Reports of Original Investigations

Tracheal pressure regulated volume assist ventilation in acute respiratory failure

[Ventilation débit-assistée régulée par pression trachéale dans les cas d'insuffisance respiratoire aiguë]

Tomislav Mirkovic MD,* Vesna Paver-Erzen MD PhD,* Tomislav Klokocovnik MD PhD,†
Ashvini Gursahaney MD,‡ Paul Hernandez MD,‡ Stewart B. Gottfried MD‡

Purpose: Proportional assist ventilation (PAV) uses volume assist (VAV) and flow assist ventilation (FAV) to reduce elastic and resistive effort, respectively. Proportional assist ventilation may be difficult to apply clinically, particularly due to FAV related considerations. It was hypothesized that regulating tracheal (Ptr) rather than airway opening pressure (Pao), to overcome endotracheal tube related resistive effort, during VAV would provide an effective alternative method of ventilation. We therefore compared the effects of Pao and Ptr regulated VAV on breathing pattern and inspiratory effort.

Methods: In seven intubated patients, flow, volume, Pao, Ptr, esophageal and transdiaphragmatic pressure were measured during VAV (0–80% respiratory system elastance) using Pao vs Ptr to regulate ventilator applied pressure. Breathing pattern and the pressure-time integral of the inspiratory muscles ($\dot{P}_{mus} \cdot dt$) and diaphragm ($\dot{P}_{di} \cdot dt$) were determined.

Results: Compared to spontaneous breathing, the respiratory rate to tidal volume ratio, or rapid shallow breathing index (RSBI), improved progressively with increasing VAV (130 ± 64 vs 70 ± 35 , VAV 0 vs 80%; $P < 0.05$) while inspiratory effort fell ($\dot{P}_{mus} \cdot dt = 39.6 \pm 7.5$ vs 28.5 ± 7.2 cm H₂O·sec·L⁻¹, $\dot{P}_{di} \cdot dt = 35.4 \pm 7.8$ vs 24.2 ± 5.9 cm H₂O·sec·L⁻¹, VAV 0 vs 80%; $P < 0.05$) due to a decrease in elastic related effort. At any given level of support, there was further reduction in RSBI, $\dot{P}_{mus} \cdot dt$, and $\dot{P}_{di} \cdot dt$ (which averaged 23.6 ± 2.7 , 33.7 ± 4.4 , and $38.5 \pm 5.1\%$, respectively; $P < 0.05$) for Ptr compared to Pao regulated VAV due to a decrease in resistive effort.

Conclusions: Tracheal pressure regulated VAV can be a simple and effective method of partial ventilatory support in acute respiratory failure. Further work will be needed to determine its efficacy and potential benefit relative to PAV and other modes of ventilation in routine clinical practice.

CAN J ANESTH 2007 / 54: 6 / pp 420–429

Objectifs : La ventilation assistée proportionnelle (PAV) a recours à la ventilation volume-assistée (VAV) et à la ventilation débit-assistée (FAV) pour réduire les efforts élastique et résistif, respectivement. La PAV peut être difficile à mettre en pratique cliniquement, surtout à cause de considérations relatives à la FAV. L'hypothèse a été émise que la régulation de la pression trachéale (Ptr) plutôt que de la pression d'ouverture des voies aériennes (Pao), afin de vaincre la résistance de la sonde endotrachéale, durant la VAV serait un mode de ventilation alternatif efficace. Ainsi nous avons comparé les effets de la VAV régulée par Pao et par Ptr sur les courbes respiratoires et l'effort inspiratoire.

Méthodes : Les mesures suivantes ont été observées chez sept patients intubés : débit, volume, Pao, Ptr, pressions œsophagienne et transdiaphragmatique durant la VAV (0–80 % d'élastance respiratoire) en utilisant soit la Pao, soit la Ptr afin de réguler la

From the Clinical Departments for Anesthesiology and Surgical Intensive Care,* and Cardiovascular Surgery,† UMC Ljubljana, Slovenia; and the Divisions of Respiratory and Critical Care Medicine,‡ Department of Medicine, McGill University Health Centre and Meakins-Christie Laboratories, McGill University, Montreal, Quebec, Canada.

Address correspondence to: Dr. Stewart B. Gottfried, McGill University Health Centre, Royal Victoria Hospital, 687 Pine Avenue West, Room M4.10, Montreal, Quebec H3A 1A1, Canada. Phone: 514-934-1934, ext. 36117; Fax: 514-843-1695; E-mail: stewart.gottfried@muhc.mcgill.ca

Supported in part by Inspiraplex, Respiratory Health Network of Centres of Excellence, Medical Research Council of Canada, Association Pulmonaire du Québec.

Accepted for publication February 13, 2006.

Revision accepted February 22, 2007.

Final revision accepted March 19, 2007.

This article is accompanied by an editorial. Please see Can J Anesth 2007; 54: 407–13.

pression générée par le respirateur. Les courbes respiratoires et l'intégrale pression-temps des muscles inspiratoires ($\int P_{mus} \cdot dt$) et du diaphragme ($\int P_{di} \cdot dt$) ont été déterminées.

Résultats : Comparé à la respiration spontanée, le ratio fréquence respiratoire : volume courant, ou index de respiration superficielle (RSBI), s'est progressivement amélioré avec une augmentation de la VAV (130 ± 64 vs 70 ± 35 , VAV 0 vs 80 % ; $P < 0,05$), alors que l'effort inspiratoire a décliné ($\int P_{mus} \cdot dt = 39,6 \pm 7,5$ vs $28,5 \pm 7,2$ cm H₂O·sec·L⁻¹, $\int P_{di} \cdot dt = 35,4 \pm 7,8$ vs $24,2 \pm 5,9$ cm H₂O·sec·L⁻¹, VAV 0 vs 80 % ; $P < 0,05$) en raison de la diminution de l'effort élastique. A tous les niveaux de soutien, on a observé une diminution plus importante du RSBI, $\int P_{mus} \cdot dt$, et $\int P_{di} \cdot dt$ (atteignant en moyenne $23,6 \pm 2,7$, $33,7 \pm 4,4$, et $38,5 \pm 5,1$ %, respectivement ; $P < 0,05$) pour la VAV réglée par Ptr comparée à celle réglée par Pao en raison de la diminution de l'effort résistif.

Conclusions : La VAV réglée par pression trachéale peut constituer une méthode d'assistance respiratoire partielle simple et efficace dans le cas d'insuffisance respiratoire aiguë. Des travaux supplémentaires seront nécessaires afin de déterminer son efficacité et ses bienfaits potentiels par rapport à la PAV et à d'autres moyens de ventilation mécanique courants dans la pratique clinique.

PROPORTIONAL assist ventilation (PAV) is a novel mode of partial ventilatory support where pressure is applied by the ventilator in proportion to patient-generated volume and flow.^{1,2} By adjusting the proportionality between applied pressure and volume (volume assist ventilation, VAV) as well as applied pressure and flow (flow assist ventilation, FAV), it is possible to specifically reduce the elastic and resistive work of breathing performed by the patient.^{1,2} In addition to being able to set ventilator support according to the nature and magnitude of respiratory impairment, these features theoretically provide for automatic adjustment of assistance to changing ventilatory demand facilitating patient-ventilator synchrony.¹⁻⁴

Proper setting of VAV and FAV parameters requires 1) measurement of respiratory mechanics be reliable and 2) total respiratory system elastance (Ers) and resistance (Rrs) remain relatively stable, linear functions of inspired volume and flow.^{1-3,5} This poses a particular challenge for Rrs and implementation of FAV. Reliable bedside measurements of Rrs in mechanically ventilated patients are often difficult to obtain, due in large part to the endotracheal tube. Substantial *in vivo* increases in tube resistance are frequent, often quite variable, and considerably increase patient effort during assisted modes of ventilation.⁶⁻⁹ Respiratory system resistance is also highly flow dependent, primarily due to the flow resistive properties of the endotracheal

tube.^{7,10} Failure to take this into account during FAV may lead to under-assistance as well as over-assistance, resulting in patient-ventilator asynchrony, frequent alarms, and increased caregiver intervention.^{1,2,5,11,12} Clinical acceptance of PAV has been disappointing as a result of such considerations.^{13,14}

Automatic tube compensation (ATC) is a ventilatory modality designed to overcome the added flow resistance of an artificial airway by applying positive pressure in relationship to flow based on *in vitro* determination of tube resistance and continuous measurement of inspiratory flow and airway opening pressure (Pao) during pressure preset modes of ventilation.¹⁰ Despite commercial availability on newer microprocessor-based ventilators, ATC has been shown to be significantly less effective than expected due to a number of technical considerations.¹⁰ Moreover, even under optimal conditions ATC cannot compensate for the expected increase in endotracheal tube resistance that occurs *in vivo* due to secretions, tube deformation, or reduced airway patency for other reasons.^{6,8,15,16}

Investigators have demonstrated that direct recordings of tracheal pressure (Ptr) via an intraluminal catheter can be used to overcome *in vivo* values of endotracheal tube resistance during continuous positive airway pressure or pressure support ventilation.^{10,17} We hypothesized that the limitations described above for PAV and ATC might be addressed by using Ptr rather than Pao to regulate the positive pressure applied during VAV alone without the addition of FAV. As an initial step toward examining this hypothesis, the objective of the present study was to compare the effects of Ptr and Pao regulation of ventilator applied pressure on breathing pattern and inspiratory effort at varying levels (0–80% Ers) of VAV in patients with acute respiratory failure of diverse etiology.

Methods

Subjects

Intubated patients mechanically ventilated for management of acute respiratory failure in the intensive care units of McGill University Health Centre were reviewed. Seven patients who were clinically stable for the preceding 24 hr, were able to tolerate limited periods of decreased ventilatory support, and could provide informed consent were studied (Table I). Individuals with cardiovascular instability, clinically significant bleeding, pneumothorax, tube thoracostomy, or a contraindication to esophagogastroduodenal catheter placement were excluded. The institutional Ethics Committee approved the investigative protocol and written informed consent was obtained.

TABLE I Patient characteristics

Patient	Gender	Age (yr)	Tube (ID, mm)	Ventilator days	F _I O ₂	PEEP (cm H ₂ O)	PEEPi,dyn * (cm H ₂ O)	Diagnosis
1	F	67	8.0 ET	19	0.50	5	0	sepsis, acute lung injury
2	F	68	8.0 ET	11	0.45	4	0.6 ± 0.5	pneumonia, chronic alcoholism
3	F	79	8.0 TT	58	0.35	4.5	0.7 ± 0.3	CABG, diaphragm paralysis
4	M	64	8.5 ET	3	0.50	5	0	pneumonia, ARDS
5	F	57	8.0 TT	77	0.55	7.5	2.9 ± 0.7	COPD, pneumonia
6	M	64	8.0 ET	15	0.40	9	3.8 ± 0.7	COPD, pneumonia
7	F	65	7.5 ET	36	0.60	8	0.8 ± 0.3	pneumonia, diabetes

ET = endotracheal tube; TT = tracheostomy tube; ID = internal diameter; F_IO₂ = fractional inspired oxygen concentration; PEEP = positive end-expiratory pressure; PEEPi,dyn = dynamic intrinsic positive end-expiratory pressure; CABG = coronary artery bypass graft; ARDS = adult respiratory distress syndrome; COPD = chronic obstructive pulmonary disease. *Mean values ± SD determined during spontaneous unassisted breathing as part of the study protocol.

Equipment

Flow was measured with a heated pneumotachograph (Fleisch # 2) and differential pressure transducer (MP-45, ± 2 cm H₂O, Validyne Corp., Northridge, CA, USA). Volume was obtained by integration of the flow signal. Tracheal pressure was measured using a polyethylene sidehole catheter (internal diameter 1.4 mm, outer diameter 1.9 mm) with one end positioned 1–2 cm proximal to the carinal end of the endotracheal (or tracheostomy) tube.⁷ The other end was attached to a differential pressure transducer (MP-45, ± 100 cm H₂O, Validyne Corp., Northridge, CA, USA) and a continuous low-flow gas source (0.2 L·min⁻¹) to ensure catheter patency.¹⁸ Fractional inspired oxygen concentration was identical to the ventilator setting (see below). Preliminary testing confirmed that this had no effect on ventilator operation or patient parameters. Airway opening pressure was recorded from a polyethylene catheter of similar length connecting a sideport of the airway adapter to an identical differential pressure transducer. Airway opening pressure and P_{tr} were also connected to separate limbs of a three-way stopcock, the latter attached to the pressure sensing port used to regulate the positive pressure applied by the prototype ventilator (see below). By turning the stopcock, either P_{ao} or P_{tr} could be readily selected to regulate ventilator applied pressure. Esophageal (P_{es}) and gastric pressure (P_{ga}) were measured by means of identical balloon-catheter systems connected to separate differential pressure transducers (MP-45, ± 100 cm H₂O, Validyne Corp., Northridge, CA, USA). The esophageal catheter was positioned so that changes in P_{es} and P_{ao} during occluded inspiratory efforts at end expiration were nearly identical.¹⁹ Transdiaphragmatic pressure (P_{di}) was determined by subtracting P_{es} from P_{ga}. Signals were digitized using a 12-bit analogue-to-digital converter (Model # 2801A, Data Translation

Inc., Marlborough, MA, USA) and recorded at a sampling rate of 100 Hz for subsequent analysis.

Experimental protocol

Patients were connected to a prototype ventilator capable of providing PAV as well as conventional modes of ventilation.^{3–5} A standard ventilator circuit containing low compliance tubing of fixed length with the humidifier omitted was utilized. The F_IO₂ and positive end-expiratory pressure (PEEP) applied during routine mechanical ventilation were used and remained unchanged throughout the study. Trigger sensitivity was set at ~1 cm H₂O below PEEP. Medical management was otherwise continued as previously prescribed. Systemic blood pressure, heart rate, electrocardiogram, and S_aO₂ were monitored. A physician not involved in the study was present to provide for patient care.

In the semi-recumbent position, Ers and Rrs were determined during PAV utilizing incremental levels of VAV and FAV (“runaway” method) as previously described.^{1,2} Pulmonary mechanics were also computed using multiple linear regression analysis²⁰ for subsequent comparison. Thereafter, five levels of VAV equal to approximately 0, 20, 40, 60, and 80% of the individual’s previously determined Ers were applied for five- to ten-minute periods in random order. Flow assist ventilation was set to zero. This was performed twice, once using P_{ao} to regulate ventilator applied pressure and the other P_{tr}. The order was determined by a standard coin toss. To avoid undue discomfort as well as to provide a comparable functional state, patients were returned to routine mechanical ventilation in the assist-control mode for ten to 15 min between the two conditions.

FIGURE 1 Graphical determination of pressure-time integral of inspiratory effort (A) and positive pressure applied by the ventilator (B) for airway opening (left) and tracheal pressure (right) regulated volume assist ventilation at one level of support. VAV 60% (Pao) = airway opening pressure regulated volume assist ventilation at 60% of respiratory system elastance; VAV 60% (Ptr) = tracheal pressure regulated volume assist ventilation at 60% of respiratory system elastance; Pes = esophageal pressure; Pao = airway opening pressure. A: area A = chest wall related elastic effort; area B = lung related elastic effort; area C = resistive related effort. Upper boundary of area A (bold line) represents static elastic recoil pressure of chest wall. Lower boundary of area C (bold line) represents dynamic esophageal pressure during inspiration. Area between dynamic and static relationships indicates total inspiratory effort performed by patient. B: area D = resistive related ventilator pressure; area E = elastic related ventilator pressure; area F = positive end-expiratory pressure (PEEP) related ventilator applied pressure.

Data analysis

Approximately 20–30 consecutive breaths from the latter half of each experimental period were analyzed. Tidal volume (V_T) was determined from the digitally integrated flow signal. The duration of inspiration (T_I), expiration (T_E), and total respiratory cycle (T_{TOT}) were assessed from the flow record. From these, respiratory rate (RR), minute ventilation ($\dot{V}_E$), duty cycle (T_I/T_{TOT}), and mean inspiratory (V_T/T_I) and expira-

tory (V_T/T_E) flow were obtained. Additionally, the coefficient of variation ($CV = SD \cdot 100 / \text{mean}$) was determined for selected breathing pattern parameters (V_T , RR, and T_I/T_{TOT}).²¹

To determine the pressure-time integral for the inspiratory muscles ($\int P_{mus} \cdot dt$), the P_{cs} -time and static chest wall recoil pressure-time relationship were aligned and the enclosed area from the onset of inspiratory effort to the transition from inspiratory to expiratory flow measured (Figure 1A).^{3–5} The static volume-pressure relationship of the chest wall predicted according to age and gender was used, assuming the relationship to be linear over the experimental V_T range.²² The flow-resistive properties of the chest wall were not considered in this analysis. Inspiratory effort was partitioned into elastic, resistive, and intrinsic PEEP components as previously described.^{5,23} The area under the P_{di} -time relationship was also measured. The pressure-time integral of the inspiratory muscles ($\int P_{mus} \cdot dt$) and the diaphragm ($\int P_{di} \cdot dt$) were calculated for a one-minute period and expressed per litre $\dot{V}_E$. To estimate the assistance provided by the ventilator during Pao and Ptr regulation of VAV, the pressure-time integral of Pao ($\int P_{ao} \cdot dt$) was also obtained. This was further divided into the pressure applied to overcome Ers, Rrs, and total PEEP (i.e., both intrinsic PEEP and PEEP externally applied through the ventilator circuit (Figure 1B)).^{24,25}

Statistical analysis

All values are presented as means $\pm$ SD. Analysis of variance (ANOVA) for repeated measurements and paired Neuman-Keul post-hoc test were used to compare results for VAV (20–80%) to spontaneous unsupported breathing (VAV 0%). A similar approach was used to compare Pao and Ptr regulated trials at each level of VAV (0–80%). A paired Student's *t* test was used for comparison between values of Ers and Rrs calculated by multiple linear regression analysis and the “run away” method with PAV. *P* values < 0.05 were considered significant for all analyses.

Results

Respiratory mechanics measurements determined with the PAV “runaway method” and multiple regression analysis in all patients are provided in Table II. Elastance of the respiratory system with both methods were very similar. Respiratory system resistance measured with the PAV approach and lung resistance obtained by regression analysis, assuming chest wall flow resistance to be negligible, were also comparable.

An experimental record comparing Pao and Ptr regulated VAV is shown in Figure 2. Spontaneous

TABLE II Comparison of respiratory mechanics determined with PAV runaway method and multiple linear regression analysis during VAV trials

	VAV 0%		VAV 20%		VAV 40%		VAV 60%		VAV 80%		$\bar{E}_L^*$	E_{CW}	$\bar{E}_{RS}$	$\bar{R}_L^*$	$E_{RS,PAV}$	$R_{RS,PAV}$
	E_L	R_L	E_L	R_L	E_L	R_L	E_L	R_L	E_L	R_L						
1	31.4	8.3	31.9	8.4	32.2	9.1	32.4	7.5	32.4	8.7	32.1 ± 0.5	8.6	40.7	8.4 ± 0.5	40	8.5
2	25.1	11.3	25.1	12.1	24.9	14.4	25.3	12.7	22.4	13.8	24.6 ± 2.1	8.6	33.2	12.9 ± 1.6	32.5	12.5
3	22.5	8.2	26.3	6.4	23.8	11.2	21.8	8.6	18.3	11.6	22.5 ± 3.4	8.6	31.1	9.2 ± 2.4	30	10
4	17.6	15.8	18.1	16.0	14.8	10.1	15.5	16.4	18.1	17.8	16.8 ± 1.9	7.1	23.9	15.1 ± 3.2	25	15
5	6.6	25.3	6.4	5.7	10.6	23.6	8.5	26.4	6.7	27.1	8.0 ± 2.1	8.6	16.6	24.8 ± 1.3	17.5	25
6	10.7	17.5	13.4	15.6	12.1	17.2	14.8	15.7	12.4	16.2	12.6 ± 1.6	7.1	19.7	16.4 ± 1.1	20	17
7	8.8	23.9	10.9	20.5	9.4	20.1	9.5	21.5	9.5	21.2	9.6 ± 0.8	8.6	18.2	21.4 ± 1.6	20	20

PAV = proportional assist ventilation; VAV = volume assist ventilation. Parameters determined using multiple linear regression analysis based on equation of motion: E_L = lung elastance; $\bar{E}_L$ = mean lung elastance; R_L = lung resistance; $\bar{R}_L$ = mean lung resistance. Predicted values of chest wall elastance (E_{CW}) were added to $\bar{E}_L$ to obtain mean total respiratory system elastance ($\bar{E}_{RS}$). Chest wall resistance considered negligible so that $\bar{R}_L$ approximates total respiratory system resistance. $E_{RS,PAV}$ = total respiratory system elastance determined with PAV runaway method; $R_{RS,PAV}$ = total respiratory system resistance determined with PAV runaway method. Units for elastance = cm H₂O·L⁻¹; units for resistance = cm H₂O·L⁻¹·sec. *Mean values $\pm$ SD for VAV 0–80% trials.

FIGURE 2 Experimental record comparing airway opening (ao) and tracheal pressure (tr) regulated volume assist ventilation (VAV) at three levels of support (0, 40, and 80% respiratory system elastance) in one patient. Pao = airway opening pressure; Ptr = tracheal pressure; Pes = esophageal pressure; Pga = gastric pressure; Pdi = transdiaphragmatic pressure.

TABLE III Breathing pattern parameters during airway opening (Pao) and tracheal pressure (Ptr) regulated volume assist ventilation (VAV)

	VAV 0%(Pao)	VAV 0%(Ptr)	VAV 20%(Pao)	VAV 20%(Ptr)	VAV 40%(Pao)	VAV 40%(Ptr)	VAV 60%(Pao)	VAV 60%(Ptr)	VAV 80%(Pao)	VAV 80%(Ptr)
V_T (mL)	274 ± 68	310 ± 79**	298 ± 79	343 ± 71**	335 ± 95*	372 ± 71**	350 ± 84*	402 ± 87**	378 ± 82*	445 ± 103**
RR (min ⁻¹)	32.4 ± 10	28.9 ± 9.7	30.5 ± 8.2	26.9 ± 8.2	27.8 ± 9.1*	25.7 ± 8.9	26.3 ± 9.3*	24.1 ± 7.7**	24.7 ± 8.9*	21.4 ± 7.1**
$\dot{V}_E$ (L·min ⁻¹)	9.07 ± 2.86	8.98 ± 2.86	9.07 ± 2.86	9.24 ± 3.21	9.29 ± 2.75	9.57 ± 4.71	9.21 ± 2.96	9.67 ± 2.70	9.37 ± 2.87	9.53 ± 2.94
T_I (sec)	0.60 ± 0.16	0.66 ± 0.16	0.65 ± 0.16	0.71 ± 0.18	0.72 ± 0.15*	0.75 ± 0.29	0.77 ± 0.32*	0.81 ± 0.32	0.83 ± 0.45*	0.91 ± 0.42
T_E (sec)	1.21 ± 0.56	1.41 ± 0.56**	1.32 ± 0.64	1.52 ± 0.66**	1.44 ± 0.62	1.58 ± 0.53**	1.51 ± 0.52*	1.68 ± 0.58**	1.59 ± 0.71*	1.89 ± 0.79**
T_I/T_{TOT}	0.332 ± 0.061	0.318 ± 0.061	0.329 ± 0.061	0.318 ± 0.074	0.334 ± 0.056	0.322 ± 0.062	0.338 ± 0.071	0.325 ± 0.079	0.343 ± 0.082	0.325 ± 0.071**
V_T/T_I (mL·sec ⁻¹)	456 ± 93	469 ± 77	458 ± 72	484 ± 124	465 ± 95	496 ± 121	455 ± 87	495 ± 123	456 ± 100	489 ± 113
V_T/T_E (mL·sec ⁻¹)	226 ± 56	220 ± 50	226 ± 77	226 ± 63	232 ± 47	236 ± 61	232 ± 50	239 ± 66	238 ± 53	236 ± 77
PEEP _{idyn} (cm H ₂ O)	1.26 ± 0.84	1.18 ± 0.87	1.32 ± 1.03	1.03 ± 0.61	1.18 ± 0.61	1.20 ± 0.92	1.16 ± 0.82	0.88 ± 0.29	1.29 ± 0.82	1.06 ± 1.03
RR/VT (min ⁻¹ ·L ⁻¹)	130 ± 64	103 ± 57	111 ± 56	83 ± 34	100 ± 54	75 ± 35	81 ± 39*	64 ± 30**	70 ± 35*	53 ± 26**

Values are means ± SD. V_T = tidal volume, RR = respiratory rate, $\dot{V}_E$ = minute ventilation, T_I = inspiratory time, T_E = expiratory time, T_I/T_{TOT} = inspiratory duty cycle, V_T/T_I = mean inspiratory flow, V_T/T_E = mean expiratory flow, PEEP_{idyn} = dynamic intrinsic positive end-expiratory pressure; VAV P = airway opening pressure regulated volume assist ventilation, VAV P = tracheal pressure regulated volume assist ventilation. * $P < 0.05$ vs Pao regulated VAV 0%; ** $P < 0.05$ Pao vs Ptr regulated VAV at same percentage support.

unsupported breathing (VAV 0%) improved considerably with VAV, being less rapid and shallow while inspiratory effort was reduced as indicated by tidal excursions of P_{es} and P_{di} . For any given level of support, however, V_T was larger and inspiratory effort less with Ptr compared to Pao regulation of ventilator applied pressure. The magnitude of positive pressure applied at the airway opening during Ptr regulated VAV was greater, accounting for these effects.

Table III provides group mean data summarizing the effects of Pao and Ptr regulated VAV on breathing pattern. Compared with spontaneous breathing, V_T rose significantly as VAV was increased with a corresponding fall in RR such that there was no significant change in $\dot{V}_E$. There was a corresponding reduction in the ratio of RR to V_T , often referred to as the rapid shallow breathing index.²⁶ When Ptr rather than Pao was used to regulate ventilator applied pressure during VAV, V_T was larger at all levels of support and RR lower with no difference in $\dot{V}_E$. RR/ V_T was decreased. V_T variability, reflected by the coefficient of variation, was greater with Ptr regulated VAV at the higher levels of support (Table IV). The coefficient of variation of other breathing pattern parameters was not significantly altered by Pao or Ptr regulated VAV.

The influence of Pao and Ptr regulation of VAV on respiratory timing is shown in Table III. Both T_I and T_E lengthened proportionally with increasing VAV so that there was no change in T_I/T_{TOT} in comparison to spontaneous breathing. The use of Pao vs Ptr to regulate ventilator applied pressure had no effect on T_I for any given level of VAV. The trend toward a reduction in T_I/T_{TOT} with Ptr regulated VAV reached statistical significance at the highest level of support (VAV 80%). Both V_T/T_I and V_T/T_E were unchanged with increasing VAV and were no different between Pao and Ptr regulated trials.

Figure 1 depicts the graphical determination of the pressure-time integral of inspiratory effort (A) and positive pressure applied by the ventilator (B) for both Pao and Ptr regulated VAV at one level of support in a representative patient. The pressure required by the patient and ventilator to overcome Rrs, Ers, and PEEP are identified separately. Group mean data for inspiratory effort and ventilator applied pressure for all experimental conditions are provided in Figures 3 and 4. Total inspiratory effort was high during spontaneous breathing, in keeping with ventilator-dependent acute respiratory failure, and comparable for elastic and resistive components. Effort related to intrinsic PEEP was modest. Increasing VAV produced a graded reduction in total inspiratory effort that was specifically due to the decrease in elastic related effort with little or no

TABLE IV Coefficient of variation for selected breathing pattern parameters during airway opening (Pao) and tracheal pressure (Ptr) regulated volume assist ventilation (VAV)

	VAV 0% (P)	VAV 0% (P)	VAV 20% (P)	VAV 20% (P)	VAV 40% (P)	VAV 40% (P)	VAV 60% (P)	VAV 60% (P)	VAV 80% (P)	VAV 80% (P)
CV, V_T (%)	5.9 ± 4.2	8.1 ± 4.2	6.7 ± 4.2	9.4 ± 6.9	8.1 ± 4.1	8.8 ± 10.3	6.5 ± 4.5	13.2 ± 11.3	9.3 ± 6.4	16.9 ± 13.6*
CV, RR (%)	4.9 ± 3.7	6.3 ± 3.6	5.3 ± 3.7	6.7 ± 3.9	5.7 ± 4.5	7.2 ± 6.6	5.2 ± 3.9	7.8 ± 8.7	5.9 ± 6.6	10.8 ± 9.7
CV, T_I/T_{TOT} (%)	5.0 ± 3.7	6.3 ± 3.7	5.3 ± 3.9	6.8 ± 6.1	5.9 ± 3.2	7.9 ± 9.7	5.9 ± 7.1	8.9 ± 12.9	5.2 ± 6.6	8.5 ± 13.2

Mean values ± SD for coefficient of variation (CV) for tidal volume (V_T), respiratory rate (RR), and inspiratory duty cycle (T_I/T_{TOT}) are shown. * $P < 0.05$ Pao vs Ptr regulated VAV at same percentage support.

FIGURE 3 Pressure-time integral for the inspiratory muscles (left) and the diaphragm (right) at each level of airway opening and tracheal pressure regulated volume assist ventilation. fP_{mus} = inspiratory muscle effort; fP_{di} = diaphragmatic effort; ao = airway opening pressure regulated volume assist ventilation; tr = tracheal pressure regulated volume assist ventilation; VAV = volume assistant ventilation; $fP_{mus,el(cw)}$ = chest wall related elastic effort; $fP_{mus,RES}$ = resistive related effort; $fP_{mus,el(lung)}$ = lung related elastic effort; $fPEEPi,dyn$ = intrinsic PEEP related effort; NS = not significant. Data expressed as means ± SD for all patients. * $P < 0.05$, $^{**}P < 0.005$, $^{***}P < 0.001$: airway opening vs tracheal pressure regulated VAV at same percentage support.

change in inspiratory effort related to Rrs and intrinsic PEEP. Results were comparable for the diaphragm as well as the inspiratory muscles in general. In contrast, resistive effort was markedly reduced when Ptr rather than Pao was used to regulate ventilator applied pressure during VAV. Resistive effort was similar for all levels of VAV, and fell by approximately half with Ptr regulated support. Inspiratory effort related to Ers and intrinsic PEEP was no different between Ptr and Pao regulated VAV. Results for the inspiratory muscles and diaphragm were again very similar.

Figure 4 shows that ventilator applied pressure used

FIGURE 4 Pressure-time integral for positive pressure applied by the ventilator at each level of airway opening and tracheal pressure regulated volume assist ventilation. ao = airway opening pressure regulated volume assist ventilation; tr = tracheal pressure regulated volume assist ventilation; VAV = volume assistant ventilation; fP_{ao} = pressure-time integral of ventilator applied pressure; fP_{aoRrs} = pressure-time integral of resistance related ventilator applied pressure; fP_{aoErs} = pressure-time integral of elastance related ventilator applied pressure; fP_{aoPEEP} = pressure-time integral of positive end-expiratory pressure related ventilator applied pressure; NS = not significant. Data expressed as means ± SD for all patients. * $P < 0.05$, $^{**}P < 0.005$, $^{***}P < 0.001$: airway opening vs tracheal pressure regulated volume assist ventilation at same percentage support.

to overcome Ers ($fP_{ao,el}$) rose with increasing VAV and was no different between Pao and Ptr regulated support. The applied pressure related to total PEEP

($\dot{V}_{ao} P_{EEPtot}$) was relatively small when breathing spontaneously and remained unchanged during VAV with either P_{ao} or P_{tr} regulation. The positive ventilator pressure attributable to R_{rs} ($\dot{V}_{ao} P_{res}$) during spontaneous breathing with P_{ao} regulation was modest and changed little with increasing VAV. However, the positive pressure applied by the ventilator to overcome R_{rs} was dramatically greater during P_{tr} regulated VAV and similar for all levels of assistance.

Discussion

Previous investigations have examined the impact of PAV on respiration using some combination of VAV and FAV.^{4,5,12,21,27–30} Navalesi and coworkers specifically characterized the consequences of increasing levels of VAV on total work of breathing over a wide range of support.³ The reduction in elastic work achieved with VAV was offset in part by an increase in resistive work so that the decrease in total work of breathing was less than expected. This is in some contrast to our current findings, where VAV exclusively reduced the inspiratory effort due to E_{rs} with no significant effect on the patient effort required to overcome R_{rs} . The reasons for this discrepancy are not entirely clear, but are most likely due to improvements in operating characteristics of the prototype ventilator between the two investigations (particularly response time and phase relationships between ventilator applied pressure *vs* flow and volume).

The pattern of breathing in patients with acute respiratory failure is generally rapid and shallow irrespective of the underlying disease.²⁶ This was true during unassisted spontaneous breathing in this study population. The observed improvement in breathing pattern was most significant when P_{tr} rather than P_{ao} was used to regulate ventilator applied pressure during VAV. There were notable qualitative differences in respiratory timing, however, comparing P_{ao} and P_{tr} regulated VAV. The latter findings are in keeping with steady-state loading experiments in normal subjects, where inspiration is relatively shortened during elastic loading but increased by the addition of an inspiratory resistive load.³¹

In addition to being slower and deeper, V_T variability also increased significantly with P_{tr} regulation of ventilator applied pressure during VAV. This has been previously noted with conventional PAV (i.e., VAV+FAV) and attributed to mechanical unloading and improved neuromechanical coupling.^{2,5,12,21} The influence of tube compensation, particularly as applied here using P_{tr} to regulate ventilator applied pressure, on breathing pattern variability has not been examined previously. These data are in contrast to other conven-

tional modes of partial ventilatory support, particularly pressure support ventilation, where the manner in which positive pressure is applied limits the amount of variability observed.^{1,2,4,5,12}

From a clinical perspective, P_{tr} regulated VAV offers a number of distinct practical advantages over conventional PAV requiring separate adjustment of both VAV and FAV settings. The use of a single parameter (i.e., VAV) would simplify setting the ventilator, both initially and thereafter as changes in clinical status dictate. Reliable measurement of E_{rs} can be readily obtained during spontaneous breathing with VAV without resorting to hyperventilation, sedation, or paralyzing agents to ensure adequate muscle relaxation. Using P_{tr} to automatically adjust ventilator pressure to compensate for *in vivo* changes in inspiratory endotracheal tube and circuit resistance would further simplify ventilator management and patient care. This would be of particular benefit when using a heat and moisture exchanger, where unrecognized fluid accumulation and altered resistance can cause respiratory distress and associated complications.^{6,8} Similar issues may apply for closed system suction devices.¹⁶ Using P_{tr} to regulate ventilator pressure would also overcome the failure of FAV to take into account the prominent flow dependence of endotracheal tube resistance, and the resulting potential for the development of patient-ventilator asynchrony, frequent alarms, and the need for caregiver intervention and ventilator adjustments.^{12–14,21,26,27}

It should be recognized that the effective use of P_{tr} regulated VAV suggests that intrinsic R_{rs} exclusive of the endotracheal tube is not excessive. This may not be true for some patients, particularly those with severe chronic obstructive pulmonary disease (COPD). In 13 ventilator-dependent patients with COPD, for example, Wrigge *et al.* found lower respiratory system resistance to average 6.58 ± 3.59 cm $H_2O \cdot L^{-1} \cdot sec$.²¹ The empiric addition of a low to moderate level of FAV (e.g., 4–10 cm $H_2O \cdot L^{-1} \cdot sec$) may be warranted in this setting when inspiratory effort remains elevated with P_{tr} regulated VAV and PEEP adjusted to offset intrinsic PEEP.^{21,29} In this regard, the response to P_{tr} regulated VAV in the two individuals with known COPD in this study did not appear to differ from the other patients.

Continuous flow through the intraluminal P_{tr} catheter was used to maintain its patency. This system worked well with P_{tr} regulated VAV for periods of up to two hours without incident. One recent model ventilator currently provides a similar intraluminal catheter system to continuously monitor P_{tr} , although recorded values do not influence ventilator operation (Avea,

Viasys Healthcare, Yorba Linda, CA, USA). The routine clinical use of Ptr regulated VAV would obviously require additional rigorous safeguards and redundancy to ensure patient safety and proper ventilator support if secretions or other factors were to interfere with accurate continuous measurement of Ptr.

In conclusion, VAV reduces the inspiratory effort required to overcome Ers and improves breathing pattern in patients with acute respiratory failure. The use of Ptr to regulate ventilator pressure during VAV further reduces inspiratory effort and improves breathing pattern by directly eliminating the workload imposed by *in vivo* inspiratory resistance of the endotracheal tube and ventilator circuit. Tracheal pressure regulated VAV appears to be a simple and effective method of partial ventilatory support in acute respiratory failure in the intensive care unit setting. Further work will be required to confirm the efficacy and potential benefit over conventional PAV or other modes of ventilation in routine clinical practice.

Acknowledgements

The authors sincerely thank Dr. Magdy Younes for providing the prototype PAV ventilator and the participating physicians, nurses, and respiratory therapists at the McGill University Health Centre for their cooperation and assistance.

References

- 1 Younes M. Proportional assist ventilation, a new approach to ventilatory support. *Theory. Am Rev Respir Dis* 1992; 145: 114–20.
- 2 Younes M. Proportional assist ventilation. In: Tobin MJ (Ed.). *Principles and Practice of Mechanical Ventilation*. New York: McGraw-Hill; 1994: 349–69.
- 3 Navalesi P, Hernandez P, Wongs A, Laporta D, Goldberg P, Gottfried SB. Proportional assist ventilation in acute respiratory failure: effects on breathing pattern and inspiratory effort. *Am J Respir Crit Care Med* 1996; 154: 1330–8.
- 4 Ranieri VM, Giuliani R, Mascia L, et al. Patient-ventilator interaction during acute hypercapnia: pressure-support vs. proportional-assist ventilation. *J Appl Physiol* 1996; 81: 426–36.
- 5 Ranieri VM, Grasso S, Mascia L, et al. Effects of proportional assist ventilation on inspiratory muscle effort in patients with chronic obstructive pulmonary disease and acute respiratory failure. *Anesthesiology* 1997; 86: 79–91.
- 6 Cohen IL, Weinberg PF, Fein IA, Rowinski GS. Endotracheal tube occlusion associated with the use of heat and moisture exchangers in the intensive care unit. *Crit Care Med* 1988; 16: 277–9.
- 7 Navalesi P, Hernandez P, Laporta D, et al. Influence of site of tracheal pressure measurement on in situ estimation of endotracheal tube resistance. *J Appl Physiol* 1994; 77: 2899–906.
- 8 Villafane MC, Cinnella G, Lofaso F, et al. Gradual reduction of endotracheal tube diameter during mechanical ventilation via different humidification devices. *Anesthesiology* 1996; 85: 1341–9.
- 9 Haberthur C, Fabry B, Stocker R, Ritz R, Guttman J. Additional inspiratory work of breathing imposed by tracheostomy tubes and non-ideal ventilator properties in critically ill patients. *Intensive Care Med* 1999; 25: 514–9.
- 10 Elsasser S, Guttman J, Stocker R, Mols G, Priebe HJ, Haberthur C. Accuracy of automatic tube compensation in new-generation mechanical ventilators. *Crit Care Med* 2003; 31: 2619–26.
- 11 Du HL, Ohtsui M, Shigeta M, et al. Expiratory asynchrony in proportional assist ventilation. *Am J Respir Crit Care Med* 2002; 165: 972–7.
- 12 Varelmann D, Wrigge H, Zinserling J, Muders T, Hering R, Putensen C. Proportional assist versus pressure support ventilation in patients with acute respiratory failure: cardiorespiratory responses to artificially increased ventilatory demand. *Crit Care Med* 2005; 33: 1968–75.
- 13 Ambrosino N, Rossi A. Proportional assist ventilation (PAV): a significant advance or a futile struggle between logic and practice? *Thorax* 2002; 57: 272–6.
- 14 Vitacca M. New things are not always better: proportional assist ventilation vs. pressure support ventilation. *Intensive Care Med* 2003; 29: 1038–40.
- 15 Bishop MJ. Endotracheal tube lumen compromise from cuff overinflation. *Chest* 1981; 80: 100–1.
- 16 Glass C, Grap MJ, Sessler CN. Endotracheal tube narrowing after closed-system suctioning: prevalence and risk factors. *Am J Crit Care* 1999; 8: 93–100.
- 17 Messinger G, Banner MJ, Blanch PB, Layon AJ. Using tracheal pressure to trigger the ventilator and control airway pressure during continuous positive airway pressure decreases work of breathing. *Chest* 1995; 108: 509–14.
- 18 Macklem PT, Mead J. Resistance of central and peripheral airways measured by a retrograde catheter. *J Appl Physiol* 1967; 22: 395–401.
- 19 Baydur A, Behrakis PK, Zin WA, Jaeger M, Milic-Emili J. A simple method for assessing the validity of the esophageal balloon technique. *Am Rev Respir Dis* 1982; 126: 788–91.
- 20 Dechman GS, Chartrand DA, Ruiz-Neto PP, Bates JH. The effect of changing end-expiratory pressure on respiratory system mechanics in open- and closed-chest anesthetized, paralyzed patients. *Anesth Analg* 1995;

- 81: 279–86.
- 21 Wrigge H, Golisch W, Zinserling J, Sydow M, Almeling G, Burchardi H. Proportional assist versus pressure support ventilation: effects on breathing pattern and respiratory work of patients with chronic obstructive pulmonary disease. *Intensive Care Med* 1999; 25: 790–8.
 - 22 Estenne M, Yernault JC, De Troyer A. Rib cage and diaphragm-abdomen compliance in humans: effects of age and posture. *J Appl Physiol* 1985; 59: 1842–8.
 - 23 Aslanian P, El Atrous S, Isabey D, *et al.* Effects of flow triggering on breathing effort during partial ventilatory support. *Am J Respir Crit Care Med* 1998; 157: 135–43.
 - 24 Marini JJ. Pressure-controlled ventilation. *In:* Tobin MJ (Ed.). *Principles and Practice of Mechanical Ventilation*. New York: McGraw-Hill; 1994: 349–69.
 - 25 Crooke PS, Head JD, Marini JJ, Kotchkiss JR. Patient-ventilator interaction: a general model for nonpassive mechanical ventilation. *IMA J Math Appl Med Biol* 1998; 15: 321–37.
 - 26 Yang KL, Tobin MJ. A prospective study of indexes predicting the outcome of trials of weaning from mechanical ventilation. *N Engl J Med* 1991; 324: 1445–50.
 - 27 Grasso S, Puntillo F, Mascia L, *et al.* Compensation for increase in respiratory workload during mechanical ventilation. Pressure-support versus proportional-assist ventilation. *Am J Respir Crit Care Med* 2000; 161: 819–26.
 - 28 Passam F, Hoing S, Prinianakis G, Siafakas N, Milic-Emili J, Georgopoulos D. Effect of different levels of pressure support and proportional assist ventilation on breathing pattern, work of breathing and gas exchange in mechanically ventilated hypercapnic COPD patients with acute respiratory failure. *Respiration* 2003; 70: 355–61.
 - 29 Appendini L, Puro A, Gudjonsdottir M, *et al.* Physiologic response of ventilator-dependent patients with chronic obstructive pulmonary disease to proportional assist ventilation and continuous positive airway pressure. *Am J Respir Crit Care Med* 1999; 159: 1510–7.
 - 30 Marantz S, Patrick W, Webster K, Roberts D, Oppenheimer L, Younes M. Response of ventilator-dependent patients to different levels of proportional assist. *J Appl Physiol* 1996; 80: 397–403.
 - 31 Cherniack NS, Altose MD. Respiratory responses to ventilatory loading. *In:* Horbein TF (Ed.). *Regulation of Breathing*. New York: Marcel Dekker; 1981: 905–64.