OCCASIONAL REVIEW

Proportional assist ventilation (PAV): a significant advance or a futile struggle between logic and practice?

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Thorax 2002;**57**:272–276

Proportional assist ventilation is a promising addition to other more conventional modes of mechanical ventilation with the theoretical advantage of improving patient-ventilator interaction. It may also be of use as a diagnostic tool in the control of breathing in mechanically ventilated patients.

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The most important reason for starting mechanical ventilation is usually to restore pulmonary gas exchange in patients with acute respiratory failure in order to reverse life threatening hypoxaemia and/or progressive respiratory acidosis.[1] For many years frequent measurement of arterial blood gas tensions has been the only physiological evaluation in these patients and the chief guide to setting the mode and pattern of ventilatory assistance.[2] In the 1980s two factors contributed substantially to a change in this conventional attitude. Firstly, a growing amount of research indicated that respiratory muscle malfunction, overload, or "fatigue" had a pivotal role in the pathophysiology of acute respiratory failure.[3] Secondly, pressure support ventilation (PSV)—a mode of mechanical ventilation whose primary goal is to unload the patient's respiratory muscles[4]—became widely popular and was increasingly used in the intensive care unit (ICU), so reduction of the patient's inspiratory effort and work of breathing (WOB) became a major goal of mechanical ventilation and one of the most frequent reasons for instituting ventilatory support.[1]

However, while measurement of blood gas tensions and pH has become increasingly easy in recent years and is extensively used in the clinical setting, the assessment of respiratory muscle function is not generally used in critically ill patients and is basically restricted to use in research protocols, largely because the methods available for measuring inspiratory effort and WOB are accurate and reliable but are not suitable for routine use in the ICU.[5] Because of the lack of physiological monitoring of respiratory muscle function, the ventilator is set essentially by common practice and the effects of mechanical ventilation on inspiratory effort and WOB are not directly measured.[2]

PATIENT-VENTILATOR INTERACTION

Severe dyspnoea and a rapid and shallow pattern of breathing are generally considered to be reliable signs of respiratory distress and impending ventilatory pump failure.[3] The institution of mechanical ventilation aims to relieve dyspnoea and to decrease the patient's respiratory frequency while increasing tidal volume (V_T).[1] In general, the ventilator is set so that the patient's respiratory muscles have only to trigger the mechanical breath with a minimum effort and then can relax while the ventilator does all the work. Most modern microprocessor equipped ventilators provide a continuous display of flow, volume, and airway pressure signals so that poor adaptation of the patient to the ventilator settings can be easily observed and treated to prevent, not only patient-ventilator dyssynchrony, but also the expenditure of considerable effort by the patient over the period of mechanical inflation after the trigger phase.[6 7]

Although in some patients the inspiratory activity penetrates physiologically into the mechanical breath because the respiratory motor output cannot switch off immediately after triggering, the respiratory muscles are generally silent in the second part of mechanical lung inflation.[7] This passive inspiration is advantageous because it rests the respiratory muscles which must recover from overwork. However, from the control of breathing standpoint, it is one of the fundamental mechanisms underlying patient-ventilator dyssynchrony because the mechanical inspiration goes into the neural expiratory time.[8] Under these circumstances mismatching between the neural "duty cycle" and the mechanical "duty cycle" occurs causing "wasted" inspiratory effort during expiration.[8–10] This effort during expiration is ineffective in bringing the ventilatory pattern under the patient's control because the elastic recoil present in the system is greater than the negative pleural pressure swing. Although the consequences of "wasted" or "ineffective" efforts have not been fully elucidated, it is certain that they exert an unnecessary burden on the patient's respiratory muscles which should be unloaded by mechanical ventilation.[9 10]

There are several causes of poor patient-ventilator interaction which can be due to both underassistance and overassistance.[7] During mechanical ventilation the thorax is under the influence of two oscillatory pumps—one governed by

Abbreviations: PAV, proportional assist ventilation; PSV, pressure support ventilation; WOB, work of breathing; CVF, chronic ventilatory failure; ARF, acute respiratory failure; V_T, tidal volume; E, elastance; R, resistance; FA, flow assist; VA, volume assist; PEEP, positive end expiratory pressure; CPAP, continuous positive airway pressure; NPPV, non-invasive positive pressure ventilation; Pdi, transdiaphragmatic pressure; Poes, oesophageal pressure; Pao, pressure at the airway opening.

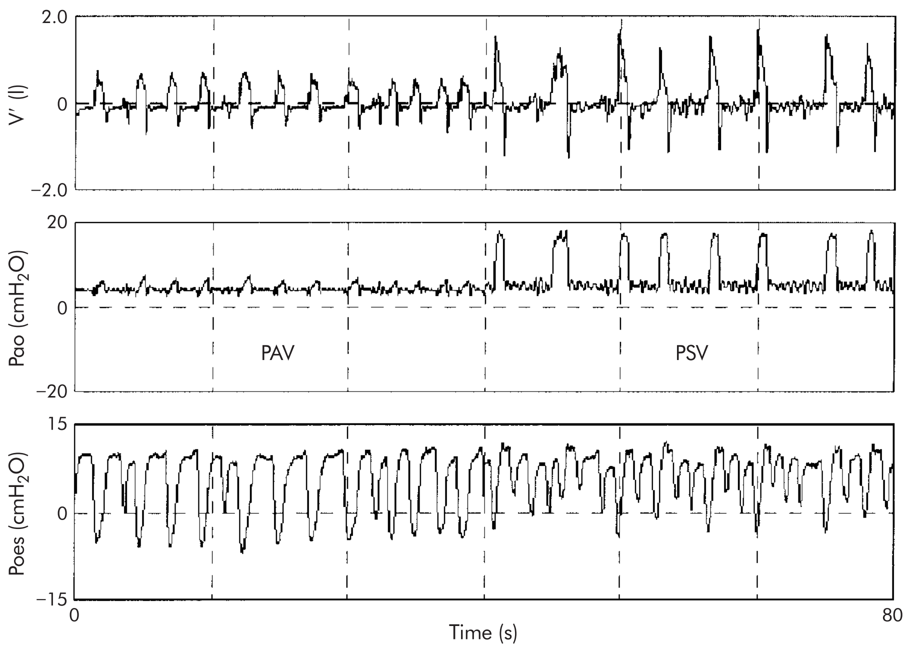

Figure 1 Representative trace from a patient with chronic ventilatory failure due to COPD during proportional assist ventilation (PAV) (left) and pressure support ventilation (PSV) (right) showing pressure at the airway opening (Pao) and oesophageal pressure (Poes). With the greater level of assistance during PSV, the occurrence of ineffective efforts increases compared with PAV.

the patient's central control and the other by the caregiver who sets the ventilator according to her/his clinical judgement. The two systems should work in harmony to achieve the goals of mechanical ventilation.[1] However, this is not always the case and a poor patient-ventilator interaction can substantially impair the management of acute respiratory failure.[7 9]

PROPORTIONAL ASSIST VENTILATION

Proportional assist ventilation (PAV) was proposed as a powerful means of improving the patient-ventilator interaction by bringing one of the two oscillatory pumps—the mechanical ventilator—under the control of the other—the patient's central control of breathing.[11 12] It is the only mode of ventilation designed on a physiological basis where the technical solutions offered by ventilators did not come first.[11]

PAV is a form of synchronised partial ventilatory assistance with the peculiar characteristic that the ventilator generates pressure in proportion to the patient's instantaneous effort—that is, the more the patient pulls, the more pressure the machine generates. Thus, with PAV the ventilator amplifies the patient's inspiratory effort without any preselected target volume or pressure. The aim of PAV is to allow the patient to attain whatever ventilation and breathing pattern seems to fit the ventilatory control system. PAV therefore assumes control of the breathing system and a condition in which the neuroventilatory uncoupling is determined by the discrepancy between the high ventilatory demand and the insufficient capability of the ventilatory pump to cope with the workload. PAV provides a sort of "additional muscle" under the complete control of the patient's ventilatory drive for determining the depth and frequency of the breaths.[12]

PAV follows the equation of motion, one of the fundamentals of respiratory mechanics, which states that the pressure applied by the respiratory muscles (Pmus) to the system is used to overcome the elastic (E) and resistive (R) opposing forces. The former is proportional to the volume (V) displacement whereas the latter is proportional to the airflow rate (V′), neglecting inertia:

$$\text{Pmus} = \text{E} \times \text{V} + \text{R} \times \text{V}' \qquad (1)$$

PAV provides ventilatory assistance in terms of flow assist (FA, cm H_2O/l/s) and volume assist (VA, cm H_2O/l) which can specifically unload the resistive and elastic burdens, respectively. With PAV the pressure applied to inflate the respiratory system results from a combination of the patient's inspiratory effort and the positive pressure applied by the ventilator to the airway opening (Pao), this depending upon the levels of VA and FA set by the caregiver, such that Equation 1 becomes:

$$\text{Pmus} = \text{V} \times (\text{E} - \text{VA}) + \text{V}' \times (\text{R} - \text{FA}) \qquad (2)$$

With PAV there is no target flow, volume, or pressure and the responsibility of guiding the ventilatory pattern is shifted completely from the caregiver to the patient with the purpose of improving the patient-ventilator interaction as shown by the example in fig 1. However, the few clinical studies performed during invasive mechanical ventilation which have compared PSV and PAV[13–16] have failed to show any significant systematic superiority of PAV over PSV. Nevertheless, in these studies PAV allowed a greater variability in V_T than PSV in the face of an increased ventilatory demand. Furthermore, it was shown that both invasive and non-invasive PAV could improve arterial blood gas tensions and alveolar ventilation as well as unloading the respiratory muscles in both acute[17–19] and chronic patients.[20 21]

PAV in chronic ventilatory failure

A preliminary study indicated that, in resting awake stable patients with chronic ventilatory failure due to either chronic obstructive pulmonary disease (COPD) or restrictive chest wall disease (RCWD), non-invasive application of PAV set at the patient's level of comfort improved the breathing pattern and minute ventilation while unloading the inspiratory muscles with an excellent patient-ventilator interaction. Similar results were obtained with PSV, but PAV achieved these physiological benefits at a lower level of mean airway pressure (Pao).[22] This may be relevant since some data have shown that non-invasive positive pressure ventilation (NPPV) can significantly reduce cardiac output in patients with stable COPD.[23]

PAV and PEEP/CPAP

Clearly, in patients with COPD some level of positive end expiratory pressure (PEEP) or continuous positive airway pressure (CPAP) must be set by the ventilator to counterbalance the intrinsic PEEP (PEEPi) which is systematically present in patients with COPD, particularly during exacerbations.[24] If an adequate level of PEEP is not set by the

Table 1 Comparison between elastance (E) and resistance (R) and the levels of assistance

Reference	Diagnosis	Assessment of E and R	E (cm H_2O/l)	R (cm H_2O/l/s)	VA (cm H_2O/l)	FA (cm H_2O/l/s)
Bianchi *et al*[40]	Stable CVF: COPD	Run away	10.5 (4.6)	3.8 (1.7)	8.6 (3.6)	3 (1.3)
Vitacca *et al*[18]	ARF: COPD	Oesophageal balloon	17.6 (12.4)	22.4 (8)	15.6 (4.9)	4.4 (1.7)
Polese *et al*[21]	Stable CVF: COPD	Oesophageal and gastric balloons	15.8 (8)	15 (7.6)	13.9 (4.1)	4.1 (1.3)
Porta *et al*[22]	Stable CVF: COPD	Oesophageal and gastric balloons	16.4 (16.8)	15.3 (7.9)	12.2 (5.6)	4.7 (2.7)
	RCWD		18.2 (12.4)	8.1 (4.1)	27.8 (8)	6.9 (2.7)

VA = volume assist; FA = flow assist; ARF = acute respiratory failure; CVF = chronic ventilatory failure; COPD = chronic obstructive pulmonary disease; RCWD = restrictive chest wall disease.

ventilator, the patient's inspiratory effort may be smaller than PEEPi and not sufficient to trigger the ventilator. Under those circumstances patient-ventilator dyssynchrony occurs, independent of the mode of ventilatory assistance.[7 25] In addition, application of PEEP further reduces the magnitude of the inspiratory effort in patients with COPD receiving either PSV[26] or PAV[27] because of acute exacerbations. Due to the low levels of PEEPi, patients with stable COPD do not seem to get the same advantage from external PEEP,[28] although this was suggested by one study of PSV.[29]

Setting of PAV

Theoretically, implementation of PAV requires knowledge of the patient's respiratory mechanics. In fact, appropriate regulation of VA, FA, and PEEP entails measurement of the patient's resistance, elastance, and PEEPi. Without these measurements there is a significant risk of either underestimating or overestimating the ventilatory load and conceivably of either underassisting or overassisting the patient, thus hampering the success of ventilatory assistance.[12]

Respiratory mechanics in ventilator dependent patients with silent respiratory muscles can be easily assessed by using, for instance, the interrupter technique[30] or even with on line computerised measurements.[31] This condition may occur during controlled mechanical ventilation or in a research setting but is far less likely in clinical practice during assisted mechanical ventilation. Minimally invasive techniques such as the oesophageal balloon for measuring inspiratory effort and WOB can also be used in research protocols but are rarely used in routine clinical practice. A comparison of elastance and resistance in patients measured with the oesophageal balloon technique and the levels of FA and VA, respectively, is shown in table 1. It can be seen that, while VA approaches the elastance value, FA remains well below the degree of resistance.

In these studies the elastance of individual patients was determined by means of the "run away" technique (fig 2) as originally proposed by Younes and colleagues.[12] However, although the percentage assist was substantially different for FA and VA, this did not alter the fundamental operation of PAV in terms of synchrony between ventilator and patient.[21] In these studies the end of the PAV ventilatory cycle always occurred during the declining phase of the transdiaphragmatic pressure (Pdi), just as during spontaneous breathing, and did not extend beyond the point where Pdi reached baseline. In these conditions the PAV ventilatory mode did not compromise the time available for expiratory flow. The patients were getting less assistance than it was previously thought but, since all the patients felt comfortable and no patient-ventilator dyssynchrony occurred, it is difficult to know whether a more precise level of assistance was really needed.

To facilitate the assessment of patient's respiratory mechanics for the implementation of PAV at the bedside for clinical purposes, Younes and colleagues recently proposed new methods for the non-invasive determination of inspiratory resistance[32] and passive elastance[33] during PAV in the ICU. Farrè *et al*[34] have also proposed that the forced oscillation technique applied by the ventilator during non-invasive PAV could be useful in assessing ventilatory resistance. Although viewed with interest and intellectual curiosity, these techniques should be tested to assess whether they meet the need of simplicity and reliability required by clinical practice in order to fill the gap between the compelling logic of PAV and the apparent lack of exciting results coming from its application in "real life".[2] As previously mentioned, PAV accomplished the

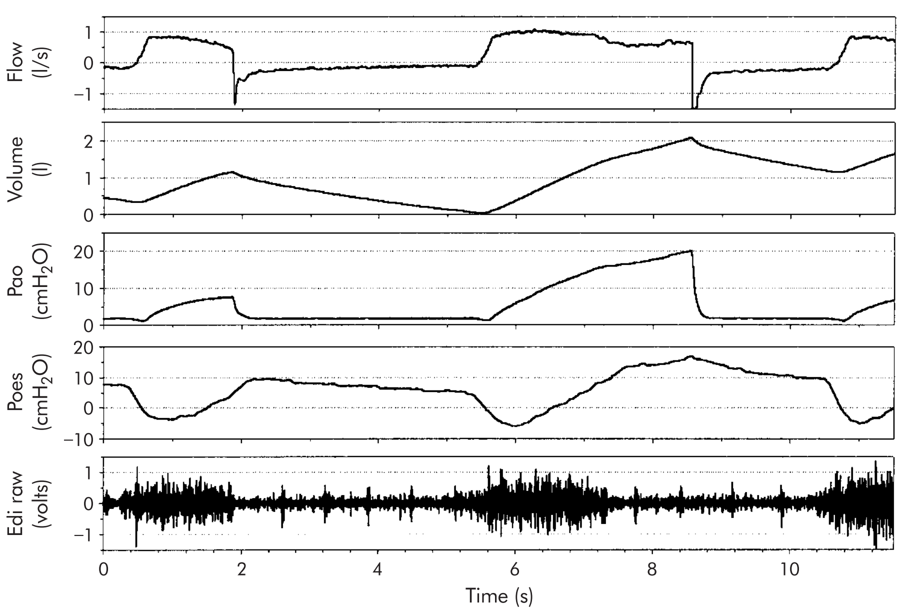

Figure 2 Representative trace from a patient with chronic ventilatory failure due to COPD during PAV showing flow, volume, and pressure at the airway opening (Pao), oesophageal pressure (Poes), and surface electromyography of the diaphragm (Edi raw). First breath: PAV supported breath; second breath: "run away" phenomenon illustrated by the continuation of positive pressure after the end of the patient's inspiratory effort into the neural expiration. This trace shows that the amount of pressure delivered by the ventilator in the second breath exceeded the patient's elastic recoil opposing force.

goals of mechanical ventilation but failed to show any significant systematic superiority over PSV, although in some circumstances as, for example, in the patient illustrated in fig 1, the patient-ventilator interaction improved substantially by switching the patient from PSV to PAV.

PAV and NPPV

Non-invasive positive pressure ventilation (NPPV) was considered to be an application in which PAV should provide good advantages over more conventional modes of ventilatory assistance. Indeed, cooperation by the patient is essential for the success of NPPV since it is set primarily to match the patient's comfortable breathing pattern. Although PAV was effective in achieving the goals of NPPV in studies in patients with acute respiratory failure[18 19] as well as in short term studies on chronic patients,[20 21] no significant systematic superiority over NPPV in the PSV mode was found when the two modes of assistance were compared.[22 35] It is unclear whether a better setting of PAV tailored to the patient's respiratory mechanics would have produced different results more in line with the convincing logic of PAV. In this respect, the methods recently proposed by Farrè *et al*[34] and Younes *et al*[32 33] for non-invasive measurement of elastance and resistance in the clinical setting during PAV may open new possibilities which deserve further attention and investigation.

In clinical practice the elastic assist is usually determined by gradually increasing the gain until overassistance occurs with excessive volumes and pressures (fig 2). The gain can then be set either at the maximum level (100%) or at a lower level such as 60% or 80% of the maximum. The resistive assist is determined by empirical values of the patient's resistance or by looking for the optimal comfort with different peak flows. It is surprising to see that, using this latter approach, some authors found values of resistive assist much lower than predicted (table 1).[21 22] This may be related to the second specific problem of PAV during NPPV—namely, leaks. Leakage of the mask will be measured as patient effort by the ventilator and assisted accordingly; this may necessitate lowering the assistance markedly. Clinical experience seems to indicate that excellent results can be obtained with this mode, however, provided that close monitoring is performed and that specific training has been given.[20–22]

Future applications of PAV

New areas in which PAV may theoretically provide clinical benefits for patients as well as intellectual satisfaction for physicians may be the application of PAV during sleep,[36–38] for weaning off ventilation,[27] to assist exercise,[39–41] and in neonatology.[42] In these conditions the possibility for patients to control their mechanical support should provide a better level of comfort than with more conventional methods.

PAV might also be a powerful tool for studying the control of breathing in patients with acute or chronic ventilatory failure. Since the patient's central control and neuromuscular drive governs the level and pattern of ventilatory assistance, any abnormality in the central controller as, for instance, during periods of apnoea or blunted drive should be revealed by PAV. PAV may therefore become a diagnostic tool for research purposes in poorly explored areas such as the control of breathing in mechanically ventilated patients.

CONCLUSIONS

Different modes of mechanical ventilation are currently available to tailor the level and pattern of ventilatory assistance to the individual patient's ventilatory demand and diagnosis. PAV is a new addition to other more conventional and widely used modes of mechanical ventilation with the theoretical advantage of improving patient-ventilator interaction. However, adequate guidelines for the proper setting of PAV on the lung mechanics of individual patients, in accordance with the theoretical background of PAV, are not yet available, especially for non-invasive delivery. PAV successfully achieves the goals of mechanical ventilation in terms of arterial blood gas tensions, respiratory mechanics, and patient relief at a significantly lower airway pressure than PSV. In addition, in some patients PAV substantially improves the patient-ventilator interaction during NPPV. However, prospective clinical trials to investigate whether PAV has real advantages over the existing modes of mechanical ventilation in long term clinical settings have not yet been concluded.

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