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Inspiratory pressure/maximal inspiratory pressure ratio: a predictive index of weaning outcome

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Abstract. *Objective:* To compare the accuracy of $P_I/P_I max$ ratio and other commonly used indices in predicting weaning outcome.
Design: A prospective study.
Setting: Intensive care unit.
Patients: 31 stable intubated patients ready to undergo weaning trial.
Methods: A simple method was developed to measure the P_I and $P_I max$ in intubated patients. The accuracy of $P_I/P_I max$ ratio and other commonly used indices in predicting outcome were compared. All indices were measured prior to weaning trial using standardized methods.
Measurements and results: Minute ventilation of the successful patients (13.00±0.67 (SE) l/min) was not significantly different from the failure patients (10.64±1.26 l/min, $p = 0.10$). The P_I and $P_I max$ for the successful patients (11.48±1.25 cmH_2O and 47.77±4.48 cmH_2O, respectively) and the unsuccessful patients (14.32±2.31 cmH_2O and 40.16±4.55 cmH_2O, respectively) were also not significantly different ($p = 0.28$ and 0.24, respectively). The $P_I/P_I max$ ratio was lower for the weaning successes (0.26±0.03) than for the weaning failures (0.36±0.04, $p < 0.05$). The threshold value of 0.3 for $P_I/P_I max$ provided the best separation between weaning success and failure patients. The combined usage of rapid shallow breathing index and $P_I/P_I max$ ratio provided the highest accuracy with sensitivity of 0.81 and specificity of 0.93.
Conclusion: The $P_I/P_I max$ ratio provided a good separation between the patients who were successfully weaned and those who failed. It provides additional discriminative power to f/V_T.

Key words: Weaning prediction – Ventilator – Weaning index – Rapid shallow breathing – Breathing pattern

The purpose of having weaning indices is to identify the earliest time that a patient can resume spontaneous breathing, and to identify patients who are at risk for cardiorespiratory embarrassment during a weaning trial. In order for weaning indices to be useful, they should be easily measurable at the bedside with simple instruments. In addition, weaning indices should assess many different physiological functions and provide insight into the reasons for ventilator dependency. In a previous investigation, Yang and Tobin [1] have demonstrated that a rapid shallow breathing pattern frequently developed in patients who could not be weaned from the ventilator, and an index that quantitates the degree of rapid shallow breathing was a very accurate predictor of weaning outcome. Its onset is often immediate after the discontinuation of ventilator support. The reason the patient adopts this breathing pattern remains unclear.

Failure to wean from mechanical ventilation has frequently been attributed to impaired gas exchange function [2], alteration of respiratory center output [3], or respiratory muscle fatigue due to the imbalance between respiratory load and the ability to meet that demand [4]. It is suspected that respiratory muscle fatigue may be an important factor responsible for difficult weaning. In normal subjects, it has been demonstrated that respiratory muscle fatigue is likely to occur if the average inspiratory pressure during tidal breathing exceeds 40% of the maximal inspiratory pressure for an extended time [5]. Given the frequent occurrence of respiratory muscle fatigue during weaning, it is reasoned that the ratio of inspiratory pressure (P_I) to maximal inspiratory pressure ($P_I max$) among patients with a successful weaning outcome may be lower than those of the patients with an unsuccessful weaning outcome. The direct measurement of $P_I/P_I max$ ratio should be useful in predicting the likely outcome of a trial of weaning. In the current study, direct measurements of inspiratory pressure, maximal inspiratory pressure, and their ratio were obtained in the patients who were considered for a weaning trial. The results of P_I, $P_I max$, and $P_I/P_I max$ were compared between the patients who were successfully weaned and those who failed. Furthermore, the accuracy of $P_I/P_I max$ ratio, traditional weaning indices (maximal inspiratory pressure and minute ventilation ($\dot{V}_E$)) [6], and newly developed indices (respiratory frequency (f), tidal volume (V_T), rapid shallow index (f/V_T)) of weaning outcome were examined.

Methods and materials

There were 31 patients recruited from the medical intensive care units of Hermann Hospital, Houston, Texas. The general characteristics of the patients are shown in Table 1.

At the time of study, all patients were clinically stable and considered ready to be weaned from mechanical ventilation by his/her primary physician. The measurements were standardized and measured by the investigator. All the patients underwent a weaning trial by T-piece. The findings of the current investigation were not made available to the primary physician, and, thus, did not influence the physician's decision regarding extubation. Overall 16 patients had a successful weaning outcome and 15 patients failed a weaning trial. The study was approved by the Institutional Ethics Committee.

Before the weaning trial, $\dot{V}_E$, f, V_T, f/V_T, P_I, $P_I$max, and P_I/P_Imax ratio were obtained. Minute ventilation was measured with a calibrated spirometer (Boehringer Laboratory, Wynnewood, PA) attached to the endotracheal tube. Immediately after discontinuation of ventilator support, respiratory frequency and minute ventilation were measured while the patient spontaneously breathed room air for 1 min. Respiratory frequency was the number of breaths over 1 full minute of spontaneous breathing. The averaged tidal volume (V_T) was calculated by dividing the minute ventilation into the respiratory frequency ($\dot{V}_E/f$). The rapid shallow index was then calculated as the quotient of f/V_T [1].

After the measurements of spontaneous breathing, the patient was placed back on the ventilator temporarily for at least 5 min or until the patient's SaO_2 and heart rate had returned to the previous baseline values. When the patient's clinical condition became stable, P_I and $P_I$max measurements were performed. A T-piece adaptor was equipped with a one-way valve attached to the one end and a pressure transducer attached to the other end. A one-way valve was used during this maneuver so that only the exhalation was allowed while the inhalation was prevented. The middle port of the T-piece would be attached to the tip of the endotracheal tube when the patient was ready to undergo measurements. The ventilatory support was discontinued briefly before the measurements. The patient was allowed to breathe spontaneously for 20–30 s to establish a stable pattern of breathing. The T-piece was attached to the endotracheal tube during the expiratory phase. The airway was occluded at the end of expiration to assess the intrinsic PEEP under zero-flow condition. The intra-alveolar pressure should equilibrate with the endotracheal pressure during the brief airway occlusion. The occlusion was then released after the first one or two breaths so that the patient can continue to exhale but not able to inhale. This ensured that the $P_I$max was measured at a lung volume below functional residual capacity (near residual volume). P_I was taken as the negative inspiratory pressure of the first breath after airway occlusion, while the $P_I$max was the most negative inspiratory pressure swing achieved over 20 s of airway occlusion. P_I was measured from the initiation of inspiratory effort to the most negative pressure deflection of the first breath. Thus, intrinsic PEEP, if present, should be accounted for. The occlusion pressure of the first two breaths has been shown to closely reflect the intra-alveolar pressure swing of the breaths prior to the occlusion [7, 8]. The details of the method of assessing $P_I$max have previously been published [9].

Table 1. General characteristics of patient group

Characteristics	Success	Failure
Age, years	55 ± 3.5	59 ± 5.3
Sex	11M : 5F	9M : 6F
Indications for intubation		
Neuromuscular disorders	6	3
Airway obstruction	3	5
Pneumonia	3	3
ARDS	1	3
Congestive heart failure	3	1

Outcome definitions

The weaning success group consisted of patients who were able to sustain spontaneous breathing for ≥24 h after extubation (Table 2). The failure group included patients in whom ventilatory support was reinstituted at the end of a weaning trial because of respiratory rate ≥ 30 min with clinical evidence of distress, hemodynamic instability or significant deterioration in arterial blood gas ($PaCO_2 \geq 50$ mmHg, pH ≤ 7.32, or $PaO_2 \leq 60$ mmHg on FIO_2 and higher) or who required reintubation within 24 h of discontinuation of ventilatory support due to the deterioration of respiratory conditions.

Statistical analysis

The mean values of f, V_T, $\dot{V}_E$, f/V_T, P_I, $P_I$max, and P_I/P_Imax ratio of the weaning success patients and weaning failure patients were calculated. Respiratory frequency, V_T, $\dot{V}_E$, f/V_T, P_I, $P_I$max, P_I/P_Imax ratio of both groups of patients were also compared by using unpaired Student's *t*-test.

A traditional decision analysis technique was used to assess the accuracy of indices. True positives (TP) were defined as those patients whose test predicted weaning success and who actually succeeded. True negative (TN) were those patients whose test predicted weaning failure and who actually failed. False positive (FP) were patients test predicted to wean successfully but who actually failed. False negatives (FN) were patients predicted to fail but who actually succeeded. Standard formulae were used to calculate the sensitivity (TP/(TP+FN)), specificity (TN/(TN+FP)), positive predictive value (TP/(TP+FP)), and negative predictive value (TN/(TN+FN)) for each index [10].

Results

There were 16 patients successfully weaned and 15 patients failed weaning trial. Of the failed patients 8 had a high respiratory rate with apparent distress clinically, 4 had hypercapnia and acidosis, 2 had severe hypoxemia, and one patient developed hemodynamic instability.

An example of inspiratory pressure tracing during airway occlusion is shown in Fig. 1. P_I is the negative inspiratory pressure of the first breath, and the $P_I$max is the most negative pressure achieved during 20s airway occlusion. The results of f, V_T, f/V_T, $\dot{V}_E$, P_I, $P_I$max, and P_I/P_Imax of all 31 patients who underwent a trial of weaning are shown in Table 2. The mean values of P_I, $P_I$max, and $\dot{V}_E$ for those patients with a successful outcome and those patients with an unsuccessful outcome were not significantly different. However, f, V_T, f/V_T,

Table 2. Group mean values of weaning indices[a]

Index	Success	Failure	*p*-Value
f (breaths/min)	28.00 ± 1.94	36.93 ± 2.92	< 0.05
V_T (ml/breath)	497.27 ± 52.79	289.60 ± 28.19	< 0.01
f/V_T (br/min/l)	65.26 ± 7.11	143.30 ± 15.03	< 0.01
$\dot{V}_E$ (l/min)	13.00 ± 0.67	10.64 ± 1.26	0.11
P_I (cmH_2O)	11.48 ± 1.25	14.32 ± 2.31	0.28
$P_I$max (cmH_2O)	47.77 ± 4.48	40.16 ± 4.55	0.24
P_I/P_Imax	0.26 ± 0.03	0.36 ± 0.04	< 0.05

[a] Values are mean ± standard errors, all *p*-values are two-tailed probabilities

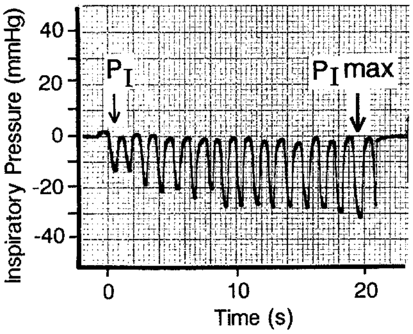

Fig. 1. The *small arrow* indicates the pressure of the first breath while the *large arrow* indicates the maximal negative inspiratory pressure achieved during 20 s of airway occlusion. Note the presence of intrinsic PEEP, which is the positive deflection above the zero before the first breath. The pressure of the first breath reflects the average spontaneous inspiratory pressure

and P_I/P_Imax ratio for the weaning success patients were significantly different from those of weaning failure patients ($p < 0.05$, 0.01, 0.01, 0.05, respectively).

The threshold values used for f, V_T, f/V_t, $P_I$max and $\dot{V}_E$ were 38 breaths/min, 325 ml/breath, 100 breaths/min/l, -15 cmH_2O, and 15 l/min, which have been previously established in the literature [1]. The threshold value used for P_I/P_Imax was 0.3. This threshold value was chosen because it had the lowest number of false classifications.

Sensitivity, specificity, positive and negative predictive values of the weaning indices in predicting outcome are shown in Table 3. The sensitivity was highest for V_T and $P_I$max at 1.0, while the f/V_T was slightly lower. The specificity was highest for f/V_T, and P_I/P_Imax and V_T are slightly lower. Overall tidal volume and rapid shallow breathing index were the most accurate predictors of the weaning outcome while the new index, P_I/P_Imax ratio, was slightly less accurate. However, its accuracy is much higher than the traditional indices, $\dot{V}_E$ and $P_I$max. Four of 16 patients who were successfully weaned had a P_I/P_Imax ratio greater than 0.3, while 10 of 15 weaning failure patients had a value greater than 0.3. Among 14 patients in whom inspiratory pressure per breath exceeded 30% of maximal inspiratory pressure achieved, 10 failed their weaning trial. Of 17 patients in whom inspiratory pressure per breath was less than 30% of maximal inspiratory pressure, 12 patients had a successful weaning outcome. In other words, there is 72% chance of weaning failure when the ratio is above 0.3, and there is 71% chance of weaning success when the ratio is below 0.3.

When rapid shallow breathing index and P_I/P_Imax ratio were used in combination (that $f/V_T \leq 100$ and $P_I/P_I\text{max} \leq 0.3$ predicts weaning success, and all the other combinations predict weaning failure), the overall diagnostic accuracy was further improved. This combination had a sensitivity of 0.81, specificity of 0.93, positive predictive value of 0.93, and negative predictive value of 0.83. The combination of these indices by far gave the highest specificity and positive predictive value.

Table 3. Sensitivity, specificity, positive and negative predictive values of each index

Index	Sensitivity	Specificity	Positive predicted value	Negative predicted value
f (≤ 38 breaths/min)	0.88	0.47	0.64	0.78
V_T (≥ 325 ml/breath)	1.00	0.67	0.76	1.00
f/V_T (≤ 100 br/min/l)	0.94	0.73	0.79	0.92
$\dot{V}_E$ (≤ 15 l/min)	0.81	0.20	0.52	0.50
$P_I$max (≤ -15 cmH_2O)	1.00	0.13	0.55	1.00
P_I/P_Imax (≤ 0.3)	0.75	0.67	0.71	0.72
f/V_T and P_I/P_Imax	0.81	0.93	0.93	0.83

Discussion

The major findings of this study are that there is a significant difference in P_I/P_Imax ratio between weaning success and weaning failure patients and that this ratio may be an additional useful index in predicting weaning outcome. The measurement was easily obtained during the routine measurement of the weaning indices. Furthermore, this new index complemented the most accurate index (f/V_T) currently employed.

$P_I$max and $\dot{V}_E$ are the traditional indices employed to predict weaning outcome. In the study by Sahn and Lakshminaryan [5], they reported that a successful weaning outcome was likely if $P_I$max value was less than -30 cmH_2O and a weaning failure was likely if $P_I$max was greater than -20 cmH_2O; they also reported that a $\dot{V}_E$ of ≥ 10 l/min was useful in predicting weaning failure. However, other investigators have subsequently found that $P_I$max [11, 12] and $\dot{V}_E$ criteria [11, 13, 14] were associated with a high rate of false positive and false negative results. Our results are consistent with the findings of the latter investigators that there was no clear cut separation between the weaning success and failure patients. Since weaning failure is usually multi-factorial, it is not surprising that $P_I$max or $\dot{V}_E$ alone is not accurate in predicting weaning outcome. In comparison to the routinely measured weaning indices, we found that P_I/P_Imax was significantly more discriminatory than $P_I$max and $\dot{V}_E$. The reason for its better predictive power may reflect the fact that P_I/P_Imax takes into account of the balance between the mechanical impediment to breathing and the ability of respiratory muscles to overcome the impediment.

The current study demonstrated that rapid shallow breathing index and tidal volume are the two most accurate predictors of weaning outcome. The sensitivity and specificity of these indices are consistent with the findings of our previous investigation [1]. While they are the most accurate predictors of weaning outcome, the reason for the development of rapid shallow breathing remains unclear. It could be caused by the combination of muscle weakness and impaired pulmonary mechanics. However, respiratory muscle fatigue was unlikely to be the cause since the patient adopted this breathing pattern immediately after resuming spontaneous breathing (before they had a chance to develop fatigue). Instead, rapid shallow breathing pattern probably reflects the body's response to a large mechanical load. In a recent study by Mador and Acevedo [14], it was shown that, in healthy adults, muscle fatigue alone would not induce rapid shallow breathing. However, a rapid but not shallow breathing pattern developed when respiratory muscle fatigue and increased load were present simultaneously. Whether the same physiology applies to sick patients undergoing weaning trial will require further investigations. Although P_I/P_Imax ratio is not as discriminatory as the f/V_T, it appears that P_I/P_Imax provided additional discriminatory power to the rapid shallow breathing index. When used in combination with f/V_T index, it further increased the predictive power than either index alone. In fact, the combination of f/V_T and P_I/P_Imax by far had the highest positive predictive value of all predictive indices at 0.93. This means that 93% of the patients who had f/V_T of less than 100/min/l and P_I/P_Imax ratio of less than 0.3 will be successfully weaned from ventilator. However, the high positive predictive value came at the expense of lower negative predictive value. Indeed, when compared to the f/V_T, the overall diagnostic accuracy increased only slightly from 0.84 to 0.88. It should be stressed that an index with high specificity or positive predictive value is valuable because this means the number of false positives (the patient who was predicted to have successful weaning outcome yet failed weaning trial) is small. In other words, the chance of having a successful weaning outcome is excellent if both indices predict success, whereas a negative predictive value in either one of these indices should alert the physician to be more judicious about the weaning trial.

The prevalence rate of respiratory muscle fatigue among the patients with respiratory failure is not known. It has been demonstrated that diaphragmatic muscle fatigue will occur when the average trans-diaphragmatic pressure during tidal breathing persistently exceeds 40% of the maximal trans-diaphragmatic pressure [4]. Indeed, we found that a patient is likely to encounter difficulties during weaning when the P_I/P_Imax ratio is greater than 0.3. The difference in ratios between this study and previous investigations might be explained by several factors. First, the current investigation employed P_I and $P_I$max, which reflected the pressure-generating capacity of all the respiratory muscles. In contrast, the previous investigation examined trans-diaphragmatic pressure, which mainly assessed the diaphragmatic function. Whether the accessory respiratory muscles have the same fatigue threshold as the diaphragm is not clear. Second, our study subjects had severe medical illnesses while the previous study used only the healthy subjects in their investigations. It is possible that the respiratory muscles of the patients with severe illness have a lower fatigue threshold. In addition to P_I/P_Imax ratio, other investigators have found that duty cycle of a breath was also an important determinant in the development of respiratory muscle fatigue [16], and that fatigue occurred when the time-tension index (the product of P_I/P_Imax and duty cycle) exceeded 0.15. Unfortunately, we did not make direct measurements of respiratory duty cycle (T_I/T_{tot}), thus the time-tension index could not be calculated. In a recent study comparing the breathing pattern of patients with chronic obstructive pulmonary disorders with hypercapnia and those without hypercapnia, Grassino et al. found a significant difference in the P_I/P_Imax ratio, but not in the T_I/T_{tot} between the two groups of patients [17]. The average T_I/T_{tot} was 0.41 for hypercapnic patients and 0.42 for non-hypercapnic patients. Indeed, in most clinical situations T_I/T_{tot} does not deviate markedly from 0.4 [18]. Thus, it appears that the P_I/P_Imax ratio is the major determinant of muscle fatigue. If the average duty cycle in our patients was assumed to be 0.4, the time-tension index for the weaning successful group would be 0.125, while that of the weaning failure group would be 0.18. The data is consistent with the possibility that patients who failed weaning trial developed a breathing pattern leading toward fatigue.

The question whether inspiratory pressure measured at the endotracheal tube during airway occlusion closely reflects the intrathoracic pressure swing during spontaneous breathing was recently investigated by Maltais et al. [7]. These authors did not find any difference between the intra-thoracic pressure swing during spontaneous breathing and inspiratory pressure measured at the endotracheal tube of the first two breaths after the airway occlusion. Similarly, we compared the preocclusion esophageal pressure change with the pressure measured at the airway of the first occluded breath. In a preliminary report of 11 patients, we found that the pressure measured at the endotracheal tube was 9% higher than the esophageal pressure change. Thus, it is likely that P_I measured at the endotracheal tube closely estimates the inspiratory pressure during spontaneous breathing. Further studies should be helpful to confirm these findings.

The major advantage of the current method lies in its simplicity. All of the measurements can be obtained by a respiratory therapist in a simple maneuver without expensive or complicated equipments or challenging directions. P_I/P_Imax ratio provides information about the balance between respiratory load and respiratory capacity. This information may be helpful in identifying the possible respiratory fatigue that prevents the patient from weaning from ventilatory support. With the addition of respiratory pattern monitoring currently available in many ICUs, the time-tension index can be readily calculated and should provide more information about the balance between the load and capacity.

In summary, we have developed a simple method to assess the balance between inspiratory pressure and maximal inspiratory pressure. This index provides a better separation between the weaning success and failure patients than the traditionally used indices. It also provides additional discriminative power to the rapid shallow index in predicting weaning outcome. Lastly, this index also has the attractiveness of using non-invasive instrumentation that respiratory therapists are familiar.

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