emphysema may fail to wean despite having a low RSBI.17 Last, we did not measure auto-positive end-expiratory pressure, which may

![Figure 3. Cox-regression plots of the time course from admission to the PCU to successful weaning based on groups defined by the RSBI and Cst on admission to the PCU.](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/22033/)
have resulted in the underestimation of Cst in patients with emphysema. In addressing these concerns, we found that the impact of Cst on TTW was not different in patients with emphysema vs those without emphysema, and emphysema was not associated with delayed weaning (Table 3). However, we could not completely include that the absence of a significant impact of emphysema on TTW was not simply due to the relatively low number of such patients in our data. In that regard, it is interesting to note that the exclusion of patients with emphysema from our data set only reinforced our results.

Our use of the RSBI differs from its original description as a predictor of weaning success at the time of its measurement in an ICU setting. Rather, we use it as a predictor of TTW in a long-term ventilator unit. In that setting, it is noteworthy that ROC plots indicate that the RSBI remains a useful predictor of long-term weaning success (area under the ROC curve, 0.68; C-statistic, 0.004), albeit with lower sensitivity and specificity than those in an ICU setting (at the RSBI 105 cutoff, 67% and 57%, respectively). Moreover, a review of the ROC curve coordinates suggests that there is no particular advantage in altering the RSBI 105 cutoff (eg, sensitivity and specificity at an RSBI cutoff of 125 were 66% and 60%, respectively).

There is no consensus among studies as to the length of time not receiving mechanical ventilation before a patient is considered successfully weaned, with some considering 24 h, 48 h, 72 h, or 1 week as different criteria for weaning success. We adopted a cutoff of 48 h predominantly because it was a value that would not be at the extremes of the values in the studies reviewed and would therefore allow a more direct comparison of our results to those studies, and also because we considered that a return to mechanical ventilation past that period would only involve a minority of patients. Nevertheless, larger studies have increasingly adopted a 1-week period of freedom from mechanical ventilatory support as a criterion for weaning success. A review of our data supports this. Five patients who had stopped receiving mechanical ventilation for 48 h had to resume mechanical ventilation from 3 to 5 days after the initiation of the weaning trial. Alternatively, none of the patients who weaned for >5 days had to return to receiving mechanical ventilation. Using a 1-week cutoff as a criterion of weaning success reduces the percentage of patients weaned modestly to 51% (from 56%) but did not change our findings concerning determinants of weaning, the interaction between RSBI and Cst, or the results of our multivariate analysis.

Another issue is whether the size of the tracheostomy tube may have had an impact on weaning or on our measurements. An adequately sized tube was one criterion for admission to the PCU and, overall, median airways resistance in our patients was 13 cm H2O s/L with a positive (leftward) skew to the distribution (70% of patients had a “normal” reading of <15 cm s/L, and 96% of patients had an airway resistance of < 20 cm s/L). Moreover, airways resistance was not predictive of the failure to wean (data not shown).

As is apparent from the raw numbers reported in Table 3, some of the characteristics of interest could not be collected in all patients due to an inability to complete the required maneuver or unsatisfactory waveforms (RSBI and Cst), tests that were not ordered within the time frame required for inclusion (albumin, echocardiography), or missing data. However, TTW distribution and weaning success rates were similar in those with vs those without missing characteristics, suggesting that these omissions did not result in a systematic bias.

Although our study was designed and implemented before the publication of evidence-based guidelines for weaning, our protocols incorporate many of the salient recommendations of this document including the use of a therapist-driven weaning protocol, an effort to identify and address the impediments to weaning, a formal assessment of readiness to wean, implementation of a single daily spontaneous breathing trial as the initial weaning modality, and the use of a nonfatiguing form of ventilatory support (in our case, pressure-support ventilation) for individuals failing spontaneous breathing trials. Our use of a systematically applied weaning protocol that conforms to evidence-based guidelines should therefore help to ensure that our findings are generalizable to other similarly managed units.

In further addressing the generalizability of our findings, our weaning success rate of 56% is quite comparable to the 50 to 75% success rate reported in several other studies of patients receiving long-term ventilation and our overall TTW distribution is similar to that of another study (Fig 4).

The results of our study are also concordant with those of other studies in showing that TTW was not prolonged in patients of advanced age, and consequently that age should not be the sole consideration in decisions about mechanical ventilation. Our results similarly agree with those of Schonhofer et al who found that the APACHE II score does not predict weaning outcome. Although a higher APACHE II score tended to be associated with higher TTW in our study (Table 3), this was probably due to the significant effect of creatinine level and the use of dialysis, both subcomponents of the APACHE II score, on TTW.
The most striking difference between our study and others is that we were unable to confirm the importance of albumin level as a predictor of weaning success. For instance, the albumin level within 2 weeks of admission to the PCU was 2.1 g/dL in those who failed to wean and 2.2 g/dL in those who successfully weaned (p = 0.75). We were also unable to confirm the importance of albumin as a predictor of weaning success using ROC curves, or as a predictor of TTW when used as a continuous variable in a Cox regression model. This result is at odds with those of others. While this may reflect differences between those different studies in albumin levels at hospital admission, it is not possible to confirm this from a review of the available data reported in those studies.

In conclusion, our study is concordant with other studies of long-term respiratory care units in showing a high weaning success rate and in identifying several predictors of a successful weaning outcome. We extend these data by showing that in a multivariate model, only the lung parameters we reviewed (ie, RSBI combined with Cst), and creatinine level remain independently associated with TTW, particularly in patients without emphysema. Our study suggests that further interventions to accelerate weaning should focus on the prevention and treatment of lung and renal dysfunction, and more specific determinants of weaning outcome should be sought in patients with emphysema. The time-based outcome data in our report may be helpful in the planning of resource allocation, selection criteria, and decision making concerning patient disposition.

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