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# *Adaptive Support and Pressure Support Ventilation Behavior in Response to Increased Ventilatory Demand*

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***Background:*** **Dual-control modes of ventilation adapt the pressure delivery to keep a volume target in response to changes in respiratory mechanics, but they may respond poorly to changes in ventilatory demand. Adaptive support ventilation (ASV), a complex minute volume-targeted pressure-regulated ventilation, was compared to adaptive pressure ventilation (APV), a dual-mode in which the pressure level is adjusted to deliver a preset tidal volume, and to pressure support ventilation (PSV) when facing an increase in ventilatory demand.**

***Methods:*** **A total of 14 intensive care unit patients being weaned off mechanical ventilation were included in this randomized crossover study. The effect of adding a heat-and-moisture exchanger to augment circuit dead space was assessed with a same fixed level of ASV, PSV, and APV.**

***Results:*** **Arterial blood gases, ventilator response, and patient respiratory effort parameters were evaluated at the end of the six periods. Adding dead space significantly increased minute ventilation and $Paco_2$ values with the three modes. Indexes of respiratory effort (pressure-time index of respiratory muscles and work of breathing) increased with all ventilatory modes after dead-space augmentation. This increase was significantly greater with APV than with PSV or ASV ($P < 0.05$). The assistance delivered during APV decreased significantly with dead-space from 12.7 ± 2.6 to 6.7 ± 1.4 cm $H_2O$, whereas no change occurred with ASV and PSV.**

***Conclusions:*** **ASV and PSV behaved differently but ended up with similar pressure level facing acute changes in ventilatory demand, by contrast to APV (a simple volume-guaranteed pressure-control mode), in which an increase in ventilatory demand results in a decrease in the pressure support provided by the ventilator.**

VOLUME-TARGETED pressure-regulated modes of ventilation control tidal volumes (VT) through variable levels of pressure and are referred to as dual-control modes.[1] A target VT is achieved by regulating the inspiratory airway pressure (PINSP) in a so-called negative closed loop, *e.g.*, if the patient's VT is above the optimal VT, PINSP is reduced and *vice versa*. A recent study found that in cases of increased respiratory demand above the set target, a reduction in PINSP is obtained with subsequent potentially harmful increase in respiratory muscle effort.[2] This is a major drawback of these modes, which may adapt adequately to changes in respiratory mechanics but adapt poorly to changes in respiratory demand.[1–4]

Adaptive support ventilation (ASV) is a more complex mode (table 1) recently approved by the Food and Drug Administration and provides automatic ventilation in which minute volume (MV) is controlled through a VT-respiratory rate (RR) combination based on respiratory mechanics. In patients unable to trigger a breath (passive or paralyzed patients), the ventilator generates a pressure-controlled breath, automatically adjusting inspiratory pressure and timing to achieve the target VT and RR. The target VT-RR combination is based on the Otis equation, which determines an RR that minimizes work of inspiration for a clinician-set MV on the basis of the time constant of the respiratory system.[5,6] The time constant can be estimated on a breath-by-breath basis by the expiratory time constant (RCEXP) obtained from the expiratory flow-volume curve.[6–8]

In patients able to trigger a breath (active patients), the ventilator generates pressure support breaths, automatically adjusting PINSP to achieve the target VT, and it delivers additional pressure-controlled breaths if the patient's RR is below the target RR.[9–11] The usual patient response to an increased VT is a decrease in RR, and *vice versa*. Thus, the RR is usually also indirectly modified by the ventilatory setting, although not strictly controlled. Considering actively breathing patients ASV is adjusting the PINSP like a dual-control mode; in case of increased respiratory demand, a similar response could be expected (table 1). Conversely, ASV is more sophisticated than a "simple" dual mode, because of the moving RR-VT target according to change in respiratory mechanics,[9,10] because of the control of MV that prevents alveolar hypoventilation, and because of a set of rules designed to avoid dead space ventilation, risk of barotraumas, or excessive dynamic hyperinflation. The target VT is defined by the clinician-set MV and the calculated time constant. The patient-desired MV is not part of the loop. Time constant is monitored continuously, and a change in MV can by itself induce a change in the time constant and subsequently in the target VT.

In conventional pressure support ventilation (PSV), which is largely used in mechanically ventilated patients

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**Table 1. Main Characteristics of the Three Evaluated Ventilatory Modes and Their Differences**

| | PSV | ASV | APV |
|---|---|---|---|
| User setting | Inspiratory pressure | Minute ventilation | Tidal volume |
| Main algorithm characteristics | Fixed inspiratory pressure | For the set minute ventilation, inspiratory pressure is automatically adjusted to obtain an optimal combination of respiratory rate and tidal volume | Inspiratory pressure is automatically adjusted to obtain the tidal volume set by the user |
| Controlled variable(s) | Inspiratory pressure | Tidal volume and respiratory rate | Tidal volume |
| Type of breath | Assisted; pressure-targeted breaths | Controlled and assisted; pressure-targeted breaths | Assisted; pressure-targeted breaths |
| Pressure-delivered characteristics | Constant | Breath-by-breath variable | Breath-by-breath variable |
| Volume-delivered characteristics | Variable | Variable | Constant |
| Automatic adjustments to respiratory mechanics | No | Optimal combination of respiratory rate and tidal volume varies depending on the expiratory time constant | Yes |
| Cycling-off criteria | Percent of peak flow | Time in controlled breaths – percent of peak flow in assisted breaths | Percent of peak flow |
| Safety rules | No | Intend to limit auto-PEEP, volutrauma, and dead space ventilation | No |

For ASV mode, breath can be controlled or assisted. For PSV and APV, each breath is assisted, *i.e.*, patient-triggered and supported; respiratory rate, inspiratory time, and flow are variable and controlled by the patient. For the three modes, inspiratory flow is variable and decelerating. The following setting parameters are similar for the three modes when breaths are assisted: inspiratory and expiratory triggers, rise time, PEEP, and inspired oxygen fraction.

APV = adaptive pressure ventilation; ASV = adaptive support ventilation; PEEP = positive end-expiratory pressure; PSV = pressure support ventilation.

during weaning, the level of assistance delivered by the ventilator remains fixed regardless of the ventilatory demand of the patient (increase or decrease in minute ventilation and/or inspiratory effort)[1,4] (table 1). We therefore designed the current study to compare ASV to a simple dual mode of ventilation (adaptive pressure ventilation [APV]) and to PSV in a group of mechanically ventilated patients whose respiratory demand was artificially increased.

The *a priori* hypothesis was that in case of increased respiratory demand, the level of support may be decreased with APV but not (or not systematically) with ASV and not with PSV. This work has been presented previously in abstract form.[12]

## Material and Methods

### *Patients*

Fourteen patients were prospectively enrolled. They had been on mechanical ventilation *via* an endotracheal tube for more than 48 h and were ventilated with PSV levels of 10 to 20 cm $H_2O$ above 5 cm $H_2O$ of positive end-expiratory pressure (PEEP). The following exclusion criteria were used: coma or need for sedation, contraindication to eso-gastric catheter insertion, hemoglobin level below 8 g/dl, body temperature above 38.5°C, and poor tolerance of PSV defined either as a RR greater than 30 breaths/min and VT lower than 6 ml/kg or visible use of the accessory inspiratory muscles.

The experimental protocol was approved by the Ethics Committee of the Saint-Eloi Teaching Hospital (Comité Consultatif des Personnes Participants à la Recherche Biomédicale Montpellier, France), and written informed consent was provided by patients or next of kin.

### *General Ventilatory Settings*

The three ventilatory modes (PSV, APV, and ASV) were delivered by the same ventilator (Galileo; Hamilton Medical AG, Rhazuns, Switzerland) and were set to match similar MV. The rise time (50 ms), flow trigger (5 l/min), and expiratory trigger sensitivity (50%) were identical with the three modes. In half of the patients, however, the expiratory trigger sensitivity in APV was set at 25% and not 50% like in ASV and PSV. The extrinsic PEEP level was set at 5 cm $H_2O$ and kept constant throughout the study, and $F_{IO_2}$ was set to achieve oxygen saturation greater than 95%. The main characteristics of the three ventilatory modes and their differences are summarized intable 1.

### *Pressure Support Ventilation (PSV)*

Before randomization in one of the three ventilatory modes, PSV was applied first for 5 min to allow determination of the inspiratory pressure level that achieved a VT between 6 and 8 ml/kg of predicted body weight with an RR between 20 and 30 breaths/min; the resulting values of VT were used to set APV, and the resulting values for minute ventilation were used to set ASV.

### *Adaptive Support Ventilation*

ASV has been fully described in previous papers.[9,11,13] At the onset of mechanical ventilation, the ventilator delivers three test breaths, during which $RC_{EXP}$ is determined from the expiratory flow volume curve.[7,8,14] MV

is set by the clinician and controlled through a VT-RR combination based on the breath-by-breath estimation of $RC_{EXP}$,[7,8,14] according to the minimal work of breathing concept developed by Otis.[6] Subsequently and on a breath-by-breath basis, two simultaneous closed loops continuously regulate (1) $P_{INSP}$ to achieve the target VT and (2) inspiratory and expiratory times to achieve the target RR in passive patients and in active patients when the patient's rate is below the target RR.

To avoid extreme and potentially dangerous values of VT and RR, ASV uses on a breath-by-breath basis a safety window for target VT and RR values. The minimal target VT is defined as twice the anatomical dead space estimated from the predicted body weight. The maximal target VT is defined as the maximal clinician-set pressure times the dynamic compliance of the total respiratory system. The minimal value for the target RR is 5 breaths/min, which is used in the present study to avoid controlled breaths. All the evaluated breaths were patient-triggered in the current study during all six periods of the study. The maximal value for the target RR is defined as the ratio $20/RC_{EXP}$.

*Adaptive Pressure Ventilation*

APV is a pressure-controlled mode that starts by determining the patient's volume/pressure response on a sequence of three test breaths, volume/pressure being defined as: VT/(peak pressure – extrinsic PEEP). According to the volume/pressure value, the lowest $P_{INSP}$ to be applied to achieve the targeted VT is calculated. The minimal $P_{INSP}$ is 5 cm $H_2O$ above extrinsic PEEP. The adaptive controller compares the monitored VT to the targeted VT and if the patient's actual VT is higher or lower than the target volume, $P_{INSP}$ is gradually adjusted (by 2 cm $H_2O$ steps) down to extrinsic PEEP + 5 cm $H_2O$ and up to high-pressure alarm limit minus 10 cm $H_2O$. As with PSV, the patient controls the RR, inspiratory time, and flow.

*Protocol and Increase in Ventilatory Demand*

A protocol similar to a previously reported protocol[2] has been used. The effects of PSV, APV, and ASV given in a random order were assessed during a 20-min baseline period (dead space off) followed by a 20-min period adding a heat-and-moisture exchanger representing a dead space of 100 ml between the endotracheal tube and the Y-piece of the ventilatory circuit (dead space on). The values of VT and minute ventilation obtained before randomization in PSV mode, in which inspiratory pressure was set to achieve a VT between 6 and 8 ml/kg of predicted body weight with an RR between 20 and 30 breaths/min, were used to set the selected minute ventilation in ASV and the desired VT in APV. We also tried to refine the settings in baseline condition for ASV and APV modes (dead space off) on a case-by-case basis in such a way that esophageal pressure ($P_{ES}$) and/or transdiaphragmatic pressure swings were approximately of the same magnitude in PSV mode (dead space off).[15]

*Measurements*

All measurements were performed during the last 5 min of the three ventilatory modes that were randomized with dead space on and off for each, *i.e.*, six following study periods: PSV-dead space off, PSV-dead space on, APV-dead space off, APV-dead space on, ASV-dead space off, ASV-dead space on. The air flow rate was measured using a heated and calibrated pneumotachograph (Fleisch #1; Fleisch, Lausanne, Switzerland) that was linear over the experimental flow range. Airway pressure was measured close to the pneumotachograph by using a differential pressure transducer (MP45, $\pm$100 cm $H_2O$; Validyne, Northridge, CA). $P_{ES}$ and gastric pressure ($P_{GA}$) were measured using a double balloon catheter (Marquat, Boissy-Saint-Léger, France) inserted through a nostril after topical anesthesia and then advanced until the distal and proximal balloons were in the stomach and midesophagus, respectively. Each balloon was filled with 0.5–1 ml of air, and the catheter connected to its own differential pressure transducer (MP45, $\pm$100 cm $H_2O$; Validyne). Placement of the esophageal balloon was assessed using the airway occlusion test[16], and placement of the gastric balloon was assessed by checking that smooth manual pressure on the abdomen produced $P_{GA}$ fluctuations and that swallowing produced a sharp $P_{ES}$ peak related to esophageal contraction with no $P_{GA}$ peak.[17] Transdiaphragmatic pressure was obtained by subtracting the $P_{ES}$ signal from the $P_{GA}$ signal (transdiaphragmatic pressure = $P_{GA}$–$P_{ES}$). Flow and pressure signals were digitized at 128 Hz and sampled using an analog-to-digital converter system (MP100; BIOPAC Systems, Santa Barbara, CA). After elimination of artifacts caused by coughing or esophageal spasms, 15–20 consecutive breaths were used to compute mean values. VT was computed by integration of the flow signal, and RR, inspiratory and expiratory times, duty cycle, and mean inspiratory flow rate were determined from the flow signal. Minute ventilation was calculated as the product of VT by RR. Dynamic lung compliance was calculated as the ratio of mean VT to the changes in transpulmonary pressure ($P_{ES}$ – airway pressure) during inspiration.

*Data Analysis and Assessment of Patient Effort*

Patient inspiratory effort was evaluated on the basis of pressure indexes and inspiratory work of breathing. The $P_{ES}$ and transdiaphragmatic pressure swings, the $P_{ES}$–time product and the transdiaphragmatic pressure-time product were calculated as previously described.[15,18] Inspiratory work of breathing was computed from $P_{ES}$ and VT loops as previously described.[15,18] The inspiratory work of breathing per breath was calculated from a Campbell diagram by computing the area enclosed be-

tween the inspiratory Pes–VT curve and the static Pes–volume curve of the chest wall, using a theoretical value for chest wall compliance (4% of the predicted value for the vital capacity per cm $H_2O$). Although the use of this theoretical value may result in some error, this was expected to be identical for all periods and not affecting the validity of comparisons. Inspiratory work of breathing is expressed as joules per breath as the work per volume unit (joules per liter) or as the work per time unit (joules per minute). Blood samples were obtained for arterial blood gas analysis (ABL 520 analyzer; Radiometer, Copenhagen, Denmark) at the time of respiratory measurements through a 20-gauge catheter inserted in a radial or femoral artery. Standard three-lead monitoring electrodes continuously recorded heart rate and rhythm. Systolic and diastolic arterial blood pressures were continuously monitored through the radial artery signal. Oxygen saturation was continuously monitored using pulse oxymetry.

*Statistical Analysis*

Values are expressed as mean ± SD or median (interquartile range) according to the type of variable distribution. Data were analyzed by a multiple-way analysis of variance (MANOVA) with the ventilatory modalities as the between-groups factor, the dead space on/off, and the random order as the repeated-measures factors. When a significant F ratio was obtained, differences between the data were isolated with the *post hoc* Tukey multiple comparison tests. Values between dead space on and dead space off were compared using parametric or nonparametric tests according to their distribution. We also compared the increase of inspiratory effort expressed in percentage of baseline value induced by the added dead space between the three modes. Differences at the level of $P < 0.05$ were considered statistically significant. Statistical analysis was performed using SAS/STAT software version 8.1 (SAS Institute, Cary, NC).

## Results

The etiology of respiratory failure of the 14 patients were postoperative acute respiratory failure (n = 9), pulmonary infection (n = 3), and acute pancreatitis (n = 2). No patient was tracheotomized. For the following parameters, the values are expressed in mean ± SD: age, 64 ± 9 yr; height, 168 ± 8 cm; weight, 72 ± 14 kg; duration of mechanical ventilation, 13 ± 6 days. The mean values of the main ventilatory parameters are presented in table 2, and blood gas and hemodynamic parameters are presented in table 3. None of the study parameters (ventilatory pattern, inspiratory effort, and hemodynamics) differed significantly among PSV, ASV, and APV during the baseline period (tables 2, 3, and 4). With PSV and ASV, tolerance was good during the baseline and dead-space periods in all patients. With APV, however, three patients (nos. 5, 9, and 14) experienced overt clinical respiratory distress during the dead-space period, which has to be stopped prematurely. The data for the dead-space APV period in these three patients were therefore recorded for about 5–10 min after addition of dead space.

Adding dead space significantly increased minute ventilation and $Paco_2$ values with PSV, ASV, and APV (tables 2 and 3). Dead space significantly increased minute ventilation by 18%, 19% and 21% in PSV, APV and ASV respectively (table 2). In PSV, minute ventilation had been increased through a 22% increase in RR as compared to 1.2% increase in VT (table 2 and fig. 1) and this

**Table 2. Effects of Dead Space Addition on Breathing Pattern and Mechanics Under PSV, ASV, and APV**

| | PSV | | ASV | | APV | | |
|---|---|---|---|---|---|---|---|
| Mode Dead Space | Off | On | Off | On | Off | On | MANOVA |
| RR, breaths/min | 20.1 ± 3.2 | 24.7 ± 4.8 | 19.6 ± 3.6 | 24.2 ± 4.7 | 20.5 ± 3.5 | 24.1 ± 4.2 | * |
| VT, ml | 549 ± 153 | 556 ± 146 | 585 ± 108 | 592 ± 126 | 560 ± 110 | 559 ± 103 | |
| VE, l/min | 11.7 ± 3.1 | 13.9 ± 3.1 | 11.4 ± 2,4 | 13.9 ± 2.6 | 10.7 ± 2.1 | 12.8 ± 2.7 | *§ |
| Ti, s | 0.9 ± 0.1 | 0.9 ± 0.2 | 0.9 ± 0.2 | 0.9 ± 0.1 | 1.3 ± 0.2 | 1.2 ± 0.3 | |
| Te, s | 2.1 ± 0.3 | 1.7 ± 0.4 | 2.2 ± 0.5 | 1.8 ± 0.5 | 2.0 ± 0.3 | 1.6. ± 0.5 | * |
| Ti/Ttot, % | 31.3 ± 6.0 | 36.0 ± 6.7 | 28.6 ± 4.1 | 34.6 ± 6.9 | 40.1 ± 5.9 | 44.9 ± 8.7 | *‡ |
| VT/Ti, l/min | 0.63 ± 0.19 | 0.65 ± 0.19 | 0.69 ± 0.14 | 0.68 ± 0.18 | 0.44 ± 0.11 | 0.45 ± 0.11 | |
| RR/VT, breaths · $min^{-1}$ · $l^{-1}$ | 37.4 ± 10.4 | 43.8 ± 17.0 | 34.9 ± 12.1 | 40.5 ± 15.7 | 37.1 ± 7.1 | 41.3 ± 12 | * |
| Pinsp, cm $H_2O$ | 12.0 ± 3.4 | 11.9 ± 3.2 | 12.3 ± 3.4 | 12.8 ± 3.6 | 12.7 ± 2.6 | 6.7 ± 1.4† | *‡ |
| PEEPi, cm $H_2O$ | 1.8 ± 1.1 | 2.8 ± 1.8 | 2.1 ± 1.2 | 3.6 ± 1.9 | 2.2 ± 1.2 | 4.7 ± 2.1† | *‡§ |
| Dynamic lung compliance, ml/cm $H_2O$ | 69 ± 19 | 59 ± 18 | 68 ± 20 | 61 ± 21 | 72 ± 30 | 60 ± 22† | *‡§ |

Dynamic lung compliance was calculated as the ratio of mean VT to the changes in transpulmonary pressure (Pes – Paw) during inspiration. * $P < 0.05$ effect of dead space addition; † $P < 0.05$ *vs.* corresponding PSV (*post hoc*); ‡ $P < 0.05$ effect of ventilatory mode; § $P < 0.05$ interaction of effects of dead space and ventilatory mode.

APV = adaptive pressure ventilation; ASV = adaptive support ventilation; MANOVA = multiple analysis of variance; PEEPi = intrinsic positive end-expiratory pressure; Pinsp = inspiratory airway pressure delivered by the ventilator above PEEP; PSV = pressure support ventilation; RR = respiratory rate; Ti = inspiratory time; Te = expiratory time; Ttot = total respiratory time; VT/Ti = mean inspiratory flow; VE = volume per minute; VT = tidal volume.

**Table 3. Effects of Dead Space on Arterial Blood Gas and Hemodynamic Parameters Under PSV, ASV, and APV**

| | PSV | | ASV | | APV | |
|---|---|---|---|---|---|---|
| Mode Dead Space | Off | On | Off | On | Off | On |
| pH | 7.46 ± 0.06 | 7.45 ± 0.06 | 7.47 ± 0.06 | 7.45 ± 0.06* | 7.46 ± 0.06 | 7.43 ± 0.05* |
| $Pao_2$, mmHg | 133 ± 59 | 140 ± 60 | 134 ± 65 | 140 ± 62 | 132 ± 58 | 141 ± 48 |
| $Pao_2/Fio_2$, mmHg | 271 ± 82 | 280 ± 92 | 268 ± 74 | 280 ± 86 | 257 ± 63 | 282 ± 92 |
| $Paco_2$, mmHg | 36.3 ± 5.4 | 38.5 ± 7.2* | 35.8 ± 4.5 | 37.7 ± 6.7* | 35.3 ± 6.0 | 40.0 ± 6.7* |
| HR, breaths/min | 91 ± 18 | 92 ± 18 | 93 ± 19 | 94 ± 19 | 94 ± 19 | 98 ± 18 |
| SBP, mmHg | 135 ± 28 | 138 ± 26 | 136 ± 23 | 140 ± 27 | 135 ± 25 | 138 ± 31 |
| DBP, mmHg | 70 ± 10 | 70 ± 5 | 67 ± 9 | 68 ± 7 | 69 ± 8 | 70 ± 7 |

* $P < 0.05$ effect of dead space addition.

APV = adaptive pressure ventilation; ASV = adaptive support ventilation; DBP = diastolic blood pressure; HR = heart rate; PSV = pressure support ventilation; SBP = systolic blood pressure.

was also the case with APV and ASV (table 2). PINSP was kept constant in PSV and ASV but significantly decreased with APV from 12.7 ± 2.6 to 6.7 ± 1.4 cm $H_2O$ ($P < 0.01$) (table 2).

Respiratory effort indexes at the end of the six studied conditions are summarized in table 4. Dead space increased respiratory muscle effort with the three modes (table 4 and fig. 2) but significantly more with APV as compared to PSV or ASV ($P < 0.05$).

## Discussion

The main result of the current study is that ASV and PSV behaved differently but ended up with similar pressure levels facing acute changes in ventilatory demand resulting from the addition of a dead space. By contrast, the same increase in ventilatory demand with APV resulted in a decrease in the pressure support provided by the ventilator, which is opposite from the desired response and a much larger increase in respiratory effort than with the other modes (table 4, fig. 2).

### *Adaptive Support Ventilation*

To our knowledge, this is the first study to evaluate the patient behavior and ventilator response of the ASV mode when ventilatory demand was increased by addition of dead space to the circuit. We reported in case of increase ventilatory demand that ASV is adjusting the level of ventilatory support in a way similar to PSV and that the increase of the patient's inspiratory effort was similar in both ASV and PSV.

As described in the method section and in previous publications,[10,11,19–22] ASV incorporates a pressure regulation algorithm to achieve the optimal VT. This optimal RR-VT combination gives the desired minute ventilation. As compared to a "simple" dual mode, the VT-targeted, pressure regulation loop of ASV is only one piece in a more sophisticated system, also including an RR regulation system, an MV guarantee, and safety rules based on the breath-to-breath evaluation of the patient's RCEXP. Each part makes this mode different from a simple dual mode like APV and volume support ventilation.[1–3,23]

One important feature is the possibility for ASV to track the changes in respiratory mechanics through repeated measurements of the expiratory time constant. Although we did not record time constant during the experiment, we found a decrease in dynamic compliance associated with RR increase (table 2). According to the ASV algorithm, a decrease in compliance is followed

**Table 4. Effects of Dead Space on Inspiratory Muscle Effort Under PSV, ASV, and APV**

| | PSV | | ASV | | APV | | |
|---|---|---|---|---|---|---|---|
| Mode Dead Space | Off | On | Off | On | Off | On | MANOVA |
| ΔPes, cm $H_2O$ | 4.1 ± 2.9 | 8.1 ± 5.1 | 4.8 ± 7.4 | 8.9 ± 6.1 | 4.4 ± 3.2 | 12.5 ± 5.2† | *‡§ |
| PTPes, cm $H_2O \cdot s$ | 4.2 ± 2.2 | 6.9 ± 3.3 | 4.3 ± 3.7 | 7.6 ± 3.4 | 5.2 ± 3.1 | 11.6 ± 4.6† | *‡§ |
| PTPes × RR, cm $H_2O \cdot s^{-1} \cdot min^{-1}$) | 80.6 ± 44.5 | 163.7 ± 75.3 | 85.1 ± 83.1 | 180.6 ± 85.5 | 97.6 ± 54.6 | 256.9 ± 87.1† | *‡§ |
| ΔPdi, cm $H_2O$ | 4.0 ± 3.1 | 8.3 ± 6.1 | 4.8 ± 7.4 | 8.8 ± 6.2 | 4.5 ± 3.3 | 12.5 ± 5.2† | *‡§ |
| PTPdi, $cmH_2O \cdot s$ | 3.8 ± 3.6 | 6.9 ± 3.8 | 4.1 ± 3.6 | 7.4 ± 3.3 | 4.8 ± 3.1 | 15.5 ± 14.3† | *‡§ |
| PTPdi × RR, cm $H_2O \cdot s^{-1} \cdot min^{-1}$ | 76.4 ± 70.9 | 166.5 ± 81.3 | 86.4 ± 79.4 | 186.8 ± 73.9 | 89.8 ± 60.6 | 257.3 ± 132.8† | *‡§ |
| WOB, J/l | 0.41 ± 0.24 | 0.81 ± 0.37 | 0.50 ± 0.58 | 0.88 ± 0.58 | 0.44 ± 0.26 | 1.09 ± 0.48† | *‡§ |
| WOB, J/min | 5.3 ± 4.3 | 12.1 ± 8.3 | 7.7 ± 11.1 | 14.3 ± 11.8 | 6.1 ± 4.7 | 15.7 ± 9.6† | *‡§ |

* $P < 0.05$ effect of dead space addition; † $P < 0.05$ *vs.* corresponding PSV (*post hoc*); ‡ $P < 0.05$ effect of ventilatory mode; § $P < 0.05$ interaction of effects of dead space and ventilatory mode.

APV = adaptive pressure ventilation; ASV = adaptive support ventilation; ΔPDI = transdiaphragmatic pressure; ΔPES = esophageal pressure; MANOVA = multiple analysis of variance; PSV = pressure support ventilation; PTPDI = transdiaphragmatic pressure-time product; PTPES = esophageal pressure-time product; WOB = work of breathing.

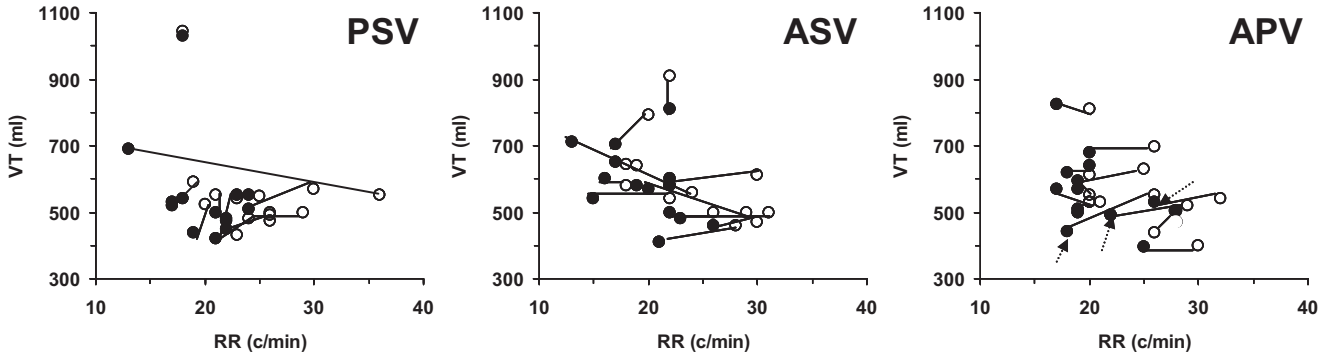


**Fig. 1. Individual effects of added dead space on respiratory rate (*RR*) and tidal volume (*VT*) during pressure support ventilation (*PSV*), adaptive ventilation (*ASV*), and adaptive pressure ventilation (*APV*); *closed circles* = baseline; *open circles* = dead space on. In APV, the three *arrows* indicate the three patients (nos. 5, 9, 14) who experienced overt clinical respiratory distress during the dead space on period that had to be stopped prematurely.**

by a decrease in the targeted VT and eventually by the level of pressure support. In parallel, added heat and moisture exchanger induced most probably an increase in airway resistances; according to the ASV algorithm, an increase in airway resistances is followed by an increase in the targeted VT and eventually by the level of pressure support. The net effect is likely to be a minor or no change in the targeted VT and subsequently on the level of support. This was confirmed by recalculating the ASV targeted VT according to the Otis equation.[6] For example, with a compliance of 68 ml/cm $H_2O$ (table 2) and a resistance of 5 cm $H_2O \cdot l^{-1} \cdot s^{-1}$ in dead space on, the targeted VT was 500 ml. With a compliance of 61 ml/cm $H_2O$ as observed in dead space on (table 2) and a resistance of 6 cm $H_2O \cdot l^{-1} \cdot s^{-1}$, the targeted VT was the same, *i.e.*, 500 ml. Therefore it seems that the similar delivered pressure in PSV and ASV resulted from a very different behavior, and a complex heat and moisture exchanger–induced modification in respiratory mechanics explains the lack of change of support level with ASV.

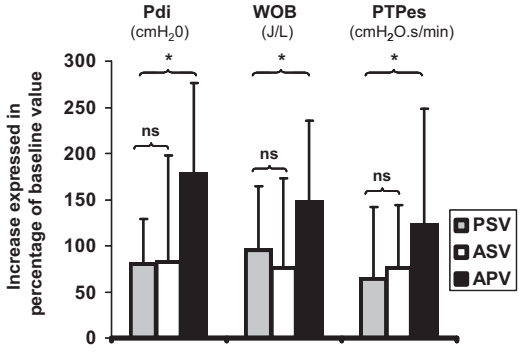


**Fig. 2. Increase in the main respiratory effort parameters: transdiaphragmatic pressure (*PDI* ), work of breathing (*WOB, J/l*), and pressure-time product of the respiratory muscles (*PTPES, cm $H_2O$ s $min^{-1}$* ) with added dead space expressed in percentage of baseline value for the three modes: pressure support ventilation (*PSV*), adaptive ventilation (*ASV*), and adaptive pressure ventilation (*APV*). Note that no significant difference was observed between PSV and ASV. However, the increases with APV were significantly greater than those with PSV and ASV. * $P < 0.05$.**

In ASV, minimum minute ventilation is the only specific setting that must be chosen by the clinician, and it is based on patient's body weight. That is why we choose in the current study to match the three modes to deliver at baseline a ventilatory assist to obtain the same minute ventilation. Moreover, in the present study, during each setting, ventilatory demand was increased by adding dead space without ventilator readjustment. Particularly, the PEEP of 5 cm $H_2O$ remained constant throughout the six study periods. We speculate that this low level, as often applied in this kind of patients, did not influence the results.

ASV has been shown able to reduce the duration of weaning in postcardiac surgery patients.[21] In such relatively easy-to-wean patients, respiratory muscles are often able to overcome an increase in the respiratory demand. Conversely, in intensive care unit patients after prolonged mechanical ventilation, *i.e.*, more than 3 days, the weaning phase might be associated with an imbalance between respiratory muscle capacity and load. In such patients, a preliminary investigation showed that ASV was able to provide similar support at rest compared to a synchronized intermittent mandatory ventilation plus PSV mode of ventilation.[11]

Weiler *et al.*[24] have shown that ASV adapted much better than controlled mechanical ventilation to maintain alveolar ventilation in response to changes in respiratory system compliance induced by lateral positioning during renal surgery. The same authors[22] evaluated the ASV response upon switching from 2-lung to 1-lung ventilation during thoracic surgery. The ASV algorithm maintained a safe VT and preserved minute ventilation as lung volume and compliance were altered. These studies[1,9,22,24] demonstrate the feasibility of allowing the ventilator to automatically select ventilation variables and to make changes in response to patient effort and lung mechanics, but they do not evidence that ASV is superior to other ventilation modes, which need further investigations.

### *Adaptive Pressure Ventilation*

In ASV and APV, the patient VT is adjusted to a target VT through PINSP regulation. In ASV and APV, changing

the patient VT affects the RR and eventually the time constant. As the time constant is changing, the target VT is changing in ASV and not in APV, where the target VT is set by the user. Therefore the main difference between ASV and APV regarding VT is that the target is fixed and set by the user in APV as compared to variable and depending on the time constant in ASV. As previously reported,[2] in a simple dual mode like APV or volume support ventilation, which are volume-guaranteed pressure-control modes, an increase in ventilatory demand leads to a decrease in pressure support. A simple volume-guaranteed pressure-control mode may conceivably result in respiratory distress in clinical settings as observed in 3 of the 14 included patients in the current study and 2 of the 10 evaluated patients in our previous study[2] a few minutes after adding dead space and using a simple dual-mode. The results obtained in the current study for the ventilator behavior when ventilatory demand was artificially increased in APV confirmed those reported in our previous study with volume support ventilation in terms of a decrease of pressure support and the proportion of inspiratory effort increase (tables 2 and 4, fig. 2). However, some differences in breathing pattern exist regarding patient response during PSV between the two studies; they are probably explained mainly by the expiratory trigger setting. The impact of the expiratory trigger setting on patient-ventilator interaction was emphasized recently in several studies both in PSV[11,25–27] and in volume-guaranteed pressure-control mode such as volume support ventilation.[28] In the current study performed with the Galileo ventilator (Hamilton), the expiratory trigger sensitivity was adjusted at 50% of the inspiratory peak flow; in our previous study,[2] it was fixed at 5% on the Servo 300 (Maquet, Lund, Sweden). Indeed, with the Servo 300 ventilator, dead space increase induced no significant increase in RR (24.8 ± 6.6 to 25.9 ± 6.6 c/min, $P = 0.31$) and a significant increase in VT (479 ± 116 to 532 ± 164 ml, $P = 0.01$); the current study, the addition of dead space induced a significant increase in RR (20.1 ± 3.2 to 24.7 ± 4.8 c/min, $P = 0.02$) and no significant change in VT (549 ± 153 to 556 ± 146 ml, $P = 0.52$). Such a response has been previously described in a study by Ranieri *et al.* comparing PSV to proportional assist ventilation.[24] Elsewhere, inspiratory time was moderately longer during the APV condition in comparison to ASV and PSV modes. It may be explained by the fact that he expiratory trigger sensitivity (breath termination cycle) in APV in half of the patients was set at 25% and not 50% like in ASV and PSV. Longer inspiratory time means more support,[29] but with conflicting results on the energetic indexes (table 4) depending on how much the patient is synchronized with the ventilator. In any case, we don't believe the higher baseline inspiratory time should invalidate the change in the level of support observed with APV. The current study was designed to compare changes induced by added dead space and not the absolute baseline values. The mean changes in energetic indexes was much higher in APV (+163%) as compared to ASV (111%) and PSV (103%) (table 4). Moreover, from a physiologic point of view, APV is depending only on respiratory muscles output; the more the muscles are able to generate a VT and the less support given by the ventilator. ASV is depending on the respiratory muscles output as well, but it takes also into account the change in respiratory mechanics (by changing the target). Basically in clinical condition, changes in respiratory muscle output are very often associated with change in respiratory mechanics. From a practical point of view, ASV offers more by automatically switching from pressure-controlled breath to pressure-support breath as soon as the patient is able to trigger the breath (and back to pressure-controlled if for any reason the patient stops triggering the breath) and by a set a dynamic safety rules that limits dynamic hyperinflation and volo/barotrauma. The current study was obviously not designed to evidence these aspects (already published in postoperative cardiac surgery patients[21]), but to respond to a specific question on how ASV was behaving in cases of increase respiratory demand as compared to PSV and APV.

*Future Directions*

A recently published International Consensus Conference on weaning[30] indicates that ASV may be seen as closed loop ventilation that needs further investigation to help patients weaning from the mechanical ventilator. In this context, it is reassuring to find that ASV did not react poorly with an increase in demand, in contrast to other dual-modes.

One limitation of the current physiologic trial is that we only studied a homogeneous group of patients (mainly postoperative acute respiratory failure), and it would be interesting to evaluate ASV and APV mode in more patients with different pathologies, such as chronic obstructive pulmonary disease and/or obese patients through observational and/or therapeutic studies. It might also be interesting to compare ASV with the Smart Care system,[31] a closed-loop knowledge-based algorithm introduced in an Evita XL (Drager, Lübeck, Germany) ventilator to act as a computer-driven weaning protocol that can reduce mechanical ventilation duration and intensive care unit length of stay when compared to a physician-controlled weaning process.[32]

In conclusion, our findings show that ASV and PSV, which have different working principles, behaved differently but ended up with similar delivered inspiratory pressures facing acute changes in ventilatory demand, by contrast to APV (a simple volume-guaranteed pressure-control mode) in which an increase in ventilatory demand results in a decrease in the pressure support provided by the ventilator, opposite from the desired

response. The observation of unchanged inspiratory pressure with ASV is probably explained by opposite effects of minute ventilation and respiratory mechanics on the target.

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## References

1. Branson RD, Johannigman JA: What is the evidence base for the newer ventilation modes? Respir Care 2004; 49:742–60
2. Jaber S, Delay JM, Matecki S, Sebbane M, Eledjam JJ, Brochard L: Volume-guaranteed pressure-support ventilation facing acute changes in ventilatory demand. Intensive Care Med 2005; 31:1181–8
3. Ranieri M: Optimization of patient-ventilator interactions: Closed-loop technology to turn the century. Intensive Care Med 1997; 23:936–9
4. Branson R: Understanding and implementing advances in ventilator capabilities. Curr Opin Crit Care 2004; 10:23–32
5. Otis A, Fenn W, Rahn H: Mechanics of breathing in man. J Appl Physiol 1950; 2:592–607
6. Otis A: The work of breathing, Section 3: Respiration, Handbook of Physiology. Edited by Fenn WO, Rahn H. Washington DC, American Physiological Society, 1964, pp 463–76
7. Lourens MS, van den Berg B, Aerts JG, Verbraak AF, Hoogsteden HC, Bogaard JM: Expiratory time constants in mechanically ventilated patients with and without COPD. Intensive Care Med 2000; 26:1612–8
8. Brunner JX, Laubscher TP, Banner MJ, Iotti G, Braschi A: Simple method to measure total expiratory time constant based on the passive expiratory flow-volume curve. Crit Care Med 1995; 23:1117–22
9. Brunner JX, Iotti GA: Adaptive support ventilation (ASV). Minerva Anestesiol 2002; 68:365–8
10. Laubscher TP, Frutiger A, Fanconi S, Jutzi H, Brunner JX: Automatic selection of tidal volume, respiratory frequency and minute ventilation in intubated ICU patients as start up procedure for closed-loop controlled ventilation. Int J Clin Monit Comput 1994; 11:19–30
11. Tassaux D, Dalmas E, Gratadour P, Jolliet P: Patient-ventilator interactions during partial ventilatory support: a preliminary study comparing the effects of adaptive support ventilation with synchronized intermittent mandatory ventilation plus inspiratory pressure support. Crit Care Med 2002; 30:801–7
12. Jaber S, Verzilli D, S Matecki S, Wysocki M, Eledjam J, Brochard L: Adaptive support ventilation (ASV) *versus* pressure support ventilation (PSV) *versus* volume-guaranted pressure-support (abstract). Intensive Care Med 2005; 742: S192
13. Campbell RS, Branson RD, Johannigman JA: Adaptive support ventilation. Respir Care Clin N Am 2001; 7:425–40
14. Lourens MS, Ali L, van den Berg B, Verbraak AF, Bogaard JM, Hoogsteden HC, Babuska R: Estimation of expiratory time constants *via* fuzzy clustering. J Clin Monit Comput 2002; 17:15–22
15. Jaber S, Fodil R, Carlucci A, Boussarsar M, Pigeot J, Lemaire F, Harf A, Lofaso F, Isabey D, Brochard L: Noninvasive ventilation with helium-oxygen in acute exacerbations of chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2000; 161:1191–200
16. Baydur A, Behrakis P, Zin W, 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
17. Diehl JL, Lofaso F, Deleuze P, Similowski T, Lemaire F, Brochard L: Clinically relevant diaphragmatic dysfunction after cardiac operations. J Thoracic Cardiovasc Surg 1994; 107:487–98
18. Brochard L, Harf A, Lorino H, Lemaire F: Inspiratory pressure support prevents diaphragmatic fatigue during weaning from mechanical ventilation. Am Rev Respir Dis 1989; 139:513–21
19. Cassina T, Chiolero R, Mauri R, Revelly JP: Clinical experience with adaptive support ventilation for fast-track cardiac surgery. J Cardiothorac Vasc Anesth 2003; 17:571–5
20. Gruber PC, Gomersall CD, Leung P, Joynt GM, Ng SK, Ho KM, Underwood MJ: Randomized controlled trial comparing adaptive-support ventilation with pressure-regulated volume-controlled ventilation with automode in weaning patients after cardiac surgery. ANESTHESIOLOGY 2008; 109:81–7
21. Sulzer C, Chiolero R, Cassina T, Chassot P, Mueller X, Revelly J: Adaptive support ventilation for fast tracheal extubation after cardiac surgery: A randomized controlled study. ANESTHESIOLOGY 2001; 95:1339–45
22. Weiler N, Eberle B, Heinrichs W: Adaptive lung ventilation (ALV) during anesthesia for pulmonary surgery: Automatic response to transitions to and from one-lung ventilation. J Clin Monit Comput 1998; 14:245–52
23. Ranieri V, Giuliani R, Mascia L, Grasso S, Petruzelli V, Puntillo N, Perchiazzi G, Fiore T, Brienza A: Patient-ventilator interaction during acute hypercapnia: Pressure support *versus* proportional assist ventilation. J Appl Physiol 1996; 81:426–36
24. Weiler N, Eberle B, Latorre F, von Paczynski S, Heinrichs W: Adaptive lung ventilation (AVL). Evaluation of new closed loop regulated respiration algorithm for operation in the hyperextended lateral position. Anaesthesist 1996; 45:950–6
25. Tassaux D, Michotte JB, Gainnier M, Gratadour P, Fonseca S, Jolliet P: Expiratory trigger setting in pressure support ventilation: From mathematical model to bedside. Crit Care Med 2004;32: 1844–50
26. Tassaux D, Gainnier M, Battisti A, Jolliet P: Impact of expiratory trigger setting on delayed cycling and inspiratory muscle workload. Am J Respir Crit Care Med 2005; 172:1283–9
27. Brochard L: When ventilator and patient's end of inspiration don't coincide: What's the matter? Am J Respir Crit Care Med 2002; 166:2–3
28. Sottiaux TM: Patient-ventilator interactions during volume-support ventilation: Asynchrony and tidal volume instability–a report of three cases. Respir Care 2001; 46:255–62
29. Tokioka H, Tanaka T, Ishizu T, Fukushima T, Iwaki T, Nakamura Y, Kosogabe Y: The effect of breath termination criterion on breathing patterns and the work of breathing during pressure support ventilation. Anesth Analg 2001; 92:161–5
30. Boles JM, Bion J, Connors A, Herridge M, Marsh B, Melot C, Pearl R, Silverman H, Stanchina M, Vieillard-Baron A, Welte T: Weaning from mechanical ventilation. Eur Respir J 2007; 29:1033–56
31. Bouadma L, Lellouche F, Cabello B, Taille S, Mancebo J, Dojat M, Brochard L: Computer-driven management of prolonged mechanical ventilation and weaning: A pilot study. Intensive Care Med 2005; 31:1446–50
32. Lellouche F, Mancebo J, Jolliet P, Roeseler J, Schortgen F, Dojat M, Cabello B, Bouadma L, Rodriguez P, Maggiore S, Reynaert M, Mersmann S, Brochard L: A multicenter randomized trial of computer-driven protocolized weaning from mechanical ventilation. Am J Respir Crit Care Med 2006; 174:894–900