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Evaluation of indexes predicting the outcome of ventilator weaning and value of adding supplemental inspiratory load

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Abstract. *Objective:* To assess the diagnostic accuracy of several measured and calculated indexes for early prediction of weaning outcome, and to study the value of supplemental inspiratory load in improving the accurate prediction of successful weaning. *Design:* Prospective study. *Setting:* ICU of a University Hospital. *Patients:* Thirty consecutive patients under prolonged mechanical ventilation and without chronic obstructive pulmonary disease (COPD). *Interventions:* Forty weaning trials were performed. Data were recorded at 15, 30 (adding inspiratory flow resistance), 60 and 120 min. *Measurements and main results:* The threshold values and the accuracy of three indexes were determined: Inspiratory airway occlusion pressure at 0.1 sec. (P01) to maximum inspiratory pressure ratio (P01/MIP), inspiratory effort quotient (IEQ), and the ratio of respiratory frequency to tidal volume (F/Vt). All three were useful predictors for weaning success with a diagnostic accuracy between 82%–87%. At 15 min of spontaneous breathing, a P01/MIP ratio <0.14 predicts weaning success with a sensitivity of 82% and specificity of 83%. In our group of patients no reintubation was necessary. The application of mechanical inspiratory load significantly increased P01 values (3.16 ± 1.22 to 3.60 ± 1.19, $p<0.001$). The degree of the P01 increase did not provide prediction of weaning outcome. *Conclusions:* a) P01/MIP, IEQ and F/Vt ratio were accurate, early predictors of weaning outcome. b) The addition of a moderate mechanical inspiratory load did not enhance the diagnostic accuracy of P01 measurements. c) In our patients, a period of two hours seemed to be sufficient for development and detection of weaning failure.

Key words: Ventilator weaning – Respiratory muscles – Respiratory insufficiency – Mechanical ventilation

For years, attempts have been made to obtain functional quantitative parameters which are useful when deciding whether to interrupt respiratory assistance or not, incorporating more and more complex and numerous variables [1–17]. The objective is to predict as soon as possible whether the patient will be able to maintain spontaneous breathing indefinitely, and to achieve and early identification of those who must continue mechanical ventilation. We studied the diagnostic accuracy of three calculated indexes to predict weaning outcome: P01/MIP ratio [16]. Inspiratory effort quotient (IEQ) [5], and the ratio of respiratory frequency to tidal volume (F/Vt) [15]. We compared these indexes with several traditional criteria.

The most common cause of ventilatory assistance dependency is an imbalance between the level of ventilation needed by the patient and the ability of the patient's respiratory systems to respond [18, 19]. During each breath the respiratory muscles cannot indefinitely sustain pressures that exceed a percent of their maximum inspiratory pressure at functional residual capacity (FRC) [20]. P01/MIP relates the inspiratory drive and the effectiveness of muscular contraction during each breath to the maximum capacity to generate pressure. Similarly, IEQ expresses the quotient between muscular effort during normal respiration and the maximum inspiratory pressure.

For a given level of ventilation, energy output is minimized by increasing respiratory frequency and limiting the depth of each breath, a common finding in patients in whom a weaning trial fails [11]. F/Vt ratio reflects the amount of rapid shallow breathing, which appears to provide, during the first minute after the machine is disconnected, a reliable indicator of the ability to be weaned from mechanical ventilation [15].

Repeated measurements during weaning trials were performed for clinical assessment of respiratory pattern, and for determination of the best moment to perform these measurements after disconnection. Lastly, we assessed the value of adding supplemental inspiratory flow resistance to enhance the predictive accuracy of P01 measurements. The response of P01 to respiratory loading by inspiring CO_2 can predict the result of weaning trials: the failure of a rise in CO_2 to augment respiratory effort may signal exhausted respiratory reserves [17]. However, the changes in the inspiratory drive promoted by chemoreceptors occur slowly and continue until chemical conditions reach an equilibrium [21]. We studied the more rapid neuromuscular response using inspiratory flow resistance during a short period of time.

Methods and materials

Patients

Forty weaning trials wer performed on 30 patients (9 women and 21 men) aged 22–79 years (mean±SD: 56.7±14.9). None had COPD. All of them were being ventilated with a Servo ventilator 900C (Siemens-Elema AB, Solna, Sweden) and were included in our study when they met the following conditions:

1) Prolonged mechanical ventilation (>48 h).

2) Improved respiratory process, stable hemo-dynamics, being conscious and cooperative, nasotracheal intubation and adequate airway aspiration, absence of hyperthermia, no administration of respiratory depressant drugs, no important nutritional deficiencies or diet rich in carbohydrates.

3) With the following gasometric data:

$PO_2 \gtrsim 75$ mmHg, $pH > 7.30$ and stable, and $PCO_2 < 45$ mmHG, while being ventilated with the following respiratory pattern:

$Vt = 10$ ml/kg, 12–14 breaths/min, $FiO_2 \lesssim 0.5$, $I:E = 1:2$, $PEEEP = 0$.

4) The patients had previously been informed and had expressed their consent.

Protocol

With the patient in semiseated position, the respirator is switched off and spontaneous respiration is started (commencement of the weaning trial) across a T-circuit building with: a gas blender (Oxygen Blender Bird; Bird Corporation, Palm Springs, California), a 6-litre gas reservoir bag, a Fleisch no. 2 flow transducer (Fleisch, Lausanne, Switzerland) plugged in a Compliance Test Mark III (Gould Godart BV, Bilthoven, The Netherlands), a Statham P23 transducer (Statham Instruments, Hato Rey, PR) for measuring tracheal pressure, a switch device which allows the reduction of the inspiratory circuit bore and thus increases resistance up to the desired level, and a device for inspiratory airway occlusion using a latex balloon inflated with air by means of a syringe [22].

The same FiO_2 was applied as during mechanical ventilation. With a gas flow of 60 l/min the circuit had the following characteristics: Dead space = 70 ml, inspiratory resistance = 2.4 cmH_2O/l/s, expiratory resistance = 1.7 cmH_2O/l/s. Arterial blood gases were measured with an AVL 945 Automatic Blood Gas System analyzer (AVL, Graz, Austria) immediately following blood extraction.

The first data were recorded 15 min after discontinuation of assisted ventilation. At 30 min, inspiratory resistance was increased for a short time period up to a level considered as moderate (10 cmH_2O/l/s), starting data recording 20 s later, which lasted no longer than 5 min. Flow resistance was then withdrawn and new measurements were accomplished at 60 and 120 min.

Respiratory support was reinstituted when at any moment one of the following conditions was fulfilled: $PaO_2 \lesssim 65$ mmHg with $FiO_2 = 0.5$, PCO_2) >50 mmHg, $pH \lesssim 7.30$, cardiac frequency >130 beats/min, evidence of increasing respiratory effort and dyspnea, arrhythmias, bradycardia, angina, restlessness, disorientation or decreasing consciousness [9]. The patient remained at respiratory rest until a new attempt of extubation could be initiated.

After 120 min of spontaneous respiration, those with no need of ventilatory support were extubated, provided they fulfilled the following extubation criteria: $PaO_2 > 65$ mmHg with $FiO_2 \lesssim 0.5$, PIM < -20 cmH_2O, $pH > 7.30$ and stable, respiratory frequency $\lesssim 40$/min. After extubation, patients received adequate pharmacological treatment, respiratory physiotherapy, humidified inspiratory gas and appropriate staff attention.

Weaning from mechanical ventilation was considered a failure when the patient could not be extubated but required respiratory support. Once the established criteria had been met and the patient was extubated, weaning was considered a success. All patients who needed reintubation for respiratory reasons within 48 h after extubation were classified as unsuccesful extubations, whereas the opposite were considered successful extubation cases.

Records

Measured parameters were: Arterial pH, PaO_2 (mmHg), $PaCO_2$ (mmHg), PaO_2/PAO_2, heart rate (beats/min), tidal volume in ml (Vt), minute volume in ml (VE), respiratory frequency (F), maximum inspiratory pressure in cmH_2O (MIP) measured at FRC, and occlusion pressure at 0.1 s in cmH_2O (P01). Simultaneous recording on a Honeywell VR-12 polygraph (Electronics for Medicine, Pleasantville, N.Y.) of the inspiratory and expiratory flow, tidal volume, tracheal pressure (paper speed:10 mm/s) was performed. Volume calibration, measured by pneumotachograph, was carried out with 1-liter super syringe. Tidal volume at each respiration was measured for one minute and divided by the respiratory frequency, thus trying to minimize the effect which physiological variations in the respiratory pattern could have on ventilation measurements. The total length of each respiratory cycle (Ttot) was calculated dividing 60 by the respiratory frequency. To obtain the inspiratory time value (Ti), the number of respirations carried out during a minimum of one minute was analyzed, and the average was calculated.

To record P01, airway occlusion was performed as many times as necessary in order to avoid possible response modifications by anticipation or experience. All the advice available in this respect was taken into account [23–25]. After each occlusion (paper speed 50 mm/s, range of 25 mm = 6.5 cmH_2O), a minimum of 8–10 normal respirations were allowed for. MIP measurement was carried out at functional residual capacity (FRC), for which patients had to perform maximal volitional inspiration at the end of normal expiration. The performance was repeated three times, selecting the highest value.

Calculated parameters were: Mean inspiratory flow (Vt/Ti) in ml/s, inspiratory duty cycle (Ti/Ttot), F/Vt ratio, inspiratory effort quotient (IEQ) and P01/maximum inspiratory pressure ration (P01/MIP) [18]. $IEQ = (k\ Vt/Cdyn) \times (Ti/Ttot)/MIP$ [5]. K is a constant which depends on the shape of the inspiratory driving pressure wave. In ICU patients k should reach about 0.75.

Dynamic compliance (Cdyn) = corrected Vt/(peak pressure−positive end expiratory pressure). Corrected Vt = Vt−compressible respirator volume. The compressible volume of the SERVO 900C was calculated according to the method described by Demers et al. [26]. Pulmonary gas exchange was assessed by the PaO_2/PAO_2 ratio.

Student's *t*-test was used to compare mean values, and a probability smaller than 0.05 was considered significant. We calculated the diagnostic efficacy of each index with respect to successful weaning [27].

- Sensitivity $(S) = TP/(TP+FN) \times 100$; Specificity $(E) = TN/(TN+FP) \times 100$
- Positive predictive value $(V+) = TP/(TP+FP) \times 100$
- Negative predictive value $(V-) = TN/(TN+FN) \times 100$
- Diagnostic accuracy $(DA) = (TP+TN)/(TP+TN+FP+FN) \times 100$

TP = True positive. FP = False positive. TN = True negative. FN = False negative.

Results

In Table 1, the individual clinical characteristics of patients are shown. There were 28 cases (70%) of successful weaning (extubated patients), and 12 (30%) of weaning failure. The latter presented the following objective criteria for weaning failure: PIM > -20 mH_2O on 4 occasions, FR >40 min in 3 cases, $PaCO_2 > 50$ mmHg in 2 cases, and cardiac frequency >130 beats/min accompanied by arterial hypertension in one case. In addition dyspnea and evidence of increasing respiratory effort

Table 1. Clinical characteristics of patients, baseline lung mechanics and gas exchange status. P01/MIP and F/Vt values prior to extubation and before reinstitution of mechanical ventilation

Patient no.	Age	Weight (kg)	Diagnosis	Mechanical ventilation (days)	Cdyn	PaO_2/PAO_2	P01/MIP	F/Vt
Successes (n = 28)								
1	49	60	Fat embolism	25	27	0.27	0.11	71
2	43	52	Cardiac failure	3	22	0.42	0.08	53
3e	52	60	Thoracic trauma	12	29	0.24	0.10	110
4b	66	67	Pulmonary embolism	15	39	0.46	0.13	70
5	70	69	Sepsis	4	24	0.31	0.13	55
6	51	92	Thoracic trauma	6	37	0.30	0.12	56
7	77	49	Pulmonary embolism	14	24	0.40	0.09	115
8	24	90	Sepsis	15	34	0.34	0.09	49
9	24	58	Pancreatitis	7	26	0.58	0.05	91
10c	44	69	Sepsis	32	26	0.52	0.12	80
11b	72	72	Sepsis	14	30	0.43	0.15	99
12	64	68	Bronchoaspiration	4	35	0.39	0.06	68
13	37	60	Pneumonia	13	27	0.62	0.04	54
14	64	58	Hemorragic shock	4	27	0.27	0.12	75
15	48	82	Thoracic trauma	6	35	0.32	0.14	61
16	70	63	Hemorragic shock	7	28	0.39	0.13	53
17b	74	88	Pneumonia	19	38	0.46	0.15	105
18	74	49	Cardiac failure	3	24	0.67	0.07	89
19	55	94	ARDS	22	34	0.39	0.05	56
20	45	88	Sepsis	6	36	0.49	0.10	61
21	48	70	Mitral insufficiency	8	27	0.51	0.15	78
22	22	78	Hemoptysis	4	35	0.65	0.08	59
24	76	72	Pneumonia	3	27	0.64	0.07	44
25b	67	64	ARDS	11	28	0.29	0.11	83
26	79	50	Bronchoaspiration	4	27	0.26	0.10	51
28	62	71	Thoracic trauma	24	28	0.53	0.05	70
29	40	116	Bronchoaspiration	6	32	0.68	0.16	33
30	56	89	Thoracic trauma	7	35	0.41	0.10	71
Mean	55	71		11	30	0.43	0.10	71
SD	17	16		8	5	0.13	0.03	21
Failures (n = 12)								
3a	52	60	Thoracic trauma	3	22	0.24	0.26	110
3b	52	60		5	21	0.25	0.25	103
3c	52	60		7	24	0.24	0.23	102
3d	52	60		9	25	0.29	0.20	114
4a	66	67	Pulmonary embolism	13	30	0.42	0.17	97
10a	44	69	Sepsis	20	23	0.42	0.29	118
10b	44	69		29	25	0.40	0.22	96
11a	72	72	Sepsis	7	24	0.36	0.15	124
17a	74	88	Pneumonia	17	36	0.41	0.22	115
23	75	59	Pneumonia	6	22	0.43	0.20	80
25a	67	64	ARDS	6	24	0.26	0.33	98
27	57	87	Diaphragmatic paralysis	9	27	0.56	0.14	76
Mean	59	68		11	25	0.35	0.22	103
SD	11	10		7	3	0.10	0.05	15
Success vs failures	ns	ns		ns	$p<0.05$	ns	$p<0.001$	$p<0.001$

Cdyn, dynamic compliance (ml/cmH_2O)

were evident in all these cases. In the two remaining patients, respiratory assistance was re-established at 30 min due to subjective criteria of dyspnea, diaphoresis and increasing respiratory effort. The resumption of assisted ventilation was necessary in the first 30 min in 6 weaning attempts, 1 at 40 min and 5 at 120 min. In our study there were no reintubations, that is, success in weaning was also success in extubation (see Discussion).

Figure 1 shows two sets of clumping illustrating the values of P01/MIP, IEQ and F/Vt before respirator reinstitution in our 12 unsuccessful ventilator weaning attempts, and also shows the values prior to extubation for the 28 successful cases (mean values difference in the three indexes: $p<0.001$). All patients with P01/MIP <0.14 or IEW <0.19 could be extubaed, while those with values over 0.16 (P01/MIP) or 0.23 (IEQ) needed re-

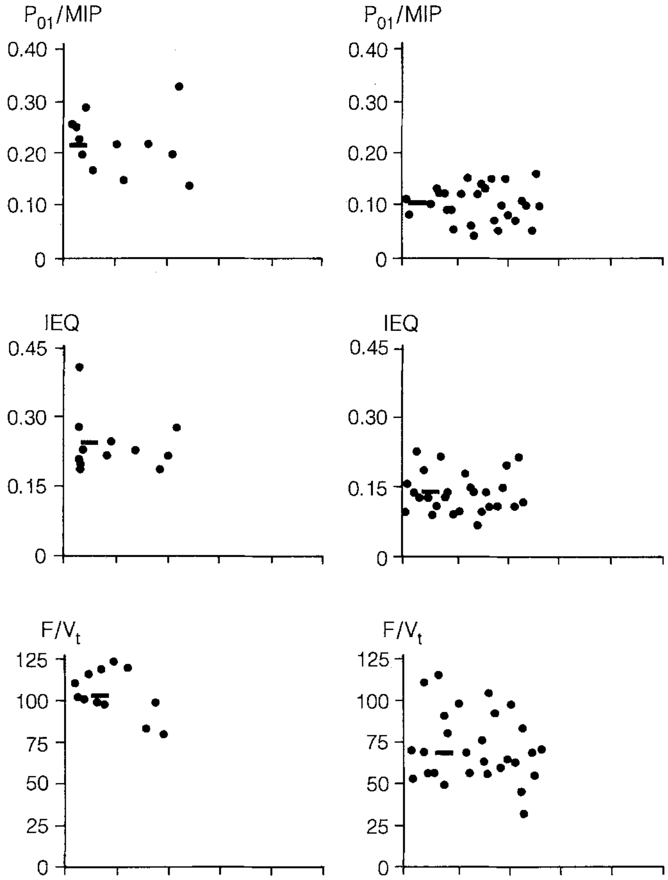

Fig. 1. On the *left*: P01/MIP, IEQ and F/Vt in weaning failure before reinstatement of respiratory assistance ($n = 12$). On the *right*, values in successfully weaned patients prior to extubation ($n = 28$). There is an "intermediate zone" of overlapping between 0.14–0.16 in P01/MIP and 0.19–0.23 in IEQ values. F/Vt showed important overlapping. Difference in mean values (failure vs success) in the three indexes: $p < 0.001$

spiratory assistance. F/Vt showed overlapping values. We selected as threshold values those which discriminated best between successfully and unsuccessfully weaned patients.

Table 2 shows the accuracy of some selected critical threshold values of measured parameters and calculated indexes as indicators to resume mechanical ventilation during a T-trial. We establish their diagnostic efficacy as predictors of success in ventilator weaning after 15, 60 and 120 min of spontaneous respiration (Table 3).

Between 15 and 60 min of spontaneous respiration, the successfully weaned patients ($n = 28$) experienced an elevation in VE ($p < 0.05$), and F ($p < 0.01$) values, with no significant posterior variations until the end of the 120 min trial. Four patients in the failure group (3 c, 10 b, 11 a and 23) showed significant increases in P01 ($p < 0.05$), F ($p < 0.05$), Vt/Ti ($p < 0.05$) and VE ($p < 0.05$) from the beginning to the end of the weaning attempt. In our group of patients, at any moment of the trial, unsuccessful ventilator weaning patients showed significantly higher values of F ($p < 0.001$), VE ($p < 0.05$), P01 ($p < 0.05$) and Ti/Ttot ($p < 0.01$) than those successfully weanded, while MIP ($p < 0.001$) and Vt ($p < 0.05$) were smaller.

Table 2. Diagnostic efficacy of threshold values of measured and calculated indexes as indicators to resume mechanical ventilation during weaning trial

Index	Sensitivity	Especificity	Positive predictive value	Negative predictive value	Diagnostic accuracy
P01/MIP	(12/12)	(23/28)	(12/17)	(23/23)	(35/40)
≥0.14	100%	82%	71%	100%	87.5%
IEQ	(12/12)	(23/28)	(12/17)	(23/23)	(35/40)
≥0.19	100%	82%	71%	100%	87.5%
F/Vt	(10/12)	(23/28)	(10/15)	(23/25)	(33/40)
≥96	83%	82%	66%	92%	82.5%
F	(9/12)	(23/28)	(9/14)	(23/26)	(32/40)
≥35	75%	82%	64%	88%	80%
MIP	(9/12)	(23/28)	(9/14)	(23/26)	(32/40)
≥ −23	75%	82%	64%	88%	80%
P01	(9/12)	(17/28)	(9/20)	(17/20)	(26/40)
≥3.4	75%	61%	45%	85%	65%
VE	(9/12)	(18/28)	(9/20)	(18/22)	(27/40)
≥12.5	75%	64%	45%	86%	67.5%
Vt	(7/12)	(21/28)	(7/14)	(21/26)	(28/40)
≤360	58%	75%	50%	81%	70%

Definitions of abbreviations: P01/MIP, P01/maximum inspiratory pressure ratio; IEQ, inspiratory effort quotient; F/Vt, frequency/tidal volume ratio (breaths/min/liter); F, respiratory frequency (breaths/min); MIP, maximum inspiratory pressure at FRC (cmH_2O); P01, inspiratory airway occlusion pressure at 0.1 s (cmH_2O); VE, minute ventilation (liters/min); Vt, tidal volume (ml)

Table 3. Accuracy of each index as indicators for successful weaning after 15, 60 and 120 min of spontaneous breathing

Index	Sensitivity	Especificity	Positive predictive value	Negative predictive value	Diagnostic accuracy
Values after 15 min					
P01/MIP	(23/28)	(10/12)	(23/25)	(10/15)	(33/40)
<0.14	82%	83%	92%	67%	82.5%
IEQ	(23/28)	(9/12)	(23/26)	(9/14)	(32/40)
<0.19	82%	75%	88%	64%	80%
F/Vt	(24/28)	(8/12)	(24/28)	(8/12)	(32/40)
<96	86%	67%	86%	67%	80%
Values after 60 min					
P01/MIP	(23/28)	(4/5)	(23/24)	(4/9)	(27/33)
<0.14	82%	80%	96%	44%	82%
IEQ	(22/28)	(5/5)	(22/22)	(5/11)	(27/33)
<0.19	79%	100%	100%	45%	82%
F/Vt	(23/28)	(3/5	(23/25)	(3/8)	(26/33)
<96	82%	60%	92%	37%	79%
Values after 120 min					
P01/MIP	(23/28)	(5/5)	(23/23)	(5/10)	(28/33)
<0.14	82%	100%	100%	50%	85%
IEQ	(23/28)	(5/5)	(23/23)	(5/10)	(28/33)
<0.19	82%	100%	100%	50%	85%
F/Vt	(24/28)	(4/5)	(24/25)	(4/8)	(28/33)
<96	86%	80%	96%	50%	85%

Definitions of abbreviations: P01/MIP, P01/maximum inspiratory pressure ratio; IEQ, inspiratory effort quotient; F/Vt, frequency/tidal volume ratio (breaths/min/liter)

Inspiratory load

The application of inspiratory flow resistance ($n = 34$) shows that loading increases P01 (3.16±1.22 versus

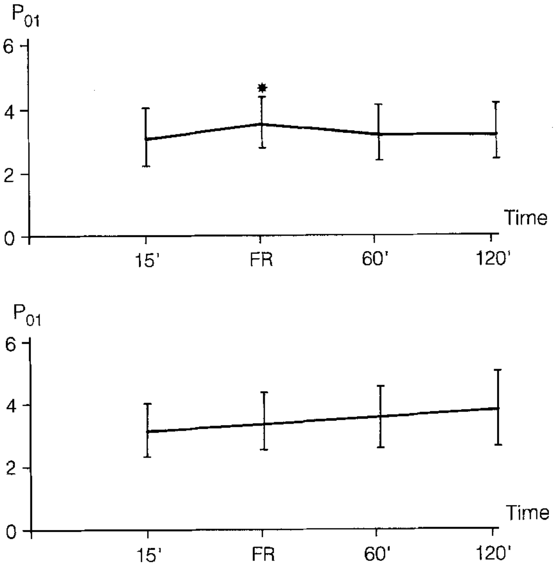

Fig. 2. *Top:* Time course of P01 during successfully weaned patients ($n = 28$) (X±SEM). * The external inspiratory load increases P01 ($p < 0.01$). *Bottom:* Time course of P01 during weaning in attempts requiring reinstitution of assisted respiration after 120 min of spontaneous breathing ($n = 5$) (X±SEM). No significant P01 differences comparing paired mean values at any moment of the trial. *FR*, Inspiratory flow resistance

3.60±1.19, $p < 0.0001$). Figure 2 (top) shows the time course of the P01 (mean±SEM) throughout the trial in patients with successful weaning ($n = 28$). In this group, the use of inspiratory flow resistance increases the P01 ($p < 0.01$); once the loading is withdrawn, the P01 descends significantly ($p < 0.05$), and there are no further variations until extubation is performed 120 min later. Figure 2 (bottom) shows the time course of P01 (mean±SEM) during T-trial with patients requiring ventilator reinstitution after 120 min of spontaneous respiration ($n = 5$). Table 4 shows the degree of P01 increase after application of inspiratory flow resistance in successful and unsuccessful weaning trials. Comparing both groups, the difference in the P01 increases as a result of respiratory loading is not significant.

Discussion

As predictors of the outcome of weaning from mechanical ventilation, we studied the diagnostic accuracy of several indexes obtained at patients' bedside during two hours of spontaneous breathing across a T-circuit. The population studied was limited to patients undergoing prolonged mechanical ventilation (48 h) and, in contrast to a large number of previous studies [15, 17, 25], none of the patients had COPD. Pulmonary hyperinflation in COPD patients generates a series of important geometric alterations and, in consequence, the diaphragm and the other respiratory muscles operates with severe mechanical disadvantages [19, 28]. We therefore consider that this type of patients should be studied separately as a subgroup.

Table 4. Airway occlusion pressure (P01) before and during external inspiratory flow resistive load

	P01 basal	P01 FR	P01 FR/P01 basal
All attemps ($n = 34$)	3.16±1.22	3.60±1.19	1.13
Weaning success ($n = 28$)	3.09±1.22	3.52±1.05	1.13*
Weaning failure ($n = 5$)	3.12±0.93	3.40±1.04	1.08*

P01 basal, P01 at 15 min of spontaneous respiration; P01 FR, P01 value after adding supplemental external inspiratory flow resistance
* Comparing both groups, the degree of increase in P01 is not significant

In our group of patients no reintubation was necessary; thus, success in weaning was also success in extubation. The time period of 120 min seems to be sufficient for the development and detection of unsuccessful weaning. The definition of weaning success is fairly objective (spontaneous ventilation for >48 h), but it is more difficult to define weaning failure objectively. We cannot assure that the patients reconnected to the ventilator because they did not tolerate 2 h of T-piece would have needed reintubation in case of early extubation by a more aggressive physician. The lack of objective criteria for weaning failures is a problem found in all studies on discontinuation of mechancial ventilation and makes it difficult to compare the accuracy of predictive indexes in different studies. Of our 12 failed weaning attempts, 10 met objective criteria for weaning failure. In our patients, independently of the value of all weaning indexes, the ability to maintain spontaneous respiration for 120 min, keeping $PaO_2 > 65$ mmHg ($FiO_2 \lesssim 0.5$), $PaCO_2 < 50$ mmHg, pH over 7.30, breathing frequency under 40 min, cardiac frequency <130, and MIP at FRC less than -20 cmH_2O is an accurate indicator of successful weaning, with a specificity (absence of false positives) of 100%.

MIP was obtained recording maximum inspiratory pressure after normal expiration, i.e. with a lung volume near FRC. Other authors have proposed a standard, reproducible form to measure MIP at residual volume in intubated patients, the patient's cooperation not being necessary [29]. The maximum active muscular force, however, is achieved at a lung volume similar to that in an elastic rest situation, which occurs at lung volumes close to FRC [30]. All our patients were with nasotracheal intubation, without respiratory depressants, conscious, cooperative, sufficiently informed and able to make a voluntary maximum inspiratory effort. Theoretically, all the patients who require prolonged mechanical ventilation as a consequence of severe lung pathology and whose extubation may be complex should be conscious, with a sufficient degree of cooperation, maintain a minimum of efficient cough and carry out physiotherapy exercises if necessary. Under these conditions our patients were able to perform voluntary maximum inspiration at FRC.

Maximum inspiratory pressure provides information about inspiratory muscle force, but to judge endurance any single indicator must reflect both breathing capability and the amount of ventilation required by the patient [18, 19]. Roussos et al. studied respiratory muscle endurance, relating the inspiratory muscle pressure necessary during normal respiration to the maximum capacity to generate pressure, and finding a critical threshold above which the respiratory effort cannot be maintained indefinitely [20]. Two suggested indexes (P01/MIP and IEQ) are based on relating the muscular effort each breath to the MIP. All our patients with P01/MIP <0.14 or IEQ <0.19 could be successfully extubated, while those with values over 0.16 or 0.23 respectively required the reinstitution of mechanical ventilation (intermediate zone for P01/MIP: 0.14–0.16, and for IEQ: 0.19–0.23). At a value of P01/MIP <0.14, at 15 min after having started ventilator weaning, patients could be successfully weaned and extubated with a sensitivity of 82% and a specificity of 83%. For IEQ the specificity drops to 75%. Both indexes seem to conserve their predictive power during weaning, and at two hours their specificity is 100%.

For a given level of ventilation, the respiratory work becomes diminished by rapid shallow breathing (a common finding in patients in whom a weaning trial fails), which can therefore be an adaptation to avoid fatigue. In our group of patients, at any moment of the trial, unsuccessful ventilator weaning patients showed significantly higher values of F, VE, P01 and Ti/Ttot than successfully weaned, while Vt and MIP were smaller. These findings indicate rapid shallow breathing, greater inspiratory drive and less inspiratory muscular strength in unsuccessfully weaned patients. The problem is whether rapid shallow breathing is a sign of adaptation to decrease respiratory work, or whether it suggests incipient respiratory decompensation, tachypnea not always indicating the presence of overt fatigue [18]. An increase in respiratory rate and fall in tidal volume should serve to alert the clinician that the patient may be breathing against a fatiguing load, but these changes may not be accurate predictors of long-term performance [31]. The F/Vt ratio reflects the amount of rapid shallow breathing, and it appears to be the single most accurate index to early prediction of weaning outcome [15]. In our patients, a threshold value of F/Vt $\gtrsim 96$ is an indicator of weaning failure with a sensitivity of 83% and a specificity of 82%. During weaning trials the diagnostic efficacy of this index was slightly less accurate than those which reflect the balance between respiratory demands and respiratory muscle reserve (P01/MIP and IEQ).

The patients who failed to wean promptly developed rapid shallow breathing, but their respiratory pattern may undergo changes from the beginning to the end of the weaning trial, generally consisting of an increase in the respiratory drive, minute volume and respiratory rate [11, 31]. We have found that the respiratory pattern in the successfully weaned patients is not stable after respiratory support is discontinued, presenting an increase in VE and respiratory frequency between 15 and 60 min. Thus, the prediction of the outcome could theoretically be less accurate if the extubation criteria used are determined too early during a weaning trial. In addition, although the indexes studied were useful indicators of the ability to be weaned during the first 15 min after the machine is disconnected, with the classic criteria utilized in the protocol of this study it appears that a 2 h period has a high predictive power (specificity 100%) of successful trials of weaning. This seems to be enough time to detect the patients who will fail to wean and to select those who can be extubated with success, while a P01/MIP >0.14, an IEQ >0.19 or F/Vt ratio >96 can indicate to the clinical that mechanical ventilation should be reinstated. Following two hours of spontaneous respiration, these indexes predict weaning success and successful extubation with a sensitivity between 82%–86% and a specificity between 80%–100%.

Inspiratory load

Increase in central respiratory drive during weaning failure has been found in intensive care patients with different pathologies [12, 13, 25]. Montgomery et al. studied 11 patients with heterogeneous causes of respiratory failure, showing that the response of P01 to respiratory loading by inspiring CO_2 can predict the result of weaning trials, given that the failure of a rise in CO_2 to augment respiratory effort may signal exhausted respiratory reserves [17]. The use of hypercapnia as a method of respiratory laod during weaning is not convenient because the neuromuscular mechanisms promoted by chemoreceptors occur slowly and continue until chemical conditions reach an equilibrium [21]. We have used the increase in inspiratory flow resistance as the respiratory overload method because the early respiratory adjustment and compensation of external mechanical load is due to reflexes caused by the stimulation of mechanoreceptors, and to the intrinsic properties of the respiratory muscles [21]. This rapid response facilitates studying the neuromuscular compensatory capacity while maintaining the loading during a short time period, since it should not significantly interfere in the respiratory effort performed during weaning trial.

The application of inspiratory flow resistance increases P01 in patients with successful weaning; once the load is withdrawn, P01 decreases significantly and there are no variations later until extubation is performed. The patients requiring ventilator reinstitution do not behave in a uniform manner, and no significant P01 differences are registered when comparing paired mean values at any moment of the trial. Given the level of inspiratory resistance used, the degree of respiratory drive increase does not yield a prediction of weaning outcome. We have not been able to distinguish between successes and failures using a respiratory flow resistance of $10\,cmH_2O/l/s$, which in our opinion means that either (a) the stimulus promoted by mechanoreceptors and respiratory muscles in response to mechanical load used was inferior to that produced by chemoreceptors as a response to a hypercapnic challenge that raised end-tidal CO_2 approximately 10 mmHg, or (b) an exhausted inspiratory drive does not reflect a true pathophysiologic determinant of the outcome of weaning. We therefore cannot confirm Montgomery's findings. Thus, the addition of a mechanical, external and moderate inspiratory load during a weaning trial does not enhance the diagnostic accuracy of P01 measurements.

In summary, P01/MIP, IEQ and F/Vt ratio were accurate indicators to resume mechanical ventilation during weaning trial, and were accurate predictors of weaning outcome after 15 min of discontinuation of mechanical ventilation, its predictive power remaining acceptably stable throughout two hours of spontaneous breathing. The use of selected classical criteria together with the ability to maintain spontaneous respiration for two hours seems to be, in our study, as accurate as more sophisticated tests predicting successful weaning. This time period seems to be sufficient for development and detection of weaning failure. During weaning the respiratory pattern is not stable, undergoing significant changes after the moment the machine is disconnected. Thus, in spite of the possibilities of early weaning outcome prediction, we suggest two hours of weaning trial, a time period which does not seem excessive if we take into consideration that these are patients who require prolonged mechanical ventilation as a conseqeunce of severe lung pathology and whose extubation is potentially complex. During weaning, the threshold values of the indexes studied are accurate indicators to alert the clinician that the patient may be breathing against a fatiguing load and needs assisted respiration. After two hours of spontaneous breathing, all three indexes are accurate indicators of successful extubation, and the choice of one depends on its diagnostic efficacy and ease of calculation. Finally, while admitting that an exhausted inspiratory drive is a determinant factor in weaning outcome, the addition of a moderate mechanical inspiratory load did not enhance the accuracy of P01 measurements predicting weaning outcome. Further studies, increasing the number of patients using higher levels of external and mechanical inspiratory load, are necessary.

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