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The Timed Inspiratory Effort Index as a Weaning Predictor: Analysis of Intra- and Interobserver Reproducibility

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BACKGROUND: Prolonged ventilatory weaning may expose patients to unnecessary discomfort, increase the risk of complications, and raise the costs of hospital treatment. In this scenario, indexes that reliably predict successful liberation can be helpful. OBJECTIVE: To evaluate the intra- and interobserver reproducibility of the timed inspiratory effort index as a weaning predictor. METHODS: This prospective observational study included subjects judged as able to start liberation from mechanical ventilation. For the intra-observer analysis, the same investigator performed 2 measurements in each selected patient with an interval of 30 min a rest. For interobserver analysis, 2 measurements were obtained in another sample of subjects, also with an interval of 30 min rest, but each of one performed by a different investigator. The Bland-Altman diagram, the coefficient concordance of kappa, and the Pearson correlation coefficient were used to compare the measurements. The performance of the timed inspiratory effort index was assessed by receiver operating characteristic curves. Values of *P* < .05 were considered significant. RESULTS: We selected 113 subjects (43 males; mean ± SD age, 77 ± 14 y). Fifty-six (49.6%) achieved successful liberation, and 33 (29%) died in the ICU. The mean ± SD duration of mechanical ventilation was 14.4 ± 6.7 d. The Bland-Altman diagrams that addressed intra- and interobservers agreement showed low variability between measurements. Values of the concordance coefficients of kappa were 0.82 (0.68–0.95) and 0.80 (0.65–0.94), and of the linear correlation coefficients, 0.86 (0.77–0.91) and 0.89 (0.82–0.93) for the intra- and interobservers measurements, respectively. The mean ± SD values for the area under the curve for each pair of the intra- and interobserver measurements were 0.96 ± 0.07 versus 0.94 ± 0.07 (*P* = .41) and 0.94 ± 0.05 versus 0.90 ± 0.07 (*P* = .14), respectively. CONCLUSIONS: The variability of the measurement of the timed inspiratory effort index by intra- and interobservers showed very high reproducibility, which reinforced the index as a sensible, accurate, and reliable outcome predictor of liberation from mechanical ventilation.
Key words: ventilatory weaning; mechanical ventilation liberation; inspiratory muscles; variability; reproducibility; accuracy. [Respir Care 0;0(0):1–●. © Daedalus Enterprises]

Introduction

Mechanical ventilation is an essential therapy for patients with acute respiratory failure. Weaning is the process of transition from mechanical ventilation to spontaneous breathing in patients who remained on mechanical ventilation for ≥24 h.[1,2] It should be emphasized that the withdrawal of the patient from mechanical ventilation may be more difficult than maintenance. Some researchers describe weaning as an obscure area of intensive care and

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comment that, even with specialists, this stage of ventilatory care can be considered a mixture of art and science.[2-4]

The use of mechanical ventilation can cause ventilator-induced diaphragm dysfunction and generate changes in muscle structure and contractility, which results in reduced respiratory muscle strength, a process that can start as early as 18 h after mechanical ventilation.[5-7] Many researchers agree that the ventilator-induced diaphragm dysfunction can prolong weaning and is associated with an increased ICU stay and with hospital mortality.[6,8-11] In this regard, indexes that could evaluate for the presence of ventilator-induced diaphragm dysfunction and reliably predict a successful weaning would be helpful. The maximum inspiratory pressure (P_{Imax}) was the first respiratory index described in the literature as a predictor of ventilatory liberation. Perhaps due to the lack of standardization in its measurement, the performance of P_{Imax} as a weaning predictor is poor in most studies.[12-15]

In the search for an index with better predictive power for mechanical ventilator liberation, we considered the combination of parameters (respiratory center stimulation and muscle response) that may be crucially impaired in patients on mechanical ventilation. The timed inspiratory effort index is a recently proposed weaning index that seems to be able to indicate readiness for mechanical ventilation liberation while providing a quick test of diaphragm strength, especially in patients on long-term mechanical ventilation associated with neurologic and neuromuscular diseases. Accordingly, the index showed better performance than those previously reported in a number of studies.[16-18] Thereby, the aim of this study was to evaluate the reliability of the timed inspiratory effort index as a weaning predictor by analyzing its intra- and interobserver variability and reproducibility.

QUICK LOOK

Current knowledge

Premature discontinuation as well as unnecessary delay of liberation from mechanical ventilation have been associated with poor outcomes. Clinical judgment alone may not be enough for the guidance of the timing of withdrawal from mechanical ventilation. A recently proposed ventilator weaning predictor, the timed inspiratory effort index, combines the ability to generate an inspiratory pressure with the time needed to achieve the maximum inspiratory pressure.

What this paper contributes to our knowledge

The high accuracy and reproducibility of the timed inspiratory effort index reinforce this weaning predictor as a reliable complementary tool for the clinician. This information may allow more specific programming of respiratory therapy for this population of critically ill patients.

Methods

This was a prospective, observational study that involved subjects on mechanical ventilation admitted to the ICU of a general hospital from March 2017 to June 2018. The ethics committee of the Federal Fluminense University approved the study under the number CAAE 43049615.0000.5243. Informed consent was obtained from every patient, whenever possible, or from his or her next of kin. Enrollment criteria included patients >18 y of age, with an endotracheal or tracheostomy tube, who were judged as able to start the weaning process. They should also have resolution of the acute phase of the disease that led to mechanical ventilation and an adequate level of consciousness and cough reflex. Accordingly, subjects should have their infection under control, stable cardiovascular status (heart rate $\leq$ 120 beats/min and systolic blood pressure between 90 and 160 mm Hg, no or minimal use of vasopressors), stable metabolic status, hemoglobin > 10 g/dL, adequate oxygenation (arterial oxygen saturation > 90% with $F_{IO_2} \leq 0.4$ or $P_{aO_2}/F_{IO_2} \geq 150$) with final positive expiratory pressure $\leq$ 8 cm H_2O), adequate frequency ($\leq$35 breaths/min), pressure support $\leq$ 20 cm H_2O, and no significant respiratory acidosis (pH > 7.30). We excluded patients with tracheal stenosis, intracranial pressure > 20 mm Hg, on sedation, with severe cardiac insufficiency or hemodynamic instability, signs of systemic infection or reinfection during the liberation process, or discontinuation due to other complications.

Procedures and Definitions

All the subjects in the study were on mechanical ventilation with Extend XT (TAEMA, Air Liquide, Paris, France) and were continuously monitored by using the DX 2010 multi-parameter monitor (Dixtal, São Paulo, São Paulo, Brazil), which records the electrocardiogram, heart rate, S_{pO_2}, and systemic arterial pressure. At any sign of instability, the test was interrupted and the subject was returned to mechanical ventilation. For measurements of P_{Imax} and the

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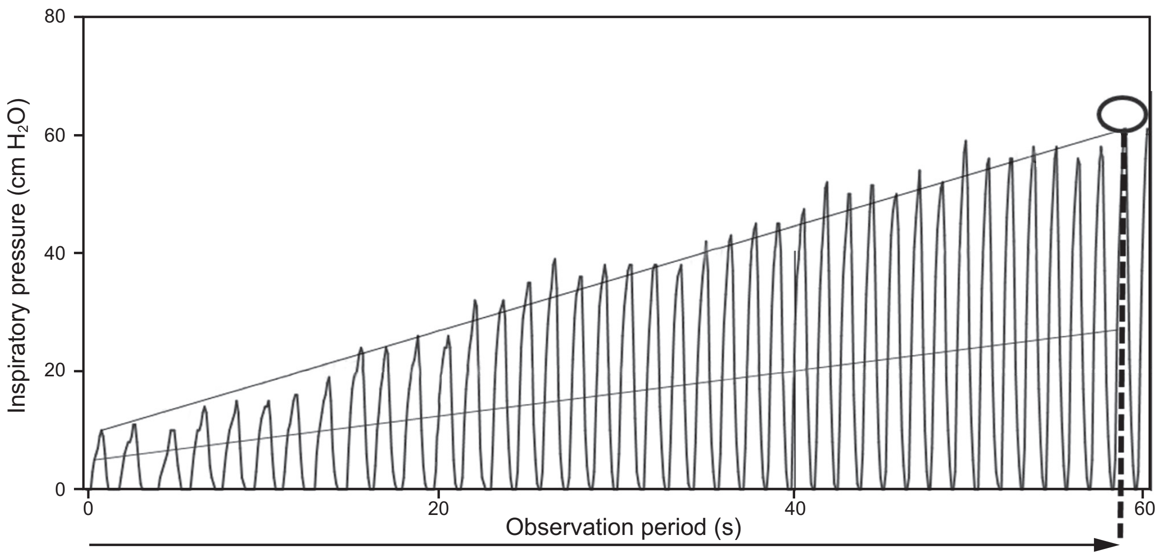

Fig. 1. Typical record, which demonstrates that the maximum inspiratory peak pressure (61 cm H_2O, vertical dashed line) over 60 s of observation was achieved at 58.2 s. In this test, the timed inspiratory effort index was 1.04 cm H_2O/s.

timed inspiratory effort index, the digital vacuometer (Magnamed, São Paulo, São Paulo, Brazil), with a scale of 300 cm H_2O and an increment of 0.1 cm H_2O and a time interval of 100 ms, was used. The method used was the occlusion of the airway during inspiration with a unidirectional valve,[19,20] with the subjects positioned in the supine position, and the head elevated at 45°. The cuff was hyperinflated to prevent air leak during measurement. After tracheal aspiration, the subjects remained connected to the mechanical ventilator to rest for 2 min on 100% oxygen.[13,14,16-18] After hyperoxygenation, the ventilator was disconnected, and the subject breathed spontaneously. After 10 s of spontaneous breathing, the digital manometer was connected to the artificial airway at the end of a normal expiration (at FRC). The airway was occluded for 60 s while the values were recorded, which corresponded to each inspiratory effort.[13,14,16-18]

For the intra-observer analysis, the same respiratory physiotherapist performed 2 measurements in each selected subject, with a 30-min rest period on pressure-support ventilation. For interobserver analysis, 2 measurements were obtained by different respiratory physiotherapists on another group of subjects, which also provided a 30-min rest period between tests. The timed inspiratory effort index was calculated as the ratio of the P_{Imax} registered after the first 30 s of observation to the corresponding time to reach this value of P_{Imax}, while keeping the airway occlusion with a unidirectional valve for up to 60 s. The timed inspiratory effort index = P_{Imax}(after 30 s of start, cm H_2O)/time (in s) to achieve this value of P_{Imax}. A typical record of inspiratory pressures by time is shown in Figure 1.

Liberation was considered successful if spontaneous breathing was maintained for >48 h after mechanical ventilation withdrawal. The decision to return to mechanical ventilation was taken by a respiratory physiotherapist and the attending physician (both did not have access to the results of the timed inspiratory effort index measurement). Criteria to interrupt periods of spontaneous breathing during the T-piece trial were as follows: agitation and/or anxiety, reduced level of consciousness, diaphoresis, dyspnea, and/or cyanosis, oxygen saturation measured from an arterial blood sample < 90% or P_{aO_2} < 60 mm Hg, with F_{IO_2} > 0.4, P_{aCO_2} > 50 mm Hg or increased in >8 mm Hg, arterial pH < 7.33 or decreased by ≥0.07, frequency > 35 breaths/min or increased by 50% for ≥5 min, heart rate >140 beats/min or a sustained increase or decrease > 20%, mean blood pressure > 130 mm Hg or <70 mm Hg, and tachyarrhythmias.[2,12-14,16,17,18,21]

Statistical Analysis

The sample size was calculated to be able to evaluate the differences in the order of 20% between groups with a power of 80% and an alpha error of 5%, in which a minimum number of 35 individuals was found for each studied group. The results were expressed as mean ± SD for continuous variables with normal distribution and, alternatively, as median and 95% CI. Category variables were expressed as frequencies. The differences between the continuous variables and the frequencies were evaluated by using the Wilcoxon test and the chi-square test, respectively.

The obtained values of the timed inspiratory effort index were evaluated as to their ability to predict weaning by calculating the area under the receiver operating characteristic curve. The areas under the receiver operating characteristic curve were compared by using the method of Hanley and

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Table 1. Subject Characteristics based on Weaning Outcome

Variable	Total	Weaning		*P* (Success vs Failure)
		Success	Failure	
Sample, *n* (%)	113	56 (49.6)	57 (50.4)	NA
Males/females, *n*	43/70	17/39	26/31	.14
Race (White/Black), *n*	67/46	34/18	33/28	.87
Age, mean ± SD y	77 ± 14	75.2 ± 15.3	78.6 ± 13.6	.21
APACHE II score, mean ± SD	18.9 ± 5.5	17.7 ± 5.0	20 ± 5.9	.03
Duration of MV, mean ± SD d	14.4 ± 6.7	12.8 ± 6.4	16.1 ± 6.6	<.01
P_{aCO2} before test, mean ± SD mm Hg	40.9 ± 4.3	40.2 ± 3.9	41.7 ± 4.7	.07
Deaths in the ICU, *n* (%)	33 (29.2)	12 (10.6)	21 (18.6)	.07
Tracheostomy, *n* (%)	63 (55.8)	24 (21.3)	39 (34.5)	<.01

NA = not applicable
APACHE = Acute Physiology and Chronic Health Evaluation
MV = mechanical ventilation

Table 2. Values Obtained with the Same Observer (Group Intra-observation, *n* = 60)

Variable	Examination, Median (95% CI)		*P*
	First	Second	
$P_{Imax,\ cm\ H_2O}$	44.5 (36.8–49)	44 (38.8–48)	.13
Time to achieve $P_{Imax,\ s}$	49.9 (47.5–53.6)	48.5 (43.1–53)	.30
Timed inspiratory effort index	0.87 (0.73–1.01)	0.85 (0.79–1.01)	.16

P_{Imax} = maximum inspiratory pressure

Table 3. Values Obtained with Different Observers (Group Interobservation, *n* = 53)

Variable	Second Observer	Third Observer	*P*
$P_{Imax,\ cm\ H_2O}$	49 (44–55.1)	51 (43.8–55.1)	.30
Time to achieve $P_{Imax,\ s}$	48.4 (42.3–53.6)	49 (45.8–54.3)	.99
Timed inspiratory effort index	1.02 (0.88–1.16)	1.02 (0.88–1.13)	.33

Data are median (95% CI).
P_{Imax} = maximum inspiratory pressure

McNeil.[22] Specifically for the analysis of intra- and interobserver reproducibility, the Bland-Altman diagram and the inter-rater agreement statistic (kappa) were used. Values of $P < .05$ were considered significant. Statistical analysis was performed by using the statistical program SPSS, version 18.0 (Chicago, Illinois) and the MedCalc statistical program, version 11.4.2.0. (Mariakerke, Oost-Vlaanderen, Belgium).

Results

One hundred and thirteen subjects were selected (43 males, mean ± SD age, 77 ± 14 y). Fifty-six (49.6%) underwent successful liberation, and 33 (29%) died in the ICU. Tracheotomy was necessary in 63 subjects (55.8%), the mean ± SD duration of mechanical ventilation was 14.4 ± 6.7 d, and the mean ± SD APACHE (Acute Physiology and Chronic Health Evaluation) II score was 18.9 ± 5.5 (Table 1). The median and 95% CI of the intra-observer examinations with regard to P_{Imax}, time to achieve P_{Imax}, and timed inspiratory effort index are depicted in Table 2. In this setting, no statistically significant difference was found between measurements: $P = .13$ for P_{Imax}, $P = .30$ for the time to reach P_{Imax}, and $P = .16$ for the timed inspiratory effort index. Correspondent results for the interobserver examinations are in Table 3. Again, statistically significant differences were not found, with $P = .30$ for P_{Imax}, $P = .99$ for the time to reach P_{Imax}, and $P = .33$ for the timed inspiratory effort index.

The Bland-Altman diagrams that addressed intra- and interobserver agreement for these variables are in Figure 2. Values for the concordance coefficients of kappa of the intra- and interobservers were median weighted Kappa (95% CI) 0.82 (0.68–0.95) and 0.80 (0.65–0.94), respectively. Similar findings were found for linear correlation coefficients of the intra- and interobservers r2 (95% CI) linear regression of Pearson 0.86 (0.77–0.91) and 0.89 (0.82–0.93), respectively (Fig. 3). When evaluating the weaning predictive power of the measurements of the intra-observer data by receiver operating characteristic curves, no statistically significant difference was found between the curves (0.96 ± 0.07 vs 0.94 ± 0.07; $P = .41$); the analysis of the interobserver data showed comparable results (0.94 ± 0.05 vs 0.90 ± 0.07; $P = .14$) (Fig. 4).

Discussion

P_{Imax} was recommended as a weaning predictor by an International Consensus Conference[2]; however, even

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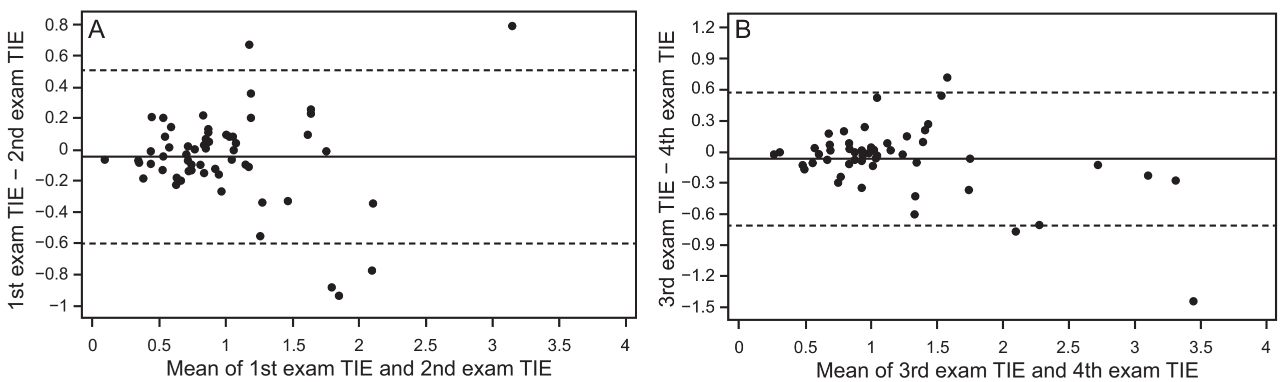

Fig. 2. A Bland-Altman diagram of the intra- (A) and interobservers (B). TIE = timed inspiratory effort. Center lines show means, and dotted lines denote ±1.96 SD.

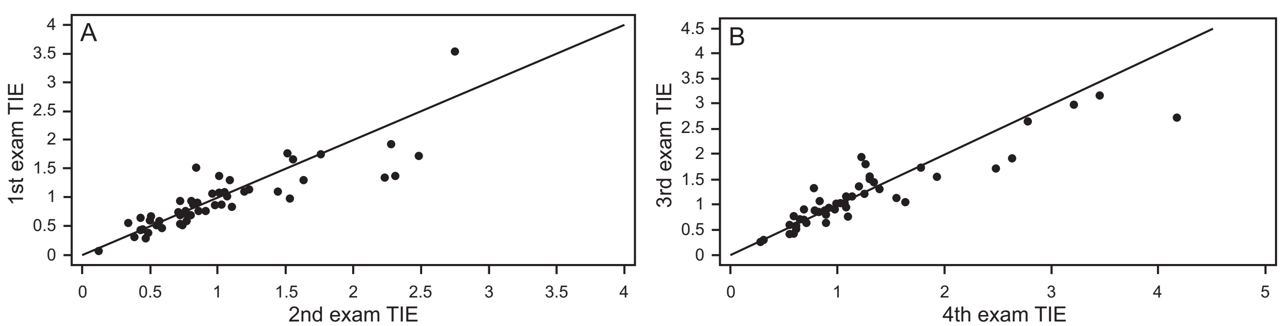

Fig. 3. Linear Pearson correlation of the intra- (A) and interobservers (B). TIE = timed inspiratory effort.

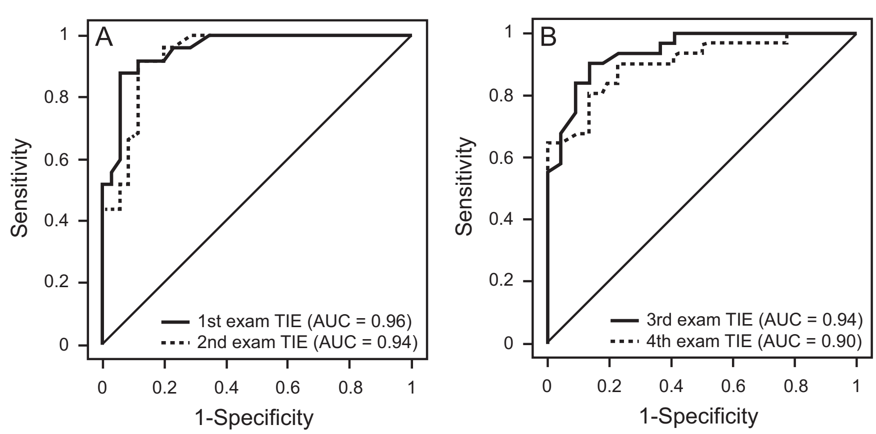

Fig. 4. The area under the receiver operating characteristic curve, evaluating the TIE index as a predictor of weaning success of the intra- (A) and interobservers (B). TIE = timed inspiratory effort.

when measured by adopting the unidirectional inspiratory valve, the index performs below expectation in this regard.[12-15,17,19,20] The timed inspiratory effort index is a new weaning index, easy to perform at bedside and that has been reported to be more accurate.[14,17,18] The aim of the present study was to assess the reliability and reproducibility of the timed inspiratory effort index to better validate the measure as a useful weaning predictor. For this purpose, we resorted to a traditional analysis of intra- and interobserver measurements. The studied sample consisted of older subjects, with a predominance of females. They had a high APACHE II score, prolonged duration of mechanical ventilation, and a high rate of tracheostomy. In this scenario, the mortality rate (29.2%) cannot be seen as a surprise. The features of our subjects were common to the ones found in most of the ICUs worldwide. Half of the subjects underwent successful liberation, a number also consistent with previous studies.[10,14,18,23]

As an initial approach to accomplish the study purpose, the median of the 2 intra-observer measurements were compared, and no statistical significant difference was found. The same occurred with the 2 measurements of the interobserver were compared. These findings demonstrated that the timed inspiratory effort values may be easily and reproducibly obtained. The graphic analysis of the Bland-Altman diagrams showed that the mean line of either intra- or the interobserver data crossed the y axis close to the zero value. In addition, most of the values in both graphics were within the limits of $\pm$1.96 SD. The kappa concordance coefficients were 0.82 and 0.80 for the intra- and interobservers, respectively, which denoted very good agreement between measurements. Accordingly, the linear correlation coefficients were 0.86 and 0.89 for the intra- and interobservers, which indicated a high correlation between measurements.

Historically, few weaning predictors were recommended for clinical practice, mainly due to their low accuracy and reproducibility. In previous studies, the values for the accuracy of the timed inspiratory effort index (referred to as the area under the receiver operating characteristic curve) ranged from 0.90 to 0.96, which expressed a better performance than other predictive indexes described in the literature.[14,17,18] Interestingly, the values for the areas under the curve in the present study also ranged from 0.90 to 0.96. More importantly, no statistical difference was observed between the curves of each of the 2 sets of measurements for the intra- or interobserver data. Given the nature of the study, design limitations were restricted to those that pertained to the pre-established methods used to analyze intra- and interobserver reproducibility. However, it should be commented that it seemed prudent to preclude measurements of the timed inspiratory effort index in circumstances such as elevated intracranial pressure, risk of abdominal content evisceration, acute coronary artery disease, flail chest, and unstable heart failure.

Conclusions

The results of the present study, which addressed the variability of the measurement of the timed inspiratory effort index by intra- and interobservers, showed a very high reproducibility, which reinforced the index as a sensible, accurate, and reliable outcome predictor with regard to liberation from mechanical ventilation. Accordingly, analysis of our data suggested that a measure might be sufficient to make a decision in clinical settings.

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