Predictors of weaning outcome in chronic obstructive pulmonary disease patients

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ABSTRACT: Several threshold values for predicting weaning outcome from mechanical ventilation have been proposed. These values, however, have been obtained in nonhomogeneous patient populations. The aim of the present study was to determine the threshold values in chronic obstructive pulmonary disease (COPD) patients and compare them to those reported for nonhomogeneous patient populations.

The initial weaning trial included 81 COPD patients. Fifty-three of them underwent a successful weaning trial, whereas 28 failed it. The latter were enrolled into the present investigation, and were restudied during a subsequent successful trial. The weaning indices used were those reported in the literature.

The threshold values obtained were within 10% of those reported for a nonhomogeneous patients population only for tidal volume and effective compliance. The classification error was <20% for maximal inspiratory pressure (MIP), occluded inspiratory pressure swing (ΔP_i)/MIP, rapid and shallow breathing (respiratory frequency/tidal volume), and compliance, rate, oxygenation, pressure index (CROP), whereas the area under the receiver operating characteristic curves was >0.9 only for ΔP_i /MIP and CROP.

In conclusion, the threshold values obtained in chronic obstructive pulmonary disease patients who failed the first weaning attempt differed from those previously reported. Although a gold standard weaning index is not available for chronic obstructive pulmonary disease patients, the occluded inspiratory pressure swing/maximal inspiratory pressure and compliance, rate, oxygenation, pressure index may be candidates for such a role.

Eur Respir J 2000; 15: 656–662.

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Keywords: Chronic obstructive pulmonary disease
classification error
receiver operating characteristic
threshold values
weaning indices

Received: April 22 1999

Accepted after revision November 29 1999

This study was supported, in part, by a grant from the Ministero dell'Università e della Ricerca Scientifica e Tecnologica

Numerous indices have been proposed for the prediction of weaning outcome from mechanical ventilation. Only a few, however, are of good diagnostic accuracy. YANG and TOBIN [1] established the threshold values of a battery of different weaning indices reflecting respiratory mechanics, pulmonary gas exchange, control of breathing and inspiratory muscle function in a highly nonhomogeneous patient population. Then they assessed the predictive power of the threshold value for each index in another nonhomogeneous patient population, and found that the rapid and shallow breathing index (the ratio of respiratory frequency (f_R) to tidal volume (V_T)) was the most accurate predictor of weaning outcome. However, the abnormalities of respiratory mechanics, gas exchange, control of breathing and inspiratory muscle function vary markedly among patients who require mechanical ventilation for different aetiologies [2–7]. Accordingly, the threshold values of the weaning indices should be assessed in homogeneous patient populations.

The aim of this study was to determine the threshold values of previously proposed weaning indices in a population of chronic obstructive pulmonary diseases (COPD) patients. The same patients were studied first during a failed weaning trial (WF) and then during a successful trial (WS).

Materials and methods

Patients

The initial weaning trial included 81 COPD patients admitted to the authors' intensive care unit (ICU; S. Anna Hospital) for management of acute respiratory failure (ARF). Fifty-three of them underwent a WS, and 28 a WF. The latter were enrolled in the present investigation, and were restudied during a subsequent WS. The anthropometric characteristics of the patients are given in table 1. The diagnosis of COPD was based on clinical history, chest radiography and lung function tests (forced expiratory volume in one second (FEV₁)/forced vital capacity (FVC) <70% of the predicted value), according to American Thoracic Society criteria [8]. The FEV₁/FVC at the time of discharge from the ICU was available for 22 patients and averaged $46 \pm 11\%$ pred. The predicted values were those of MORRIS *et al.* [9]. The ARF was due to different aetiologies (table 1): 19 patients had airway infection, characterized by wheezing, increased sputum production, cough, fever and elevation of the white blood cell count; five had pneumonia as evidenced by typical radiographic findings. In three cases the cause of ARF

Table 1. – Anthropometric and clinical characteristics of chronic obstructive pulmonary disease patients

Patient No.	Sex	Age yrs	Weight kg	Cause of ARF	tICU days	tWF days	tWS days	FEV1* L	FVC* L
1	M	69	95	Pneumonia	11	5	6	0.93	1.90
2	F	76	48	Airway infection	45	15	33		
3	F	76	90	CHF; airway infection	14	7	10	0.89	1.33
4	M	76	113	Airway infection	18	7	11	1.32	2.18
5	F	74	100	CHF; airway infection	22	9	15		
6	F	78	50		10	5	7	0.56	0.90
7	M	66	80	Airway infection	26	12	21	0.63	1.59
8	F	75	48	Airway infection	28	17	20	0.47	0.95
9	F	81	80	Airway infection	12	6	9	0.50	1.20
10	M	72	85	Pneumonia	35	20	28	0.92	1.80
11	M	75	70	Pneumonia	15	7	13	0.64	1.50
12	F	69	58	Airway infection	19	9	13	0.92	1.31
13	M	65	78	Sepsis	42	13	15	0.78	1.20
14	M	67	40	Airway infection	17	7	12		
15	F	65	71		14	5	7	0.78	1.56
16	M	77	50	Airway infection	19	8	13	0.52	1.58
17	F	67	53	Airway infection	17	9	15	0.43	0.90
18	F	67	58	Airway infection	24	8	17	0.39	0.73
19	F	63	70	CHF; airway infection	37	12	26	0.91	1.87
20	M	65	93	Airway infection	10	5	7	0.57	1.47
21	F	74	49	Airway infection	13	5	8		
22	M	79	53	Airway infection	9	5	7		
23	M	82	75	Airway infection	15	6	8	0.58	1.30
24	F	74	45	Airway infection	14	6	8		
25	F	65	75		9	5	8	0.32	0.96
26	F	65	87	NHL; airway infection	25	15	21	0.60	1.41
27	M	67	67	Pneumonia	9	5	6	0.37	1.64
28	M	79	70	Pneumonia	15	5	8	0.68	1.46
Mean		72	70		19	8	13	0.67	1.39
SD		6	19		10	4	8	0.25	0.38

*: measurements made at time of discharge from intensive care unit (ICU). ARF: acute respiratory failure; tICU: time in ICU; tWF: time on mechanical ventilation before a failed weaning trial; tWS: time on mechanical ventilation before a successful weaning trial; FEV1: forced expiratory volume in one second; FVC: forced vital capacity; M: male; F: female; CHF: congestive heart failure; NHL: non-Hodgkin's lymphoma.

could not be determined. All patients were hypercapnic when they were transferred to the ICU. At the time of discharge from the ICU, their arterial carbon dioxide tensions (P_{a,CO_2}) amounted to 7.3 ± 1.1 kPa (55 ± 8 mmHg). On discharge, only three patients were not hypercapnic ($P_{a,CO_2} < 5.7$ kPa (43 mmHg)), suggesting that most of the patients (90%) had undergone acute on chronic respiratory failure.

The duration of mechanical ventilation at the time of the WF and the WS is shown in table 1. On average, 4.8 ± 3.9 days elapsed between the two trials. The study was approved by the Institutional Ethics Committee and informed consent was received from the patients or next of kin.

Patients were intubated with endotracheal tubes of 8.0–8.5 mm internal diameter. During the day they were ventilated with assist-control (A/C) mode or pressure support ventilation using a Servo 900C ventilator (Siemens-Elema, Solna, Sweden), as decided by their attending physician. Overnight, however, they were all placed on A/C mode ventilation. The decision to attempt a weaning trial, extubate a patient or reinstitute mechanical ventilation was made by the primary physician who was blinded to the study design and did not know the values of the various weaning indices used in the present study (table 2). Such decisions were made according to the routine clinical

Table 2. – Threshold values for predicting weaning outcome

Weaning index	Threshold value	
	Previous studies*	Present study
f_R breaths·min ⁻¹	≤38	≤25
$\dot{V}_T$ mL	≥325	≥340
$\dot{V}_T/BW$ mL·kg ⁻¹	≥4	≥5
$\dot{V}'_E$ L·min ⁻¹	≤15	≤8.6
VC/BW mL·kg ⁻¹	≥10	≥13
MIP cmH ₂ O	≥15	≥44
$P_{a,O_2}/P_{A,O_2}$	≥0.35	≥0.46
$C_{rs,eff}$ mL·cmH ₂ O ⁻¹	≥22	≥24
$C_{rs,st}$ mL·cmH ₂ O ⁻¹	≥33	≥54
$\Delta P_{i/MIP}$	≤0.3	≤0.41
$f_R/\dot{V}_T$ breaths·min ⁻¹ ·L ⁻¹	≤100	≤84
CROP mL·breath ⁻¹ ·min ⁻¹	≥13	≥16

*: from [1], except for vital capacity (VC)/body weight (BW) and inspiratory pressure swing (ΔP_i)/maximal inspiratory pressure (MIP), which were from [10] and [11], respectively. f_R : respiratory frequency; $\dot{V}_T$: tidal volume; $\dot{V}'_E$: minute ventilation; P_{a,O_2} : arterial oxygen tension; P_{A,O_2} : alveolar oxygen tension; $C_{rs,eff}$: effective compliance of the respiratory system; $C_{rs,st}$: static compliance of the respiratory system; CROP: compliance, rate, oxygenation, pressure index ($C_{rs,eff} \times 1/f_R \times P_{a,O_2}/P_{A,O_2} \times MIP$).

criteria of the authors' department, namely: 1) consciousness (normal orientation and thought processes); 2) haemodynamic stability without need for vasoactive drugs and absence of arrhythmias; 3) metabolic and electrolyte balance ($\text{pH} \geq 7.35$ and serum sodium, potassium, chlorine, calcium and magnesium ion concentrations within normal range); 4) normal kidney function (serum creatinine levels and azotaemia within normal range); 5) normal liver (no coagulopathy or hyperbilirubinaemia and transaminase activity within normal range); 6) normal digestive system function (no vomiting, diarrhoea or constipation); 7) near-resolution of the immediate cause of ARF (decreased sputum production, cough, wheezing and white blood cell count associated with absence of fever; and resolution of pneumonia on radiography); and 8) arterial oxygen saturation (Sa,O_2) $>90\%$ with inspiratory oxygen fraction ≤ 0.4 during mechanical ventilation. A WS was registered when the patient was capable of spontaneous breathing during a 2-h T-piece weaning trial followed by extubation, which did not require reinstitution of mechanical ventilation within 48 h. A WF was registered when the 2-h weaning trial was terminated because of respiratory distress and cardiovascular instability (tachypnoea, increased accessory muscle activity, diaphoresis, facial signs of distress, tachycardia, arrhythmias and hypotension) or if Sa,O_2 and/or the pH fell below 88% and 7.3, respectively. Extubation failure was defined when reinstitution of mechanical ventilation was required <48 h after extubation. The latter was required in only two subjects: patient No. 10 18 h after extubation because of respiratory acidosis and paradoxical breathing, and patient No. 19 after 36 h because of respiratory distress associated with fever. None of the patients exhibited upper airway problems (e.g. oedema) after extubation.

Weaning indices

The weaning indices used consisted in those previously used, listed in table 2 together with the corresponding threshold values.

Procedure and data analysis

Immediately before the weaning trials, the patients were ventilated in A/C mode with constant flow, with the ventilator settings adjusted to achieve the lowest levels of minute ventilation ($\dot{V}'_E$) and an $\dot{f}_R$ compatible with relaxation of the respiratory muscle, without the need for sedatives or muscle relaxants. During passive mechanical ventilation, the following variables were read from the ventilator dials: $\dot{V}_T$ during mechanical ventilation ($\dot{V}_{T,MV}$), peak airway pressure (P_{peak}) and, with end-expiratory and end-inspiratory occlusions of >3 s, the static end-expiratory ($PEEP_{\text{tot}}$) and end-inspiratory (P_{plateau}) occlusion pressures. The following criteria were used to confirm that the measurements had been obtained during relaxation: 1) no trigger activation, 2) stability of peak airway pressure during ≥ 10 respiratory cycles; and 3) attainment of a plateau during the 3-s end-inspiratory and end-expiratory airway occlusions. For each variable, the mean value of three measurements was calculated.

The internal transducers of the ventilator underwent checks and calibration throughout the study period. In order to reduce the effect of the compliance of the system connecting the subjects to the ventilator on the respiratory mechanics measurements, a single length of standard low-compliance adult tubing was used and the humidifier omitted from the inspiratory line. The compliance of the system connecting the subjects to the ventilator was $0.1 \text{ L}\cdot\text{kPa}^{-1}$. The arterial oxygen tension (P_{a,O_2})/alveolar oxygen tension (P_{A,O_2}) was also measured during this period of mechanical ventilation.

From the above measurements, the following indices were computed: a) static respiratory compliance ($C_{rs,st}$): $C_{rs,st} = \dot{V}_{T,MV} / (P_{\text{plateau}} - PEEP_{\text{tot}})$; and b) effective respiratory compliance ($C_{rs,eff}$): $C_{rs,eff} = \dot{V}_{T,MV} / (P_{\text{peak}} - PEEP_{\text{tot}})$ [10].

Spontaneous breathing. After the data during mechanical ventilation had been collected, the patients were disconnected from the ventilator and underwent the weaning trial, breathing spontaneously through the endotracheal tube with supplemental oxygen (T-tube). The inspired O_2 concentration was adjusted to obtain an Sa,O_2 of $\geq 90\%$. Cardiac frequency, $\dot{f}_R$ and Sa,O_2 were continuously monitored in order to verify haemodynamic and respiratory stability. All data were collected within the 5th and 10th min after the beginning of the T-piece trial. During this period, all patients exhibited haemodynamic and respiratory stability.

The respiratory variables were measured as follows. First, $\dot{f}_R$ and $\dot{V}'_E$ were measured for 1 min during the first 2–3 min of the weaning trial using a calibrated Wright respirometer (Ferraris Medical, Enfield, UK). $\dot{V}_T$ was calculated by dividing $\dot{V}'_E$ by $\dot{f}_R$. Next, VC was measured with the same device by asking the patient to inspire and expire maximally. This manoeuvre was repeated three times at a comfortable frequency of once every 40 s and the highest value selected. In all instances, before each subsequent VC measurement, the Sa,O_2 , cardiac frequency and $\dot{f}_R$ had returned to baseline values. Subsequently, the inspiratory pressure swing (ΔP_i) was obtained by measuring the amplitude of the negative swing in airway pressure during an occluded inspiration from functional residual capacity (FRC) [11]. Airway occlusions were performed using a noiseless pneumatic shutter (Mallinckrodt, Mirandola, Italy) placed on the inspiratory line of a two-way valve connected to the proximal end of the endotracheal tube. Occlusion of the inspiratory line during a control expiration allowed expiration but prevented inspiration. The equipment dead space (excluding the endotracheal tube) was 23 mL. The shutter was controlled remotely by a physician and the ΔP_i read on an aneroid manometer (NIF-Kit; Markos, Monza, Italy). The ΔP_i value was derived from the mean of three repeated measurements performed at the comfortable frequency of one every 1 min. Using the same device, maximal inspiratory pressure (MIP) was determined by maintaining the airway occluded at FRC for ≥ 20 s, as described by MARINI *et al.* [12]. The maximal value from three repeated manoeuvres was accepted.

During the measurement of $\dot{V}'_E$, VC and MIP, the O_2 supply was temporarily suspended. However, during these brief periods the Sa,O_2 always remained $>90\%$.

Some of the weaning indices used are based on measurements made solely during mechanical ventilation (e.g. $C_{rs,eff}$) or spontaneous breathing (e.g. fR/V_T), whereas others include measurements made under both conditions (e.g. compliance, rate, oxygenation, pressure index (CROP, $C_{rs,eff} \times 1/fR \times P_{a,O_2}/P_{A,O_2} \times MIP$).

Statistical analysis

Data are presented as mean $\pm$ SEM. The approximate degree of normal distribution was calculated for each index. Student's paired data t-test was used for analysing normally distributed data and Wilcoxon rank-sum pair analysis was used in cases in which this approximation was valid in terms of kurtosis and skewness. The Bonferroni adjustment was utilized in assessing the differences between a WF and a WS. A p-value of <0.05 was taken as statistically significant.

The threshold values proposed by other authors for various weaning indices were used to evaluate their predictive power in the present patient population (table 2).

The following standard formulae were used to calculate the predictive power of the threshold values for each index: 1) sensitivity=true positive/(true positive+false negative); 2) specificity=true negative/(true negative+false positive); and 3) diagnostic accuracy=(true positive+true negative)/(true positive+true negative+false positive+false negative). A true positive result was defined as occurring when a patient's test predicted a WS and weaning succeeded; a true negative result as occurring when a test predicted a WF and weaning failed; a false positive result when a test predicted a WS but weaning failed, and a false negative result when a test predicted a WF but weaning succeeded.

Based on the present results, the threshold values of the weaning indices in table 2 and their relative classification errors were computed *de novo* using discriminant analysis. The classification error, which was calculated as [(false negative+false positive)/(true positive+true negative+false positive+false negative)] $\times$ 100, represents the proportion of patients who are not classified correctly by a test. The predictive power of each index was also assessed using receiver operating characteristic (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. The area under the ROC curve for each index summarizes the per-

formance of that index in predicting weaning outcome. In order to overcome the problem of underestimation of the area related to the rating method reported in the literature, a calculation system in which each point on the ROC curve was determined by changing the diagnostic judgement threshold along the curve of positive sample distribution percentiles was adopted [13–15].

Results

As shown in table 3, in the present COPD population, most indices were significantly different between a WF and a WS. The corresponding threshold values, calculated by the discriminant analysis method, are given in table 4 together with the classification error and the area under the ROC curve. The classification error was <20% for MIP, $\Delta P_i/MIP$ and CROP, whereas the area under the ROC curves was >0.9 only for $\Delta P_i/MIP$ and CROP.

The threshold values obtained in the present COPD population were within 10% of those reported for a nonhomogeneous patient population only for V_T and $C_{rs,eff}$ (table 2). The other threshold values differed markedly, especially those for $fR/V'E$, $C_{rs,st}$ and MIP. Figure 1 depicts the individual values of MIP, fR/V_T and CROP obtained in the present subjects during a WF and a WS together with the threshold values obtained in the present study and in the literature (table 2).

In the present COPD population, the predictive power of the threshold values of the various weaning indices reported in the literature were assessed in a nonhomogeneous patient population (table 2). As shown in table 5, the diagnostic accuracy was rather low, except for that of CROP.

Discussion

The main finding of the present study is that the threshold values of the weaning indices obtained previously in a nonhomogeneous population of patients differ from those pertaining to COPD patients (table 2). This is not surprising in view of the fact that the abnormalities in respiratory mechanics, pulmonary gas exchange, control of breathing and inspiratory muscle function differ among patients who require mechanical ventilation for different aetiologies [2–7]. Accordingly, threshold values should be determined separately for different patient populations.

Table 3. — Values of different weaning indices in 28 chronic obstructive pulmonary disease patients during a failed weaning trial (WF) and a successful weaning trial (WS)

	fR breaths· min ⁻¹	V_T mL	V_T/BW mL·kg ⁻¹	$V'E$ L·min ⁻¹	VC/BW mL·kg ⁻¹	MIP cmH ₂ O	$P_{a,O_2}/$ P_{A,O_2}	$C_{rs,eff}$ mL· cmH ₂ O ⁻¹	$C_{rs,st}$ mL· cmH ₂ O ⁻¹	ΔP_i cmH ₂ O	$\Delta P_i/MIP$	fR/V_T breaths· min ⁻¹ ·L ⁻¹	CROP mL·breath ⁻¹ · min ⁻¹
WF Mean	28	292	4.3	8.1	11.1	38	0.4	21.6	57.6	16.4	0.51	106	11.6
SD	4	102	1.3	2.8	4.9	7	0.1	6.8	18.5	3.8	0.10	37	4.5
WF Mean	24	387	5.8	8.9	15.2	53	0.5	25.3	51.4	14.9	0.32	69	31
SD	4	131	1.7	2.3	5.6	11	0.1	7.1	17	4.0	0.08	26	16
p-value	0.001	0.001	0.001	NS	0.001	0.001	0.001	0.001	NS	0.05	0.001	0.001	0.001

fR : respiratory frequency; V_T : tidal volume; BW: body weight; $V'E$: minute ventilation; VC: vital capacity; MIP: maximal inspiratory pressure; P_{a,O_2} : arterial oxygen tension; P_{A,O_2} : alveolar oxygen tension; $C_{rs,eff}$: effective compliance of the respiratory system; $C_{rs,st}$: static compliance of the respiratory system; ΔP_i : inspiratory pressure swing during airway occlusion; CROP: compliance, rate, oxygenation, pressure index ($C_{rs,eff} \times 1/fR \times P_{a,O_2}/P_{A,O_2} \times MIP$).

Table 4. – Threshold values of different weaning indices obtained in the present study

	$C_{rs,st}$ mL· cmH ₂ O ⁻¹	$V'E$ L·min ⁻¹	$C_{rs,eff}$ mL· cmH ₂ O ⁻¹	ΔP_i cmH ₂ O	$P_{a,O_2}/$ P_{A,O_2}	VC/BW mL·kg ⁻¹	V_T mL	V_T/BW mL·kg ⁻¹	f_R breaths· min ⁻¹	f_R/V_T breaths· min ⁻¹ ·L ⁻¹	MIP cmH ₂ O	$\Delta P_i/MIP$	CROP mL·breath ⁻¹ · min ⁻¹
Threshold	54	8.6	24	19.5	0.46	13	340	5.0	25	84	44	0.41	16
Classification	43	43	40	36	32	35	34	32	30	28	19	16	17
error %													
ROC curve	0.59	0.63	0.66	0.67	0.73	0.74	0.74	0.76	0.77	0.79	0.88	0.91	0.93
area													
SEM	0.08	0.08	0.07	0.07	0.06	0.07	0.07	0.07	0.07	0.04	0.05	0.04	0.04

Threshold value and classification error were calculated by discriminant analysis. $C_{rs,st}$: static compliance of the respiratory system; $V'E$: minute ventilation; $C_{rs,eff}$: effective compliance of the respiratory system; ΔP_i : inspiratory pressure swing during airway occlusion; P_{a,O_2} : arterial oxygen tension; P_{A,O_2} : alveolar oxygen tension; VC: vital capacity; BW: body weight; V_T : tidal volume; f_R : respiratory frequency; MIP: maximal inspiratory pressure; CROP: compliance, rate, oxygenation, pressure index ($C_{rs,eff} \times 1/f_R \times P_{a,O_2}/P_{A,O_2} \times MIP$); ROC: receiver operating characteristic.

In the present study, the values of different weaning indices during a WF and a subsequent WS were assessed in the same 28 COPD patients, and the corresponding threshold values computed (table 4). The patients included two subjects (Nos.10 and 19) who had to be reintubated within 36 h after extubation. Since weaning and extubation failure may be regarded as distinct outcomes with different causes, the assessment of the parameters in tables 3 and 4 was repeated after exclusion of patients No. 10 and No. 19. The weaning threshold, classification error, ROC area and diagnostic accuracy remained virtually the same.

The classification error was lowest for $\Delta P_i/MIP$ (16%), CROP (17%) and MIP (19%) and the corresponding ROC curve areas were highest (0.91, 0.93 and 0.88, respectively) (table 4). Clearly, the present threshold values for weaning indices need to be tested prospectively in future studies in COPD patients, which should also take into account the effect of duration of mechanical ventilation on weaning outcome [1]. However, the results of a recent study of VALLERDÙ *et al.* [16] suggest that the present threshold value for f_R/V_T , which is lower than that proposed by YANG and TOBIN [1] (84 *versus* 100 breaths·min⁻¹·L⁻¹), is probably valid in COPD patients. They measured f_R/V_T in 13 COPD patients who were successfully weaned and 20 patients who failed weaning. The respective values for a WS and a WF were 59 ± 32 and

110 ± 50 breaths·min⁻¹·L⁻¹, which are close to those of the present study (table 3). Furthermore, using a threshold value of ≤ 100 breaths·min⁻¹·L⁻¹, they found a diagnostic accuracy similar to that of the present study (0.76 *versus* 0.71). Unfortunately these authors did not compute the threshold value of f_R/V_T using their data. It is likely, however, that it would have been <100 , as in the present study (table 4). This is also supported by VASSILAKOPOULOS *et al.* [17], who studied 10 COPD patients at two time points (during a WF and then a WS) and found similar f_R/V_T values to those in the current study (97 ± 44 breaths·min⁻¹·L⁻¹ at failure and 51 ± 11 breaths·min⁻¹·L⁻¹ at success), indicating that in COPD a threshold of <100 breaths·min⁻¹·L⁻¹ should separate weaning failure from success. It should be noted that in the study of VASSILAKOPOULOS *et al.* [17] the duration of mechanical ventilation did not play a prominent role in determining the weaning threshold.

Except for V_T and $C_{rs,eff}$, the threshold values of the weaning indices of the present COPD population differed markedly from those found in previous studies on non-homogeneous populations of patients (table 2). This is especially true for f_R , $V'E$, MIP, and $C_{rs,st}$.

According to YANG and TOBIN [1], the threshold values of f_R and $V'E$ for predicting weaning outcome are $f_R \leq 38$ breaths·min⁻¹ and $V'E \leq 15$ L·min⁻¹, respectively. These values, however, pertain to a nonhomogeneous

Fig. 1. – Individual values of three weaning indices obtained during a failed weaning trial (WF) and subsequently during a successful trial (WS) involving 28 chronic obstructive pulmonary disease patients. a) maximal inspiratory pressure (MIP); b) respiratory frequency (f_R) to tidal volume (V_T) ratio; and c) compliance rate, oxygenation, pressure index (effective compliance of the respiratory system $\times 1/f_R \times$ arterial oxygen tension/alveolar oxygen tension $\times$ MIP). : threshold values from the literature (table 2); - - - : threshold values of the present study. For further information, see text.

Table 5. – Sensitivity, specificity and diagnostic accuracy of different weaning indices using threshold values from previous studies*

	$C_{rs,st}$ mL· cmH ₂ O ⁻¹	V'_E L·min ⁻¹	f_R breaths· min ⁻¹	MIP cmH ₂ O	$P_{a,O_2}/$ P_{A,O_2}	VC/BW mL·kg ⁻¹	V_T mL	$\Delta P_i/MIP$	$C_{rs,eff}$ mL· cmH ₂ O ⁻¹	V_T/BW mL·kg ⁻¹	f_R/V_T breaths· min ⁻¹ ·L ⁻¹	CROP mL·breath ⁻¹ · min ⁻¹
Sensitivity	0.86	0.75	1.0	1.0	0.96	0.86	0.57	0.36	0.71	0.89	0.36	0.96
Specificity	0.11	0.21	0	0	0.32	0.46	0.71	0.96	0.64	0.46	0.54	0.79
Diagnostic accuracy	0.48	0.48	0.50	0.50	0.64	0.66	0.66	0.66	0.68	0.68	0.71	0.87

*: in table 2. Sensitivity=true positive/(true positive+false negative); Specificity=true negative/(true negative+false positive); diagnostic accuracy=(true positive+true negative)/(true positive+false negative+false positive+true negative). $C_{rs,st}$: static compliance of the respiratory system; V'_E : minute ventilation; f_R : respiratory frequency; MIP: maximal inspiratory pressure; P_{a,O_2} : arterial oxygen tension; P_{A,O_2} : alveolar oxygen tension; VC: vital capacity; BW: body weight; V_T : tidal volume; ΔP_i : inspiratory pressure swing during airway occlusion; $C_{rs,eff}$: effective compliance of the respiratory system; CROP: compliance, rate, oxygenation, pressure index ($C_{rs,eff} \times 1/f_R \times P_{a,O_2}/P_{A,O_2} \times MIP$).

population. In COPD patients with ARF, both f_R and V'_E during spontaneous breathing are in general much lower than this [18–20]. This is in line with the present results: in both WF and WS patients, f_R and V'_E were in most instances <38 breaths·min⁻¹ and ≤ 15 L·min⁻¹, respectively (table 3). Furthermore, V'_E did not differ substantially among the WS and WF patients. Accordingly, in COPD, the thresholds for f_R and V'_E were necessarily lower than those obtained by YANG and TOBIN [1] in a nonhomogeneous population (table 2).

In the present COPD patients, the $C_{rs,st}$ measured during mechanical ventilation were relatively high (table 3), reflecting the fact that, in COPD patients with ARF, the $C_{rs,st}$ does not differ significantly from that of normal subjects [4, 10], except on the first day of mechanical ventilation, when they exhibit marked dynamic hyperinflation and hence their V_T impinges on the flat upper part of the static volume/pressure curve of the respiratory system [2]. It should be noted, however, that during spontaneous breathing trials COPD patients may exhibit markedly enhanced dynamic hyperinflation (DH) with concomitant decrease in $C_{rs,st}$. This enhanced DH is closely associated with weaning failure [19, 20]. This may explain why $C_{rs,st}$ as well as $C_{rs,eff}$, measured during mechanical ventilation, are of poor predictive power for weaning outcome (table 4).

The threshold values of MIP obtained in the present COPD patients differed markedly from that of YANG and TOBIN [1] (44 versus 15 cmH₂O). Since the same method was used in both studies [12], this discrepancy probably mainly reflects differences between the populations studied. The present MIP threshold is also higher than that reported by other investigators (~30 cmH₂O) for a nonhomogeneous patient population [11] and for a group consisting predominantly of postoperative patients with a mean duration of mechanical ventilation of 36 h [21]. Since these investigators also used the occlusion method of MARINI *et al.* [12] to assess MIP, it is likely that the present high MIP threshold value reflects the different patient populations studied. It should be noted that, in COPD patients, MIP depends markedly on the extent of DH, which in turn is modulated by several mechanisms (e.g. V'_E , respiratory pattern and expiratory flow limitation). Decreased DH should result not only in increased MIP but also in a decrease in inspiratory load of breathing (decreased intrinsic positive end-expiratory pressure and

increased $C_{rs,st}$). Accordingly, it is not surprising that, in COPD patients, MIP had a relatively high predictive power for weaning outcome, the ROC area amounting to 0.88 (table 4). COUSSA *et al.* [5] predicted that COPD patients with ARF require a MIP of <35 cmH₂O in order to be successfully weaned. In the present COPD patients, the MIP threshold value amounted to 44 cmH₂O (table 4).

Although in the present COPD patients MIP, an expression of inspiratory muscle strength, exhibited a relatively low classification error (19%) (table 4), the latter could be further reduced by indices which in addition to MIP also take into account inspiratory muscle activity ($\Delta P_i/MIP$) as well as gas exchange and respiratory mechanics (CROP).

In the present COPD patients, the f_R/V_T threshold of 100 breaths·min⁻¹·L⁻¹ was associated with a relatively high classification error (28%), contrary to the results obtained by YANG and TOBIN [1] in a nonhomogeneous patient population. This probably reflects the fact that in COPD patients the f_R/V_T threshold for predicting weaning outcome is lower than that reported by these authors (84 versus 100 breaths·min⁻¹·L⁻¹). A lower f_R/V_T threshold in COPD patients would be expected in view of their relatively low f_R (see above). It should be noted, however, that the predictive value of f_R/V_T for weaning outcome found in the present COPD patients was similar to that observed by several authors in nonhomogeneous patient populations [22–26].

The magnitude of the area under the ROC curve allows estimation of the predictive power independent of a specific threshold value. The large ROC curve areas of $\Delta P_i/MIP$ and CROP indicate that these indices potentially have a high predictive power for weaning outcome in COPD patients (table 4). Weaning failure in the present patients, in whom the extrapulmonary and metabolic abnormalities had already been corrected, was probably mainly due to excessive respiratory impedance and/or decreased inspiratory muscle strength. The results of this study indicate that the balance between load and strength is taken into account by weaning indices such as $\Delta P_i/MIP$ and CROP, which can be measured at the bedside.

Patients should be weaned as soon as they can sustain spontaneous ventilation. Some experienced ICU physicians have the capacity to successfully predict whether or not a patient is ready for extubation solely on clinical examination. This, however, is not always the case. In fact,

in the present initial weaning trial on 81 COPD patients, the ICU physicians correctly predicted a WS in only 53 (65%) cases. Using MIP, ΔP_i /MIP and CROP, a higher success rate would be expected (table 4). Thus, physiological weaning indices may help in such decision-making. A weaning index is clinically useful if: 1) it is related to the physiological mechanisms underlying ARF, 2) its diagnostic accuracy is adequate, and 3) its measurement is easy and reproducible. At present, a gold standard weaning index is not available, particularly for COPD patients. However, the present results suggest that ΔP_i /MIP and CROP may be good candidates for such a role.

The main result of the present study is that, in chronic obstructive pulmonary disease patients who had already failed a first weaning attempt, the threshold values of most weaning indices differed from those of a whole nonhomogeneous population of mechanically ventilated patients undergoing a weaning trial.

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