Research article

Development and prospective validation of a model for predicting weaning in chronic ventilator dependent patients

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Abstract

Background: Approximately ten percent of patients placed on mechanical ventilation during acute illness will require long-term ventilator support. Unfortunately, despite rehabilitation, some will never be liberated from the ventilator. A method of predicting weaning outcomes for these patients could help conserve resources and minimize frustrating failed weaning attempts for this population. The objective of this investigation was to identify predictors of weaning outcome for patients admitted to a chronic ventilator unit (CVU).

Methods: This was a retrospective analysis with prospective validation. The study setting was a 25 bed CVU within a rehabilitation hospital. The training group consisted of 43 patients referred to our facility for weaning after > 3 weeks of mechanical ventilation. A multivariate model to predict weaning outcome was constructed in this group and applied to a prospective group of 31 patients followed during an 18-month period.

Results: A modified Glasgow Coma Scale (GCS) and the presence of sustained spontaneous respirations (SSR), defined as the presence of 2 breaths recorded above the ventilator settings on four occasions, were highly predictive of weaning success within six months of CVU admission. Patients with a modified GCS $\geq$ 8 were 6.5 times more likely to wean than those with a modified GCS < 8 (95% confidence interval 1.6–26.3) and those with SSR were 25.5 times more likely to wean than those without SSR (95% confidence interval 4.3–51.9).

Conclusions: In our population of CVU patients, simple parameters that were available on admission and did not directly reflect cardiopulmonary function were useful predictors of weaning outcome.

Background

The number of acutely ill hospitalized patients placed on mechanical ventilation has increased over the past 20 years, perhaps by as much as 50% per decade. [1] Many of these patients are elderly or have multiple medical problems, and as a result, often need prolonged periods of rehabilitation prior to successful weaning from mechanical ventilation. While only 5–10% of patients require more than 3 weeks of ventilator support, these patients consume 35–50% of intensive care resources. [2]

Table 1: Characteristics of Training and Prospective Groups by Weaning Outcome

	Training Group		Prospective Group		
	Weaned n = 18 (SD)	Not Weaned n = 25 (SD)	Weaned n = 19 (SD)	Not Weaned n = 12 (SD)	p-value
Age, years	62 (+/-18)	60 (+/-16)	57 (+/-15)	54 (+/-25)	NS
Sex, male (%)	9 (45%)	13 (57%)	9 (68%)	9 (57%)	NS
Months of ventilation prior to admission	3.6 (+/-10)	2.2 (+/-4.2)	1.6 (+/-6)	1.9 (+/-6)	NS

NS = not significant, SD = standard deviation

Early transfer from the acute care unit to a specialized chronic ventilator unit (CVU) capable of providing intensive rehabilitation, respiratory, and nutritional services has been associated with cost savings and improved outcome. [3] However, not all patients cared for in these facilities can ultimately be weaned from mechanical ventilation. A method of predicting the likelihood of successful weaning could improve outcomes while conserving resources.

Several predictors of weaning outcome for patients in CVUs have been described. [4,5] Because most focus on pulmonary parameters, they have usually been applied to patients with respiratory causes of ventilator dependence. Much less information exits regarding prediction of weaning outcomes in more heterogeneous CVU populations, particularly those suffering a major neurolgic event. Thus, we sought to identify variables predictive of weaning success in our population of chronic ventilator dependent patients.

Methods
Setting
The study was conducted in a 25-bed CVU, which is part of university affiliated chronic care hospital staffed by a team of pulmonologists, internists, nurses, respiratory therapists and rehabilitation specialists, including a medical director who is a pulmonologist. The unit was also staffed by two rotating pulmonary physicians and a medical house officer. Three to four nurses and two respiratory therapists were on the floor at all times. Physical therapy, occupational therapy, nutritional services and speech/swallow therapy were available. All of these rehabilitaion services were offered for patients able to participate. The majority of patients were admitted directly from the critical care setting after more than three weeks of ventilator support. Patients were transferred to the CVU if they were hemodynamically stable and did not require continuous cardiac monitoring (invasive and non-invasive telemetry). The occurrence of critical care delirium was not recorded, although no patient was receiving continuos intravenous sedation or narcotics at the time of CVU

transfer. Perceived rehabilitation or weaning potential were not used as admission criteria. Patients who became unstable in the CVU were transferred to an acute care facility unless otherwise directed.

All patients admitted to the CVU were ventilated via a surgically placed tracheostomy. Daily rounds were made by a pulmonary specialist, during which patients were assessed for weaning potential. No formal weaning protocol was followed, although all patients were assessed for their weaning based on their ability to initiate and maintain adequate unsupported respiratory efforts. All patients were weaned with either progressive pressure support or T-piece trials during which time vital signs, oxyhemoglobin saturation and end-tidal carbon dioxide monitoring was performed. The length of these trials was based the patients tolerance, but typically were initiated at 30 minutes duration and then extended until several daily trials of 4–6 hours could be completed. Appropriate patients were then progressed to unsupported breathing via the tracheostomy with oxygen supplementation, and if possible tracheotomy decanullation. The tracheotomy tube was not removed in patients who were felt unable to protect their airway, despite successful ventilator liberation.

Study Design
The model to predict weaning outcome was developed on a training group of 43 patients admitted during a two-year period and validated on a separate prospective group of 59 patients admitted to the CVU during the subsequent 18 months. No aspect of staffing or documentation changed during this time.

Data Collection
Demographic information including age, sex, referring facility, past medical history, duration of mechanical ventilation prior to admission and diagnosis were extracted from medical records. Patients were classified into one of five diagnostic categories as the primary cause for prolonged mechanical ventilation: 1) obstructive lung disease (i.e., chronic obstructive pulmonary disease, asthma,

2) acute lung injury (i.e., acute respiratory distress syndrome, pneumonia, toxic exposure), 3) post-operative, 4) neurologic catastrophe (i.e. cerebral vascular accident (CVA/ICB), anoxic encephalopathy (AE), spinal cord disease (SCD), sub-dural or sub-arachnoid hemorrhage (SDH/SAH), or alternate neurologic diagnosis including seizures and neuropathies), and 5) other (such as malignancy, trauma). In the prospective group of patients admission arterial blood gas values were also recorded.

In addition to the patient demographics and diagnoses described above, a modified Glasgow Coma Scale (GCS) and the presence of sustained spontaneous respirations (SSR) were assessed upon admission to the CVU. The modified GCS was obtained from two sources: the nurse's intake record and the physician's admission findings. The GCS scoring system includes a numeric code for motor, eye and verbal response. [6] However the verbal component has been criticized as difficult to reliably score in intubated patients, despite a variety of proposed techniques for designating a verbal score. [7] In addition, several investigators have recently reported that the verbal component of the GCS can be omitted without compromising reliability and predictive validity of the score, especially in patients suffering a neurologic event. [8,9] Since all our patients had a tracheostmy and were unable to speak, only the motor and eye scores were recorded, and the maximum value of this modified GCS was 10. The highest recorded score was chosen in cases in which the nurse's intake record and physician's admission findings were discordant. The modified GCS at three and six months from admission was also recorded (obtained from nursing re-evaluation forms completed on all patients).

The presence of sustained spontaneous respirations (SSR) was determined from multiple sources. Patients were classified as having SSR if either the physician's history, nursing intake sheet, or respiratory therapy logs recorded more than two respirations above the ventilator settings on four separate occasions within the first several days of admission. The patient's SSR status was also assessed during the pulmonologist's determination of each patient's ability to wean. To minimize the effects of the ventilator such as minute ventilation and respiratory rate leading to respiratory depression and absent SSR, respiratory alkalosis and over sedation were sought for all patients without SSR. When these were found the ventilator was adjusted and the level of support decreased and/or sedation was minimized and the presence of SSR reassessed. Ventilator support was decreased with a reduction in the machine delivered respiratory rate and minute ventilation. No patient was receiving intravenous sedation/narcotics, however, several patients were receiving intermittent doses of oral anxiolytics/pain medications at the time of

CVU admission. In the majority of patients these were subsequently discontinued or minimized, and only given on an "as-needed" basis. The SSR status, obtained from the same sources at three and six months, was also recorded. Although neither the GCS nor the SSR had previously been validated as weaning predictors in the chronic ventilator population, these parameters were chosen because they were felt to represent reasonable potential weaning predictors in our CVU population.

Study Endpoints
Patients included in analysis were followed until they were weaned, or for at least six months from the time of CVU admission. If a patient failed to wean within 6 months they were considered a weaning failure in the analysis. Successful weaning was defined as >2 weeks of liberation from mechanical ventilation for 24 hours per day within six months of admission to the CVU.

Statistics
Statistical analysis was performed using SPSS (version 6.0) and GB STAT (version 6.5) statistical software. Variables associated with weaning success on univariate analysis were used to construct a multivariate model using forward stepwise logistic regression to construct a multivariate model. Statistical significance was considered for variables with a p level of <0.05. Predictors of weaning in the training group were applied to the prospective group. Predictor accuracy for the training group was expressed using predicted and observed values for SSR status and modified GCS in determining weaning outcome.

Results
Complete data were available for all 43 patients in the training group. Thirty-one of the 59 patients in the prospective group were followed until weaned, or for at least six months and were included in the analysis. The remaining 28 patients died before six months, were transferred to an acute care facility, or were discharged to home prior to an attempt at weaning. These patients were excluded from the statistical analysis.

Demographic information including admission diagnosis for the 74 patients who completed the study is presented in Tables 1 and 2. The training and prospective groups were similar with respect to age, sex, duration of prior ventilation and admission diagnosis. There was no significant difference between the weaned and non-weaned groups for the training and prospective groups for any of the parameters shown in Table 1 and 2. A total of 37 patients were admitted with a neurologic diagnosis, which was the largest diagnostic category for both groups. The primary diagnosis in the majority (17 patients) was AE. Eight patients had suffered a CVA/ICB, 5 had either a SDH/SAH,

Table 2: Admission Diagnosis for Training and Prospective Groups by Weaning Outcome

Diagnosis	Training Group		Prospective Group		
	Weaned n = 18 (%)	Not Weaned n = 25 (%)	Weaned n = 19 (%)	Not weaned n = 12 (%)	p-value
Obstructive lung disease	1 (6)	1 (4)	2 (10)	1 (8)	NS
Acute lung injury	7 (39)	4 (16)	5 (27)	3 (25)	NS
Post surgery	2 (11)	1 (4)	2 (10)	0	NS
Other (cancer, trauma)	2 (11)	3 (12)	2 (10)	1 (8)	NS
Neurologic event	6 (33)	16 (65)	8 (43)	7 (59)	NS

NS = not significant

3 had SCD and 4 had another neurologic diagnosis, including neuropathy, seizures and CNS infection.

Eighteen patients in the training group (42%) and 19 patients (61%) in the prospective group weaned from mechanical ventilation within six months of CVU admission. Within the largest diagnostic combined category, patients with AE were unlikely to wean from mechanical ventilation, with only 24% being liberated from the ventilator in 6 months. Outcomes for other neurologic diagnosis were variable, and the small number of patients in each diagnostic category limits interpretation. Less than 40% of patients with a SCD or a CVA/ICB weaned, while >50% of those with a SDH/SAH or alternate neurologic diagnosis were successfully weaned.

One training group patient was off mechanical ventilation for 24 hours and one for 72 hours before resumption of ventilator support was required. Both of these patients were classified as weaning failures. All other patients in both groups weaned from mechanical ventilation remained off the ventilator for at least two weeks. Patients who successfully weaned did not differ in age, sex or duration of prior mechanical ventilation from those who failed to wean from mechanical ventilation for > 2 weeks within 6 months of CVU admission (Tables 1 &2). Two patients over the age of 76 successfully weaned, including one patient over the age of 90.

The duration of ventilation for the 37 patients who weaned in both groups was also similar (data not shown). Twenty-five patients weaned in three months or less, while 12 patients weaned within three to six months. Only two patients weaned from mechanical ventilation after six months (both in the training group). These patients were classified as weaning failures in the analysis.

Univariate analysis of variables associated with weaning success in the training group demonstrated that the modified GCS, SSR status and the presence of a neurologic or acute lung injury diagnosis determined at the time of CVU admission were all significant predictors of weaning outcome. Arterial blood gas values obtained in the prospective group, including the pH, PaO_2/FiO_2 ratio and alveolar-arterial PO_2 gradient did not correlate with a patient's ability to wean. Likewise, patient age, sex and duration of prior mechanical ventilation failed to predict weaning outcome. On multivariate analysis, only the modified GCS and the presence of SSR, determined at the time of admission, were predictive of weaning outcome. Patients with a modified GCS ≥ 8 were 6.5 times more likely to wean than those with a modified GCS < 8 (95% confidence interval 1.6–26.4, p=.0002) and those with SSR were 25.5 times more likely to wean than those without SSR (95% confidence interval 4.3–51.90, p=.006). Only one patient without SSR weaned within 6 months of admission. However, she had been heavily sedated at the time of SSR assessment. In no other patient was sedation or respiratory alkalosis found to account for a lack of SSR at the time of admission. When the single patient who was off mechanical ventilation for 72 hours was included as a weaning success in the analysis these results did not change significantly.

Two patients developed SSR after admission and were successfully weaned at seven and 11 months. However, these patients were included as weaning failures because they failed to wean within 6 months. No other patient in the training or prospective groups had a substantial change in the modified GCS or SSR status during follow-up at 3 and 6 months after admission.

Predicted values for modified GCS and SSR derived from the training group, and observed values for weaning outcome in the prospective group were closely correlated. (Figures 1 and 2). When the modified GCS value and SSR status were combined to predict weaning outcome, the predicted and observed values of weaning outcome were also similar. In the training group, a modified GCS ≥ 8 and the presence of SSR correctly predicted weaning out-
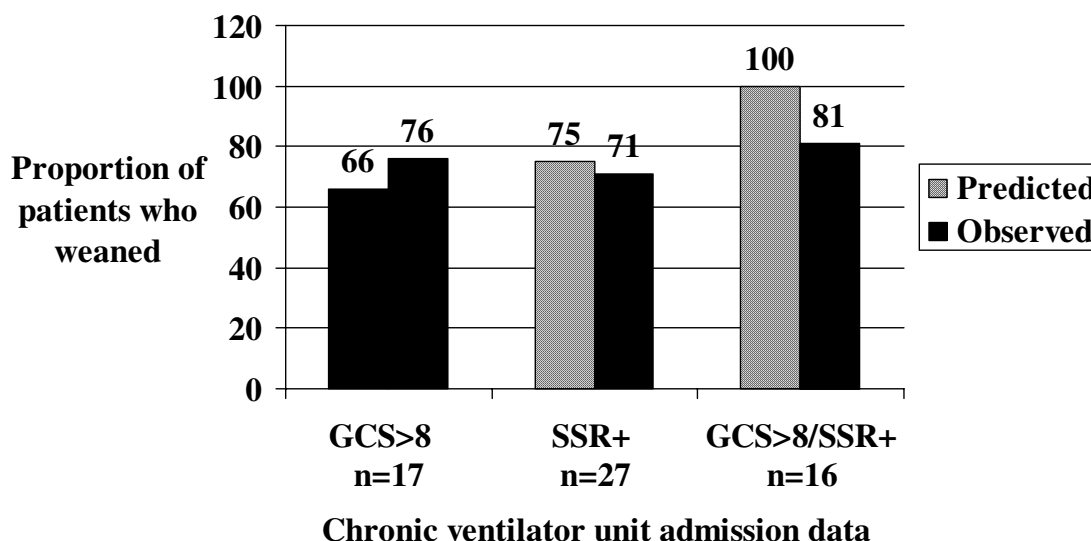
Figure 1
Predicted and Observed Values of Weaning Success in the Validation Cohort. Positive predictive values were calculated from the development cohort and applied to the validation cohort. Predicted and observed proportions of patients successfully weaned are shown.

come in 81% of patients, while a modified GCS <8 and a negative SSR predicted weaning failure in 100% of patients.

The SSR status and modified GCS value correctly predicted weaning outcome for patients admitted with various diagnoses. When data was combined for both groups of patients a positive SSR status correctly predicted weaning outcome in 84% of patients with acute lung injury, 72% of patients with a neurologic event, 80% of patients with obstructive lung disease, 100% of post-operative patients and 71% of patients admitted with another diagnosis such as trauma. Within the sub-categories of patients with a neurologic diagnosis, SSR status correctly predicted weaning outcome in 82% of those with AE, 100% in those with a C-spine injury or alternate diagnosis, but in ≤ 50% of those with SDH/SAH or ICB.

Likewise, the modified GCS value also correctly predicted weaning outcome correctly for the combined training and prospective groups. A modified GCS ≥ 8 predicted weaning success in 84% of patients with acute lung injury, 72% of patients with a neurologic event, 80% of patients with

obstructive lung disease, 66% of post-operative patients and 71% of patients with an alternate diagnosis. Again, the GCS status was more likely to correctly predict weaning outcome in patients with AE (82%) and the GCS performed better than the SSR status in patients with SDH/ICB, correctly predicting weaning outcome in 100%. However the accuracy of this parameter was 66% in SCD and ≤ 50% in patients with CVA/ICB or other neurologic diagnosis.

The final disposition of the 74 patients who successfully weaned from mechanical ventilation is shown in Table 3. Most patients were discharged home or to a long-term facility, which provided care for patients with tracheostomy tubes not requiring mechanical ventilation. Some patients remained in the CVU after weaning.

Discussion
This study suggests that a modified GCS and the presence of SSR are useful predictors of weaning for selected patients admitted to a CVU. These predictors can be applied at the time of admission, and appear to be primarily useful in CVU patients who have suffered a major neu-
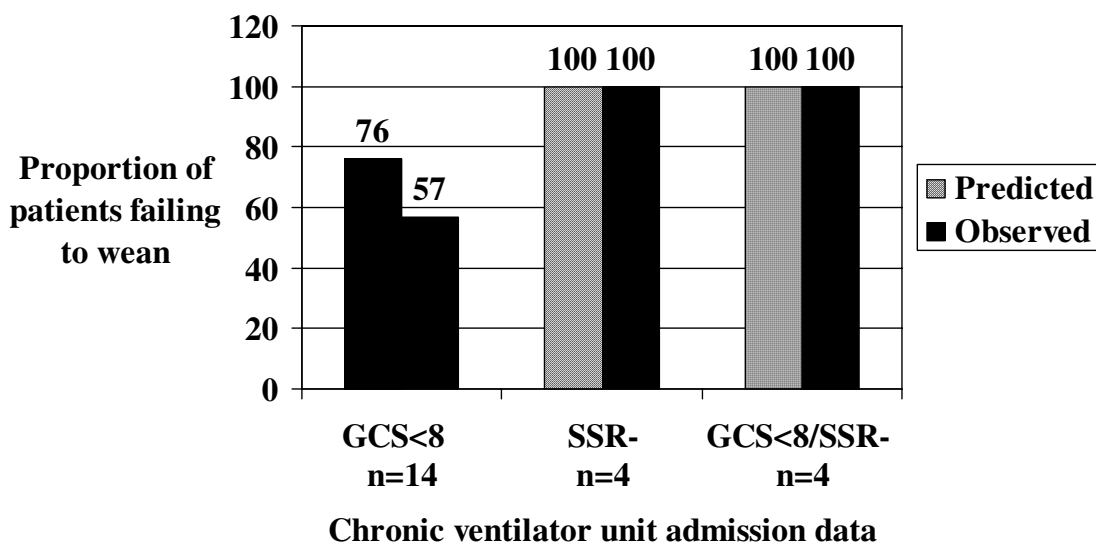
Figure 2
Predicted and Observed Values of Weaning Failure in the Validation Cohort. Negative predictive values were calculated from the development cohort and applied to the validation cohort. Predicted and observed proportions of patients failing to wean are shown.

Table 3: Final Disposition for the Training and Prospective Groups

Disposition	Training Group		Prospective Group	
	Weaned (n = 18)	Not Weaned (n = 25)	Weaned (n = 19)	Not Weaned (n = 12)
Home	6 (27%)	0	6 (32%)	0
Chronic Care	10 (56%)	1 (4%)	7 (37%)	1 (8%)
Acute Care	1 (6%)	7 (28%)	4 (21%)	3 (25%)
Deceased	0	11 (44%)	2 (11%)	2 (17%)
Remained in Chronic Ventilator Unit	1 (6%)	6 (24%)	0	6 (50%)

rologic event. Although our scoring system also successfully predicted weaning outcomes in patients with a variety of underlying disorders, the small sample size makes it difficult to draw conclusions about the utility of this model in these groups.

Patients included in this analysis were followed until successful weaning or for at least six months. This interval was considered to be reasonable since the majority of

patients admitted to a CVU require some period of rehabilitation prior to weaning attempts. Patients were required to be free from mechanical ventilation for at least two weeks to avoid misclassification of patients who tolerated only a brief period of unassisted breathing.

Thirty-seven of the patients included in the study had a neurologic diagnosis, which may have contributed to the utility of the GCS in predicting weaning outcomes. The

GCS and SSR status were more likely to predict weaning outcome correctly in the patients with AE, but had variable accuracy in the other diagnostic groups included in this analysis. This may reflect the small sample size of the other diagnostic categories. In addition, it is difficult to determine if these parameters truly predict weaning outcome, or are simply related to the patients underlying nuerologic condition. However, other investigators have also reported on the utility of the GCS in determining weaning outcomes. In one series that included 109 neurosurgical patients a GCS of 8 or greater was associated with weaning success (67% versus 21% for a GCS of less than 8). [10] The GCS has also been used to determine timing of tracheostomy in "unweanable" neurosurgery patients. [11] Direct comparison between our study and other investigations is limited by our modification of the GCS for the verbal score. In our population the modified GCS also correctly predicted weaning outcome in 83% of patients with a respiratory diagnosis, suggesting that the interaction between lung mechanics, respiratory muscle strength and sensorium reflected by this score are important determinates of weaning. However, many of these patients also had an underlying history of neurologic disease.

The presence of SSR also appears to be an accurate a predictor of weaning. Patients without SSR were extremely unlikely to wean unless a correctable respiratory depressant could be identified. Only one patient who did not have SSR at the time of admission due to sedation weaned within six months. In most patients, the lack of SSR reflected profound neurologic injury due to primary nervous system abnormalities and again may be a marker of underlying illness rather than an independent predictor of "weanability". Four patients who had a primary respiratory diagnosis were unable to maintain SSR at the time of admission. Three of these patients with a history of neurologic disease or over sedation also had a modified GCS of <8. One patient with severe chronic obstructive pulmonary disease had a modified GCS of 10, but was unable to maintain SSR, possibly due to poor respiratory muscle function or diminished respiratory drive. Two patients in the study developed SSR after admission, and were successfully liberated from the ventilator after six months. Thus, a change in the SSR status might be useful for identifying patients who can successfully wean even after prolonged CVU admission.

Several other scoring systems to predict weaning success in the chronic ventilator population have been described. [4,5] One system, derived from patients with primarily respiratory causes of ventilator dependence, incorporating several measures of pulmonary function (static compliance, airway resistance dead space to tidal volume ratio, arterial carbon dioxide partial tension ($PaCO_2$), and frequency/tidal volume) was used to derive a score predicting weaning in a cohort of 72 patients. In the 38 patients who completed a 42-day trial of weaning the model had a positive and negative predictive value of 83 and 100%, respectively. [4] The success of the model reflected the high percentage of patients with respiratory diagnoses, which increased the applicability of the pulmonary mechanics. Patients with severe neurologic impairments were excluded from the study, and no formal assessment of neurologic status was included.

Predictors of successful ventilator weaning and survival in COPD patients have also been investigated. In 42 consecutive COPD patients with acute respiratory failure requiring mechanical ventilation for >21 days, neuromuscular drive, maximal inspiratory pressure, frequency to tidal volume ratio, serum protein level and the PaCO2 were found to vary between patients who successfully weaned and those who did not. None of these indices predicted long-term survival. [12] In another cohort of COPD patients on mechanical ventilation for >14 days, survival at one year was associated with pre-morbid level of activity, FEV1, serum albumin level and severity of dyspnea. [13] The populations in these investigations were more homogenous, possibly explaining the accuracy of indices for ventilator weaning which reflect pulmonary physiology. In addition, our study is limited by the small number of patients with isolated pulmonary disease, and the lack of respiratory physiology data available.

In another study, a summary score incorporating the alveolar-arterial oxygen tension gradient, blood urea nitrogen and gender (A+B+G score) was an accurate predictor of weaning from mechanical ventilation for >1 week in a large cohort of CVU patients. [5] In our investigation gender failed to predict weaning outcomes. However, the A+B+G score was derived from a population of patients that differed considerably from ours. This underscores the conclusions of the original investigation recommending external validation of predictive models, and their application to similar populations. [5]

In both of these models, duration of prior ventilation was not found to predict weaning success. [4,5] These results are similar to our findings. In the population from which the A+B+G score was derived, younger patients had a higher rate of weaning success. However, the physiologic difference between patients ages 68 and 71 years old was not felt to be significant. [5] Age failed to predict weaning outcomes in our model, perhaps related to the small number of patients who were either very young or old.

Numerous other reports have provided details on weaning success and outcomes for chronic ventilator patients. [14-16] Direct comparisons among them are limited

because of differences in patient populations, definitions of chronic ventilator dependency and admission criteria. As an example, many CVUs require that patients have rehabilitation and weaning potential prior to admission. In addition, institutions with a large percentage of postoperative patients appear to have higher rates of weaning success. In mixed populations of CVU patients weaning success and long-term survival have been reported to be less than 40% by several investigators, which is similar to our findings. [15,16]

There are several potential limitations to this study. Pulmonary function data and pre-admission nutritional information were unavailable for analysis and might have impacted weaning outcomes. Forty-seven percent of patients in the prospective group were excluded from the analysis because they died before completing the six-month follow-up, or were transferred to another ventilator facility. The effect that these patients would have had on the accuracy of the models is uncertain. It is possible that some of these patients ultimately weaned in another ventilator facility. There were a large percentage of patients with a primary neurologic cause of ventilator dependence in both groups, and this may account for the ability of the GCS and SSR to predict weaning. In addition, standard weaning parameters such as the negative inspiratory force and rapid shallow breathing index were not routinely collected on our patients.

Conclusions
Despite the limitations noted above, the modified GCS and SSR defined in this investigation are potentially useful predictors of long-term weaning potential in similar CVU populations with a large percentage of neurologic patients. The ability of these parameters to predict weaning outcomes in CVU cohorts with a higher percentage of cardio-pulmonary disease remains unclear. Application of these weaning parameters at the time of admission to similar populations of CVU patients may help conserve resources while permitting aggressive weaning efforts to be focused on patients with a better chance of weaning success. Weaning should be reconsidered after the initial evaluation for patients in whom potential respiratory depressants can be identified, or who have a substantial change in their neurologic status.

Abbreviations
CVU=chronic ventilator unit: SSR=sustained spontaneous respirations; GCS=Glasgow Coma Scale: APACHE=acute physiologic and chronic health evaluation: $PaCO_2$= arterial carbon dioxide partial tension

Competing Interests
None declared.

Authors Contributions
KH: data collection, study design, analysis, manuscript drafting

PB: statistical analysis, manuscript drafting

MJB: study design and coordination

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