

# A randomized, controlled trial of the role of weaning predictors in clinical decision making\*

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**Objective:** Weaning predictors are often incorporated in protocols to predict weaning outcome for patients on mechanical ventilation. The predictors are used as a decision point in protocols to determine whether a patient may advance to a spontaneous breathing trial. The impact of including predictors in a weaning protocol has not been previously studied. We designed a study to determine the effect of including a weaning predictor (frequency-tidal volume ratio, or  $f/V_T$ ) in a weaning protocol.

**Design:** Randomized, blinded controlled trial.

**Setting:** Academic teaching hospitals.

**Patients:** Three hundred and four patients admitted to intensive care units at three academic teaching hospitals.

**Interventions:** Patients were screened daily for measures of oxygenation, cough and secretions, adequate mental status, and hemodynamic stability. Patients were randomized to two groups; in one group the  $f/V_T$  was measured but not used in the decision to wean ( $n = 151$ ), but in the other group,  $f/V_T$  was measured and used, using a threshold of 105 breaths/min/L ( $n = 153$ ). Patients

passing the screen received a 2-hr spontaneous breathing trial. Patients passing the spontaneous breathing trial were eligible for an extubation attempt.

**Measurements and Main Results:** Groups were similar with regard to gender, age, and Acute Physiology and Chronic Health Evaluation II score. The median duration for weaning time was significantly shorter in the group where the weaning predictor was not used (2.0 vs. 3.0 days,  $p = .04$ ). There was no difference with regard to the extubation failure, in-hospital mortality rate, tracheostomy, or unplanned extubation.

**Conclusions:** Including a weaning predictor ( $f/V_T$ ) in a protocol prolonged weaning time. In addition, the predictor did not confer survival benefit or reduce the incidence of extubation failure or tracheostomy. The results of this study indicate that  $f/V_T$  should not be used routinely in weaning decision making. (Crit Care Med 2006; 34:2530–2535)

**KEY WORDS:** adult; weaning parameters; weaning predictors; weaning protocol; ventilator weaning

Invasive mechanical ventilation is lifesaving for patients with acute respiratory failure, but it is also associated with substantial risks. Therefore, once adequate recovery occurs, efforts focus on liberating (wean-

ing) the patient from the ventilator as expeditiously as possible. For the past 3 decades, the standard of care has been to use one or more bedside physiologic measurements—*weaning predictors*—to decide if a patient is ready to breathe spontaneously as the first step to liberation (1). Specifically, it has been considered unsafe to discontinue mechanical ventilation if the vital capacity or tidal volume is reduced, the negative inspiratory force is inadequate, or the respiratory rate is too fast, or if a pattern of a rapid and shallow breathing is present during a brief trial of spontaneous breathing. Although these weaning predictors have been extensively studied, their direct impact on outcome has never been investigated. To address this issue, we conducted a randomized, controlled trial to specifically examine the role of weaning predictors in clinical decision making.

## METHODS

The objective of the study was to identify the effect of incorporating a weaning predictor

in a daily screen to assess weaning readiness on the duration of mechanical ventilation. To test the hypothesis that including a weaning predictor (frequency-tidal volume ratio, or  $f/V_T$ ) in a daily screen would not reduce weaning time or total duration of mechanical ventilation, all mechanically ventilated patients admitted to the intensive care units (ICUs) of three tertiary care medical centers were considered for enrollment. The study was conducted at the medical ICUs at Tufts-New England Medical Center (T-NEMC) and St. Elizabeth Medical Center and at the multidisciplinary ICU of the Ottawa Hospital General Campus. A team of critical care medicine physicians supervising fellows and resident physicians led the ICUs at the three sites. The institutional review boards of the participating hospitals approved the study design and protocol; patients or their surrogates provided informed consent.

## Patient Selection

All adult patients were eligible once mechanically ventilated for  $\geq 24$  hrs. Exclusion criteria for enrollment were age  $\leq 18$  yrs, inability to obtain an informed consent, an expected survival  $< 48$  hrs, primary neurologic event without

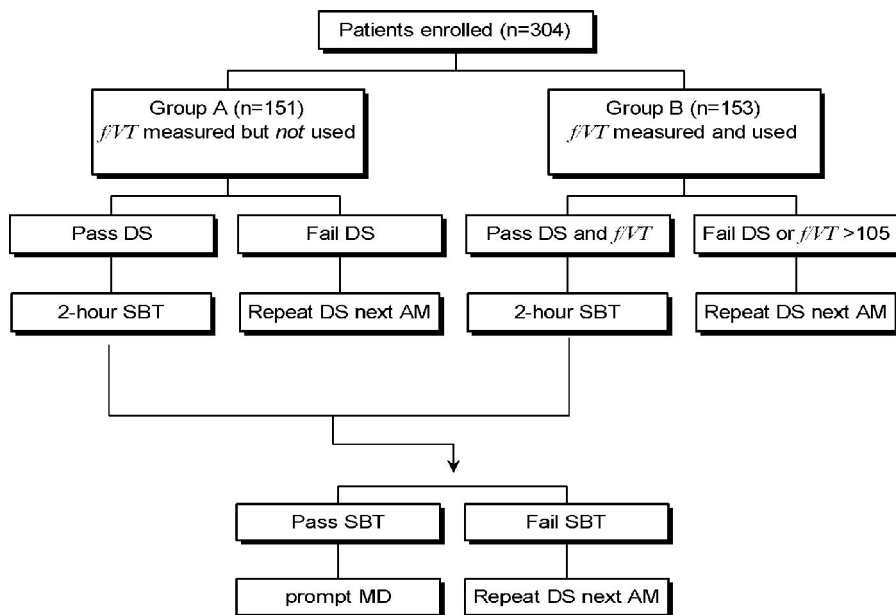
\*See also p. 2676.

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The authors have not disclosed any potential conflicts of interest.

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DOI: 10.1097/01.CCM.0000236546.98861.25



**Figure 1.** Patients enrolled in the study underwent a daily screen (DS) to assess for weaning readiness. To pass the DS, five criteria had to be satisfied: The patient a) had a  $\text{PaO}_2/\text{FiO}_2 \geq 150$  or oxygen saturation  $>90\%$  at  $\text{FiO}_2 \leq 0.4$ ; b) was on positive end-expiratory pressure  $\leq 5$  cm  $\text{H}_2\text{O}$ ; c) had a mean arterial pressure of  $\geq 60$  mm Hg without vasopressor agents; d) was awake or easily arousable; and e) had adequate coughing during suctioning and did not require suctioning more often than every 2 hrs. Once these criteria were satisfied, a weaning predictor (frequency-tidal volume ratio, or  $f/V_T$ ) was measured but not included in the assessment of weaning readiness for group  $f/V_T-$  but was included in the weaning assessment for group  $f/V_T+$ . Patients passing daily screening criteria automatically received a 2-hr spontaneous breathing trial (SBT). A trial was considered successful and physicians were asked to approve extubation when the patient could breathe spontaneously for 2 hrs, whereas failed patients continued to be screened daily until extubation, 21 days after enrollment, performance of tracheostomy, death, or withdrawal of care. (Refer to text for details.)

expectation for recovery, or current participation in weaning trials. A research coordinator or a critical care medicine fellow who was not involved in the patients' routine care screened and enrolled eligible patients in the study at the approval of the managing physician.

### Study Methods and Protocols

Patients were randomized to two groups, and assignment was based on a computerized randomization scheme by the individual centers using opaque sealed envelopes. Patient were randomized into one group where a weaning predictor ( $f/V_T$ ) was measured but not included in the assessment of weaning readiness ( $f/V_T-$ ) or another group where the weaning predictor was measured and included in the weaning assessment ( $f/V_T+$ ) (Fig. 1). Sedation was administered at the discretion of the attending physicians. All patients underwent a daily screen (2) by a respiratory care practitioner every morning at  $\sim 7$  am—the components of the daily screen for each group are outlined subsequently. Physicians caring for the patients were blinded to randomization and daily screen results. Patients passing daily screening criteria automatically received a 2-hr spontaneous breathing trial (SBT). Five

criteria had to be satisfied to pass the daily screening: a) the ratio of  $\text{PaO}_2$  to  $\text{FiO}_2$  was  $\geq 150$  or oxygen saturation was  $>90\%$  at  $\text{FiO}_2$  of  $\leq 0.4$ ; b) the patient was on positive end-expiratory pressure  $\leq 5$  cm  $\text{H}_2\text{O}$ ; c) the mean arterial pressure was  $\geq 60$  mm Hg without vasopressor agents (dobutamine or dopamine was allowed in doses  $\leq 5$   $\mu\text{g}/\text{kg}$  body weight/min); d) the patient was awake or easily arousable; and e) the patient had adequate coughing during suctioning and did not require suctioning more often than every 2 hrs. An additional requirement for patients randomized to  $f/V_T+$  to pass the daily screen was an  $f/V_T$  that could not exceed 105 breaths/min/L (3). To measure the  $f/V_T$ , the patient was removed from mechanical ventilation and the endotracheal tube was connected to a spirometer (3). Minute ventilation was measured in the first minute after ventilator discontinuation, and the respiratory rate was counted. Tidal volume was determined by the equation  $V_T = V_E/f$ , and the  $f/V_T$  was then calculated. In patients randomized to  $f/V_T-$  group,  $f/V_T$  was measured but the results were not used to assess weaning readiness. Patients not satisfying the oxygenation or hemodynamic criteria did not have the  $f/V_T$  measurement on that day. If any of the components of the daily screen were not

met, the patient did not undergo a weaning trial that day and continued to be screened daily. The weaning consisted of a 120-min trial of spontaneous breathing performed on up to 5 cm  $\text{H}_2\text{O}$  of continuous positive airway pressure and 7 cm  $\text{H}_2\text{O}$  of pressure support. A *priori* graded criteria were set to define failure to tolerate the weaning trial and were divided into three grades (Appendix A). For the SBT to be considered failed, any one Grade I criteria, any two Grade II criteria, or one Grade II criteria with both Grade III criteria had to be met. The SBT was terminated and mechanical ventilation reinstated at the original settings if the patient's nurse, physician, or respiratory therapists, who were blinded to the randomization, identified any of the set predictors for poor tolerance. Changes of the ventilator setting were only allowed at the discretion of the managing physician. The failed trial of spontaneous breathing could be repeated once at the discretion of the managing physician. A trial was considered successful and physicians were asked to approve extubation when the patient could breathe spontaneously for 2 hrs. Patients continued to be screened daily until extubation, 21 days after enrollment, performance of tracheostomy, death, or withdrawal of care. All patients were followed until hospital discharge or death.

### Study Outcome and Variables

The primary outcome for the study was weaning time, defined as the duration of mechanical ventilation from the first daily screening until reaching a study end point (extubation, 21 days from enrollment, performance of tracheostomy, death, or withdrawal of care). The total duration of mechanical ventilation was calculated as the time from intubation until planned extubation; this included the time before randomization, mechanical ventilation time after reintubation, tracheostomy, or mechanical ventilation beyond 21 days after enrollment. Reintubation rate for failed extubation was defined as the need for reintubation within 72 hrs after an extubation. Other variables included were the ICU length of stay, hospital length of stay, and hospital mortality rate.

### Statistical Analysis

Statistical testing was two sided using a type I error rate of .05. Analyses were conducted on an intention to treat basis and performed with SPSS (version 11.5; SPSS, Chicago, IL). A sample size of 300 was estimated to obtain an 80% power, and a two-tailed significance level of .05 was used to detect a 1-day difference between groups with respect to weaning time. Chi-square tests and analysis of variance were used to compare patient characteristics by admitting diagnoses. The chi-square test with Yates' continuity correction or Fisher's exact test

Table 1. Baseline characteristics of study patients

| Characteristic                                   | f/V <sub>T</sub> Not Included<br>(n = 151) | f/V <sub>T</sub> Included<br>(n = 153) | p Value           |
|--|--|--|-------------------|
| Age, yrs   | 65.4 ± 16.8                                | 63.7 ± 16.6                            | .37 <sup>a</sup>  |
| Male gender, n (%)                               | 80 (52)                                    | 83 (55)                                | .82 <sup>b</sup>  |
| APACHE II score                                  | 21 ± 7                                     | 21 ± 7                                 | .88 <sup>a</sup>  |
| Required MV at hospital admission, n (%)         | 81 (54)                                    | 85 (55)                                | .80 <sup>b</sup>  |
| Days to randomization <sup>c</sup>               | 2 (1, 4)                                   | 2 (1, 4)                               | .11 <sup>d</sup>  |
| ICU location-randomization, n <sup>e</sup>       |  |  | >.20 <sup>f</sup> |
| ICU 1  | 55   | 55                                     |                   |
| ICU 2  | 55   | 55                                     |                   |
| ICU 3  | 41   | 43                                     |                   |
| Cause of respiratory failure, n (%) <sup>g</sup> |  |  | <sup>b</sup>      |
| ARDS   | 15 (10)                                    | 17 (11)                                | .67               |
| COPD or asthma exacerbation                      | 25 (17)                                    | 19 (12)                                | .30               |
| Pneumonia  | 43 (28)                                    | 36 (24)                                | .32               |
| Congestive heart failure                         | 9 (6)                                      | 15 (10)                                | .21               |
| Gastrointestinal or liver disease                | 5 (3)                                      | 5 (3)                                  | .98               |
| Other cardiac disease                            | 8 (5)                                      | 9 (6)                                  | .82               |
| Drug overdose                                    | 3 (2)                                      | 6 (4)                                  | .32               |
| Severe sepsis                                    | 20 (13)                                    | 12 (8)                                 | .12               |
| Surgery or trauma                                | 14 (9)                                     | 13 (8)                                 | .81               |
| Neurologic emergencies                           | 10 (7)                                     | 18 (12)                                | .12               |
| Other  | 5 (3)                                      | 7 (5)                                  | .80               |
| Comorbid conditions, n (%)                       |  |  |                   |
| Cirrhosis  | 9 (6)                                      | 7 (5)                                  | .58               |
| HIV  | 4 (3)                                      | 5 (3)                                  | .70               |
| Cancer   | 17 (11)                                    | 17 (11)                                | .96               |
| Organ transplant                                 | 2 (1)                                      | 0 (0)                                  | .15               |

f/V<sub>T</sub>, frequency-tidal volume ratio; APACHE, Acute Physiology and Chronic Health Evaluation; MV, mechanical ventilation; ICU, intensive care unit; ARDS, acute respiratory distress syndrome; COPD, chronic obstructive pulmonary disease.

<sup>a</sup>Independent two-sample *t*-test; <sup>b</sup>chi-square test with Yates' continuity correction; <sup>c</sup>data are presented as median values (interquartile range, 25th and 75th percentiles), days to randomization are considered the time from respiratory failure to enrollment in the study; <sup>d</sup>Mann-Whitney rank-sum test, data are expressed as median (interquartile range); <sup>e</sup>ICU locations are indicated in the text; <sup>f</sup>chi-square analyses compared across categories; <sup>g</sup>occasionally more than one cause of respiratory failure was present per patient. Values are expressed as mean (±SD) unless otherwise indicated. *p* < .05 was considered significant for all comparisons.

was used to test for associations between categorical variables. Continuous variables are presented as the mean ± SD and were compared using the independent two-sample Student's *t*-test. Highly skewed data were analyzed with the nonparametric Mann-Whitney rank-sum test and presented as median values and the 25th and 75th percentiles. A log-linear regression model with the Poisson-distributed outcome was used to assess the impact of assignment arm on weaning time adjusting for covariates: Log [E(Y)] = βX, where Y is weaning time in days, X is a matrix of covariates, and β is a vector of regression parameters (4). The outcome variable was well approximated by the Poisson distribution and examined by chi-square test. Candidate variables for the log-linear regression model were selected *a priori*, and variables of importance were tested including age, gender, severity of illness, location of the ICU, causes of respiratory failure, comorbid conditions, and time to randomization (Table 1). Using sequential multivariate modeling procedure, we tested the relative impact of each explanatory variable on weaning time. In the final model presented in the article, we selected the variables that were

statistically significant (<.05) in sequential multivariate modeling. These variables are age, female gender, acute disease processes, and randomization assignment to a weaning predictor (f/V<sub>T</sub>+). The results of the regression model are presented as estimates of the relative risk associated with specific covariates along with the 95% confidence interval (CI). For example, the relative risk of an increase in weaning time associated with the intervention arm would be estimated using the following equation: RR<sub>X,1</sub> = exp{β<sub>1</sub>}; CI = exp{β<sub>1</sub> ± 1.96Sβ<sub>1</sub>} where Sβ<sub>1</sub> is a standard error of a regression parameter β<sub>1</sub>.

## RESULTS

### Demographic Variables

During the study period, 1,006 patients in three ICUs were screened for eligibility, of which 304 were enrolled in the study (163 men and 141 women). For the remaining 702, either they satisfied exclusion criteria or informed consent could not be obtained. Of the 304 en-

rolled patients, 151 patients were enrolled in f/V<sub>T</sub>- group, where the weaning predictor was not included in the decision to wean, and 153 patients were enrolled in f/V<sub>T</sub>+ group.

The groups were similar in gender, age, Acute Physiology and Chronic Health Evaluation II score, the percentage of patients requiring mechanical ventilation on hospital admission, location of the ICU, acute and chronic disease processes, and days to randomization (Table 1). Protocol violations were equal among groups: 9 patients underwent an SBT in the f/V<sub>T</sub>- group without passing the daily screen compared with 16 in the f/V<sub>T</sub>+ group (*p* > .2). Extubation was delayed for 11 patients in the f/V<sub>T</sub>- group compared with 12 in f/V<sub>T</sub>+ (*p* > .2). In the f/V<sub>T</sub>- group, one patient was excluded after enrollment at the request of the attending physician and another at the request of the family.

### Study Outcomes

**Duration on Weaning Protocol.** The median duration for weaning time was 2 days for the f/V<sub>T</sub>- group (interquartile range [IQR] 1, 5) and 3 days (IQR 2, 6) for f/V<sub>T</sub>+ (*p* = .04) (Table 2). The median duration for weaning time for patients who actually underwent weaning after we eliminated those who reached other study end points (performance of tracheostomy, death, or withdrawal of care) was 2 days (IQR 1, 4) for the f/V<sub>T</sub>- group vs. 3 days (IQR 1, 4) for f/V<sub>T</sub>+ group (*p* = .03). The groups had similar total duration on mechanical ventilation, 6 (IQR 3, 10) vs. 6 (IQR 2, 11) days (*p* = .77), and the median duration for ICU stay and hospital total length of stay were 9 (IQR 6, 17) vs. 9 (IQR 5, 15) days (*p* = .64) and 19 (IQR 13, 35) vs. 19 (IQR 10, 37) days (*p* = .62), respectively. There was no difference between the groups with regard to reintubation rate (*p* = .40), all-cause hospital mortality rate (*p* = .38), tracheostomy (*p* = .30), and unplanned extubation rate (*p* = .25) (Table 3). Overall, 125 patients in each group (82.8% vs. 81.7%) were extubated while on protocol (*p* = .81). The median delay in extubation after passing an SBT was 16 mins (IQR 0, 150) for the f/V<sub>T</sub>+ group compared with 18 mins (IQR 0, 165) for the f/V<sub>T</sub>- group (*p* = .41). Extubation was delayed for ≥12 hrs in 21 patients in each group. No complication occurred during the daily screening, and no adverse event was observed with the spontaneous breathing trials. The weaning time for patients in the f/V<sub>T</sub>-

Table 2. Comparison of outcome between the two study groups

| Total Study Cohort <sup>b</sup> | f/V <sub>T</sub> Not Included | f/V <sub>T</sub> Included | p Value <sup>a</sup> |
|---------------------------------|-------------------------------|---------------------------|----------------------|
| No.                             | 151                           | 153                       |                      |
| Weaning time, days              | 2 (1, 5)                      | 3 (2, 6)                  | .04                  |
| Days on mechanical ventilation  | 6 (3, 10)                     | 6 (2, 11)                 | .77                  |
| ICU days                        | 9 (6, 17)                     | 9 (5, 15)                 | .64                  |
| Hospital days                   | 19 (13, 35)                   | 19 (10, 37)               | .62                  |

f/V<sub>T</sub>, frequency-tidal volume ratio; ICU, intensive care unit; Weaning time, time from first daily screening until the achievement of a study end point; Days on mechanical ventilation, the total duration on mechanical ventilation throughout hospitalization; ICU days, total intensive care unit length of stay expressed in days. Hospital days, total hospital length of stay expressed in days.

<sup>a</sup>Statistical testing is two sided and *p* < .05 is considered significant, with comparison analyses performed by Mann-Whitney rank-sum test; <sup>b</sup>data are presented as median values (interquartile range, 25th and 75th percentiles).

Table 3. Complications of respiratory failure

|                      | f/V <sub>T</sub> Not Included | f/V <sub>T</sub> Included | p Value |
|----------------------|-------------------------------|---------------------------|---------|
| Reintubation         | 28 (18)                       | 23 (15)                   | .40     |
| Mortality            | 40 (26)                       | 34 (22)                   | .38     |
| Tracheostomy         | 10 (7)                        | 6 (4)                     | .30     |
| Unplanned extubation | 14 (9)                        | 9 (6)                     | .25     |
| >21 days on protocol | 7 (5)                         | 5 (3)                     | .54     |

f/V<sub>T</sub>, frequency-tidal volume ratio; Extubated, successfully liberated from mechanical ventilation before hospital discharge; Reintubated, the patient required reinstitution of mechanical ventilation within 72 hrs after extubation; Mortality, all-cause hospital mortality.

Chi-square test with Yates' continuity correction was used for all comparisons with a significance level of .05. Values are number of patients (%).

group who had f/V<sub>T</sub> >105 on their first weaning attempt (n = 35) was 2 days (IQR 1, 5) in comparison (n = 30) with 4 days (IQR 3, 7) for similar patients in the f/V<sub>T</sub>+ arm with f/V<sub>T</sub> >105 on their first attempt (*p* = .015). Among the 35 patient in the f/V<sub>T</sub>- group who underwent a spontaneous weaning trial, 18 patients passed their first trial whereas 17 failed (*p* > .5). Additionally, among 30 patients with f/V<sub>T</sub> <105 on their first weaning attempt who failed their spontaneous breathing trial, 12 were in the f/V<sub>T</sub>+ arm in comparison with 18 in the f/V<sub>T</sub>- arm (*p* = 0.1). A log-linear regression model of the weaning time as the dependent variable with adjustments for age, gender, severity of illness scores, acute and chronic disease processes, time to randomization, and randomization assignment was constructed. The results of modeling were presented as the relative risks for the outcome of interest—weaning time (Fig. 2). The results of modeling demonstrated that adding a weaning predictor (i.e., f/V<sub>T</sub>) to a daily screen was independently associated with increased weaning time with an adjusted relative risk of 1.213 (95% CI, 1.087–1.354).

The adjusted relative risks of an increase in weaning time associated with

some acute conditions were also significant: 1.474 (IQR 1.240–1.753) for sepsis, 1.383 (IQR 1.133–1.689) for congestive heart failure, 1.383 (IQR 1.133–1.689) for acute respiratory distress syndrome, and 1.725 (IQR 1.410–2.110) for the presence of pneumonia. Other independent predictors identified in the model were age and female gender, with adjusted relative risks of 0.995 (IQR 0.991–0.998) for each year of age, and 1.163 (IQR 1.042–1.299) for female gender (Fig. 2). In summary, including the f/V<sub>T</sub> in the screen increased weaning time even after we adjusted for the other factors that also were associated with longer weaning times.

## DISCUSSION

Mechanical ventilation is associated with numerous complications, the risk of which may increase with longer duration of intubation (5). The development of complications, especially ventilator-associated pneumonia, increases mortality rate, prolongs stay in the ICU, and increases health care costs. Therefore, efforts to identify the earliest time at which patients can be liberated from the ventilator are indicated to minimize exposure to these complications.

Another goal of prediction is the avoidance of premature trials of spontaneous breathing. Failed trials of spontaneous breathing may precipitate respiratory muscle fatigue, as assessed by diaphragmatic tension-time index and electromyogram, or muscle injury (6–11). In normal subjects, diaphragm fatigue, induced by inspiratory resistive breathing, can take ≥24 hrs to recover. Therefore, failed spontaneous breathing trials might prolong the duration of mechanical ventilation by adversely effecting subsequent weaning efforts.

To better inform decision making, investigators have tried to identify physiologic measurements to serve as predictors of weaning outcome. More than 50 different such weaning predictors have been studied (12). These studies have been exclusively observational, with predictors measured and then correlated with weaning outcome. Weaning predictors have been used to determine eligibility for randomization in trials comparing different weaning techniques (13–15). Yet these studies did not determine the role of these tests, as patients not satisfying predictor criteria were *a priori* considered not ready for weaning.

Our study represents the first randomized, controlled trial that prospectively tested whether the use of a weaning parameter affected the rate of weaning from mechanical ventilation. We used the f/V<sub>T</sub> because, of the most extensively studied predictors, it appears to be most accurate, is independent of patient effort/cooperation, and can be easily measured at the bedside (2, 11). Bias was minimized by blinding clinicians to the daily screen results, allowing no other weaning predictor measurements, and mandating a spontaneous breathing trial for patients satisfying screen criteria. Use of the f/V<sub>T</sub> did not improve weaning outcome; in fact, in both univariate and multivariate analyses, the f/V<sub>T</sub> was associated with longer duration of weaning. Furthermore, use of the f/V<sub>T</sub> did not shorten the total duration of mechanical ventilation, the likelihood of requiring prolonged ventilation or tracheostomy, or the length of ICU or hospital stay. Patients who had weaning decisions made independent of the f/V<sub>T</sub> did not suffer a higher reintubation or mortality rate.

There are several explanations why use of a weaning predictor failed to improve outcome. A recent, comprehensive, evidence-based medicine review found that most weaning predictor measure-

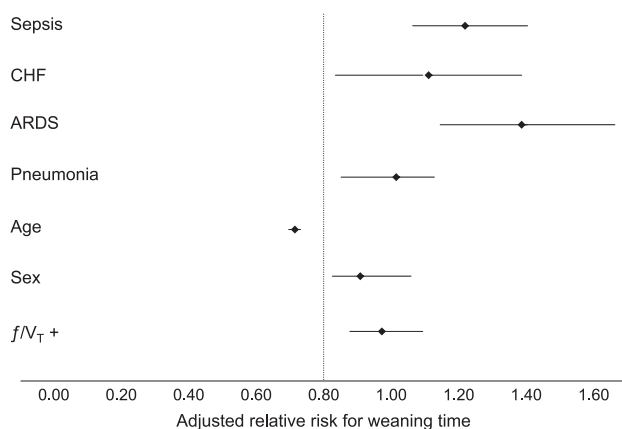


Figure 2. Adjusted relative risks with 95% confidence intervals based on the log-linear regression model for randomization arm (weaning predictor: frequency-tidal volume ratio, or  $f/V_T$ ) and six independent predictors. The results of modeling demonstrated that adding a weaning predictor to a daily screen was independently associated with increased weaning time. CHF, congestive heart failure; ARDS, acute respiratory distress syndrome.

ments fail to indicate clinically significant changes in the probability of weaning success or failure. For example, just eight of 50 predictors (minute ventilation, negative inspiratory force, maximal inspiratory pressure,  $V_T$ , respiratory frequency,  $f/V_T$ , airway occlusion pressure at 0.1 sec divided by maximal inspiratory pressure, and compliance, respiratory rate, oxygenation,  $P_{I_{max}}$ ) (3) had any predictive capacity. Only the latter two predictors were associated with the high likelihood ratios that translate into large, clinically significant changes in the probability of success or failure, but these are not easy to measure and too few patients have been studied. Of the extensively investigated predictors, the  $f/V_T$  is most accurate but even this measurement is seldom associated with more than small to moderate changes in the probability of success or failure (16). Therefore, weaning predictors may not improve outcome because the test is insufficiently accurate to inform decision making. As an example, Ely et al. (2) found that nearly one third of patients never passing a daily screen, often solely because of an  $f/V_T > 105$  breaths/L/min, were still successfully liberated from the ventilator. Our study showed that omitting the  $f/V_T$  as a screening step did not alter the duration of mechanical ventilation but accelerated the weaning process, with no adverse consequences. The weaning time was shorter in the  $f/V_T$ - group, and both groups had similar time to randomization. We suspect the absence of a statistically shorter duration of mechanical ventilation to be related to management strategies by physicians that are unrelated to the study protocol. The study protocol

was complete once a study end point was reached.

Alternatively, independent of weaning predictor accuracy, the lack of impact may derive from the nature of failed weaning trials. The premise has been that such trials must be avoided because they adversely effect outcome. There is no definitive evidence that a carefully monitored, but unsuccessful, trial of spontaneous breathing is detrimental to weaning outcome. To the contrary, in a study of 1,067 patients undergoing daily screens, only a single major complication (0.1%) could be possibly attributed to a failed SBT (17). Moreover, recent work indicates that clinically significant respiratory muscle fatigue may occur infrequently during well-monitored but failed weaning trials. Using twitch stimulation of the phrenic nerve, Laghi et al. (18) found that none of 11 patients failing weaning trials developed low-frequency fatigue. Even should fatigue develop, recovery may be much more rapid than previously thought (19, 20). The use of weaning predictors should be limited to those that indicate a trial of spontaneous breathing can be safely undertaken. Since undergoing a spontaneous breathing trial has proven to be safe, any predictor that has  $< 100\%$  negative predictive value can only impede weaning and delay extubation.

Although our study indicates no role for the routine application of the  $f/V_T$ , many other predictors are available. Unfortunately, the most promising of these either require special equipment or are too complex for easy bedside use. Because 75% of patients are easily liberated from the ventilator, it seems unlikely that

these more complicated measurements will prove useful. Nevertheless, one possible role for weaning predictors is in the evaluation of patients intolerant of spontaneous breathing with a goal of identifying reversible causes of weaning failure.

## ACKNOWLEDGMENTS

We are deeply indebted to all the nurses and respiratory therapists at Tufts-New England Medical Center, St. Elizabeth Medical Center, and Ottawa Hospital General Campus ICUs for making this study possible.

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## APPENDIX A

### Criteria Used to Define Failure to Tolerate the Spontaneous Breathing Trial

#### Grade 1 criteria

1.  $\text{PaO}_2 < 60$  mm Hg or arterial oxygen saturation  $< 90\%$  on  $\text{FiO}_2$  of  $\geq 40\%$

2. An increase in  $\text{PaCO}_2$  of  $> 10$  mm Hg from preweaning value or a decrease in the pH  $> 0.10$
3. Respiratory rate of  $> 40$  breaths/min for  $> 10$  mins
4. Decrease in the systolic blood pressure by  $> 20\%$ , or to a value  $< 80$  mm Hg

#### Grade II criteria

1. Heart rate  $> 140$  beats/min or  $< 50$  beats/min for  $\geq 5$  mins
2. A sustained increase of systolic blood pressure  $> 20\%$
3. Signs of increase of work of breathing for  $\geq 15$  mins
4. Respiratory rate exceeding 35 breaths/min for  $> 10$  mins

#### Grade III criteria

1. Diaphoresis
2. Agitation