Anesthesiology 2010; 113:378–85

Increase of Oxygen Consumption during a Progressive Decrease of Ventilatory Support Is Lower in Patients Failing the Trial in Comparison with Those Who Succeed

Giacomo Bellani, M.D., Ph.D.,* Giuseppe Foti, M.D.,† Ester Spagnolli, M.D.,‡ Manuela Milan, M.D.,§ Alberto Zanella, M.D.,§ Massimilano Greco, M.D.,† Nicolò Patroniti, M.D.,* Antonio Pesenti, M.D.‖

ABSTRACT

Background: The aim of this study was to test the hypothesis that, during weaning from mechanical ventilation, when the pressure support level is reduced, oxygen consumption increases more in patients unable to sustain the decrease in ventilatory assistance (weaning failure).

Methods: Patients judged eligible for weaning were enrolled. Starting from 20 cm H_2O, pressure support was decreased in 4-cm H_2O steps, lasting 10 min each, until 0 cm H_2O; this level was kept for 1 h. The average oxygen consumption from the last 3 min of each step, along with other ventilatory variables, was measured by indirect calorimetry (M-CAiOVX "metabolic module," Engstrom Carestation; GE Healthcare, Madison, WI) and recorded. Patients were defined as belonging to the failure group if, at any moment, they developed signs of respiratory distress according to standard criteria, or to the success group otherwise.

Results: Twenty-eight patients were studied. In most patients, the minimum oxygen consumption was not recorded at the highest pressure support applied. Sixteen patients were able to complete the weaning trial successfully, whereas 12 failed it; the success group had a minimum oxygen consumption lower than failure group (mean ± SD: 174 ± 44 *vs.* 215 ± 53 ml/min, $P < 0.05$). Moreover, although respiratory drive (assessed by P0.1) increased more in the failure group, this group had a lower increase in oxygen consumption, contradicting our hypothesis.

Conclusions: Patients failing a decremental pressure support trial, in comparison with those who succeed, had an higher baseline oxygen consumption and were not able to increase their oxygen consumption in response to an increased demand.

What We Already Know about This Topic

- An elevated oxygen consumption of respiratory muscles is associated with weaning failure

What This Article Tells Us That Is New

- Patients failing a weaning trial, in comparison with those who succeed, have a higher baseline oxygen consumption and are less able to increase it when ventilatory assistance is decreased

AFTER the acute phase of respiratory failure, when ventilatory assistance is reduced (for example, by reducing pressure support [PS] level) or discontinued, some of the patients are unable to sustain the necessary work of breathing and develop signs of fatigue, prompting the clinician to reinstitute ventilatory assistance. This occurrence, which has been termed "weaning failure," can be caused by an increased me-

* Researcher, ‡ Resident, § Research Fellow, ‖ Professor, Department of Experimental Medicine, University of Milan-Bicocca, Monza, Italy, and Department of Perioperative Medicine and Intensive Care, San Gerardo Hospital, Monza, Italy. † Staff Physician, Department of Perioperative Medicine and Intensive Care, San Gerardo Hospital.

Received from the Department of Experimental Medicine, University of Milan-Bicocca, Monza, Italy, and the Department of Perioperative Medicine and Intensive Care, San Gerardo Hospital, Monza, Italy. Submitted for publication November 5, 2009. Accepted for publication April 19, 2010. Support was provided solely from institutional and/or departmental sources. GE Healthcare (Milan, Italy) provided the equipment free of charge. The Department of Perioperative Medicine and Intensive Care, San Gerardo Hospital, has received from G.E. Healthcare funding for research on a topic different from that of the present study. Dr. Bellani received an honorarium in 2009 (USD 3,000) from G.E. Healthcare for consultancies as a member of the Respiratory Medical Advisory Board.

Address correspondence to Dr. Pesenti: Department of Experimental Medicine, University of Milan-Bicocca, Via Cadore 48, 20052 Monza, Italy. antonio.pesenti@unimib.it.

◇ This article is featured in "This Month in Anesthesiology." Please see this issue of ANESTHESIOLOGY, page 9A.

◆ This article is accompanied by an Editorial View. Please see: Schultz MJ: Weaning from mechanical ventilation: Stay poised between load and strength. ANESTHESIOLOGY 2010; 113:273–5.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are available in both the HTML and PDF versions of this article. Links to the digital files are provided in the HTLM text of this article on the Journal's Web site (www.anesthesiology.org).

chanical load (reduced compliance, increased resistance, intrinsic positive end-expiratory pressure), or a decreased ability of the patient to generate pressure, or lack of endurance.[1,2]

Whereas in normal subjects, the oxygen consumption ($\dot{V}O_2$) of respiratory muscles ($\dot{V}O_{2,\ resp}$) does not exceed 5% of the total $\dot{V}O_2$ of the body,[3] several studies demonstrated that the $\dot{V}O_{2,\ resp}$ in the patients being weaned from mechanical ventilation can be considerably higher,[4–7] and many authors, rather than focusing on the mechanical work of breathing, evaluated the role of $\dot{V}O_{2,\ resp}$ as a predictor of weaning success.[5,8–11]

In several studies,[5,6,8,12,13] $\dot{V}O_{2,\ resp}$ has been computed as the difference between the $\dot{V}O_2$ measured during controlled mechanical ventilation and during spontaneous (assisted) breathing. This approach assumes that, during controlled mechanical ventilation, the respiratory muscles of the patient, being fully relaxed, are passively displaced and that the changes in the body $\dot{V}O_2$ during the transition from controlled to assisted breathing are caused solely by changes in respiratory muscle $\dot{V}O_2$. However, such a condition might not be easily satisfied in the clinical setting, particularly because the changes in sedation level normally implemented during the transition from controlled ventilation would affect, *per se*, the total $\dot{V}O_2$ of the body.

We therefore chose to follow a different approach, and we hypothesized that during a trial of decremental PS levels, a $\dot{V}O_2$ increase would be more pronounced in patients eventually unable to sustain the PS decrease, indicating a greater $\dot{V}O_{2,\ resp}$ in these patients. We did not aim to develop an index able to predict a patient's weaning success (or failure); rather, we aimed to assess whether an increased $\dot{V}O_{2,\ resp}$ played any significant role in weaning failure, testing the hypothesis that when the PS level is reduced, $\dot{V}O_2$ increases more in those patients unable to sustain the decrease in ventilatory assistance. To estimate a patient's $\dot{V}O_2$, we used indirect calorimetry, a noninvasive and reliable method.[14]

Materials and Methods

Study Population

The protocol was approved by our institution's ethical committee (San Gerardo Hospital, Monza [MB], Italy); informed consent was obtained or deferred according to the committee recommendations. The study was performed in the eight-bed general Intensive Care Unit of a university hospital.

Patients were enrolled when being ventilated in PS for more than 24 h for acute respiratory failure and judged eligible for a test of weaning from mechanical ventilation by the attending physician.

Exclusion criteria were the following:

- Absence of resolution of the primitive disease(s)
- Hemodynamic instability requiring vasopressors
- Gas exchange impairment requiring positive end-expiratory pressure more than 10 cm H_2O and/or fractional inspired oxygen tension more than 50% to obtain a Pa_{O_2} of at least 80 mmHg
- PS level equal or greater than 20 cm H_2O
- Core body temperature more than 38°C

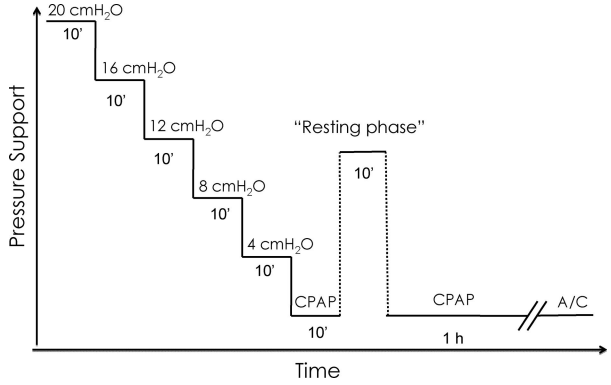

Fig. 1. Protocol schema. Pressure support level was progressively decreased to constant positive airway pressure (CPAP) and then reset to the level at which the minimum oxygen consumption had been observed (Resting phase). CPAP was then applied for 1 h or interrupted if the patient developed signs of respiratory distress (see text). Finally, a phase of assist/control (A/C) ventilation was performed to measure oxygen consumption under this condition and respiratory mechanics.

After enrollment, patients were connected to an Engstrom Carestation (General Electric, Madison, WI) with respiratory parameters unmodified from those set by the attending physician. This ventilator is equipped with the M-CAiOVX "metabolic module"[14] (General Electric); the module consists of a fast differential paramagnetic oxygen analyzer, an infrared analyzer for carbon dioxide, and a pneumotachograph to measure inspired and expired volumes. The pneumotachograph and gas sampling ports are housed in a disposable connector, placed close to the patient, between the Y-piece of the ventilatory circuit and the endotracheal tube. The signals from the pneumotachograph and the gas analyzers are synchronized to allow breath-by-breath estimations of gas exchange. The device computes online the patient's $\dot{V}O_2$ and carbon dioxide production.

Study Protocol

The decremental PS trial (fig. 1) was performed by sequentially applying the following PS levels above positive end-expiratory pressure: 20, 16, 12, 8, 4, and 0 cm H_2O and keeping each level for 10 min. At the end of the 10-min period, P0.1 (a validated index of respiratory drive[15]) was measured in triplicate. The decremental PS trial was stopped, and the PS was raised again to allow the patients to rest whenever they developed one of the following signs of respiratory distress:

- Respiratory rate more than 35 breaths/min
- Oxygen saturation measured by pulse oximetry less than 90%

- Heart rate more than 140 beats/min or variation more than 30% from baseline
- Systolic blood pressure more than 180 mmHg
- Increase in the end-tidal carbon dioxide more than 8 mmHg
- Dyaphoresis or anxiety

On the opposite, the PS level was immediately decreased (before the end of the 10-min period) to the next (lower) level if the patient developed signs of "overassistance" such as cough, tidal volume more than 15 ml/kg, or apnea for more than 15 s. At the end of the period at PS of 0 cm H_2O (*i.e.*, continuous positive airway pressure) or after the patient had met the criteria of respiratory distress, the PS was switched to the level at which the lowest $\dot{V}O_2$ had been observed, which was maintained for 10 min ("resting phase"). At the end of this phase, end-expiratory lung volume was measured by a 20% variation in inspired oxygen fraction.[16] Finally, the PS was set at the lowest level that the patient had been able to tolerate in the first phase, and this level was kept for 1 h, unless the patient developed signs of respiratory distress; in other words, the patient was kept on continuous positive airway pressure if this level had been tolerated without distress in the first phase (to verify, over a longer time span, the ability of the patient to breathe without ventilatory assistance) or at the level of PS above the one at which the patient had developed distress.

The trial was considered successful (success group) if a patient could breathe at continuous positive airway pressure for 1 h and failed (failure group) if, at any point, the patient developed any of the aforementioned signs of respiratory distress.

At the end of the trial, patients were switched to a volume assist/control ventilation for 10 min to determine $\dot{V}O_2$ in such condition and to measure respiratory system compliance and resistance by means of end-expiratory and end-inspiratory pauses,[17] analyzing only the traces of the occlusions with a flat plateau on the airway pressure.

Data Acquisition and Analysis

The Engstrom Carestation was connected to a personal computer, which recorded two types of data streams continuously.

- Continuous waveforms of airway pressure, flow, volume, carbon dioxide, and oxygen concentrations
- Breath-by-breath data on tidal volume, respiratory rate, $\dot{V}O_2$

Data from the last 3 min of each step were averaged, and we determined the lowest $\dot{V}O_2$ observed during the trial ($\dot{V}O_{2,\ min}$), and the corresponding PS level was indicated as PS_{REST}. Expiratory and inspiratory pressure time product[18] were calculated as described elsewhere.[19] Briefly, the pressure generated by respiratory muscles was calculated at any instant as the difference between the measured airway pressure and the theoretical airway pressure of a passive system:

Paw = positive end-expiratory pressure + flow*resistance + volume/compliance

Table 1. Initial Causes of Respiratory Failure in the Population Studied

Cause of Respiratory Failure	N (%)
Sepsis/septic shock	5 (18)
ALI/ARDS	5 (18)
Pancreatitis	2 (7)
Trauma	3 (11)
Cardiac arrest	2 (7)
Hemorragic shock	3 (11)
Postoperative respiratory failure	4 (14)
Other	3 (11)

ALI = acute lung injury; ARDS = acute respiratory distress syndrome.

where flow and volume are those actually measured at any instant, while resistance and compliance are measured during the phase of assist/control mechanical ventilation.

Statistical Analysis

Data are indicated as mean ± SD or median (interquartile range). Variables between the two groups (failure or success) were compared by means of unpaired Student *t* test or (for nonparametric variables, *i.e.*, Simplified Acute Physiology Score II, days on mechanical ventilation and PS_{REST}) Mann–Whitney U test or (for categorical variables *i.e.*, gender and mortality in the intensive care unit) chi-square test. Variables tested over different levels of PS were analyzed by a two-way ANOVA, having "group" (failure or success) and PS level as factors. If either the group or interaction effect resulted statistically significant we performed a *post hoc* analysis comparing, at each PS level, the two groups (Holm–Sidak method). Association between two variables was assessed by linear regression. A level of $P < 0.05$ (two-tailed) was considered as statistically significant. Statistical analyses were performed by SPSS 16.0 for Windows (SPSS, Inc., Chicago, IL) and by SigmaPlot 11.0 (Systat Software, Inc., Chicago, IL).

Results

We enrolled 28 patients, aged 67 ± 15 yr and ventilated for 30 ± 35 days. Initial causes of respiratory failure are reported in table 1.

Sixteen patients were able to complete the weaning trial successfully, and 12 failed it. Criteria determining failure of the trial were tachypnea in seven patients, excessive agitation in four patients, and increase of end-tidal carbon dioxide in one. Four patients failed the trial at a PS level of 8 cm H_2O, two failed at 4 cm H_2O, and the rest of the patients (*i.e.*, six) failed during the continuous positive airway pressure phase. Table 2 reports the main clinical parameters of the two groups, collected in the baseline phase. No difference between the two groups could be observed except for a trend toward a lower compliance in the failure group.

Figure 2 reports some examples of $\dot{V}O_2$ as a function of PS level (see also fig. 1, Supplemental Digital Content 1, which is a figure showing the entire family of curves,

Table 2. Main Demographic and Clinical Variables of Patients

Variables	Success (n = 16)	Failure (n = 12)	*P* Value
Age (years)	64 ± 18	66 ± 17	0.77
Male gender (%)	81	54	0.11
SAPS II at ICU admission	44 [31–51]	46 [39–53]	0.79
Days on mechanical ventilation	11 [6–26]	19.5 [10–42]	0.24
ICU mortality (%)	12.5	33.3	0.19
Positive end-expiratory pressure (cm H_2O)	6.4 ± 1.6	6.9 ± 2.1	0.45
Respiratory system compliance (ml/cm H_2O)	48 ± 15	37 ± 13	0.07
Respiratory system resistance (cm $H_2O \cdot L^{-1}s$)	15.9 ± 3.6	17.8 ± 4.6	0.27
Pa_{O_2}/F_{IO_2} (mmHg)	307 ± 65	283 ± 55	0.31
Pa_{CO_2} (mmHg)	46.1 ± 7.7	45.4 ± 10.6	0.84
Mean arterial pressure (mmHg)	81 ± 11	85 ± 10	0.27
Heart rate (beats/minute)	98 ± 18	84 ± 16	0.04

Data are expressed as mean ± SE or median [interquartile range].

F_{IO_2} = inspired oxygen fraction; ICU = intensive care unit; Pa_{CO_2} = arterial carbon dioxide tension; Pa_{O_2} = arterial oxygen tension; SAPS II = Simplified Acute Physiologic Score II.

http://links.lww.com/ALN/A597). In most patients, PS_{REST} did not correspond to the highest PS level; in other words, in these patients, a decreasing PS level correlated with an initial decrease in $\dot{V}O_2$ and then an increase. Figure 3 reports the frequency distribution of PS_{REST} in the two groups of patients: PS_{REST} was higher in the failure than in the success group (17 ± 3.5 *vs.* 13.7 ± 4.2 cm H_2O; $P < 0.05$).

Measurement of $\dot{V}O_2$ was reproducible. A tight correlation was found between $\dot{V}O_{2,\,min}$ (*i.e.*, measured during the decremental PS trial) and $\dot{V}O_2$ measured during the "resting phase," at the end of the decremental PS trial ($r^2 = 0.81$, $P < 0.001$; slope 0.85; see fig. 2, Supplemental Digital Content 2, which is a figure showing the correlation between these two variables, http://links.lww.com/ALN/A598).

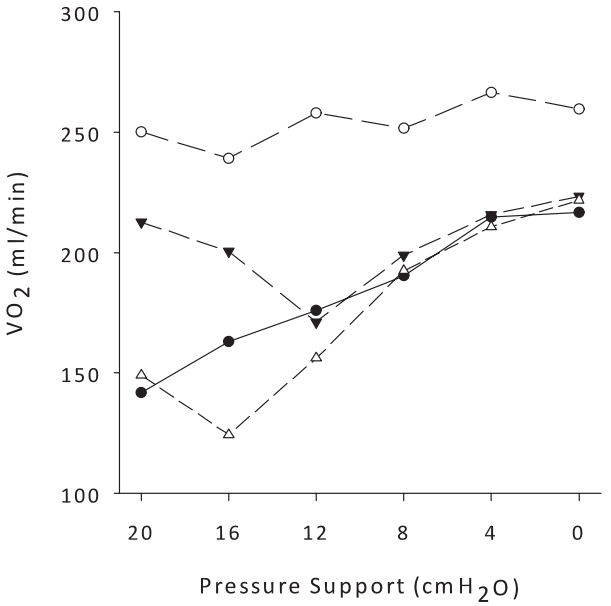

Fig. 2. Representative examples of changes in oxygen consumption ($\dot{V}O_2$) of the body associated to a decrement in pressure support (PS) level. Although in one patient (*filled circles*) the $\dot{V}O_2$ constantly increased, in two patients (*filled* and *open triangles*) the $\dot{V}O_2$ initially decreased to a minimum (resting PS level) and then progressively increased again. Finally, in one patient no systematic changes in $\dot{V}O_2$ were observed when PS level was decreased (*open circles*).

At PS_{REST}, $\dot{V}O_{2,min}$ was higher in the failure than in the success group (215 ± 53 *vs.* 174 ± 44 ml/min, respectively; $P < 0.05$); on the contrary, no difference was observed in the maximum $\dot{V}O_2$ obtained in the patients of the failure or success groups (271 ± 58 and 256 ± 65 ml/min, respectively). Accordingly, the absolute increase in oxygen consumption from $\dot{V}O_{2,\,min}$ to the maximum $\dot{V}O_2$ observed was greater in the success than in the failure group (94 ± 71 *vs.* 52 ± 24 ml/min; $P < 0.05$).

Figure 4 displays the variations of respiratory rate, tidal volume, and P0.1 after the reduction of PS: tidal volume did not differ between the failure and the success group but significantly decreased at decreasing PS levels (ANOVA: group effect, $P = 0.062$; PS effect, $P < 0.001$; interaction, $P = 0.235$). Respira-

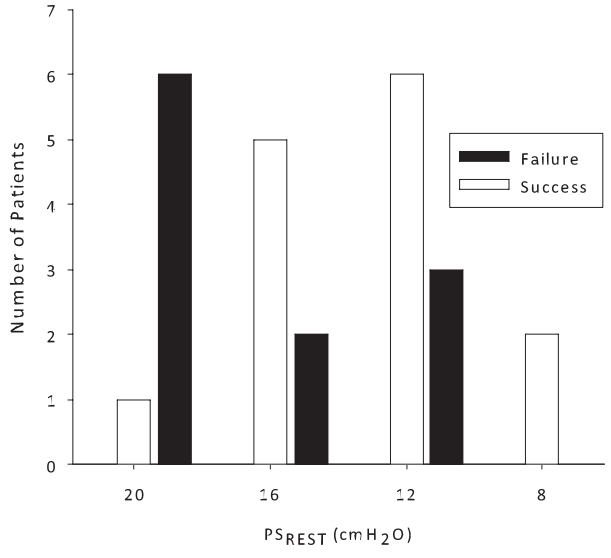

Fig. 3. For each pressure support level, the figure displays the number of patients with minimum oxygen consumption at that level.

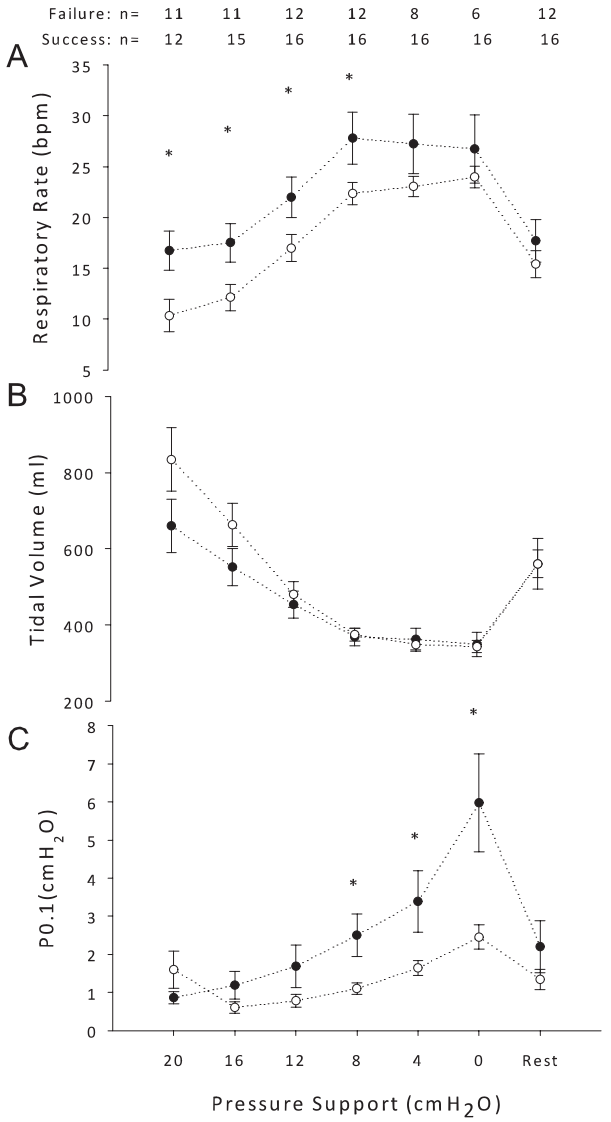

Fig. 4. The figure displays the effect of reducing pressure support on respiratory rate (*A*), tidal volume (*B*) and P0.1 (*C*) in the patients succeeding (*open circles*) and failing (*filled circles*) the weaning trial. The respiratory rate of patients failing the weaning trial tended to be higher, and P0.1 was raised more pronouncedly after a decrease in pressure support. * $P < 0.05$ *versus* success group at the same pressure support level (*post hoc* analysis by Holm–Sidak method); the number of patients at each pressure support level is indicated on top of the figure. *Error bars* represent SE.

tory rate was higher the failure group than in the success group and at lower PS levels (ANOVA: group effect, $P < 0.001$; PS effect, $P < 0.001$; interaction, $P = 0.954$); similar results were found for P0.1 (ANOVA: group effect, $P < 0.001$; PS effect, $P < 0.001$; interaction, $P < 0.001$).

The work of breathing, estimated from pressure-time product, increased more in the failure than in the success group, for a given decrease in PS (see fig. 3, Supplemental Digital Content 3, which is a figure showing the values of pressure-time product at different PS levels in the failure and success groups, http://links.lww.com/ALN/A599).

When the PS level was decreased below PS_{REST}, the $\dot{V}O_2$ increase was more pronounced in the success group than the failure group (fig. 5; ANOVA: group effect, $P < 0.001$; PS effect, $P < 0.001$, interaction, $P = 0.386$), indicating that patients able to complete the weaning trial were those who reacted to the decrease of ventilatory assistance with a greater increase in $\dot{V}O_2$.

This finding was confirmed when $\dot{V}O_2$ was plotted as a function of P0.1 at different PS levels (fig. 6): the relationship between these two variables was steeper for the success than for the failure group, indicating that for the same increase in P0.1 the $\dot{V}O_2$ would increase more in the success than in the failure group.

$\dot{V}O_2$ recorded in the phase of controlled mechanical ventilation was not significantly different from $\dot{V}O_{2,\ min}$ for patients in the success group (197 ± 58 *vs.* 174 ± 44 ml/min, P = not significant), or in the failure group (196 ± 72 *vs.* 216 ± 53 ml/min, P = not significant) (see fig. 4, Supplemental Digital Content 4, which is a figure showing the comparison between $\dot{V}O_2$ recorded in the phase of controlled mechanical ventilation and $\dot{V}O_{2,\ min}$ in the two groups of patients, http://links.lww.com/ALN/A600).

End-expiratory lung volume was similar between the success and failure groups (1,509 ± 803 *vs.* 1,665 ± 403 ml; P = not significant).

Discussion

The main findings of this work can be summarized as follows: patients able to complete a weaning trial have a baseline $\dot{V}O_2$ lower than patients failing the trial, and react to a decrease of ventilatory assistance (*i.e.*, to an increased load) with a proportionally greater increase in $\dot{V}O_2$. The finding that $\dot{V}O_2$ increased more in patients able to sustain the weaning trial than in those who failed contradicts our initial hypothesis and conflicts with some previous observations. A number of studies aimed at assessing the role of $\dot{V}O_2$ during weaning from mechanical ventilation reported that an increased $\dot{V}O_{2,\ resp}$ is associated with weaning failure[8,9,11,13,20]; other studies did not find the measurement of $\dot{V}O_{2,\ resp}$ of any use in predicting the outcome of the weaning trial.[4,5] We offer the following explanation for the discrepancy between ours and previous findings. In the presence of an intact neuromuscular function, when the ventilatory assistance is reduced, $\dot{V}O_2$ increases more in those patients who, because of a higher dead space and/or to higher resistance and elastance and/or to a greater minute ventilation, will develop a higher work of breathing. In this condition, thus, a higher $\dot{V}O_{2,\ resp}$ reflects a higher work required to breathe, and not surprisingly patients required to perform a higher work of breathing may fail their weaning trial. On the other hand, it has to be considered that if a patient is required to perform an increased workload we could assimilate the decrementing PS to a treadmill exercise: if the treadmill runs faster (*i.e.*, the PS is decreased) the patient will have to increase his/her $\dot{V}O_2$ to be able to cope with the increased demand, otherwise he/she

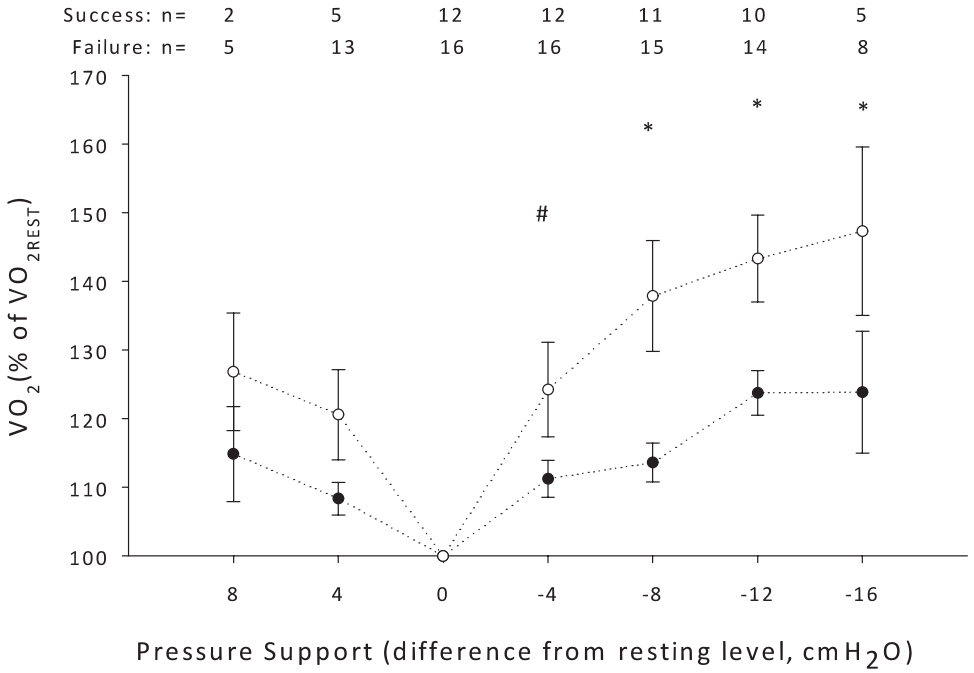

Fig. 5. Relative changes of oxygen consumption ($\dot{V}O_2$) expressed as percentage of minimum $\dot{V}O_2$ recorded in each patient at pressure support level above or below the resting level (*i.e.*, the level of pressure support associated with minimum $\dot{V}O_2$). Surprisingly, patients failing the weaning trial (*filled symbols*) had a smaller increase in $\dot{V}O_2$ when compared with patients able to complete the trial (*open symbols*) in response to a decrease of the pressure support level. * $P < 0.05$; # $P = 0.07$ *versus* success group at the same pressure support level (*post hoc* analysis by Holm–Sidak method). *Error bars* represent SE.

will fall from the treadmill (or fail the weaning trial). As a matter of fact, patients in the failure group, in spite of a large respiratory drive, increased as suggested by the P0.1 (they tried to run faster as the treadmill was running faster) could not respond to the P0.1 increase with a high enough increase in their $\dot{V}O_2$, most likely for a deterioration in muscle function. At variance for the same P0.1 increase, success patients could develop a substantial increase in $\dot{V}O_2$. This interpretation is somehow supported by sports medicine: highly trained subjects are characterized by a maximal $\dot{V}O_2$ by far greater than normal subjects. Conversely, it has been shown that in patients with failing hearts the ability of consuming oxygen is greatly impaired in comparison with matched controls and that in such patients there is a close relationship between the maximal $\dot{V}O_2$ and the muscle mass[21,22]; this finding holds true when referring specifically to respiratory muscles: maximum inspiratory strength is related to maximum $\dot{V}O_2$[23]. Adequate training results in an increase in $\dot{V}O_2$ of healthy,[24] diseased subjects,[25] and even of isolated muscles.[26] In our study, respiratory muscles of patients failing a weaning trial might have reached their "lactate threshold," shifting to anaerobic metabolism and hence becoming unable to sustain the effort for a prolonged period of time.[27]

Most of the studies showing an increased $\dot{V}O_2$ in the subjects who failed weaning were conducted on patients ventilated for a short period of time (often just 1 or 2 days): in these patients, likely to have an intact respiratory muscle function, a high $\dot{V}O_{2,\,resp}$ simply reflects a higher mechanical work of breathing while, probably, our patients ventilated for days had a decreased muscular efficiency and were not able to generate the necessary mechanical work. Interestingly, among the studies not confirming the finding that a higher $\dot{V}O_{2,\,resp}$ is associated with a weaning failure there is the paper by Hubmayr *et al.*,[5] which was conducted in a population of patients ventilated for several days. It should also be noted that patients in the failure group had a $\dot{V}O_{2,\,min}$ (*i.e.*, the minimal $\dot{V}O_2$ observed at any PS level) considerably higher than that of the success group, which might have limited the possibility of further increasing the $\dot{V}O_2$. Another factor that might aid to explain the discrepancy between ours and previous results is the different approach used: in a decremental PS trial we identified the level of support associated with the lowest $\dot{V}O_2$, and we took this as a reference; noticeably, although in the failure group the $\dot{V}O_2$ during assist/control mechanical ventilation (usually taken as a reference in previous works) decreased further, this was not the case for the failure group.

This study has a clinical implication because so far, a higher $\dot{V}O_{2,\,resp}$ has been described in the literature as a predictor of weaning failure, mainly as an indicator of an excessive work required from the patient to breathe (mirroring, in the example previously used the speed of the treadmill on which the patient is "running"). Far from challenging this solid evidence, our study proposes an additional mechanism for weaning failure: the inability of the patient to increase his/her $\dot{V}O_2$ to generate the required work of breathing in response to the increased demand (mirroring the inability of the patient to run faster on the treadmill).

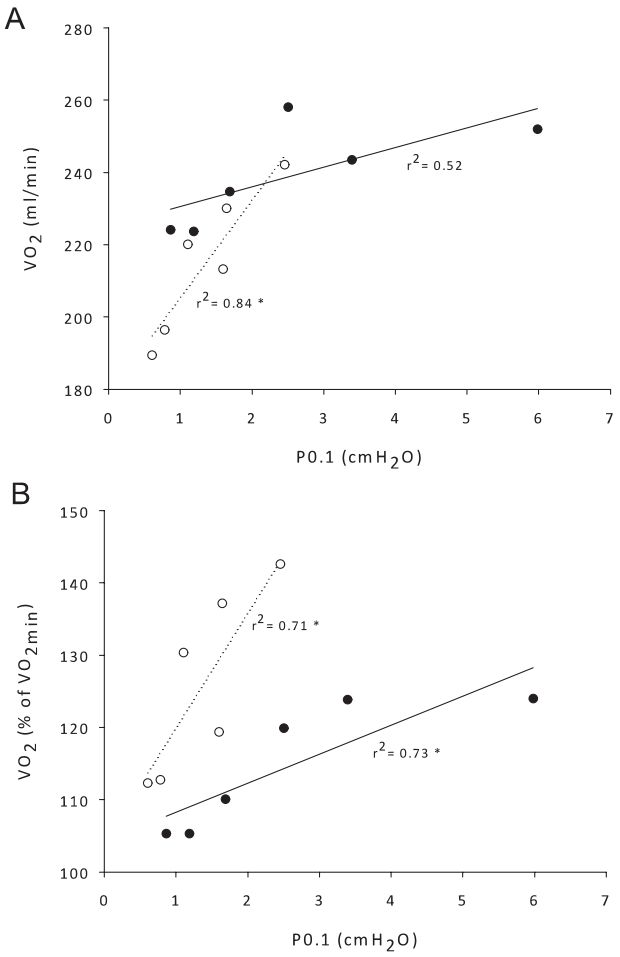

Fig. 6. Correlation between respiratory drive (expressed as P0.1) and oxygen consumption ($\dot{V}O_2$) expressed both as absolute values (*A*) or normalized for the minimum $\dot{V}O_2$ recorded during the decremental pressure support trial (*B*). Each *symbol* represents the average of the values recorded at each level of pressure support. Notice that the relationship is steeper for patients succeeding in the weaning trial (*open symbols*), indicating that for the same increase in respiratory drive these patients have a greater increase in $\dot{V}O_2$ in comparison with patients failing the trial (*filled symbols*). *, $P < 0.05$.

Another finding of the study was that, in most patients $\dot{V}O_2$ increased when ventilatory assistance was increased above a certain level: increasing PS to a level higher than the patient's need can lead to an activation of expiratory muscles, to control excessive inflation and/or to promote exhalation. This was indeed confirmed by the presence of relevant expiratory pressure-time products at high pressure support levels; this was especially true in the success patients, characterized by more favorable respiratory mechanics and, likely, muscle function. It is, however, unknown whether this finding is caused by the specific design of this study and whether it can be translated to the general population of patients undergoing spontaneous assisted ventilation.

The study has some limitations. The population is relatively limited, and we did not perform a power analysis before conducting the study. Rather, also based on previous reports on this matter, we assumed that approximately 30 patients would have constituted an adequate sample size for a physiologic study that did not aim at assessing predictors of weaning, but simply at describing one of the mechanisms of weaning failure. In any case, the nonstatistically significant differences observed should be interpreted cautiously because of the possible lack of power of our study. We used a commercial device, based on the principle of indirect calorimetry to measure $\dot{V}O_2$ in our patients; this system has the advantage of being noninvasive (requiring only a small connector at the circuit Y) and of providing continuous measurements of $\dot{V}O_2$. In our study we found a good reproducibility of the $\dot{V}O_2$ measurements obtained during two different study phases; the system has been validated mainly by comparisons with the previous Deltatrac monitor,[14,28,29] showing a good reliability. Although the different inspiratory flow profiles have not been found to affect measurement reproducibility,[30] no data are available on the potential effect of different tidal volumes or respiratory rates. Moreover, reports concerning comparisons with the reverse Fick methods, although promising, are limited.[31] The choice of maintaining each PS level for 10 min only was mandated by the necessity of keeping the protocol within a reasonable time, avoiding natural drifts of $\dot{V}O_2$. Actual capability of the patients to breathe without assistance was, however, demonstrated over a longer time span (1 h). Patients were not instrumented with an esophageal balloon, but pressure-time product was derived from airway flow and pressure tracings.[19] Not surprisingly, baseline characteristics of the patients in the failure and success groups were not perfectly balanced, with patients in the failure group having a longer (although not significantly) duration of mechanical ventilation, a trend toward a lower compliance, and a higher baseline heart rate; this imbalance might help explain why patients in the failure group were unable to increase their $\dot{V}O_2$ in response to the increased demand. Impending cardiac failure is a frequent cause of weaning failure, and it might indeed have contributed to the impossibility of the failure group to raise the $\dot{V}O_2$ adequately; unfortunately advanced hemodynamic monitoring (such as Swan–Ganz or PICCO catheters) was not available in our patients to address this issue.

Conclusion

In this study we have shown that patients who fail a weaning trial have a higher baseline $\dot{V}O_2$ and are less able to increase their $\dot{V}O_2$ when reacting to a decrease of ventilatory assistance.

References

1. MacIntyre N: Discontinuing mechanical ventilatory support. Chest 2007; 132:1049–56
2. Boles JM, Bion J, Connors A, Herridge M, Marsh B, Melot C, Pearl R, Silverman H, Stanchina M, Vieillard-Baron A, Welte T: Weaning from mechanical ventilation. Eur Respir J 2007; 29:1033–56

3. Lumb AB: Pulmonary ventilation: Mechanisms and the work of breathing, Nunn's Applied Respiratory Physiology, 5th edition. Oxford, Butterworth-Heinemann, 2000, pp 113–37
4. Annat GJ, Viale JP, Dereymez CP, Bouffard YM, Delafosse BX, Motin JP: Oxygen cost of breathing and diaphragmatic pressure-time index. Measurement in patients with COPD during weaning with pressure support ventilation. Chest 1990; 98:411–4
5. Hubmayr RD, Loosbrock LM, Gillespie DJ, Rodarte JR: Oxygen uptake during weaning from mechanical ventilation. Chest 1988; 94:1148–55
6. Weyland W, Schuhmann M, Rathgeber J, Weyland A, Fritz U, Laier-Groeneveld G, Schorn B, Braun U: Oxygen cost of breathing for assisted spontaneous breathing modes: Investigation into three states of pulmonary function. Intensive Care Med 1995; 21:211–7
7. Field S, Kelly SM, Macklem PT: The oxygen cost of breathing in patients with cardiorespiratory disease. Am Rev Respir Dis 1982; 126:9–13
8. Shikora SA, Bistrian BR, Borlase BC, Blackburn GL, Stone MD, Benotti PN: Work of breathing: Reliable predictor of weaning and extubation. Crit Care Med 1990; 18:157–62
9. Miwa K, Mitsuoka M, Takamori S, Hayashi A, Shirouzu K: Continuous monitoring of oxygen consumption in patients undergoing weaning from mechanical ventilation. Respiration 2003; 70:623–30
10. Kemper M, Weissman C, Askanazi J, Hyman AI, Kinney JM: Metabolic and respiratory changes during weaning from mechanical ventilation. Chest 1987; 92:979–83
11. Mitsuoka M, Kinninger KH, Johnson FW, Burns DM: Utility of measurements of oxygen cost of breathing in predicting success or failure in trials of reduced mechanical ventilatory support. Respir Care 2001; 46:902–10
12. Manthous CA, Hall JB, Kushner R, Schmidt GA, Russo G, Wood LD: The effect of mechanical ventilation on oxygen consumption in critically ill patients. Am J Respir Crit Care Med 1995; 151:210–4
13. Oh TE, Bhatt S, Lin ES, Hutchinson RC, Low JM: Plasma catecholamines and oxygen consumption during weaning from mechanical ventilation. Intensive Care Med 1991; 17:199–203
14. McLellan S, Walsh T, Burdess A, Lee A: Comparison between the Datex-Ohmeda M-COVX metabolic monitor and the Deltatrac II in mechanically ventilated patients. Intensive Care Med 2002; 28:870–6
15. Alberti A, Gallo F, Fongaro A, Valenti S, Rossi A: P0.1 is a useful parameter in setting the level of pressure support ventilation. Intensive Care Med 1995; 21:547–53
16. Olegård C, Söndergaard S, Houltz E, Lundin S, Stenqvist O: Estimation of functional residual capacity at the bedside using standard monitoring equipment: A modified nitrogen washout/washin technique requiring a small change of the inspired oxygen fraction. Anesth Analg 2005; 101: 206–12
17. Tobin MJ, Van de Graaff WB: Monitoring of lung mechanics and work of breathing. Principles and Practice of Mechanical Ventilation, edited by Tobin MJ. New York, McGraw-Hill, 1994; pp 967–98
18. Bellani G, Patroniti N, Weismann D, Galbiati L, Curto F, Foti G, Pesenti A: Measurement of pressure-time product during spontaneous assisted breathing by rapid interrupter technique. ANESTHESIOLOGY 2007; 106:484–90
19. Iotti GA, Braschi A, Brunner JX, Palo A, Olivei MC: Noninvasive evaluation of instantaneous total mechanical activity of the respiratory muscles during pressure support ventilation. Chest 1995; 108:208–15
20. Shikora SA, Benotti PN, Johannigman JA: The oxygen cost of breathing may predict weaning from mechanical ventilation better than the respiratory rate to tidal volume ratio. Arch Surg 1994; 129:269–74
21. Toth MJ, Gottlieb SS, Fisher ML, Poehlman ET: Skeletal muscle atrophy and peak oxygen consumption in heart failure. Am J Cardiol 1997; 79:1267–9
22. Cicoira M, Zanolla L, Franceschini L, Rossi A, Golia G, Zamboni M, Tosoni P, Zardini P: Skeletal muscle mass independently predicts peak oxygen consumption and ventilatory response during exercise in noncachectic patients with chronic heart failure. J Am Coll Cardiol 2001; 37:2080–5
23. Chua TP, Anker SD, Harrington D, Coats AJ: Inspiratory muscle strength is a determinant of maximum oxygen consumption in chronic heart failure. Br Heart J 1995; 74:381–5
24. Jones AM, Carter H: The effect of endurance training on parameters of aerobic fitness. Sports Med 2000; 29:373–86
25. Hambrecht R, Gielen S, Linke A, Fiehn E, Yu J, Walther C, Schoene N, Schuler G: Effects of exercise training on left ventricular function and peripheral resistance in patients with chronic heart failure: A randomized trial. JAMA 2000; 283:3095–101
26. McAllister RM, Terjung RL: Training-induced muscle adaptations: Increased performance and oxygen consumption. J Appl Physiol 1991; 70:1569–74
27. Bassett DR Jr., Howley ET: Limiting factors for maximum oxygen uptake and determinants of endurance performance. Med Sci Sports Exerc 2000; 32:70–84
28. Donaldson L, Dodds S, Walsh TS: Clinical evaluation of a continuous oxygen consumption monitor in mechanically ventilated patients. Anaesthesia 2003; 58:455–60
29. Singer P, Pogrebetsky I, Attal-Singer J, Cohen J: Comparison of metabolic monitors in critically ill, ventilated patients. Nutrition 2006; 22:1077–86
30. Briassoulis G, Michaeloudi E, Fitrolaki DM, Spanaki AM, Briassouli E: Influence of different ventilator modes on Vo(2) and Vco(2) measurements using a compact metabolic monitor. Nutrition 2009; 25:1106–14
31. Stuart-Andrews CR, Peyton P, Robinson GJ, Terry D, O'Connor B, Van der Herten C, Lithgow B: *In vivo* validation of the M-COVX metabolic monitor in patients under anaesthesia. Anaesth Intensive Care 2007; 35:398–405