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Breathing pattern during acute respiratory failure and recovery

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ABSTRACT: The objective of this study was to compare the breathing pattern of patients who failed to wean from mechanical ventilation to the pattern during acute respiratory failure. We hypothesized that a similar breathing pattern occurs under both conditions.

Breathing pattern, mouth occlusion pressure ($P_{0.1}$) and maximum inspiratory pressure ($P_{I,max}$) were measured in 15 patients during acute respiratory failure, within 24 h of the institution of mechanical ventilation, and in 49 patients during recovery, when they were ready for discontinuation from mechanical ventilation. The following indices were calculated: rapid shallow breathing index (respiratory frequency/tidal volume (f_R/V_T)); rapid shallow breathing-occlusion pressure index (ROP = $P_{0.1} \cdot f_R/V_T$); $P_{0.1}/P_{I,max}$; and effective inspiratory impedance ($P_{0.1}/V_T$/(inspiratory time (t_I)).

Patients who failed to wean (n=11) had a similar ROP, f_R/V_T and $P_{0.1}/P_{I,max}$ to those with acute respiratory failure despite a significantly reduced $P_{0.1}/V_T/t_I$, the value of which was comparable to that of patients who weaned successfully (n=38). The $P_{I,max}$ of patients who failed to wean was similar to that of patients who weaned successfully.

We conclude that patients who failed to wean had a breathing pattern similar to that during acute respiratory failure, despite a reduced mechanical load on the respiratory muscles and a relatively adequate inspiratory muscle strength. This suggests that strategies that enhance respiratory muscle endurance may facilitate weaning.

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The majority of patients who require assisted ventilation for acute respiratory failure (ARF) can be readily weaned from the ventilator once the precipitating factors leading to the ARF are reversed with appropriate treatment [1]. In most patients, clinical judgement together with measurement of spontaneous ventilatory parameters, such as respiratory frequency (f_R), tidal volume (V_T) and ventilation minute (V'_E), suffice to predict weaning success [2, 3]. However, some patients fail to wean and may require prolonged mechanical ventilation. During weaning trials, these patients typically exhibit a rapid shallow breathing pattern that may result in hypercapnia and impaired gas exchange [4, 5]. This breathing pattern is thought to be an adaptive mechanism that avoids the development of overt respiratory muscle fatigue [6]. When weaning failure occurs, it is usually not apparent whether this failure is primarily due to an excessive load on the respiratory muscles, inadequate inspiratory muscle strength and/or endurance, or increased ventilatory demand. The breathing pattern in patients who fail to wean is thought to be similar to that of patients during ARF [5, 7, 8]. However, breathing pattern, inspiratory muscle strength and the magnitude of inspiratory muscle load have not been compared in detail between patients who fail to wean and during ARF.

In this study, breathing pattern, inspiratory muscle strength, airway occlusion pressure ($P_{0.1}$) as an index of respiratory centre output, and the effective inspiratory impedance were measured in patients undergoing a weaning trial after resolution of the ARF and in patients with ARF. The effective inspiratory impedance *i.e.* the ratio of $P_{0.1}$, to mean inspiratory flow rate ($P_{0.1}/V_T$/inspiratory time (t_I)), reflects the load imposed on the inspiratory muscles [9]. We hypothesized that patients who fail to wean would manifest breathing patterns, inspiratory muscle strength and effective inspiratory impedance similar to those with ARF.

Materials and methods

Study subjects and design

The study was approved by the Human Studies Subcommittee of the Long Beach Veterans Affairs (VA) Medical Center (CA, USA). All patients had been admitted

Table 1. – Characteristics of the subjects studied

	ARF	FW	SW
Subjects n	15	11	38
Age yrs	66±11	72±7	63±10*
Weight kg	68±15	80±25	79±26
AV days	1.0±0.0	13.5±21.2	6.8±7.3
ET tube n	15	10	36
Tracheostomy n	0	1	2
Aetiology of ARF n			
COPD	6	2	20
CHF/AMI	2	5	7
Pneumonia	3	3	7
Miscellaneous			
Sepsis	2		
IPF	1	1	
PCP	1		
OHS			2
Encephalopathy			2

Values are presented as absolute number or mean±SD. ARF: acute respiratory failure; FW: patients who failed to wean; SW: patients who weaned successfully; AV: assisted ventilation (days of AV prior to the study); COPD: chronic obstructive pulmonary disease; CHF/AMI: congestive heart failure/acute myocardial infarction; IPF: idiopathic pulmonary fibrosis; PCP: *Pneumocystis carinii* pneumonia; OHS: obesity hypoventilation syndrome; encephalopathy: anoxic (n=1) and intracranial bleeding (n=1). *: $p<0.05$, SW compared to FW.

to the medical intensive care unit and required mechanical ventilation for ARF. The subjects studied consisted of three groups of patients: patients with ARF (n=15); patients who failed to wean (FW, n=11); and patients who weaned successfully (SW, n=38). The main causes of ARF were: exacerbation of chronic obstructive pulmonary disease (COPD); congestive heart failure or acute myocardial infarct; and pneumonia (table 1). All of the patients had an endotracheal (ET) tube of 8 or 8.5 mm with the following exceptions: in the ARF group, one patient had an ET tube of 7.5 mm; in the FW group, one patient had a tracheostomy tube; in the SW group, three patients had an ET tube of 7.5 mm and two patients had a tracheostomy tube.

Patients with ARF were studied within 24 h of the institution of mechanical ventilation. Six of the 15 patients with ARF died whilst they were on the ventilator and the remaining nine patients underwent a weaning trial once the ARF resolved. Eight of these nine patients weaned successfully and one failed to wean. The weaning data on five of the eight patients who weaned successfully were incomplete and the data were excluded. Therefore, paired data were available in only four patients during ARF and recovery, and were included in the group of patients with weaning data.

Forty five patients were recruited for another research protocol and were studied during the weaning trial. Part of the data analysis of these patients has been reported previously and served as historical control [10]. Thus, in the current study, complete weaning data were obtained in a total of 49 patients (four patients from the ARF group who underwent weaning trial, see above). Eleven of these 49 patients failed to wean and 38 were successfully weaned. Data were collected over an interval of 4 yrs, with that of the historical control group from 1989 to 1992 and that of the ARF group in 1993. Patients were weaned from the ventilator when they were ready as judged by the patients' primary team using standard weaning criteria (see below).

Prior to attempted weaning, the patients were clinically and haemodynamically stable. The patients also had to have a stable pH and an arterial oxygen tension (P_{a,O_2}) of ≥8 kPa (60 mmHg) on an inspired oxygen fraction (F_{I,O_2}) of ≤0.5. In addition, the patients met at least two of the following three standard weaning criteria: maximal inspiratory pressure ($P_{I,max}$) of <-20 cmH_2O; V'_E of <15 $L \cdot min^{-1}$; and V_T of >5 $mL \cdot kg^{-1}$. Sedatives and narcotics had been withheld 24 h prior to weaning. All patients were on the synchronized intermittent mandatory ventilation (SIMV) mode, with a rate set at 4 $breaths \cdot min^{-1}$ for ≥1 h. The weaning trial itself consisted of breathing on 5 cmH_2O flow-triggered continuous positive airway pressure (CPAP) (7200a; Puritan Bennett Corp., Carlsbad, CA, USA) for 1 h. The same weaning method has been applied both to the historical control and the patients in the current study. Failure to wean was defined as the inability to complete the 1 h trial, or completion of the trial but demonstration of any of the following signs within 48 h of discontinuation from mechanical ventilation: diaphoresis; respiratory distress; agitation; a sustained increase or decrease in cardiac frequency (f_C) of more than 20 beats $\cdot min^{-1}$; a sustained increase or decrease in mean blood pressure of greater than 15 mmHg; a P_{a,O_2} of ≤7.3 kPa (55 mmHg) on the previous CPAP F_{I,O_2}; or a decrease in pH of 0.10 units from values prior to the weaning trial. All of the patients in the weaning group completed the weaning trial; however, nine of the 11 patients in the FW group had to be re-intubated and ventilatory support resumed within 48 h. The other two patients refused re-intubation.

Methods

All measurements were made in the semirecumbent position while the patients were on CPAP. The patients in ARF were also placed on CPAP for the duration of the measurements, which lasted for 5–10 min. During weaning, measurements were obtained within 5 min from the time that the patient was placed on CPAP. Airway pressure measurements were made from a side port (proximal to the ET tube) connected to a differential pressure transducer (MP 45±100 cmH_2O; Validyne, Northridge, CA, USA). $P_{I,max}$ was measured from the end-expiratory lung volume against an occluded respiratory circuit, and held for at least 1 s. Three manoeuvres were performed and the largest value was used for analysis. In the patients who were not able to follow commands, $P_{I,max}$ was measured according to the method of MARINI *et al.* [11] with the exhalation circuit unoccluded. To obtain $P_{0.1}$, the inspiratory port of a unidirectional balloon occlusion valve (Hans Rudolph, Kansas City, MO, USA) was occluded for less than 500 ms at intervals of more than 15 s. The $P_{0.1}$ was the airway pressure decline from end-expiratory airway pressure level over 0.1 s from the onset of inspiration. Three measurements were averaged and used for data analysis.

In 31 patients, V_T was obtained from the flow signal

of a heated pneumotachograph (Fleisch No. 2; Fleisch, Lausanne, Switzerland) connected to a differential pressure transducer (MP45±2 cmH_2O; Validyne, Northridge, CA, USA). Tidal volume was measured by integrating the flow signal (8815A; Hewlett Packard, Waltham, MA, USA). Inspiratory time (t_I) and total breath cycle duration (t_{tot}) were measured from the flow signal. All signals were recorded on an 8-channel recorder (7758B; Hewlett Packard). In the remainder of the patients, V_T was measured as an average of 5–12 consecutive breaths with a volume meter (5410; Ohmeda, Englewood, CO, USA) connected directly to the proximal end of the ET tube. The volume meter was calibrated with a 3 L calibration syringe and had an accuracy of ±1%. In these patients, airway pressure was recorded on a 2-channel recorder (2200S; Gould, Cleveland, OH, USA). Inspiratory time and t_{tot} were measured from the airway pressure tracing.

Dynamic intrinsic positive airway pressure ($PEEP_i$) was measured in six of 11 patients (55%) in the FW group and 22 of 38 patients (58%) in the SW group from the oesophageal pressure (P_{oes}) as the pressure decline from onset of inspiratory effort to onset of inspiratory flow [12]. $PEEP_i$ was obtained as an average of 10 consecutive breaths. Gastric pressure was not measured in these patients; therefore, $PEEP_i$ was not corrected for expiratory muscle activity.

The following variables were calculated: f_R ($60/t_{tot}$); V'_E ($V_T \times f_R$); the rapid shallow breathing index (f_R/V_T) [13]; t_I/t_{tot}; the rapid shallow breathing-occlusion pressure (ROP) index ($P_{0.1} \cdot f_R/V_T$) [10]; and the effective inspiratory impedance ($P_{0.1}/V_T/t_I$) [9].

Because inspiratory muscle strength may affect the measurement of $P_{0.1}$, $P_{0.1}/P_{I,max}$ was also calculated [14].

Statistical analysis

Comparisons between data obtained from the three groups of patients (namely those in ARF, those who were successfully weaned (SW) and those who subsequently failed weaning (FW)), were made by one-way analysis of variance (ANOVA). If a significant difference existed between the means of the groups, the differences between means were analysed with Tukey's test. A probability (p-value) of less than 0.05 was considered significant.

Results

The subjects' characteristics are summarized in table 1. The patients who failed to wean were significantly older than those who weaned successfully. The mean (±SD) duration on mechanical ventilation prior to enrolment into the study tended to be longer in the patients who subsequently failed to wean (13.5±21.1 days, range 3–76 days) than in the patients who weaned successfully (6.8±7.3 days, range 1–34 days).

The aetiology of ARF in the majority of the SW group was COPD, although the distribution among the three groups was not significantly different (Chi-squared, p=0.23).

The ROP index, f_R/V_T, $P_{0.1}/P_{I,max}$, $P_{0.1}$ and f_R were not significantly different between FW and ARF patients (figs. 1 and 2, and table 2). However, despite failure to wean, the index of inspiratory muscle load or $P_{0.1}/V_T/t_I$ of FW patients was significantly less than that of ARF patients. In fact, FW patients had a similar $P_{0.1}/V_T/t_I$ to SW patients (fig. 2).

Table 2 shows that V_T, V'_E, and V_T/t_I were significantly higher in FW patients compared with ARF patients. As expected, SW patients had a lower ROP, f_R/V_T, and f_R compared both with ARF and FW patients. Compared with FW patients, the $P_{0.1}$ and $P_{0.1}/P_{I,max}$ were not significantly different. $P_{I,max}$ and t_I/t_{tot} were similar among the three groups.

In the FW patients, $PEEP_i$ was small and was not significantly different to that in the SW group (2.0±0.5 (±SEM) *vs* 2.0±0.4 cmH_2O, respectively).

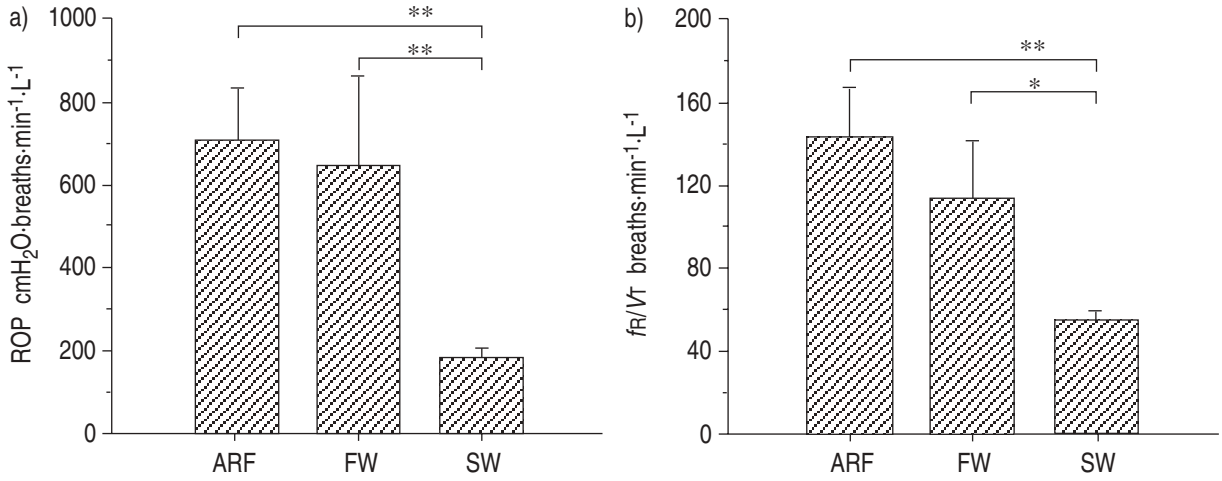

Fig. 1. – a) Rapid shallow breathing - occlusion pressure index (ROP = $P_{0.1} \cdot f_R/V_T$); and b) rapid shallow breathing index (f_R/V_T) of patients with acute respiratory failure (ARF), failed weaning (FW) and successful weaning (SW). Values are presented as mean±SEM. $P_{0.1}$: mouth occlusion pressure; f_R: respiratory frequency; V_T: tidal volume. *: p<0.05; **: p<0.01.

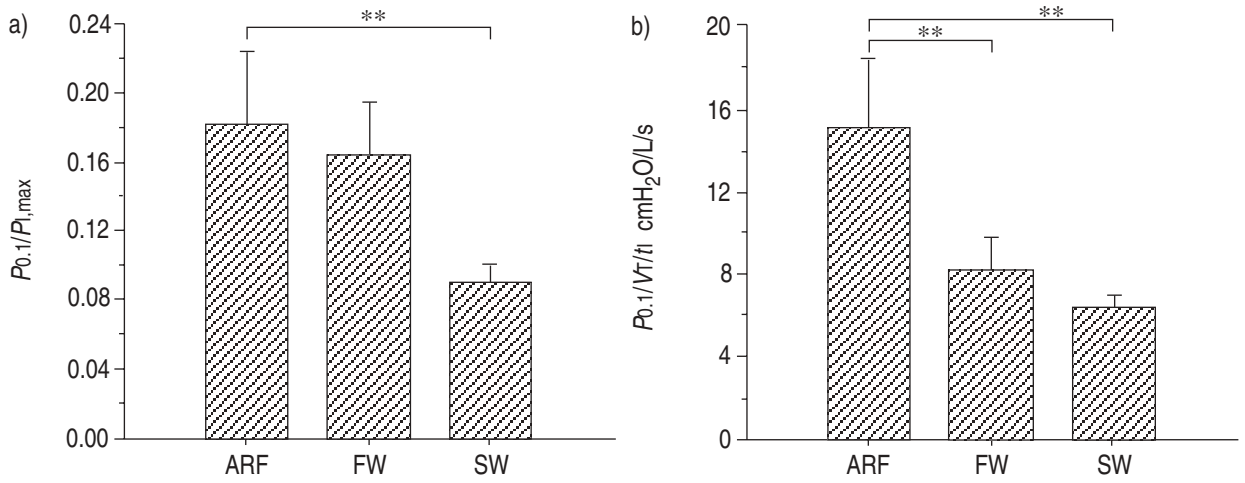

Fig. 2. – a) Ratio of occlusion pressure to maximum inspiratory pressure ($P_{0.1}/P_{I,max}$); and b) inspiratory system impedance ($P_{0.1}/V_T/t_I$) of patients with acute respiratory failure (ARF), failed weaning (FW) and successful weaning (SW). Values are presented as mean±SEM. V_T: tidal volume; t_I: inspiratory time. **: p<0.01.

Table 2. – Subjects occlusion pressure, maximum inspiratory pressure, breathing pattern and haemodynamic variables

	ARF	FW	SW
Subjects n	15	11	38
$P_{0.1}$ cmH_2O	6.5±1.6	5.2±1.3	3.2±0.2*
V_T mL	285±27	436±62*	530±28**
f_R breaths·min^{-1}	33.1±2.1	35.2±3.4	25.1±1.1**††
V'_E L·min^{-1}	9.1±0.8	13.9±1.6**	12.8±0.6*
V_T/t_I L·s^{-1}	0.38±0.03	0.59±0.07**	0.56±0.02**
t_I/t_{tot}	0.41±0.02	0.39±0.02	0.39±0.01
$P_{I,max}$ cmH_2O	36.7±4.3	33.2±4.4	43.4±3.4
Mean BP mHg	86.6±4.2	82.9±4.3	96.2±2.8
f_C beats·min^{-1}	107.5±4.3	94.4±4.3	100.1±2.3

Values are presented as mean±SEM. $P_{0.1}$: airway occlusion pressure in 0.1 ms; V_T: tidal volume; f_R: respiratory frequency; V'_E: total minute ventilation; V_T/t_I: mean inspiratory flow rate; t_I/t_{tot}: duty cycle; $P_{I,max}$: maximum inspiratory pressure; BP: blood pressure; f_C: cardiac frequency. For further definitions see legend to table 1. *,**: p<0.05, p<0.01 *vs* ARF; ††: p<0.01 *vs* FW.

Discussion

The main findings in this study are that the ROP, f_R/V_T and $P_{0.1}/P_{I,max}$ of patients who failed to wean were similar to those of patients with ARF, and yet the effective inspiratory impedance was substantially less. ARF and weaning failure are postulated to result from a decrease in respiratory muscle reserve, an increase in respiratory muscle load, or both [15]. Both respiratory muscle endurance and strength influence the balance between respiratory muscle reserve and load. Respiratory muscle load was estimated as the effective inspiratory impedance or $P_{0.1}/V_T/t_I$. During recovery, despite the significantly reduced $P_{0.1}/V_T/t_I$ compared with ARF, some patients failed to wean. In fact, the reduction in load was similar in magnitude to that of patients who weaned successfully. Likewise, the $P_{I,max}$ was similar compared with patients who weaned successfully. This observation suggests that respiratory muscle endurance may be a more important determinant than respiratory muscle strength for the success or failure to wean. Consequently, strategies that improve respiratory muscle endurance might enhance the success of weaning from mechanical ventilation.

In support of our contention is the recent study by ESTEBAN *et al.* [16], in which patients who underwent daily T-piece weaning trials were extubated sooner than with intermittent mandatory ventilation or pressure support ventilation. With T-piece weaning trials, respiratory muscle endurance is presumably enhanced. In the study by ALDRICH *et al.* [17], the adjunctive use of inspiratory resistive training in 27 patients who had been on prolonged mechanical ventilation for 3 weeks or more and failed multiple attempts at standard T-piece weaning trials, resulted in successful weaning in 12 patients, with an additional five patients weaned to nocturnal ventilatory support only. In the latter study, concurrent controls were not available and use of a T-piece was the initial method of weaning [17]. However, it appears that additional measures that improve inspiratory muscle endurance promote successful weaning.

The effective inspiratory impedance ($P_{0.1}/V_T/t_I$) is a combination of $P_{0.1}$, the pressure generated in the first 100 ms of an occluded breath, and the mean inspiratory flow of unoccluded breaths. The index, therefore, only approximates the inspiratory system impedance and needs to be interpreted with caution [9]. Nevertheless, the increase in effective inspiratory impedance during ARF suggests that the mechanical load on the respiratory muscles is increased. In patients with ARF, a similar high value of $P_{0.1}/V_T/t_I$ was also observed by FERNANDEZ *et al.* [14]. Some patients maintained a high $P_{0.1}/V_T/t_I$ when they recovered from ARF and were unable to sustain spontaneous breathing [14]. It was unclear, however, whether those patients were ready to wean, as in the present study.

The $P_{0.1}/V_T/t_I$ in the FW patients was not significantly different to that in the SW group. In the presence of $PEEP_i$, $P_{0.1}$ in the FW patients may have been underestimated, particularly when measured under static conditions. In the FW group in whom the data were available (55% of the patients), dynamic $PEEP_i$ was small and was not significantly different from that of the SW group (58%

of the patients). Only two patients in the FW group had COPD, and $PEEP_i$ was 2 cmH_2O in the one patient in whom $PEEP_i$ was measured. Furthermore, all of the patients tolerated the weaning trial and failed only after the trial was completed; therefore, increases in $PEEP_i$, if any, were not reflected in the measurement. In the presence of airflow limitation, dynamic $PEEP_i$ may underestimate static $PEEP_i$ by as much as 50–90% [18, 19]. However, this pertains both to FW and SW groups. It should be noted that 20 of the 28 patients with COPD weaned successfully; therefore, it is rather unlikely that effective inspiratory impedance in the FW group was underestimated.

$P_{I,max}$ was reduced compared to normal values but was similar between all groups (ARF, FW and SW). $P_{I,max}$ is an estimate of inspiratory muscle strength, is voluntarily or involuntarily [11] generated, and is dependent upon the intrinsic properties of the inspiratory muscles and activation of fast twitch muscle fibres [20]. $P_{I,max}$ has not been useful in characterizing patients who will fail or wean successfully [21]. Previously, others have reported that $P_{I,max}$ of patients with ARF was less compared with that during recovery [14]. Unfortunately, it is unclear whether the $P_{I,max}$ was measured within 24 h of institution of mechanical ventilation as in the present study. The $P_{I,max}$ discrepancy between the current study and that of others [14] might be related to differences in methodology.

The $P_{0.1}$ reflecting neuromuscular output, was increased in ARF, and remained increased in the FW group but decreased in the SW patients. A similar trend was observed for $P_{0.1}/P_{I,max}$ (fig. 2). During ARF, the increased mechanical load (*i.e.* elevated effective inspiratory impedance) and associated impaired gas exchange, both led to increased neuromuscular drive. The increased $P_{0.1}$ during ARF is in agreement with previous studies [22]. Although $P_{0.1}$ was larger in FW compared to SW patients, in contrast to other studies [23–25], the difference in mean $P_{0.1}$ between these groups did not achieve statistical significance. Similarly, $P_{0.1}/P_{I,max}$ did not separate the FW and SW patients. The predictive value of $P_{0.1}$ to indicate FW or SW has been questioned by others [26], who were only able to separate FW and SW patients by a difference in hypercapnic augmentation of $P_{0.1}$. Nevertheless, most studies [22–25] have demonstrated that neuromuscular output is augmented in ARF and FW patients. It should be emphasized that the present study did not address the utility of these measured variables in predicting weaning outcome, but they were used to assess differences in the physiological characteristics between FW patients and those with ARF. Neuromuscular output may be combined with rapid shallow breathing to yield the ROP index ($P_{0.1} \cdot f_R/V_T$). The ROP index was significantly different between the ARF and SW group, as well as between the FW and SW groups, as shown previously [9].

Patients with ARF demonstrated a rapid shallow breathing pattern, *i.e.* small V_T and high f_R. This contrasts to the significantly higher V_T in FW patients resulting in rapid breathing with increased V'_E (hyperventilation) (table 2). The obvious differences in V_T between ARF and FW patients can be explained by differences in mechanical load. However, both groups adopted a high f_R resulting in high f_R/V_T ratios compared to the SW group. The development of rapid shallow breathing is probably mediated *via* chemical and reflex stimuli [27]. The respiratory centre adopts an optimal breathing strategy (high f_R/V_T ratio) under stressful conditions [28]. Hence, the high f_R/V_T ratio may be a manifestation of incipient respiratory muscle fatigue.

The results and conclusions from the present study might be criticized because the patients, with the exception of four, were not studied sequentially from ARF to recovery and its consequent FW or SW outcome. A substantial proportion of the patients died during ARF. It was necessary to resort to a "historical control" for the recovery group of patients in whom the data were collected over a span of 3 yrs. Since relatively large groups of patients were studied during ARF and recovery, and since the same method of weaning was used in the historical control and four of the patients in the present study, we do not feel that the validity of our conclusions is seriously impaired. Furthermore, we were primarily interested in providing a better description of the patterns of breathing adopted during ARF and during recovery, rather than studying SW and FW groups *per se*.

In conclusion, the patterns of breathing adopted by patients who fail to wean are similar in most respects to those adopted during acute respiratory failure, despite substantial reductions in the inspiratory muscle load upon recovery from acute respiratory failure. Although inspiratory muscle strength and inspiratory muscle load are not significantly different in patients who fail to wean and patients who wean successfully, the pattern of breathing adopted in the patients who fail to wean suggests that enhancement of respiratory muscle endurance as well as institution of measures that reduce the mechanical load may improve the outcome of weaning.

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