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Work of breathing: Reliable predictor of weaning and extubation

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During the course of a critical illness, many patients become ventilator dependent. The standard assessment criteria are not always accurate in predicting potential for extubation. This investigation was designed to analyze whether the work of breathing (WOB) was a more reliable predictor of ventilator dependence. Twenty consecutive ventilator-dependent patients were prospectively studied. Nineteen required ventilator support for >2 wk and all were considered ventilator dependent because of their inability to tolerate weaning trials. The oxygen consumption ($\dot{V}O_2$) and resting energy expenditure were measured using a metabolic gas monitor. Respiratory mechanics and arterial blood gas measurements were obtained, and the deadspace to tidal volume ratio (VD/VT) was calculated. The WOB was determined by the difference in $\dot{V}O_2$ between spontaneous and mechanical ventilation, and expressed as a percentage of $\dot{V}O_2$ during mechanical ventilation.

Five of eight patients with a WOB <15% (mean 1.9) were extubated within 2 wk of study, while none of 12 patients with a WOB ≥15% (mean 34) were able to be extubated in this period. The differences in the WOB between the two groups were statistically significant (p < .01), while there was no significant difference in mechanics, $PaCO_2$, VD/VT or measured resting energy expenditure.

These data support the use of WOB determinations in evaluating extubation potential. Using a reference value for the WOB of 15%, this study had a sensitivity of 100% and a specificity of 80%. This proved to be of greater predictive value than traditional criteria. (Crit Care Med 1990; 18:157)

During the course of a critical illness, or after major surgery, many patients require ventilator support. Despite resolution of the underlying disease state, adequate nutrition, and overall clinical improvement, a significant percentage of patients will become chronically ventilator dependent. This incidence is reported to be as high as 20% (1). The inability to sustain adequate spontaneous respiration is multifactorial. Causes of respiratory failure include intrinsic lung pathology such as underlying chronic obstructive pulmonary disease as well as extrinsic etiologies such as chest wall deformity, diminished central nervous respiratory drive, and respiratory muscle dysfunction (2). Prolonged ventilator support causes respiratory muscle detraining, weakness, fatigue, and even frank atrophy.

The traditionally used criteria for weaning from ventilator support, such as arterial blood gas (ABG) determinations, vital capacity (VC), inspiratory force (IF), and minute ventilation ($\dot{V}E$) have been shown to be inaccurate for predicting potential for extubation in this group of patients (3–6). Although some of these patients display such poor respiratory mechanics that they cannot tolerate withdrawal of ventilator support, other patients will have acceptable mechanics, but cannot survive without the ventilator (4, 5).

The work of breathing (WOB) is defined as the oxygen consumption ($\dot{V}O_2$) of the respiratory muscles. It can be calculated from the difference in total body $\dot{V}O_2$ between spontaneous and mechanical ventilation, and is expressed as a percentage of $\dot{V}O_2$ during mechanical ventilation. It has been described as a useful adjunct for predicting whether a patient can be weaned from ventilator support (4, 6–8). Many techniques to measure respiratory work have been reported. Earlier attempts were impractical on a clinical basis due to complexity of design. Recently, WOB determination has been facilitated by the introduction of the portable metabolic gas monitor. This system measures the oxygen and CO_2 difference between the inspired and expired gases and then calculates the $\dot{V}O_2$ and CO_2 production ($\dot{V}CO_2$). This can be performed directly at the bedside. Using a monitor, Lewis et al. (6), in a retrospective study performed at this institution, discovered that a WOB <15% correlated well with the ability to tolerate removal of ventilator support. The purpose of this investigation was to analyze prospectively, using this criterion of 15%, whether the WOB was a more reliable predictor of ventilator dependence in the difficult-to-wean patient than the traditional criteria now in use.

PATIENTS AND METHODS

Twenty consecutive ventilated patients (11 men and nine women) in the Surgical ICU (SICU), who were identified as having weaning problems, were enrolled

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in the study. The mean age was 69.1 yr (range 48 to 84). Eighteen (90%) patients had undergone surgery. Of these patients, more than half (ten) had had cardiac surgery. Two prior patients in the study had been admitted to the SICU without prior surgery. One woman had fulminant pancreatitis and then developed respiratory failure. The other patient, a man who had received a liver transplant earlier that year, was admitted with meningitis and subsequently required ventilator support.

All but one of the patients had been ventilator dependent for >2 wk before being enrolled (one patient had been artificially ventilated for 11 days). Eight patients had been ventilator dependent for over a month before being studied. All patients displayed an intolerance to weaning either by clinical assessment or deterioration of ABG variables. All 20 patients were hemodynamically stable at time of study; none required inotropic support. There was no evidence of active sepsis and nutritional support was provided parenterally by the Nutrition Support Service. In each case, ventilator dependence was the only reason for their continued need to remain in the SICU.

Before undergoing the study, serum albumin levels and ABG were drawn. Respiratory mechanics, including VC and IF, were measured by a respiratory therapist and either exceeded or approached values considered acceptable for weaning. Patients requiring PEEP >5 cm H_2O or F_{IO_2} >0.4 were excluded from the study.

$\dot{V}O_2$, $\dot{V}E$, and resting energy expenditure (REE) measurements were performed at the bedside using a metabolic gas monitor (MGM/TWO, Utah Medical Products, Midvale, UT). Principles of operation and physical characteristics of this system of indirect calorimetry have been previously described (9–11). REE calculation from the $\dot{V}O_2$ and $\dot{V}CO_2$ involves application of the Weir equation (9). To prevent F_{IO_2} fluctuation, inspiratory gas was circuited through an oxygen blender (Bird, 3M Corp, Palm Springs, CA) en route to the ventilator (7200a, Puritan-Bennett, Lanexa, KS). Flow to the blender was regulated by an external flowmeter set at 15 L/min. The ventilator F_{IO_2} was kept at 1.0 to assure that ventilator output was derived solely from blender input.

Baseline $\dot{V}O_2$, $\dot{V}CO_2$, REE, and $\dot{V}E$ were measured during total mechanical ventilatory support. Data were collected in the steady state for approximately 20 min. The ventilator rate was then decreased in a stepwise fashion by 2 breath/min at a time. At each interval, data were collected for about 15 min to ensure an adequate sampling. Ventilator support was withdrawn as described until either the patient was able to breathe spontaneously with continuous positive airway pressure (CPAP) or became uncomfortable. At CPAP, data collecting was continued for 30 min to one hour to watch for the development of fatigue. Studies on patients unable to reach CPAP were terminated at the intermittent mandatory ventilation (IMC) level at which the patient became uncomfortable.

The oxygen cost of breathing was obtained from the difference in measured $\dot{V}O_2$ between mechanical ($\dot{V}O_{2vent}$) and spontaneous ($\dot{V}O_{2wean}$) ventilation, and was expressed as a percentage of $\dot{V}O_{2vent}$: WOB = $\dot{V}O_{2vent} - \dot{V}O_{2wean}/\dot{V}O_{2vent}$.

For patients unable to reach CPAP, the $\dot{V}O_{2wean}$ was extrapolated to its value at spontaneous respiration so that all data would be equivalent for comparison. Deadspace to tidal volume ratio (VD/VT) was calculated using the Enghoff modification of the Bohr technique with mixed expired P_{CO_2} being measured by the metabolic gas monitor. $\dot{V}O_2$ and REE measurements were standardized by BSA.

Each patient was rested the night before being studied on total ventilatory support (an IMV rate and tidal volume that supplied all of the $\dot{V}E$). Patients were kept in a constant comfortable environment and were not disturbed by family members or health care providers until the test was completed. Light sedation was used to ensure maximal ventilator tolerance and to decrease anxiety and extraneous skeletal muscle activity.

After WOB calculation, patients were separated into two groups. Group 1 consisted of all patients with a WOB ≥15%, while group 2 included all patients with WOB <15%. All patients were then followed until extubation or death. Patients extubated within 2 wk of being studied were considered extubated for the purpose of the investigation, while patients extubated >2 wk after their study were designated as not extubated. Although the primary health care team of each patient was notified of the study results, the actual weaning and decision to extubate were done by the team without further input from the investigators.

Data are presented as mean ± SEM. Differences between mean values were evaluated for statistical significance using the Student's *t*-test with $p < .05$ considered significant.

RESULTS

Table 1 depicts the results of the metabolic gas monitor studies. Patients in both groups were similar in age and size. Half of the patients in group 1 were unable to be unweaned to CPAP, while all the patients in group 2 could be studied at CPAP. There was no significant difference in REE whether predicted (pREE) by the Harris-Benedict equation or measured (mREE) between the two groups. Note the significant ($p < .01$) difference in the calculated WOB: 34% in group 1 vs. 2% in group 2. Three group 2 patients had negative values for the calculated WOB. This was due to higher $\dot{V}O_2$ measurements on total ventilator support than during spontaneous ventilation. These patients may have experienced subjective discomfort with full venti-

TABLE 1. WOB and resting energy expenditure. $\dot{V}O_{2wean}$ values are extrapolated for patients who were unable to reach CPAP. The difference in WOB between the two groups is statistically significant ($p < .01$). There were no significant differences in age, BSA, mREE, pREE, $\dot{V}O_{2vent}$ or $\dot{V}O_{2wean}$.

Patient (Sex)	Age	BSA (m^2)	Vent 1 (IMV)	$\dot{V}O_{2vent}$ (ml/min·m^2)	Vent 2 (IMV)	$\dot{V}O_{2wean}$[a] (ml/ min·m^2)	mREE (kcal/day·m^2)	pREE (kcal/day·m^2)	WOB (% Δ $\dot{V}O_2$)
Group 1									
1 (F)	75	1.74	10	82	1	139	926	743	70
2 (F)	73	1.60	8	115	2	147	963	791	28
3 (M)	62	1.80	12	124	6	220	1172	792	77
4 (M)	63	1.92	10	119	2	140	977	804	18
5 (M)	64	1.84	12	103	6	160	918	722	55
6 (M)	67	2.33	10	92	CPAP	110	788	776	20
7 (M)	62	1.85	10	113	CPAP	139	977	719	23
8 (M)	70	1.92	8	68	CPAP	80	624	690	18
9 (F)	60	1.80	10	113	2	158	1020	793	40
10 (M)	59	1.85	10	97	CPAP	115	823	783	19
11 (F)	71	1.80	8	95	CPAP	111	778	772	17
12 (M)	77	1.86	6	88	CPAP	105	764	777	19
Mean ± SEM	67 ± 2	1.86 ± 0.05		101 ± 5		135 ± 10	894 ± 40	764 ± 10	34 ± 6[b]
Group 2									
13 (F)	70	1.70	10	113	CPAP	128	860	736	13
14 (F)	78	1.70	10	126	CPAP	136	973	689	7
15 (F)	69	1.78	10	125	CPAP	138	971	770	10
16 (M)	84	1.64	10	132	CPAP	135	963	724	2
17 (F)	83	1.35	8	119	CPAP	110	825	748	−8
18 (F)	48	2.20	12	108	CPAP	95	660	773	−12
19 (M)	77	1.94	10	90	CPAP	86	604	689	−4
20 (M)	70	1.65	8	91	CPAP	97	704	784	7
Mean ± SEM	72 ± 4	1.75 ± 0.08		113 ± 5		116 ± 7	820 ± 49	739 ± 12	2 ± 3[b]

[a] Extrapolated values used when CPAP not reached.
[b] $p < .01$.
Vent 1, total ventilatory support; Vent 2, spontaneous respiration; mREE, measured REE; pREE, predicted REE.

lator support, which can increase $\dot{V}O_2$. Even when these patients are removed from the data, the WOB in group 2 is still only 8%.

Traditional respiratory variables are compared in Table 2. IF, VC, $\dot{V}E$, and $PaCO_2$ were similar for both groups. In addition, there was no significant difference in serum albumin level or VD/VT. In contrast, while no group 1 patient was extubated within 2 wk of the study, five (63%) of the eight patients in group 2 were able to be extubated within the 2 wk. Follow-up after 2 wk for the 12 patients in group 1 revealed that four died while on the ventilator, six were eventually extubated over a month after study, and the other two were extubated between 2 wk and 1 month from the study. Of the three patients in group 2 who were not extubated within the 2-wk period, one patient developed sepsis and multisystem organ failure 1 wk after study and eventually died, one patient was extubated within 3 wk of study, and the third patient could not be extubated because of problems with copious secretions and recurrent pneumonia.

Figure 1 depicts the difference in $\dot{V}O_2$ between the two groups when patients were placed on spontaneous ventilation (CPAP). Since six patients in group 1 could not reach CPAP, the data from their studies were extrapolated for comparison. Again, the $\dot{V}O_2$ measured on total ventilator support was similar between the two groups, suggesting a similar baseline metabolic state which was defined clinically as recuperative.

DISCUSSION

Respiratory insufficiency remains a serious, all too common manifestation of severe illness or the stress of major surgery. Modern ventilator support has greatly improved survival by ensuring adequate delivery of oxygen and by reducing the respiratory effort, thereby decreasing total body $\dot{V}O_2$. Unfortunately, prolonged ventilator support leads to respiratory muscle detraining, weakness, fatigue, and even atrophy. Thus, despite surviving a devastating illness, a patient may suffer from chronic ventilator dependence with its attendant high cost in terms of ongoing ICU care and risk of sepsis.

To date, there is not a test with sufficient sensitivity and specificity to predict when such patients can be weaned successfully from the ventilator. Most institutions (12) rely on $\dot{V}E$, ABG analysis, and respiratory mechanics (VC and IF). These results are specific for determining which patients will fail weaning (i.e., patients who develop hypoxemia, acidosis, tachypnea, and

TABLE 2. Comparison of weaning variables. There were no significant differences between the two groups concerning albumin, VD/VT, mechanics (IF, VC), V̇E, or Pa_{CO_2}. There were no patients in group 1 who could be extubated in 2 wk of study, while five of eight patients in group 2 were extubated in the same time period.

Patient	Albumin (g/dl)	VD/VT	IF (cm H_2O)	VC (L)	V̇E (L/min)	Pa_{CO_2} (torr)	Vent. Status
Group 1							
1	2.8	.35	−30	.700	8.8	41	NE
2	2.6	.33	−28	.500	9.9	36	NE
3	2.2	41	−24	.500	11.3	43	NE
4	2.4	.34	−40	.900	10.7	36	NE
5	2.7	.39	−22	.600	14.7	27	NE
6	2.6	.48	−42	—	12.6	42	NE
7	2.4	.59	−40	1.000	11.0	35	NE
8	3.2	.40	−18	—	11.3	46	NE
9	3.2	.17	−22	.550	7.8	31	NE
10	2.9	.32	−15	.450	8.7	36	NE
11	2.5	.39	−15	—	9.7	35	NE
12	2.9	.47	−34	—	11.2	32	NE
Mean ± SEM	2.7 ± 0.1	0.39 ± 0.03	−28 ± 3	0.650 ± 0.067	10.6 ± 0.5	37 ± 2	
Group 2							
13	2.8	.37	−65	—	8.7	31	EXT
14	2.8	.17	−26	.500	11.3	50	NE
15	2.4	.52	−30	.400	9.0	34	NE
16	2.5	.21	−38	—	10.7	41	EXT
17	2.2	.47	−28	1.100	9.2	28	EXT
18	2.1	.34	−47	.800	9.9	33	NE
19	2.6	.64	−22	—	10.4	41	EXT
20	2.2	.32	−20	—	6.2	42	EXT
Mean ± SEM	2.5 ± 0.1	0.38 ± 0.05	−35 ± 5	0.700 ± 0.137	9.4 ± 0.5	38 ± 2	

VD/VT, deadspace to VT ratio; IF, inspiratory force; NE, not extubated within 2 wk; EXT, extubated within 2 wk.

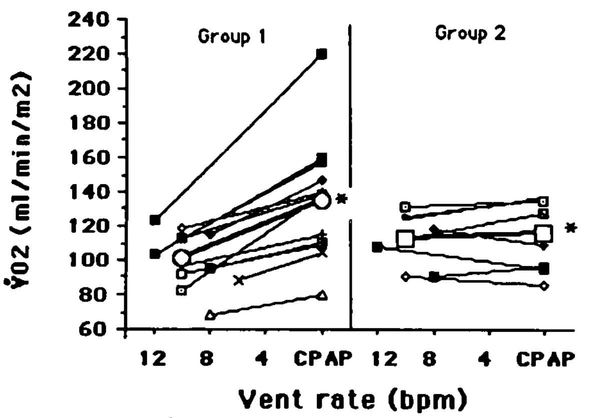

FIG. 1. Change in $\dot{V}O_2$ with decrease in ventilator support. *Large open circles* and *boxes* represent mean values. $\dot{V}O_{2vent}$ was slightly but not significantly higher in group 2. The change in $\dot{V}O_2$ as the ventilatory support was slowly withdrawn is dramatically greater for group 1. This change in $\dot{V}O_2$ represents the WOB.

increased V̇E) but are not very sensitive for predicting the potential for success. Frequently, patients are encountered in whom acceptable mechanics are found but who require reintubation within 48 h of extubation. These patients appear to have sufficient respiratory muscle strength to allow extubation, but either they do not have the reserve to overcome the development of atelectasis, mucous plugging, or an increase in oxygen demand, or they lack respiratory muscle endurance.

The limitations of respiratory mechanics as a predictor of ability to tolerate ventilator weaning are well documented. Many alternatives have been suggested. Tobin et al. (13) described their experience with analysis of the rib cage-abdominal motion patterns during respiration. In their study, muscle fatigue appeared to cause asynchronous and paradoxical movement. Unfortunately, they could not accurately apply this finding to predicting weaning potential. Another technique involved the measurement of airway occlusion pressure. This test was thought to estimate central ventilatory drive. Montgomery and colleagues (14) reported the results of a retrospective study using this procedure. In their limited investigation, seven (50%) patients required intubation. Analyzing the results of successfully extubated patients with those who were unsuccessful revealed considerable overlap. Although this method appeared inaccurate for predicting ability to wean, the investigators found that performing a hypercapnic challenge and expressing the occlusion pressure as the ratio of pressures during CO_2 stimulation and during baseline was more accurate. They acknowledged that further work in this area needs to be performed.

Many researchers have recognized the potential importance of measuring the WOB for predicting the success or failure of weaning from the ventilator. Before the development of the portable metabolic gas monitor, most determinations of WOB were cumbersome and not readily applicable to clinical practice. One of the more commonly used techniques involved estimating the inspiratory work by computing the area under a pressure-volume vs. pressure-time plot (4, 7, 15–20). Other useful techniques for measuring $\dot{V}O_2$ involve either expiratory gas collection and analysis or assessment of total body $\dot{V}O_2$ using the Fick principle (21–23). The former technique requires frequent gas sampling, is prone to technical error, and does not provide results instantly. The latter method requires insertion of a pulmonary artery catheter with its inherent risks and expense.

The metabolic gas monitor is a portable, relatively simple, accurate, and easily applicable means of measuring $\dot{V}O_2$ (9–11) which makes the calculation of the WOB a true bedside procedure. At a purchase price for the unit of about $26,000, a yearly maintenance cost of about $1,000, and a life-span of approximately 8 yr, we estimate that each study would cost <$10. In addition, 10 to 15 such studies could be easily performed weekly by a trained technician.

WOB is generally stated to be about 1% to 5% of total $\dot{V}O_2$ in healthy, spontaneously breathing volunteers (23, 24). There is abundant evidence that an increased WOB is seen with many disease states including respiratory muscle dysfunction (25). However, there are few reports concerning the application of this finding to ventilator dependence. Nishimura et al. (8) reported in an abstract the retrospective study of WOB in 11 ICU patients. Using a makeshift gas monitor, these investigators found that the group of patients successfully extubated had a WOB of 7.8% while the group that required reintubation exhibited a WOB of 20.6%. In contrast, Kemper and associates (26), also using a metabolic gas monitor, found little change in $\dot{V}O_2$ between patients extubated and those who failed. In their investigation, the WOB was 9.5% in the group of patients extubated, and 6.5% in those who were unable to wean. These results are surprising. They only measured patients for 15 to 30 min at CPAP. Perhaps a higher WOB would have been demonstrated if the patients had been studied for a longer time at CPAP. In addition, they make no mention of the criteria used for determining extubation. Both groups of patients exhibited acceptable pH, $PaCO_2$, heart rate, and $\dot{V}E$.

A recent study performed at this institution by Lewis et al. (6) served as the foundation for the present investigation. Using the same hardware and similar techniques as the present study, they retrospectively studied 30 ventilated ICU patients. They found that 88% of patients extubated within 24 h had a WOB <15% (mean 8.8), while 93% of patients not extubated had a WOB ≥15% (mean 39). Both groups of patients displayed similar respiratory mechanics, $PaCO_2$, and V_D/V_T. They concluded that patients with a WOB <15% were likely to be weaned from the ventilator.

The purpose of the present study was to test prospectively whether a WOB <15% was a more accurate predictor of the ability to wean than the traditional criteria used for many years, but acknowledged as insensitive. Twenty ventilator-dependent patients were studied. All were similar in nutritional status, age, and size. There was also no significant difference in $PaCO_2$, respiratory mechanics, or V_D/V_T between those who were extubated within 2 wk and those who were not. Most of the 20 patients had acceptable criteria for weaning (and the remainder were close), but all had failed previous attempts to wean. The only differences between these patients concerned WOB and outcome. Although the investigators had no control over weaning or the decision to extubate, 63% of patients with a WOB <15% (mean 2) were extubated within 2 wk while no patient with a WOB >15% (mean 34) was extubated in the same time period. While these results translate into a sensitivity of 100%, a specificity of 80%, and a predictive value of 85%, it must be noted that the study size was small (n = 20). Further work is necessary with a larger study population to better validate the results.

In summary, we believe that the determination of WOB in patients recovering from catabolic illness and identified by persistent ventilator dependence due to respiratory muscle weakness or poor endurance is a more accurate predictor of weaning potential than traditional criteria. This technique need not apply to those patients who are usually extubated without incident within days after major surgery, nor do we suggest its use for patients with crippling, underlying lung disease. Since weaning is labor intense and prolonged ventilation even more costly, identifying patients who can be weaned from ventilator support may provide a more efficient and cost-effective means to optimize patient care and allocation of ICU resources. Furthermore, reevaluating patients who remain ventilator dependent at subsequent intervals could assess the efficacy of respiratory muscle strengthening exercises, perhaps minimizing total time requiring artificial ventilation. The ease of determining WOB at the bedside mandates its addition to the armamentarium of the intensivist.

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