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ORIGINAL

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Respiratory load compensation during mechanical ventilation—proportional assist ventilation with load-adjustable gain factors versus pressure support

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Abstract *Rationale:* In mechanically ventilated patients respiratory system impedance may vary from time to time, resulting, with pressure modalities of ventilator support, in changes in the level of assistance. Recently, implementation of a closed-loop adjustment to continuously adapt the level of assistance to changes in respiratory mechanics has been designed to operate with proportional assist ventilation (PAV+). *Objectives:* The aim of this study was to assess, in critically ill patients, the short-term steady-state response of respiratory motor output to added mechanical respiratory load during PAV+ and during pressure support (PS). *Patients and interventions:* In 10 patients respiratory workload was increased and the pattern of respiratory load compensation was examined during both modes of support. *Measurements and results:* Airway and transdiaphragmatic pressures, volume and flow were measured breath by breath. Without load, both modes provided an equal support as indicated by a similar pressure–time product of the diaphragm per breath, per minute and per litre of ventilation. With load, these values were significantly lower ($p < 0.05$) with PAV+ than those with PS (5.1 ± 3.7 vs 6.1 ± 3.4 $cmH_2O.s$, 120.9 ± 77.6 vs 165.6 ± 77.5 $cmH_2O.s/min$, and 18.7 ± 15.1 vs 24.4 ± 16.4 $cmH_2O.s/l$, respectively). Contrary to PS, with PAV+ the ratio of tidal volume (V_T) to pressure–time product of the diaphragm per breath (an index of neuroventilatory coupling) remained relatively independent of load. With PAV+ the magnitude of load-induced V_T reduction and breathing frequency increase was significantly smaller than that during PS. *Conclusion:* In critically ill patients the short-term respiratory load compensation is more efficient during proportional assist ventilation with adjustable gain factors than during pressure support.

Keywords Inspiratory effort · transdiaphragmatic pressure · breathing pattern

Introduction

Pressure support (PS) is a widely used mode of assisted mechanical ventilation [1]. In this mode the ventilator, once triggered by the patient effort, provides a pre-set level of constant pressure until a cycling-off criterion is reached [2, 3]. As a result the patient, by altering the pressure generated by respiratory muscles, may change the inspiratory flow and thus have partial control over the mechanical breath. This ability, however, is seriously compromised in the presence of abnormal respiratory system mechanics [4].

Proportional assist ventilation (PAV) is a mode of support which amplifies the patient effort [5]. Contrary to PS, with PAV the ventilator pressure is proportional (the proportionality is pre-set) to instantaneous flow and volume

and hence to pressure generated by the respiratory muscles. Although numerous studies have shown that, compared with PS, PAV improves the synchrony between patient and ventilator [6, 7, 8, 9], the necessity of regular measurements of respiratory system mechanics imposes a major obstacle to the widespread use of this mode.

It is well known that in mechanically ventilated, critically ill patients both resistance and elastance of respiratory system may vary considerably from time to time [10, 11, 12]. This variation may change the level of assistance during PS and PAV, resulting in over- or under-assist. Over-assist may lead to ineffective efforts with PS [13, 14] and run-away phenomena with PAV [14, 15]. On the other hand, under-assist may increase inspiratory efforts during both PS and PAV [6]. Indeed, in awake patients who were being weaned from the ventilator, Grasso et al. [6] assessed ventilatory responses to added mechanical loads during PAV and PS and observed that load application caused a similar increase in inspiratory effort per breath between modes. These results indicate that with both modes, increases in respiratory system impedance may lead to impairment of neuroventilatory coupling. Thus, without regular measurements of respiratory system mechanics, the full potential benefit of PAV—the tight coupling between neural output and ventilator function [5]—may not be achieved.

Recently, methods of non-invasive determination of resistance [see section E2 of online supplement of ref. [11]) and elastance [16] of the respiratory system when patients are ventilated with PAV have been described. Based on these methods, a software has been developed (PAV+) which automatically adjusts the flow and volume gain factors such as to represent always constant fractions of the measured values of resistance and elastance of the respiratory system.

The aim of this study was to assess the short-term steady-state response of respiratory motor output to added mechanical load during PS and PAV+ in critically ill patients. Since the early reinstitution of spontaneous breathing in these patients has become an important therapeutic option to avoid the various complications associated with controlled mechanical ventilation [17, 18], the patients were studied during the acute phase of their illness. In order to eliminate behavioural responses the patients were studied during sedation.

Methods

Ten patients admitted to the intensive care unit for management of acute respiratory failure were studied. At the time of the study all patients were ventilated in PS mode. In all patients PEEP was added to improve either the oxygenation or the triggering sensitivity. None of them was eligible for a weaning t-piece trial. All patients were sedated with propofol to achieve acceptable oxygenation and patient-ventilator synchrony as judged by the primary physician. The level of sedation was such as to achieve a score of 3 on Ramsay's scale.

Measurements

Flow (V'), volume (V), and airway (Paw), oesophageal (Pes), gastric (Pga) and transdiaphragmatic (Pdi) pressures were measured breath by breath.

Initially, the patients were connected to an ICU ventilator (Puritan-Bennett 840), able to ventilate them with PS and PAV. The ventilator was equipped with software (PAV+) which, when PAV mode was activated, automatically estimated elastance (Ers_{PAV}) and expiratory resistance (Rrs_{PAV}) of the respiratory system, based on methods described previously (section E2 of online supplement of ref. [11]), [16].

With this system the caregiver sets the percentage of unloading (K, maximum 95%) and the ventilator delivers pressure as follows:

$$Paw_{(t)} = K\,[V'_{I(t)} \times (R_{tube(t)} + Rrs_{PAV}) + V_{(t)} \times Ers_{PAV}] \quad (1)$$

where $Paw_{(t)}$ is instantaneous airway pressure, R_{tube} is the flow-dependent endotracheal tube resistance, $V'_{I(t)}$ is instantaneous inspiratory flow and $V_{(t)}$ is instantaneous lung volume above end-expiratory level.

Study protocol

Initially the patients were ventilated with PS at settings determined by the primary physician and 30 min later the pressure–time product of the diaphragm per breath (PTP-Pdi/b) was calculated. Thereafter the patients were placed on PAV+ and the percentage of unloading was set at values which resulted in steady-state PTPPdi/b comparable with that obtained with PS. After determination of the percentage of unloading, in random order the patients were ventilated for 30 min with PS and PAV+ with and without increase in the workload of the respiratory system. The increase was obtained by applying sandbags to the entire surface of the anterior chest and abdominal wall such as to increase Ers_{PAV} by at least 30%. At the end of each study period, measurements of arterial blood gasses were obtained. In addition, in each experimental condition the assist level was decreased to zero (CPAP only) for one breath to document the difference between assisted and non-assisted V_T at the same chemical drive [19].

At the end of the study, the patients were placed on volume-control constant flow mode and ventilated with V_T comparable with that of assisted ventilation. The level of sedation was increased, and simultaneously breathing frequency was adjusted upward in order to lower $PaCO_2$ and inhibit respiratory muscle activity. When passive ventilation was obtained the total respiratory system mechanics were measured by the technique of rapid

airway occlusion using standard formulas [20, 21, 22]. Respiratory system mechanics were assessed with and without load application.

Data analysis

The last 2 min of each 30-min period were analysed and averaged to give the breath variables corresponding to each experimental condition. Pdi, Pga and Pes swings are reported as changes from end-expiratory value rather than from absolute zero pressure [6]. Neural and mechanical inspiratory and expiratory time were measured as previously described [23]. The rate of rise of Pdi (dp/dt), the Pdi swings (Pdi_{swings}) and the level of intrinsic PEEP (PEEPi) were also calculated [6, 24]. Inspiratory effort per breath was quantified by measuring the area under the Pdi signal from the beginning of Pdi increase to the point at which Pdi started to decline rapidly (PTPPdi/b). PTPPdi per minute (PTPdi/min) and per litre of minute ventilation (PTPPdi/L) were also calculated. PTPPdi/b was divided into that due to PEEPi and that due to inflation.

At 30%, 60% and 80% of inflation time the predicted Paw from Eq. 1 was calculated and compared with the corresponding values of observed Paw.

Data were analysed by multi-factorial analysis of variance for repeated measurements (ANOVA), followed by Tukey's test for multiple comparisons if the F-value was significant. Comparison between respiratory system mechanics measured during active and passive ventilation were made using the method of Bland and Altman [25]. All values are expressed as mean ± SD.

Results

Patients' characteristics and baseline ventilator settings are shown in Table 1.

Without load, V_T, breathing frequency, V'_E, breathing pattern and the various indices of inspiratory effort did not differ significantly between PS and PAV+ (Table 2). With PAV+, the dialled assist level (K) averaged 58 ± 15% of the measured elastance and resistance and resulted in a 73 ± 37% increase of spontaneous V_T. With PS, the average pressure level was 17.5 ± 6.1 cmH_2O and caused an increase in the spontaneous V_T by 84 ± 70%. With load, spontaneous V_T increased by 87 ± 63% with PAV+ and by 62 ± 55% with PS. With and without load, runaway breaths were not observed during PAV+. With and without load, ineffective efforts were not observed either with PAV+ or with PS.

With PAV+, the predicted and observed values of Paw at different inflation time are shown in Fig. 1. Although the predicted Paw was slightly lower and higher, respectively,

Table 1 Patients' characteristics and baseline ventilator settings

Patient (no.)	Sex (M/F)	Age (years)	Days on MV	Diagnosis on admission	PS (cmH_2O)	PEEP (cmH_2O)	FIO_2
1	M	71	6	Pneumonia	17	7	0.25
2	M	49	21	Sepsis	15	5	0.40
3	F	82	6	Aspiration	30	15	0.50
4	M	77	17	AECOPD	15	6	0.50
5	M	74	9	AECOPD	21	6	0.45
6	F	72	17	Sepsis	15	5	0.40
7	M	81	15	Sepsis	16	6	0.37
8	F	43	5	Aspiration	9	5	0.34
9	M	76	12	AECOPD	12	5	0.35
10	F	78	5	Sepsis	25	5	0.30
Mean		70	11		17.5	6.5	0.39
SD		13	6		6.2	3.1	0.08

MV mechanical ventilation, *PS* pressure support, *PEEP* positive end-expiratory airway pressure, $F_I O_2$ fractional concentration of inspired O_2, *AECOPD* acute exacerbation of chronic obstructive pulmonary disease

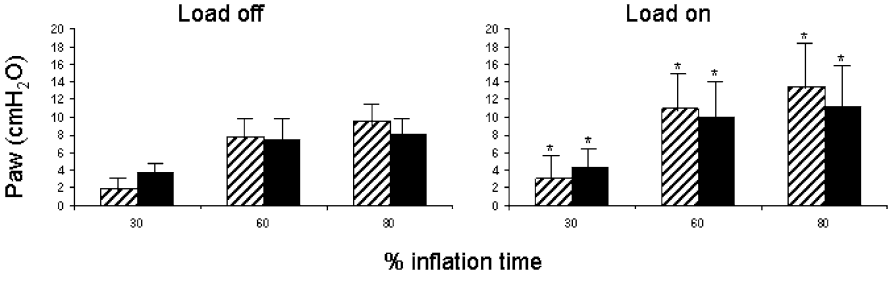

Fig. 1 Observed and predicted airway pressure (*Paw*) above positive end-expiratory pressure (mean ± SD), measured at 30%, 60% and 80% of inflation time in patients ventilated with PAV+ without and with load application. *Cross-hatched bars* observed Paw, *solid bars* predicted Paw. *Significantly different from the corresponding value without load

Table 2 Effects of load application on breathing pattern, inspiratory effort and arterial blood gasses under different experimental conditions

	PAV		PS	
	Load off	Load on	Load off	Load on
V_T (l)	0.35 ± 0.11	0.31 ± 0.10*	0.34 ± 0.11	0.29 ± 0.11*+
T_Im (s)	0.93 ± 0.2	0.87 ± 0.2	0.86 ± 0.2	0.77 ± 0.2*
Fr (breaths/min)	23.3 ± 6.1	25.8 ± 6.4	24.6 ± 5.3	29.3 ± 9.1*
V'$_E$ (l/min)	7.86 ± 2.2	7.68 ± 2.2	8.14 ± 2.0	8.10 ± 2.8
T_In (s)	0.71 ± 0.2	0.65 ± 0.2	0.67 ± 0.2	0.68 ± 0.2
T_En (s)	2.01 ± 0.5	1.78 ± 0.3	1.88 ± 0.4	1.52 ± 0.4*
Pdi_{swings} (cmH_2O)	8.08 ± 3.5	11.83 ± 7.1*	7.35 ± 4.1	14.14 ± 6.7*+
dp/dt (cmH_2O/s)	13.45 ± 6.4	20.73 ± 14.2*	12.03 ± 5.8	24.64 ± 15.7*+
PTPPdi/b (cmH_2O.s)	3.83 ± 2.3	5.13 ± 3.7*	3.20 ± 1.9	6.13 ± 3.4*+
$PTPPdi_{PEEPi}$/b (cmH_2O.s)	0.52 ± 0.6	1.94 ± 2.1*	0.54 ± 0.5	2.14 ± 1.9*
V_T/PTPPdi/b (l/cmH_2O.s)	0.14 ± 0.1	0.10 ± 0.1	0.17 ± 0.1	0.07 ± 0.1*
PTPPdi/min (cmH_2O.s/min)	80.4 ± 46	120.9 ± 78*	72.4 ± 38	165.6 ± 77*+
PTPPdi/L (cmH_2O.s/l)	11.53 ± 7.4	18.71 ± 15.1*	9.89 ± 6.5	24.36 ± 16.4*+
PaO_2 (mmHg)	92.8 ± 25.6	77.9 ± 16.7	92.9 ± 33.7	84.8 ± 33.3
PaO_2/F_IO_2	246 ± 112	190 ± 61.1*	243 ± 116	213 ± 107
$PaCO_2$ (mmHg)	49.9 ± 12.6	53.1 ± 14.1	48.7 ± 13.2	54.0 ± 16.6

V_T tidal volume, T_Im mechanical inspiratory time, *Fr* breathing frequency, V'_E minute ventilation, T_In, T_En neural inspiratory and expiratory time, respectively, *Pdi*; transdiaphragmatic pressure, Pdi_{swings} Pdi swings during inspiration, *dp/dt* the rate of rise of Pdi, *PTPPdi/b* transdiaphragmatic pressure time product per breath, $PTPPdi_{PEEP}$/b transdiaphragmatic pressure–time product per breath due to PEEPi, *PTPPdi/min*, *PTPPdi/L* transdiaphragmatic pressure–time product per minute and per litre of ventilation, respectively, PaO_2, $PaCO_2$ partial pressure of arterial O_2 and CO_2, respectively, F_IO_2 fractional concentration of inspired O_2

+Significant difference from the corresponding value with PAV+, *Significant difference from the corresponding value at load off

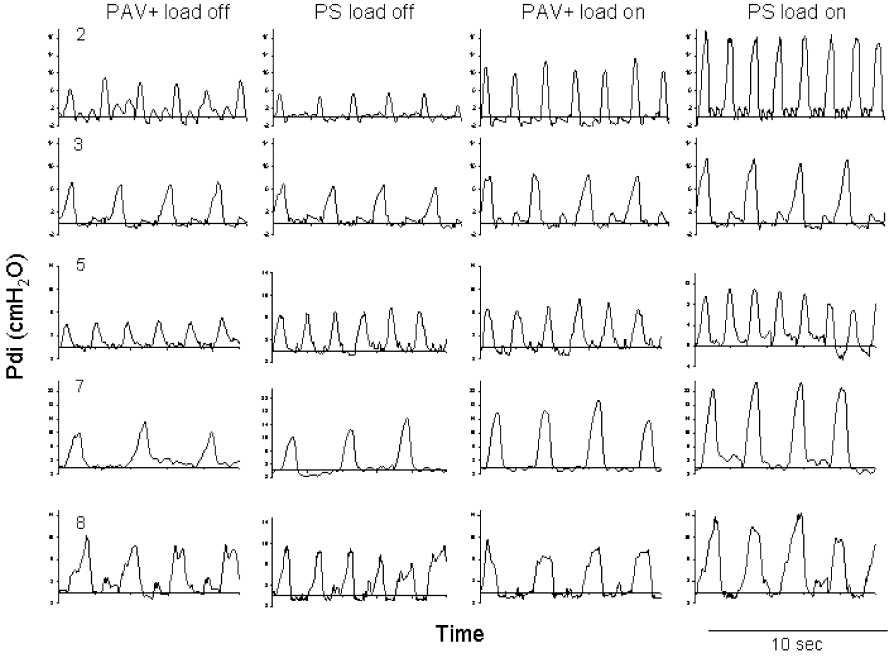

Fig. 2 Experimental records illustrating the effect of chest and abdominal binding on transdiaphragmatic pressure in five representative patients during PAV+ and during PS. Note that without load, Pdi swings were comparable between modes. With load, Pdi swings were considerable larger with PS than with PAV+

at 30% and 80% of inflation time than the actual Paw, the difference was not significant. At a given inflation time, load application significantly increased Paw (predicted and observed) compared with the corresponding values without load.

Short-term load application significantly increased elastance (Ers) and resistance (Rmin and Rmax) of the respiratory system, measured at the end of the study during controlled mechanical ventilation (Table 3). Similarly, elastance and resistance measured with PAV+ (Ers_{PAV} and R_{TOT}, respectively) increased significantly with load (Table 3). There was a significant linear relationship between Rmin and R_{TOT} and between Ers and Ers_{PAV} (Fig. S1), although there was considerable scatter in the data. Bland and Altman analysis showed a bias of –0.12 cmH_2O/l for elastance (95% CI for bias –4.0 to

Table 3 Respiratory system mechanics obtained during controlled mechanical ventilation (passive) and during PAV+ (active respiratory efforts) with and without load application

	Ers_{CMV}	Rmax	Rmin	ΔR	Ers_{PAV}	R_{TOT}	$PEEPi_{PAV}$	$PEEPi_{PS}$
Load off	27.1 ± 11.4	18.2 ± 5.9	12.3 ± 4.1	6.0 ± 3.1	25.1 ± 7.3	13.5 ± 4.5	0.8 ± 0.7	0.9 ± 0.8
Load on	37.4 ± 16.1*	20.3 ± 6.7	16.0 ± 6.8*	4.3 ± 1.9	39.2 ± 14.2*	17.0 ± 7.1*	3.2 ± 2.9*	3.5 ± 2.8*

Ers_{CMV} (cmH_2O/l), *Rmax*, *Rmin* ($cmH_2O/l/s$) passive end-inspiratory elastance, maximum end-inspiratory resistance, minimum (airway) end-inspiratory resistance, respectively, measured during volume control ventilation (passive ventilation), ΔR ($cmH_2O/l/s$); the difference between Rmax and Rmin, Ers_{PAV}(cmH_2O/l), R_{TOT} ($cmH_2O/l/s$) respiratory system elastance and total airway resistance, respectively, measured during PAV+ (active respiratory efforts), $PEEPi_{PAV}$, $PEEPi_{PS}$ (cmH_2O) intrinsic positive end-expiratory pressure (dynamic) with PAV and PS, respectively

*Significant difference from the corresponding values without load

3.8 cmH_2O/l, 95% CI for lower limit of agreement –23.4 to –9.7 cmH_2O/l, 95% CI for upper limit of agreement 9.4–22.8 cmH_2O/l) and 1.1 $cmH_2O/l/sec$ for resistance (95% CI for bias –7.9 to 10.1 $cmH_2O/l/sec$, 95% CI for lower limit of agreement –11.6 to –4.2 $cmH_2O/l/sec$, 95% CI for upper limit of agreement 6.4–13.8 $cmH_2O/l/sec$) (Figs. S2 and S3).

With both modes, load application increased $PaCO_2$ and decreased PaO_2 and PaO_2/F_IO_2 (Table 2). The difference, however, was significant only for PaO_2/F_IO_2 when the patients were ventilated with PAV+. For a given loading condition arterial blood gasses did not differ between modes.

V'_E remained constant in both modes after load application. During PS this was achieved through an increase of 20.0 ± 27.9% in breathing frequency that compensated for a reduction of 16.5 ± 13.3% in V_T. The magnitudes of the reduction in V_T (11.7 ± 11.9%) and of the increase in breathing frequency (11.7 ± 11.8%) were significantly smaller during PAV+ (Table 2). Independent of the mode, PEEPi increased significantly and to a similar extent after load application (Table 2).

In both modes all the indices of inspiratory effort increased significantly after load application (Table 2). The magnitude of the increase was significantly lower during PAV+ than that during PS. As a result, with load inspiratory effort was significantly less during PAV+ than that during PS.

Discussion

This study demonstrated that in mechanically ventilated critically ill patients an acute short-term increase in mechanical load of the respiratory system was associated with a response of respiratory motor output that differed markedly between PAV+ and PS. Although with both modes minute ventilation was preserved after load application, during PAV+ the patients were able to maintain constant minute ventilation with substantially less inspiratory effort per breath, per minute and per litre of ventilation than during PS. In addition, with PAV+ the magnitude of load-induced tidal volume reduction and breathing frequency increase was significantly smaller than with pressure support.

Chest and abdominal wall compression caused, on average, a 40% increase in passive respiratory system elastance. Similarly, passive end-inspiratory airway resistance increased by approximately 30%, probably due to lung volume decrease and airway closure [26]. In accordance with previously published findings [16], there was an acceptable agreement between respiratory system elastance obtained during controlled mechanical ventilation and that estimated with PAV+ during active respiratory efforts, although there was some scatter in the data. In addition there was acceptable agreement between expiratory resistance estimated with PAV+ and end-inspiratory airway resistance measured during controlled mechanical ventilation. The satisfactory correlation between expiratory and inspiratory resistance is most likely due to the fact that with PAV+ expiratory resistance was measured early during expiration at volumes where flow limitation rarely occurs, even in patients with obstructive lung disease [27, 28]. Thus, respiratory system mechanics estimated during active respiratory efforts approximated those obtained in passive condition.

Contrary to previous studies in critically ill patients [6], the response pattern to added mechanical load was evaluated 30 min after load application, a time interval which is sufficient to achieve a steady-state, mainly in terms of chemical stimuli. To the extent that chemical feedback is a major determinant of the response to respiratory load [23, 29], achieving stable chemical stimuli should be a prerequisite for the full response to develop.

With both modes, load application caused a deterioration of arterial blood gasses. Although with and without load arterial blood gasses were comparable between modes, with PAV+ the load-induced decrease in PaO_2/F_IO_2 ratio reached statistical significance. We do not believe that this is a mode-specific effect, since with load oxygenation was closely similar between PS and PAV+. The small number of patients studied may well account for this finding.

The load-induced increase in elastance and resistance of the respiratory system represented an increase in the respiratory workload of a magnitude sufficient to be detectable and clinically relevant [30]. Such a load in awake humans may elicit a response pattern which is partly mediated via behavioural feedback [31]. Indeed, a variable acute response to added mechanical load has been observed in humans during wakefulness [32]. We studied critically ill patients during sedation, thus eliminating or greatly attenuating the behavioural response to load application. Furthermore, the achievement of steady state should also minimize any behavioural response [31].

By study design, without load inspiratory effort, as expressed by Pdi_{swings}, dp/dt and PTPPdi/b, did not differ between the two modes. This was achieved by adjusting the assist level in PAV+. As a result, the patients maintained a comparable V_T and breathing pattern with PAV+ and PS, which were associated with similar values of PEEPi and arterial blood gasses. In addition, both modes increased the unassisted V_T to the same extent and resulted in a similar V_T/PTPPdi/b ratio, an index of neuroventilatory coupling [7]. These results indicate that intrinsic mechanical load, chemical stimuli, O_2 cost of breathing and the degree of unloading were also comparable between the two modes. Thus we are confident that respiratory load was applied against a background of an equal ventilator assistance provided by PS and PAV+.

Grasso et al. [6] assessed ventilatory responses to added mechanical loads during PS and during PAV without load-adjustable gain factors in patients during the weaning period. The magnitude of the load was comparable with that used in the present study. In this study the flow and volume assist, dialled on PAV without load, were such as to normalize patient resistive and elastic forces. Since flow and volume assist remained constant throughout, load application decreased the assist level; with load, a given inspiratory effort resulted in less inspiratory flow and volume and thus in less ventilator pressure. Grasso et al. [6] observed that load application caused a similar increase in inspiratory effort per breath, as expressed by Pdi_{swings} and PTPPdi/b, with both modes of support. The observed difference in inspiratory effort per min and per litre of ventilation between modes was solely due to a different breathing pattern adopted by the patients to compensate for the load. With PS, ventilation was maintained by a 58% increase in breathing frequency; this compensated for a 29% reduction in V_T. With PAV the changes were less marked: V_T decreased by 10% and breathing frequency increased by 14%. They assumed that with PAV the increase in inspiratory effort per breath might be reduced or eliminated by implementing a positive feedback to continuously adapt the level of assistance to changes in respiratory mechanics. The results of our study verified this assumption. We found that with load application inspiratory effort per breath was considerable lower with PAV+ than with PS, emphasizing the importance of continuous adaptation of the degree of ventilatory assistance to the changes in respiratory mechanics. However, it is of interest to note that both in our study and in that of Grasso et al. [6], patients chose to preserve minute ventilation using a mode-specific breathing pattern.

In our study with PS, although the increase in mechanical load was comparable with that used by Grasso et al. [6], the magnitude of the changes in V_T (16%) and breathing frequency (20%) was considerably lower. We studied sedated critically ill patients during the acute phase of their illness, whereas Grasso et al. [6] studied patients during wakefulness who were being weaned from the ventilator. Our patients had more severe derangement of respiratory system mechanics; as a result, on both modes without load, VT and breathing frequency were considerable lower and higher, respectively, than the values reported by Grasso et. al. [6]. In addition, in the study of Grasso et al. [6] the respiratory response to load was studied 2–3 min after load application, a time interval insufficient to achieve steady state. All these factors may account for the quantitatively different breathing pattern response to load. Particularly, behavioural feedback and state (asleep or awake) may have a great impact on the response [7, 33].

During PS the acute increase in respiratory system impedance approximately doubled the Pdi swings, inspiratory drive (expressed by dp/dt) and inspiratory effort per breath (expressed by PTPPdi/b). On the other hand, with PAV+ a similar increase in system impedance caused a modest increase (less than 50%) in these indices. With PAV+, in spite of the lower inspiratory effort, V_T was slightly but significantly higher than with PS. Since with both modes minute ventilation was preserved, breathing frequency was higher during PS than during PAV+. As a result, with load the difference in PTPPdi/min and PTPPdi/L between the two modes was further widened. To the extent that the mean pressure developed by the diaphragm is closely related to O_2 cost of breathing [34], these results indicate that with load the O_2 cost of breathing was significantly higher with PS than with PAV+. Because chemical stimuli and PEEPi increased to a similar extent with the two modes, the difference in inspiratory effort per breath and per minute, and thus in O_2 cost of breathing [34], reflected the different response of each mode to added mechanical load. With PS the level of pressure assist remained constant and independent of load, whereas with PAV+ the ventilator pressure increased with increasing load. Indeed, with PAV+ load application resulted in an approximately 50% increase in airway pressure above PEEP as indicated by Paw measured at 30%, 60% and 80% of mechanical inflation. This increase was due to (1) greater inspiratory effort and (2) manipulation of the flow and volume gain factors such as always to represent a constant fraction of the estimated values of resistance and elastance of respiratory system. The latter factor dictates that for a given inspiratory flow and volume, ventilator pressures increase with increasing elastance and

resistance of the system. It is of interest to note that with load, V_T/PTPPdi/b decreased slightly but not significantly during PAV+, whereas it decreased by more than 50% during PS. The load-adjustable gain factors most likely underlay the preservation of neuroventilatory coupling. Indeed, Grasso et al. [6] found that with both PAV and PS, load application caused an approximately 70% decrease in V_T/PTPPdi/b. These results indicate that when PAV operates with a system that continuously adapts the level of assistance to changes in respiratory mechanics, the efficacy of neuroventilatory coupling is largely independent of load. To the extent that in critically ill patients respiratory system impedance may vary considerably [10, 11, 12] this ventilator ability represents a major forward step in improving patient–ventilator synchrony [35].

Ideally, with PAV+ inspiratory effort should not be influenced by alteration in mechanical properties of the respiratory system, since the ventilator is designed to compensate for changes in mechanics by adjusting the provided pressure. This was not the case in our study, and with PAV+ all the indices of inspiratory effort increased significantly with load application. Three factors may account for this increase. Firstly, with load a substantial increase in PEEPi was observed, probably due to lung volume decrease and development of flow limitation. It is well known that when the patient is ventilated with PAV the magnitude of PEEPi has a significant impact on the actual assist due to the fact that instantaneous inspiratory flow and volume are the signals that control the delivered pressure [5, 36]. Thus in the presence of PEEPi the ventilator supports only a portion of inspiratory effort. In our study PAV+ supported 86% and 66% of the total PTPPdi/b, respectively, without and with load application. It follows that chest and abdominal wall compression by increasing PEEPi decreased significantly the supported portion of inspiratory effort, counterbalancing to some extent the advantage of continuously adapting the ventilator assistance to changes in respiratory system mechanics. Methods of triggering that shorten the delay between the beginning of inspiratory effort and initiation of ventilator breath might be of importance for PAV+ to achieve its goal [37]. Also, increasing the level of external PEEP in selected patients may partly counterbalance PEEPi and improve the ventilator performance. Secondly, $PaCO_2$ increased with load, and this may affect inspiratory effort independent of the mode. It has been shown that small increases in $PaCO_2$ (almost too small to measure) may considerably increase inspiratory effort. For example, a 1-mmHg change in $PaCO_2$ may alter the inspiratory effort by more than 20% . [38]. Thirdly, critically ill patients may exhibit a significant non-linear behaviour in pressure–volume and pressure–flow relationships during tidal breathing [27, 28, 39]. Thus, the load-induced decrease in lung volume and increase in respiratory system impedance may alter the relationship between inspiratory effort and tidal volume. It has been shown that the slope of this relationship becomes relatively flat with increasing resistance or elastance of the respiratory system [40].

This investigation was a physiological study, and great caution should be exercised in applying our findings to everyday clinical practice. The short-term steady-state response to artificially added mechanical load was evaluated. The response may be different if the load is sustained for a longer time, in which case the possible occurrence of runaway phenomena and variation in PEEPi may modify the response and affect both ventilator performance and patient's comfort. Also, we do not know the response in conscious patients or during conditions of imposed natural loads such as during bronchospasm, secretions or atelectasis.

In conclusion, our study showed that during proportional assist ventilation implementation of positive feedback to continuously adapt the level of assistance to short-term changes in respiratory mechanics increased the efficiency of the respiratory system to compensate for added mechanical load. Further studies in critically ill patients are needed to examine the response to sustained load changes and establish whether this mode influences outcome variables, such as morbidity and mortality.

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