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A PROSPECTIVE STUDY OF INDEXES PREDICTING THE OUTCOME OF TRIALS OF WEANING FROM MECHANICAL VENTILATION

KARL L. YANG, M.D., AND MARTIN J. TOBIN, M.D.

Abstract *Background.* The traditional predictors of the outcome of weaning from mechanical ventilation — minute ventilation ($\dot{V}_E$) and maximal inspiratory pressure ($P_I$max) — are frequently inaccurate. We developed two new indexes: the first quantitates rapid shallow breathing as the ratio of respiratory frequency to tidal volume (f/V_T), and the second is termed CROP, because it integrates thoracic compliance, respiratory rate, arterial oxygenation, and $P_I$max.

Methods. The threshold values for each index that discriminated best between a successful and an unsuccessful outcome of weaning were determined in 36 patients, and the predictive accuracy of these values was then tested prospectively in an additional 64 patients. Sensitivity and specificity were calculated, and the data were also analyzed with receiver-operating-characteristic (ROC) curves, in which the proportions of true positive results and false positive results are plotted against each other for a number of threshold values of an index; the area under the curve reflects the accuracy of the index.

Results. Sensitivity was highest for $P_I$max (1.00), followed closely by the f/V_T ratio (0.97). Specificity was highest for the f/V_T ratio (0.64) and lowest for $P_I$max (0.11). The f/V_T ratio was the best predictor of successful weaning, and $P_I$max and the f/V_T ratio were the best predictors of failure. The area under the ROC curve for the f/V_T ratio (0.89) was larger than that under the curves for the CROP index (0.78, $P<0.05$), $P_I$max (0.61, $P<0.001$), and $\dot{V}_E$ (0.40, $P<0.001$).

Conclusions. Rapid shallow breathing, as reflected by the f/V_T ratio, was the most accurate predictor of failure, and its absence the most accurate predictor of success, in weaning patients from mechanical ventilation. (N Engl J Med 1991; 324:1445-50.)

ALTHOUGH an experienced physician may be able to foretell the likely outcome of trying to wean a patient from mechanical ventilation, it is desirable to have predictive indexes that can be easily measured and widely applied. The purposes of such indexes are to identify the earliest time that a patient can resume spontaneous breathing and to identify patients in whom a trial of weaning is likely to fail, so that cardiorespiratory distress or collapse can be avoided. In addition, such indexes assess many different physiologic functions and may provide insight into the reasons for dependence on a ventilator.[1]

A number of indexes, such as vital capacity,[2] maximal inspiratory pressure ($P_I$max),[2,3] and minute ventilation ($\dot{V}_E$),[3-5] have been proposed as accurate predictors of the outcome of weaning, but in recent studies their predictive power has been very poor.[6-9] The discrepancy in results between the original study and more recent ones may be due to several factors, including differences in patient populations[3,6,8] or in techniques of measurement,[10] and the lack of objective criteria to define weaning outcome. Another reason why a predictive index may perform poorly is that it does not accurately reflect the true pathophysiologic determinants of the outcome of weaning.

Since many factors can be responsible for the failure of an attempt to wean a patient from mechanical ventilation, we reasoned that accurate prediction is more likely with an index that integrates a number of physiologic functions.[11] We developed two new indexes. The first is the ratio of respiratory frequency (f) to tidal volume (V_T), which quantitates the extent of rapid shallow breathing — a common finding in patients in whom a weaning trial fails.[12] The second index incorporates a measure of pulmonary gas exchange and an assessment of the relation between the demands placed on the respiratory system and the capacity of the respiratory muscles to handle them. We compared these new indexes with traditional ones with regard to accuracy. The study was divided into two parts: first, the threshold values of the indexes that discriminated best between successful weaning and weaning failure were determined; second, the accuracy of each index was assessed prospectively in an

From the Division of Pulmonary and Critical Care Medicine, the University of Texas Health Science Center at Houston (K.L.Y.), and the Division of Pulmonary and Critical Care Medicine, Hines Veterans Affairs Hospital, and the Loyola University of Chicago Stritch School of Medicine, Chicago (M.J.T.). Address reprint requests to Dr. Yang at the Division of Pulmonary and Critical Care Medicine, the University of Texas Health Science Center at Houston, 6431 Fannin, Suite 1.274, Houston, TX 77030.

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additional group of patients. The accuracy of the various indexes was also assessed with receiver-operating-characteristic (ROC) curves.[13,14]

Methods

Patients

One hundred patients (46 men and 54 women; mean age [±SE], 59.6±1.7 years) who were clinically stable and whose primary physicians considered them ready to undergo a weaning trial were recruited from our medical intensive care units. The patients had received 8.2±1.1 days of ventilator support. Their physicians were blinded to the study design and the measurements obtained, although arterial blood gas values and routine measurements by respiratory therapists ($P_I$max, thoracic compliance, and $\dot{V}_E$ and its subdivisions) were available to them. The decision to extubate a patient or reinstitute mechanical ventilation was made solely by the primary physician. The study was approved by the institutional ethics committee of the University of Texas Health Science Center.

Index of Rapid Shallow Breathing

While each patient breathed spontaneously for one minute, rapid shallow breathing was quantitated as the respiratory frequency (the number of breaths per minute) divided by the V_T in liters.

Integrative Index

The fraction of maximal inspiratory muscle strength used in each breath, or what may be termed the fraction of the inspiratory-effort reserve — i.e., the ratio of mean inspiratory pressure (P_I) to $P_I$max — is an important determinant of respiratory-muscle fatigue[15] and can be calculated as follows:

(1) Fraction of inspiratory-effort reserve per breath = P_I/P_Imax.

For a given V_T, P_I is inversely proportional to the "dynamic compliance" of the respiratory system (C_{dyn}).[16] Thus, equation 1 can be expressed as follows:

(2) Fraction of inspiratory-effort reserve per breath ∝ $(1/C_{dyn})/P_I$max.

Likewise, an index of the rate of energy expenditure per minute can be obtained by multiplying equation 2 by the respiratory rate (the number of breaths per minute):

(3) Rate of energy expenditure per minute ∝ rate/($C_{dyn} \times P_I$max).

For convenience, the elements of equation 3 can be inverted so that a high value indicates that respiratory demands are well matched by respiratory-muscle strength. A measure of gas exchange — specifically, the ratio of arterial to alveolar oxygen tension (PaO_2/PAO_2)[17] — is also incorporated, because in some patients a weaning trial fails because of impaired oxygenation rather than ventilatory-pump failure. The final form of the equation is

(4) Integrative index = ($C_{dyn} \times P_I$max $\times$ [PaO_2/PAO_2])/rate,

which we have termed the CROP index, an acronym for compliance, rate, oxygenation, and pressure.

Data Collection

During mechanical ventilation, the delivered volume was measured at the endotracheal tube with a calibrated spirometer (Boehringer Laboratory, Wynnewood, Pa.). Airway pressure was measured with a differential pressure transducer (model 78905A, Hewlett-Packard, Waltham, Mass.) attached to the endotracheal tube. The inflationary pressure needed to overcome the elastic recoil of the respiratory system was measured as the plateau in airway pressure that resulted from temporary occlusion of the expiratory tubing at end-inspiration.[18] The patient's airway was also occluded at end-expiration to detect the presence of spontaneous positive end-expiratory pressure.[19] The "static compliance" (C_{st}) of the respiratory system was calculated as volume delivered/(plateau pressure − positive end-expiratory pressure),[18] and the "dynamic compliance" (C_{dyn}) as volume delivered/(peak airway pressure − positive end-expiratory pressure).[18]

$P_I$max was measured with a calibrated differential pressure transducer. A unidirectional valve was attached to the airway, permitting expiration but not inspiration, and the most negative pressure recorded during 20 seconds of airway occlusion was taken as the $P_I$max.[10] After the discontinuation of mechanical ventilation, the patient breathed room air spontaneously for one minute, while $\dot{V}_E$ and f were measured with a spirometer; the spontaneous V_T was calculated by dividing $\dot{V}_E$ by f. Both the V_T corrected for the patient's weight (V_T/weight in kilograms) and the uncorrected value were used in the data analysis. A sample of arterial blood was collected for blood gas analysis while the patient was receiving mechanical ventilation, and pulmonary gas exchange was assessed by calculation of the PaO_2/PAO_2 ratio.[17]

Classification of Weaning Outcomes

The group that was successfully weaned consisted of 60 patients who were able to sustain spontaneous breathing for ≥24 hours after extubation.[7,9,20] The group in which weaning failed consisted of 40 patients in whom mechanical ventilation was reinstituted at the end of a weaning trial or who required reintubation within 24 hours. The patients in whom weaning failed were divided into two subgroups on the basis of their arterial blood gas values at the end of the trial.[3,12,20,21] Twenty-eight patients met objective criteria for weaning failure because they had one or more of the following: a partial pressure of carbon dioxide ≥50 torr (7 kPa) (17 patients), an increase in partial pressure of carbon dioxide of ≥8 torr (1 kPa) (18 patients), a pH of arterial blood ≤7.33 (16 patients), a decrease in pH of ≥0.07 (19 patients), or a partial pressure of oxygen ≤60 torr (8 kPa) with a fraction of inspired oxygen ≥0.5 (5 patients). The remaining 12 patients met subjective criteria for weaning failure because diaphoresis, evidence of increasing effort, tachycardia, arrhythmias, or hypotension required the reinstitution of mechanical ventilation.

Study Design

The patients were assigned to one of two data sets, depending on the order in which they entered the study. The "training set" consisted of the first 36 patients who were successfully weaned (24 patients) or in whom weaning failed according to objective criteria (12 patients). Data on these patients were used to determine which value for each index studied best differentiated the patients who were successfully weaned from those in whom weaning failed. The value selected as the threshold value was the one that resulted in the fewest false classifications. This decision was based on the assumption that the disadvantages associated with either a false positive result or a false negative result were equal, since weaning trials undertaken either prematurely or after an unnecessary delay were considered equally deleterious to a patient's health.

The predictive power of the threshold value for each index was assessed in the remaining 64 patients, who constituted the "prospective-validation set." The data for this group were subdivided in two ways — first, to compare the 36 patients who were successfully weaned with the 28 patients in whom weaning failed, and second, to compare the 36 successfully weaned patients with the 16 patients who met objective criteria for weaning failure. The clinical diagnoses of the patients in the training and the prospective-validation sets were as follows: adult respiratory distress syndrome (in 10 and 18 patients, respectively), pneumonia (9 and 9 patients), obstructive airway disease (6 and 11), central nervous system disorders (6 and 7), congestive heart failure (2 and

12), pulmonary fibrosis (0 and 2), and miscellaneous other diagnoses (3 and 5).

Statistical Analysis

A true positive result was defined as occurring when a patient's test predicted weaning success and weaning actually succeeded, a true negative result as occurring when a test predicted weaning failure and weaning actually failed, a false positive result as occurring when a test predicted weaning success but weaning failed, and a false negative result as occurring when a test predicted weaning failure but weaning succeeded. Standard formulas were used to calculate the sensitivity (true positives/[true positives + false negatives]), specificity (true negatives/[true negatives + false positives]), positive predictive value (true positives/[true positives + false positives]), and negative predictive value (true negatives/[true negatives + false negatives]) of each index.[22]

The predictive performance of each index was also assessed with ROC curves. ROC-curve analysis provides a powerful means of assessing a test's ability to discriminate between two groups of patients, with the advantage that the analysis does not depend on the threshold value selected.[13,14,23] The area under the ROC curve for each index, which summarizes the performance of that index in predicting weaning outcome, was calculated by the nonparametric method of Hanley and McNeil[24]; the technique developed by these authors was also used to compare the areas under the curves. Two sets of ROC curves were constructed for the prospective-validation data set. The first set was derived from the data on the 36 successfully weaned patients and all 28 patients in whom weaning failed, and the second set was derived from the data on the 36 successfully weaned patients and the 16 patients who met objective criteria for weaning failure.

Results

The threshold values for each index that discriminated best in the training set of data between the successfully weaned patients and the patients in whom weaning failed are shown in Table 1.

Table 1. Threshold Values of Indexes Used to Predict Weaning Outcome.

Index	Value*
Minute ventilation (liters/min)	≤15
Respiratory frequency (breaths/min)	≤38
Tidal volume (ml)	≥325
Tidal volume (ml)/patient's weight (kg)	≥4
Maximal inspiratory pressure (cm H_2O)†	≤−15
Dynamic compliance (ml/cm H_2O)	≥22
Static compliance (ml/cm H_2O)	≥33
PaO_2/PAO_2 ratio	≥0.35
Frequency/tidal volume ratio (breaths/min/liter)	≤105
CROP index (ml/breath/min)	≥13

*Threshold values were those that discriminated best in the training data set between the patients who were successfully weaned and those in whom a weaning trial failed; ≥ and ≤ indicate whether the values above the threshold value or those below it are those that predicted a successful weaning outcome.

†To convert value to kilopascals, multiply by 0.09807.

The accuracy of each index in the prospective-validation data set is shown in Table 2. Sensitivity was 1.00 for $P_I$max, which was marginally higher than the sensitivity of the f/V_T ratio or the V_T (both of which were 0.97). Specificity was highest for the f/V_T ratio (0.64) and lowest for $P_I$max (0.11). Positive predictive value was highest for the f/V_T ratio (0.78). Negative predictive value was highest for the $P_I$max (1.00), followed closely by the f/V_T ratio (0.95).

Besides examining the accuracy of the predictive indexes in the successful-weaning group and the group of all patients in whom weaning failed, we also examined the indexes' accuracy in discriminating between the successfully weaned patients and the patients who met objective criteria for weaning failure. In this second comparison, the specificities and positive predictive values of C_{dyn}, C_{st}, the PaO_2/PAO_2 ratio, and the CROP index were considerably higher (by ≥0.15), but no major differences were observed in sensitivity and negative predictive value.

We assessed the influence of the duration of mechanical ventilation on the accuracy of the predictive indexes by comparing the patients who required mechanical ventilation for ≥8 days with those who required it for shorter periods (Table 3). The accuracy was generally lower (by ≥0.15) in the patients requiring ≥8 days of mechanical ventilation, especially in terms of positive predictive value; the differences in sensitivity, specificity, and negative predictive value were smaller. The specificity of $P_I$max and the negative predictive values of f and the PaO_2/PAO_2 ratio were higher, however, in the patients requiring ≥8 days of ventilatory support.

Figure 1 shows a series of isopleths for the f/V_T ratio that represent different degrees of rapid shallow breathing. The points to the left of the isopleth representing 100 breaths per minute per liter indicate patients with a 95 percent likelihood that a weaning trial would fail, whereas the points to the right of this isopleth indicate patients with an 80 percent likelihood of successful weaning.

The areas under the ROC curves for each index are shown in Table 4, and the curves of selected indexes are shown in Figure 2. For most indexes, the areas were significantly larger than that of an arbitrary test that is expected a priori to have no discriminatory

Table 2. Accuracy of the Indexes Used to Predict Weaning Outcome.*

Index	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
Minute ventilation	0.78	0.18	0.55	0.38
Respiratory frequency	0.92	0.36	0.65	0.77
Tidal volume	0.97	0.54	0.73	0.94
Tidal volume/patient's weight	0.94	0.39	0.67	0.85
Maximal inspiratory pressure	1.00	0.11	0.59	1.00
Dynamic compliance	0.72	0.50	0.65	0.58
Static compliance	0.75	0.36	0.60	0.53
PaO_2/PAO_2 ratio	0.81	0.29	0.59	0.53
Frequency/tidal volume ratio	0.97	0.64	0.78	0.95
CROP index	0.81	0.57	0.71	0.70

*Values shown were derived from the complete prospective-validation data set, comprising 36 successfully weaned patients and 28 patients in whom weaning failed.

Table 3. Effect of Duration of Mechanical Ventilation (<8 Days or ≥8 Days) on the Accuracy of Indexes in Predicting Weaning Outcome.*

Index	Sensitivity		Specificity		Positive Predictive Value		Negative Predictive Value	
	<8 days	≥8 days	<8 days	≥8 days	<8 days	≥8 days	<8 days	≥8 days
Minute ventilation	0.79	0.75	0.75	0.08	0.65	0.35	0.40	0.33
Respiratory frequency	0.89	1.00	0.31	0.42	0.69	0.53	0.63	1.00
Tidal volume	1.00	0.88	0.50	0.58	0.78	0.58	1.00	0.88
Tidal volume/patient's weight	0.96	0.88	0.38	0.42	0.73	0.50	0.86	0.83
Maximal inspiratory pressure	1.00	1.00	0.00	0.25	0.64	0.47	1.00	1.00
Dynamic compliance	0.75	0.63	0.69	0.25	0.81	0.36	0.61	0.50
Static compliance	0.82	0.50	0.56	0.08	0.77	0.27	0.64	0.20
PaO_2/PAO_2 ratio	0.79	0.88	0.38	0.17	0.69	0.41	0.50	0.67
Frequency/tidal volume ratio	1.00	0.88	0.63	0.67	0.82	0.64	1.00	0.89
CROP index	0.82	0.75	0.56	0.58	0.77	0.55	0.64	0.78

*Values shown were derived from the complete prospective-validation data set of 64 patients, among whom 44 patients (28 who were successfully weaned and 16 who had weaning failure) required <8 days of mechanical ventilation, and 20 patients (8 who were successfully weaned and 12 who had weaning failure) required ≥8 days of mechanical ventilation.

value (i.e., 0.50), with the exception of the areas for $\dot{V}_E$ (0.40), PaO_2/PAO_2 (0.48), and P_Imax (0.61). In addition, the areas under the ROC curves for $\dot{V}_E$ and P_Imax were significantly smaller than those for the CROP index (P<0.001 and P<0.03, respectively), the f/V_T ratio (P<0.001 in both instances), V_T (P<0.001 in both instances), or f (P<0.001 and P<0.03, respectively), whereas the area under the curve for $\dot{V}_E$ was significantly smaller than those for C_{dyn} (P<0.003) and C_{st} (P<0.003). Except for the PaO_2/PAO_2 ratio, which tended to decrease the diagnostic accuracy, the areas under the ROC curves tended to become larger as additional components were incorporated into the CROP index: for C_{dyn}, the area was 0.67±0.07; for compliance and oxygenation ($C_{dyn} \times PaO_2/PAO_2$), it was 0.58±0.07; for compliance and pressure ($C_{dyn} \times P_Imax$), it was 0.73±0.06; for compliance and respiratory rate (C_{dyn}/rate), it was 0.80±0.06; for compliance, pressure, and rate together ($C_{dyn} \times P_Imax$/rate), it was 0.82±0.05; and for the CROP index it was 0.78±0.06. The area under the ROC curve for compliance, pressure, and rate was significantly larger than those for C_{dyn} (P<0.03) and compliance and oxygenation (P<0.002), the area under the curve for compliance and rate was larger than those for C_{dyn} (P<0.03) and compliance and oxygenation (P<0.002), and the area under the curve for the CROP index was larger than that of compliance and oxygenation (P<0.01), but none of the other comparisons were significant. The area under the ROC curve for the f/V_T ratio (0.89±0.05) was larger than that for the CROP index (0.78±0.06, P<0.05). The areas under the ROC curves generated by the data for the 36 successfully weaned patients and the 16 patients in whom weaning failed according to objective criteria were not significantly different from the areas generated by the data for the complete prospective-validation set of 64 patients.

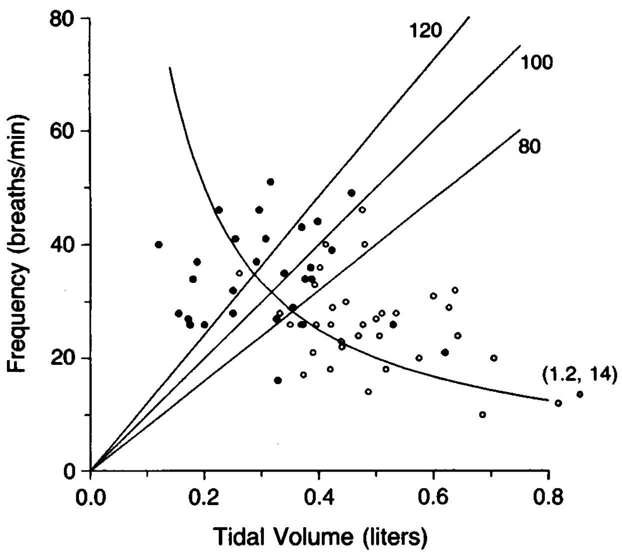

Figure 1. Isopleths for the Ratio of Breathing Frequency to Tidal Volume, Representing Different Degrees of Rapid Shallow Breathing.

For the patients indicated by the points to the left of the isopleth representing 100 breaths per minute per liter, the likelihood that a weaning trial would fail was 95 percent, whereas for the patients indicated by the points to the right of this isopleth, the likelihood of a successful weaning outcome was 80 percent. The hyperbola represents a minute ventilation of 10 liters per minute, a criterion commonly used to predict weaning outcome; apparently, this criterion was of little value in discriminating between the successfully weaned patients (open circles) and the patients in whom weaning failed (solid circles). Values for one patient (tidal volume of 1.2 liters and respiratory frequency of 14 breaths per minute) lay outside the graph.

Discussion

The predictive power of each of the two new indexes of weaning outcome, the f/V_T ratio and the CROP index, was considerably greater than that of traditional indexes, such as $\dot{V}_E$ and P_Imax.

Certain aspects of study design become particularly important when an investigation of predictors of weaning outcome is undertaken, and also when such investigations are compared.[1,25] First, the study population needs to be carefully defined. We limited our study population to medical patients, since it is generally more difficult to predict the weaning outcome in these patients than in surgical patients. Second, the technique of making the physiologic measurements needs to be clearly stated.[10,18] Third, the end points of a study need to be well defined. The definition of successful weaning is fairly straightforward (successful spontaneous ventilation for ≥24 hours is the usual one), but that of weaning failure is more difficult. Almost all investigators have defined weaning failure on the basis of abnormal arterial blood gas measurements or clinical deterioration, without stating the relative proportion of each. The lack of objective criteria for weaning failure makes it difficult to compare the performance of predictive indexes in different studies, because the patients in whom a weaning trial was considered to have failed in one study might have been weaned successfully by a more aggressive physician. Accordingly, we analyzed separately the subgroup of patients who met objective criteria for weaning failure in addition to analyzing the entire group in whom weaning failed. Fourth, the method of choosing the threshold value for an index is critical. To our knowledge, all previous investigators have used post hoc analysis to determine the threshold values that discriminated best between successfully weaned patients and patients in whom weaning failed. In contrast, we determined the optimal threshold value for each index in the first 36 patients in our study (Table 1) and then tested the accuracy of these values prospectively in the remaining patients. Finally, we used an additional technique of data analysis, the construction of ROC curves, that circumvents the chief problem inherent in the technique of classic decision analysis — namely, dependence on the threshold value that is selected.

Table 4. Area under the ROC Curve for Each Index.*

Index	Area ±SE
Minute ventilation	0.40±0.07
Respiratory frequency	0.76±0.06
Tidal volume	0.87±0.05
Tidal volume/patient's weight	0.84±0.05
Maximal inspiratory pressure	0.61±0.07
Dynamic compliance	0.67±0.07
Static compliance	0.68±0.07
PaO_2/PAO_2 ratio	0.48±0.07
Frequency/tidal volume ratio	0.89±0.05
CROP index	0.78±0.06

*Values shown were derived from the complete prospective-validation data set, comprising 36 successfully weaned patients and 28 patients in whom weaning failed.

Sahn and Lakshminarayan[3] reported that a P_Imax of ≤−30 cm of water (−3 kPa) invariably resulted in successful weaning and that a value of ≥−20 cm of water (−2 kPa) invariably resulted in weaning failure; they also reported that a $\dot{V}_E$ of ≥10 liters per minute was useful in predicting weaning failure. Subsequent investigators, however, found a high rate of false positive and false negative results when P_Imax[6,7,9,26] or $\dot{V}_E$[6,8,9] was used as a criterion. Measures of the accuracy of these threshold values in our prospective-validation set are shown in Table 5. The accuracy of indexes

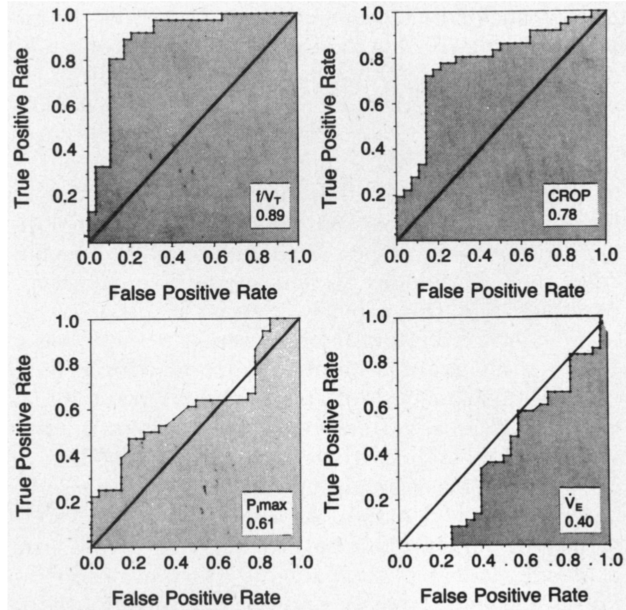

Figure 2. ROC Curves for the f/V_T Ratio, CROP Index, P_Imax, and $\dot{V}_E$ in the Prospective-Validation Data Set of 64 Patients.

The ROC curve is generated by plotting the proportion of true positive results against the proportion of false positive results for each value of a test. The curve for an arbitrary test that is expected a priori to have no discriminatory value appears as a diagonal line, whereas a useful test has an ROC curve that rises rapidly and reaches a plateau. The area under the curve (shaded) is expressed (in box) as a proportion of the total area of the graph.

of pulmonary gas exchange[18] as predictors of weaning outcome has never been subjected to detailed prospective investigation. In the prospective-validation data set, a PaO_2/PAO_2 ratio of 0.35 was found to be a relatively weak predictor of weaning outcome (Table 2), which probably reflects the fact that abnormalities of oxygenation do not frequently determine weaning failure. Other indexes that have been used to predict weaning outcome include vital capacity and maximal voluntary ventilation,[2,3] but these have also been reported to result in a high rate of false positive and false negative results[6,27]; in addition, their measurement re-

Table 5. Accuracy of Various Threshold Values for the Indexes Used to Predict Weaning Outcome.*

Index	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
P_Imax (cm H_2O)†				
≤−15	1.00	0.11	0.59	1.00
≤−20	1.00	0.14	0.60	1.00
≤−30	0.86	0.21	0.58	0.55
$\dot{V}_E$ (liters/min)				
≤10	0.31	0.61	0.50	0.40
≤15	0.78	0.18	0.55	0.38

*Values shown were derived from the complete prospective-validation data set, comprising 36 successfully weaned patients and 28 patients in whom weaning failed; ≤ indicates that the values below the value shown predict a successful weaning outcome.

†To convert values to kilopascals, multiply by 0.09807.

quires considerable cooperation on the part of the patient, making reliable data more difficult to obtain.[18]

Weaning failure is commonly multifactorial in origin, and thus an index that assesses a single physiologic function may not be optimal.[1,11] Indeed, this was borne out by the data in the present and previous studies, which showed that indexes assessing the major determinants of weaning outcome had limited diagnostic accuracy when used individually. In contrast, the CROP index, which assesses pulmonary gas exchange and the balance between respiratory demands and respiratory neuromuscular reserve, was a considerably more accurate predictor. The precise pathophysiologic basis of an elevated f/V_T ratio in patients in whom a weaning trial fails is unknown,[12] but we suspect that it is a stress response reflecting an imbalance between respiratory neuromuscular reserve and respiratory demands. As a predictor, the f/V_T ratio has several attractive features: it is easy to measure, it is independent of the patient's effort and cooperation, it has high predictive power, and fortuitously, it has a "rounded-off" threshold value (100) that is easy to remember.

Of the primary indexes, V_T was the most accurate in predicting weaning outcome. Since V_T is determined by the interaction between the amount of inspiratory pressure generated for each breath and the load placed on the respiratory system (i.e., $V_T = P_I \times C_{dyn}$), it is not too surprising that it proved to be a relatively accurate predictor. However, we are not aware of any previous study that has objectively evaluated its usefulness as a predictor of weaning outcome.

The areas under a number of the ROC curves in this study were quite large — specifically, 0.89, 0.87, and 0.77 for the f/V_T ratio, V_T, and the CROP index, respectively, which compare favorably with the areas under the ROC curves for diagnostic indexes that are considered reliable in everyday clinical practice. These include, for example, the ratio of forced expiratory volume in one second to forced vital capacity in the diagnosis of obstructive airways disease (0.86),[28] mean corpuscular volume in the diagnosis of iron-deficiency anemia (0.79),[13] and the acid phosphatase level in the diagnosis of prostatic carcinoma (0.75 to 0.80).[13] In contrast, the areas under the ROC curves for $P_I$max and $\dot{V}_E$ (0.61 and 0.40, respectively) were not significantly larger than that of an arbitrary test that is expected a priori to have no discriminatory value (i.e., a value of 0.50).

In summary, the indexes traditionally used to predict weaning outcome had limited power and were considerably inferior to the f/V_T ratio and the CROP index. The f/V_T ratio, which quantitates rapid shallow breathing, appeared to be the single most accurate index, whereas the more complex CROP index, which reflects pulmonary gas exchange and the balance between respiratory demands and respiratory-muscle reserve, was slightly less accurate.

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References

1. Tobin MJ. Weaning from mechanical ventilation. Curr Pulmonology 1990; 11:47-105.
2. Feeley TW, Hedley-Whyte J. Weaning from controlled ventilation and supplemental oxygen. N Engl J Med 1975; 292:903-6.
3. Sahn SA, Lakshminarayan S. Bedside criteria for discontinuation of mechanical ventilation. Chest 1973; 63:1002-5.
4. Stetson JB. Introductory essay. Int Anesthesiol Clin 1970; 8:767-79.
5. Pierson DJ. Weaning from mechanical ventilation in acute respiratory failure: concepts, indications, and techniques. Respir Care 1983; 28:646-62.
6. Tahvanainen J, Salmenpera M, Nikki P. Extubation criteria after weaning from intermittent mandatory ventilation and continuous positive airway pressure. Crit Care Med 1983; 11:702-7.
7. Fiastro JF, Habib MP, Shon BY, Campbell SC. Comparison of standard weaning parameters and the mechanical work of breathing in mechanically ventilated patients. Chest 1988; 94:232-8.
8. Krieger BP, Ershowsky PF, Becker DA, Gazeroglu HB. Evaluation of conventional criteria for predicting successful weaning from mechanical ventilatory support in elderly patients. Crit Care Med 1989; 17:858-61.
9. Morganroth ML, Morganroth JL, Nett LM, Petty TL. Criteria for weaning from prolonged mechanical ventilation. Arch Intern Med 1984; 144:1012-6.
10. Marini JJ, Smith TC, Lamb V. Estimation of inspiratory muscle strength in mechanically ventilated patients: the measurement of maximal inspiratory pressure. J Crit Care 1986; 1:32-8.
11. Tobin MJ. Predicting weaning outcome. Chest 1988; 94:227-8.
12. Tobin MJ, Perez W, Guenther SM, et al. The pattern of breathing during successful and unsuccessful trials of weaning from mechanical ventilation. Am Rev Respir Dis 1986; 134:1111-8.
13. Beck JB, Shultz EK. The use of relative operating characteristic (ROC) curves in test performance evaluation. Arch Pathol Lab Med 1986; 110:13-20. [Erratum, Arch Pathol Lab Med 1986; 110:958.]
14. Metz CE. Basic principle of ROC analysis. Semin Nucl Med 1978; 8:283-98.
15. Roussos CS, Macklem PT. Diaphragmatic fatigue in man. J Appl Physiol 1977; 43:189-97.
16. Milic-Emili J. Is weaning an art or a science? Am Rev Respir Dis 1986; 134:1107-8.
17. Gilbert R, Keighley JF. The arterial/alveolar oxygen tension ratio: an index of gas exchange applicable to varying inspired oxygen concentrations. Am Rev Respir Dis 1974; 109:142-5.
18. Tobin MJ. Respiratory monitoring in the intensive care unit. Am Rev Respir Dis 1988; 138:1625-42.
19. Pepe PE, Marini JJ. Occult positive end-expiratory pressure in mechanically ventilated patients with airflow obstruction: the auto-PEEP effect. Am Rev Respir Dis 1982; 126:166-70.
20. Sassoon CSH, Te TT, Mahutte CK, Light RW. Airway occlusion pressure: an important indicator for successful weaning in patients with chronic obstructive pulmonary disease. Am Rev Respir Dis 1987; 135:107-13.
21. Swartz MA, Marino PL. Diaphragmatic strength during weaning from mechanical ventilation. Chest 1985; 88:736-9.
22. Griner PF, Mayewski RJ, Mushlin AI, Greenland P. Selection and interpretation of diagnostic tests and procedures: principles and applications. Ann Intern Med 1981; 94:553-600.
23. Centor RM, Schwartz JS. An evaluation of methods for estimating the area under the receiver operating characteristic (ROC) curve. Med Decis Making 1985; 5:149-56.
24. Hanley JA, McNeil BJ. A method of comparing the areas under receiver operating characteristic curves derived from the same cases. Radiology 1983; 148:839-43.
25. Wasson JH, Sox HC, Neff RK, Goldman L. Clinical prediction rules: applications and methodological standards. N Engl J Med 1985; 313:793-9.
26. DeHaven CB Jr, Hurst JM, Branson RD. Evaluation of two different extubation criteria: attributes contributing to success. Crit Care Med 1986; 14:92-4.
27. Milbern SM, Downs JB, Jumper LC, Modell JH. Evaluation of criteria for discontinuing mechanical ventilation support. Arch Surg 1978; 113:1441-3.
28. Beck JR, Colice GL. Relative operating characteristic analysis applied to tests of pulmonary function. Semin Respir Med 1989; 10:211-7.