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## A physiologic comparison of proportional assist ventilation with load-adjustable gain factors (PAV+) versus pressure support ventilation (PSV)

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**Abstract Purpose:** To compare patient–ventilator interaction during PSV and PAV+ in patients that are difficult to wean. **Methods:** This was a physiologic study involving 11 patients. During three consecutive trials (PSV first trial—PSV1, followed by PAV+, followed by a second PSV trial—PSV2, with the same settings as PSV1) we evaluated mechanical and patient respiratory pattern; inspiratory effort from excursion P<sub>di</sub> (swing<sub>P<sub>di</sub></sub>), and pressure–time products of the transdiaphragmatic (PTP<sub>di</sub>) pressures. Inspiratory (delay<sub>tr<sub>insp</sub></sub>) and expiratory (delay<sub>tr<sub>exp</sub></sub>) trigger delays, time of synchrony (time<sub>syn</sub>), and asynchrony index (AI) were assessed. **Results:** Compared to PAV+, during PSV trials, the mechanical inspiratory time (Ti<sub>flow</sub>) was significantly longer than patient inspiratory time (Ti<sub>pat</sub>) ( $p < 0.05$ ); Ti<sub>pat</sub> showed a prolongation between PSV1 and PAV+, significant comparing PAV+

and PSV2 ( $p < 0.05$ ). PAV+ significantly reduced delay<sub>tr<sub>exp</sub></sub> ( $p < 0.001$ ). The portion of tidal volume (VT) delivered in phase with Ti<sub>pat</sub> (VT<sub>pat</sub>/VT<sub>mecc</sub>) was significantly higher during PAV+ ( $p < 0.01$ ). The time of synchrony was significantly longer during PAV+ than during PSV ( $p < 0.001$ ). During PSV 5 patients out of 11 showed an AI greater than 10%, whereas the AI was nil during PAV+. **Conclusion:** PAV+ improves patient–ventilator interaction, significantly reducing the incidence of end-expiratory asynchrony and increasing the time of synchrony.

**Keywords** Patient–ventilator synchrony · Proportional assist ventilation · Pressure support ventilation

### Introduction

The early institution of partial ventilatory support in patients recovering from acute respiratory failure (ARF) is nowadays accepted, to avoid the side effects of controlled mechanical ventilation (MV) [1–5]. Pressure support ventilation (PSV) is the most diffuse mode of partial ventilatory support, in which the ventilator applies a preset level of pressure to assist patient inspiration. Despite its uncontested clinical value, asynchronies are

likely to be produced as a consequence of machine performance, patient respiratory mechanics, and software algorithms. It is well known that the flow-based cycling on–off criteria may lead to premature or, more often, delayed termination of the end of mechanical inspiration, producing under- or over-assistance, respectively [6]. Accordingly, Beck et al. [7] demonstrated that at high PSV level, the poor patient–ventilator interaction produces the delivering of a large part of the tidal volume (VT) during the decreasing phase of diaphragm

activation. Several recent studies demonstrated that a high incidence of asynchronies during PSV may prolong the length of MV [8, 9].

Proportional assist ventilation (PAV) aims to overcome the aforementioned drawbacks. During PAV, the ventilator assistance is delivered in proportion to the patient's instantaneous flow and volume, by compensating patient resistive and elastic loads, thus amplifying the patient's own effort breath by breath [10]. Several studies showed that PAV improves patient-ventilator synchrony at the start of inspiration [11–13] but not necessarily at the end of inspiration [13–15]. Moreover, its widespread clinical use was limited by the necessity of regular measurements of respiratory mechanics (elastance and resistance). More recently, new software that is able to adapt ventilator assistance to the respiratory system mechanics (elastance and resistance, automatically and semi-continuously measured every 300 ms) has been developed (PAV+, Covidien) and clinically validated [16–18]. PAV+ allows the easier titration of ventilator support according to the patient's own respiratory mechanics: this should be translated into improved patient-ventilator interaction compared to PSV [8, 9] and thus into a larger clinical application of PAV+ than traditional PAV.

Recently, some authors compared PAV+ and PSV in patients recovering from controlled MV [19], showing that PAV+ significantly reduced the rate of weaning failure. They suggested that a significantly lower percentage of major patient-ventilator asynchronies during PAV+ could explain their results. However, the authors did not provide any formal analysis of patient-ventilator interaction and did not evaluate the asynchrony index (AI).

The aim of our study was to prospectively evaluate if PAV+, compared to PSV, is able to improve patient-

ventilator interaction by reducing minor asynchronies (inspiratory and expiratory delays) and the incidence of major asynchronies (expressed as AI), in a group of patients that are difficult to wean. To the best of our knowledge this is the first study analyzing the efficacy of PAV+ by formally evaluating patient-ventilator interaction.

## Materials and methods

The study was performed in the surgical ICU of the Policlinico Gemelli of Rome, from September 2007 to November 2009, according to the principles of the Declaration of Helsinki. The protocol was approved by our ethics committee and informed consent was obtained from each patient.

### Patients and protocol

The main characteristics of the patients enrolled in the study are listed in Table 1. Inclusion criteria were as follows: (a) 11 consecutive intubated or tracheostomized patients, (b) recovering from an episode of postoperative ARF, (c) considered difficult to wean after failing two weaning attempts. The exclusion criteria were (a) need for cardiopulmonary resuscitation; (b) a Glasgow coma scale (GCS) less than 8 or need for sedation (Ramsay score 4–5); (c) hemodynamic instability needing continuous infusion of inotropic agents, or arrhythmias; (d) evidence of cardiogenic or septic shock; (e) gastroesophageal surgery in the previous 12 months; (f) agitation or delirium requiring sedatives; (g) age greater than 18 but less than 85 years; and (h) a clinical history of chronic obstructive pulmonary disease (COPD).

**Table 1** Baseline characteristics of the patients enrolled in the study

	Sex	Age	BMI	Days of MV	Causes of ARF	PSV (cmH <sub>2</sub> O)	PEEP (cmH <sub>2</sub> O)	PaO <sub>2</sub> /FiO <sub>2</sub> baseline
1	M	76	17	26	ARDS	15	8	245
2	M	85	29	14	Pneumonia	18	7	166
3	M	81	27	23	Pneumonia	10	5	156
4	M	78	26	15	ALI	10	5	600
5	F	73	24	8	ALI	10	7	255
6	F	74	25	21	Pneumonia	10	5	325
7	M	66	24	21	ARDS	15	5	365
8	M	73	31	12	ALI	10	5	368
9	M	77	26	15	ARDS	16	10	200
10	M	85	36	24	Pneumonia	16	7	235
11	M	71	27	19	Pneumonia	14	5	200
Mean		76.2	26	18		13	6	291
SD		5.8	4.7	5.6		3.3	1.6	131.9

ALI acute lung injury, ARDS acute respiratory distress syndrome, BMI body mass index

All enrolled patients were ventilated in PSV mode with a PB 840 (Covidien Mansfield, MA, USA) with a PS set to obtain a VT of 7–8 mL/kg (mean PS  $12.7 \pm 2.9$  cmH<sub>2</sub>O), and a PEEP value set to obtain a peripheral oxygen saturation (SpO<sub>2</sub>) above 92% with FiO<sub>2</sub> ranging between 0.35 and 0.5. PSV was in all patients optimized, as proposed by Chiumello et al. [20] in patients recovering from ALI setting the fastest inspiratory rise time (0% of the breath cycle time) and setting a 40% cycling off. This cycling off was used as it was clinically best accepted by the patients.

The patients were studied in semi-recumbent position. After the end of the first trial on PSV (PSV1) the patients were switched to PAV+. During PAV+, the level of assistance, expressed as percentage of unloading, was chosen to give the same mean pressure at airway opening (Paw) level obtained during PSV1, independently from the respiratory pattern parameters (VT, and respiratory rate, RR), and was on average  $59 \pm 10\%$ . After 1 h, the patients were switched back to PSV (PSV2). Each study period lasted for 1 h. The last 3 min of each trial was recorded and the data analysis was conducted on the last 2 min of tracings. Patients parameters were continuously monitored for the whole course of the study; arterial blood gases (ABGs), hemodynamics, respiratory pattern, and patient–ventilator interaction were evaluated at the end of each study period.

## Measurements

The flow ( $V'$ ) was measured through a pneumotachograph (Fleisch No. 2; Metabo; Epalinges, Switzerland) positioned at the Y piece of the respiratory circuit. The Paw was measured through a pressure transducer with a differential pressure of  $\pm 1$  cmH<sub>2</sub>O (Digima Clic-1, ICU-Lab System; KleisTEK Engineering; Bari, Italy), positioned distally to the pneumotachograph. VT was obtained by digital integration of  $V'$  over time.

Before initiating the study two separate latex balloon-tipped catheters were placed in the middle esophagus and in the stomach, respectively, and connected to two differential pressure transducer (Digima Clic-1, ICU-Lab System; KleisTEK Engineering) to obtain the esophageal pressure (Pes) and gastric pressure (Pgas). The proper positioning was checked as previously described [21]. Transdiaphragmatic pressure (Pdi) was obtained by subtracting the esophageal pressure from the gastric pressure.

All the signals were acquired, amplified, filtered, digitized at 100 Hz, recorded on a dedicated PC, and analyzed with specific software (ICU lab 2.3, KleisTEK Advanced Electronic System, Italy).

Mechanical respiratory rate (RR<sub>flow</sub>) and mechanical inspiratory and expiratory time (Ti<sub>flow</sub> and Te<sub>flow</sub>) were determined on the flow ( $V'$ ) tracing, while patient respiratory rate (RR<sub>pat</sub>) and patient inspiratory and expiratory

time (Ti<sub>pat</sub> and Te<sub>pat</sub>) were measured on the Pdi tracing as the time between the onset of Pdi and the point at which Pdi started to fall toward baseline, as previously described [22, 23]. The amount of inspiratory effort was calculated from the tidal excursion of Pdi (swing<sub>Pdi</sub>) and as the pressure–time product of the transdiaphragmatic (PTPdi) pressure, calculated as the area under Pdi (from Pdi onset above baseline to its return to baseline) per breath (PTPdi/br), per minute (PTPdi/min), and per liter of VT generated by the patients, to determine the diaphragm effort.

The inspiratory trigger delay (delay<sub>trinsp</sub>) was calculated as the delay between the onset of the patient inspiratory effort, evaluated on the Pdi tracing, and the onset of ventilatory assistance, evaluated on the  $V'$  tracing. Similarly, the expiratory trigger delay (delay<sub>trexp</sub>) was calculated as the time lag between the offset of patient inspiration and the end of mechanical assistance as Pdi and  $V'$  fall toward the baseline, respectively. Moreover, we calculated the time of synchrony (time<sub>syn</sub>) and VT<sub>pat</sub>/VT<sub>mecc</sub>, defined as the time during which the patient inspiratory effort and the ventilatory assistance are in phase and as the percentage of VT delivered during patient inspiration, respectively. Finally, we considered a high rate of asynchrony when the AI (which represents the number of asynchrony events divided by the total respiratory rate, expressed as a percentage) was greater than 10%. The asynchronies used for the calculation of the AI were only the so-called major asynchronies: wasted efforts, autocycling, and double triggering. Minor asynchronies (delay<sub>trinsp</sub> and delay<sub>trexp</sub>) were not computed in the AI.

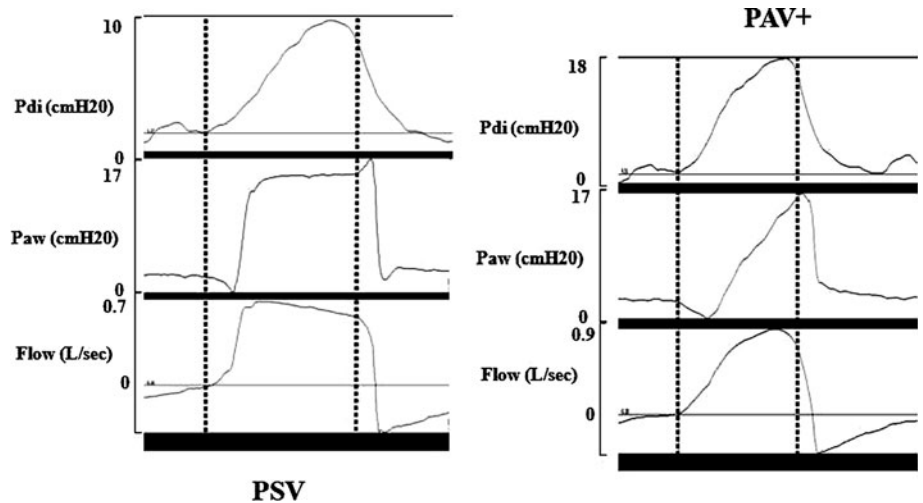
## Statistical analysis

Data are expressed as mean  $\pm$  SD. The Kruskal–Wallis test was used to detect significant differences in ABGs, respiratory pattern, inspiratory effort, and patient–ventilator synchrony between the different experimental conditions. When significant differences were detected, post-test analysis was performed using the Dunn test; *P* values less than 0.05 were considered statistically significant. The sample size of the study population was not chosen with a formal analysis, as the AI during PAV+ in this kind of patient population had never been assessed in previous studies.

## Results

All the enrolled patients completed the study protocol, without side effects. No differences were found during the whole course of the study in terms of hemodynamics. Sample tracings from a patient are shown in Fig. 1. As

**Fig. 1** Sample tracings from a patient during PSV and PAV+.  $T_{i\text{pat}}$  is represented by the two dotted lines



**Table 2** Modifications of gas exchange, respiratory pattern, and inspiratory effort during the three study periods

Parameter <sup>a</sup>	PSV1	PAV+	PSV1 versus PAV+	PSV2	PSV2 versus PAV+
pH	7.46 ± 0.07	7.45 ± 0.08	NS	7.46 ± 0.07	NS
PaO <sub>2</sub> (mmHg)	113.7 ± 34.8	118.2 ± 28.9	NS	111.5 ± 26.4	NS
PaCO <sub>2</sub> (mmHg)	41.9 ± 5.8	43.1 ± 7.8	NS	42.2 ± 5.6	NS
Peak <sub>Paw</sub> (cmH <sub>2</sub> O)	19.6 ± 5.2	18.9 ± 4.5	NS	19.7 ± 4.8	NS
Mean <sub>Paw</sub> (cmH <sub>2</sub> O)	10.8 ± 3.2	9.5 ± 2.5	NS	10.8 ± 3.1	NS
RR <sub>flow</sub> (breaths/min)	20.7 ± 5.4	22.9 ± 4.3	NS	20.5 ± 5.2	NS
RR <sub>neu</sub> (breaths/min)	22.6 ± 7.0	22.2 ± 4.3	NS	22.3 ± 6.8	NS
Ti <sub>flow</sub> (s)	1.1 ± 0.2	1.1 ± 0.4	NS	1.1 ± 0.4	NS
Ti <sub>pat</sub> (s)	0.9 ± 0.2	1.1 ± 0.4	NS	0.9 ± 0.2	<i>p</i> = 0.03
Ti/Tot <sub>flow</sub> (%)	45 ± 0.1	42 ± 0.1	NS	47 ± 0.1	NS
Ti/Tot <sub>neu</sub> (%)	40 ± 0.1	41 ± 0.1	NS	39 ± 0.1	NS
VT <sub>mecc</sub> (mL)	600.7 ± 125.8	588.2 ± 146.6	NS	598.7 ± 133.6	NS
VT <sub>pat</sub> /VT <sub>mecc</sub> (%)	71%	83%	<i>p</i> < 0.01	61%	<i>p</i> = 0.01
Swing <sub>Pdi</sub> (cmH <sub>2</sub> O)	7.8 ± 3.3	8.4 ± 2.6	NS	8.2 ± 3.1	NS
PTPdi/breath (cmH <sub>2</sub> O/s)	6.5 ± 2.9	8.7 ± 4.5	NS	5.8 ± 2.4	NS
PTPdi/min (cmH <sub>2</sub> O)	142.6 ± 63.3	182.2 ± 94.2	NS	123.2 ± 57.8	NS
PTPdi/L (cmH <sub>2</sub> O/s/L)	21.5 ± 13.7	19.1 ± 10.8	NS	25.7 ± 12.3	NS

NS not statistically significant

<sup>a</sup> Mechanical and neural respiratory rate (RR<sub>flow</sub> and RR<sub>neu</sub>, respectively), mechanical and neural inspiratory time (Ti<sub>flow</sub> and Ti<sub>neu</sub>, respectively), mechanical and neural respiratory pattern (Ti<sub>flow</sub>/Ttot and Ti<sub>neu</sub>/Ttot, respectively), mechanical and patient

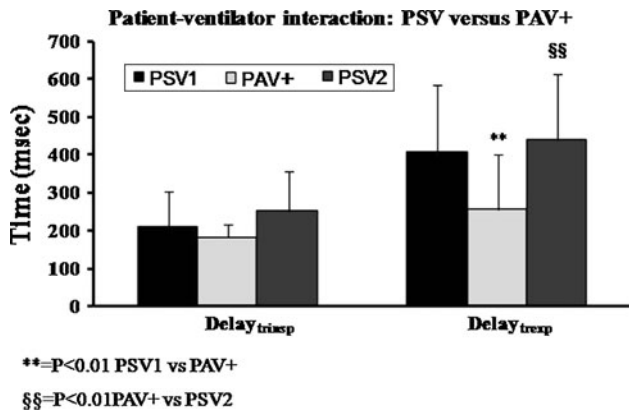
tidal volume (VT<sub>mecc</sub> and VT<sub>pat</sub>), tidal excursion of transdiaphragmatic pressure (swing<sub>Pdi</sub>), and pressure–time product of the transdiaphragmatic pressure per breath and per minute (PTPdi/breath, PTPdi/min and PTPdi/L)

shown in Table 2, no significant differences were observed between PSV1–PAV+–PSV2 in terms of gas exchange and respiratory pattern, nor Ti<sub>flow</sub>, Ti<sub>flow</sub>/Ttot, or Ti<sub>pat</sub>/Ttot (Table 2). Compared to PAV+, during PSV1 and PSV2, Ti<sub>pat</sub> was significantly shorter than Ti<sub>flow</sub> (*p* < 0.05), showing a trend toward a prolongation between PSV1 and PAV+ that was significant between PAV+ and PSV2 (*p* < 0.05).

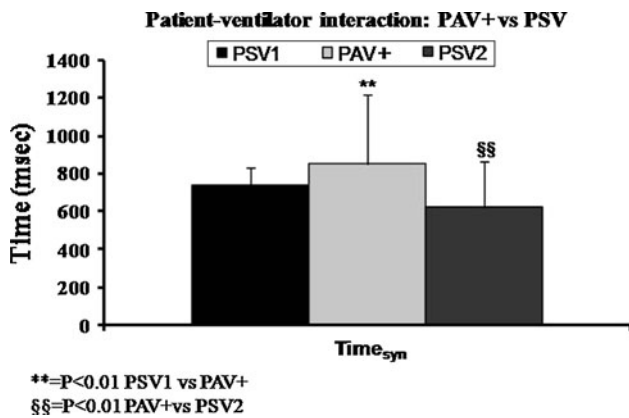
The inspiratory effort evaluated through the analysis of swing<sub>Pdi</sub> did not show significant differences between the three trials; nor did PTPdi per breath and per minute. However, all these parameters showed a trend toward an increase during PAV+ compared to the two trials of PSV.

Concerning patient–ventilator interaction, we did not observe significant differences in terms of delay<sub>trinsp</sub> during the three trials. Conversely, compared to PSV1 and PSV2, PAV+ significantly reduced delay<sub>trexp</sub> (*p* < 0.001) (Fig. 2). The reduction of delay<sub>trexp</sub> during PAV+ significantly increased the percentage of VT delivered in phase with Ti<sub>pat</sub> (VT<sub>pat</sub>/VT<sub>mecc</sub>): 83% with PAV+ versus 70 and 61% with PSV1 and PSV2, respectively, *p* < 0.01 (Table 2). No patient exhibited expiratory muscles recruitment.

Finally, the time<sub>syn</sub> was significantly longer during PAV+ than during PSV1 and PSV2 (899.6 ± 368.5 ms during PAV+ vs. 697.8 ± 280.8 ms during PSV1 and 619.9 ± 244.1 ms during PSV2, *p* < 0.001) (Fig. 3).



**Fig. 2** Inspiratory trigger delay ( $\text{delay}_{\text{trinsp}}$ ) and expiratory trigger delay ( $\text{delay}_{\text{trexp}}$ ) during PSV1–PAV+–PSV2



**Fig. 3** Time of synchrony ( $\text{time}_{\text{syn}}$ ) is the time during which patient and ventilator are in phase

During PSV (both trials) 5 patients out of 11 (45%) showed the presence of wasted effort with an AI greater than 10%, whereas no wasted effort was observed during PAV+. No autocycling was observed during the whole course of the study with both modes of ventilation.

## Discussion

We conducted this physiologic clinical study to compare patient–ventilator synchrony in patients receiving PSV and PAV+. Whereas no difference in gas exchange, respiratory pattern, and inspiratory effort was reported, PAV+ significantly decreased the  $\text{delay}_{\text{trexp}}$  and significantly increased the  $\text{time}_{\text{syn}}$ . In particular, we found that the portion of VT delivered in phase with  $T_{i\text{pat}}$  ( $\text{VT}_{\text{pat}}/\text{VT}_{\text{mecc}}$ ) was significantly higher during PAV+ compared to both trials of PSV (83% with PAV+ vs. 71 and 61% with PSV1 and PSV2, respectively,  $p < 0.01$ ).

Accordingly, both during PSV1 and PSV2 we observed an increased incidence of major asynchronies, causing an AI greater than 10%, compared to 0% during PAV+.

During the conventional modes of assisted MV, patient–ventilator asynchronies are likely to be present, and some authors demonstrated that weaning is often less successful when there is a high incidence of asynchronies [8, 9]. PAV+ could improve patient–ventilator interaction. Kondili et al. [18] evaluated the short-term response of respiratory motor output to an increased mechanical load during PAV+ and PSV in a group of ten critically ill patients. At similar gas exchange, the load-on trial increased RR and VT, the latter significantly smaller during PAV+ than during PSV ( $p < 0.05$ ). Moreover, the authors found that, whereas without load both modalities provided an adequate ventilator assistance, the increased inspiratory effort induced by the increased load was significantly lower during PAV+ than during PSV ( $p < 0.05$ ), concluding that the short-term compensation to an increased mechanical load is more efficient during PAV+ than during PSV.

More recently, the same group investigated the efficacy of PAV+ and PSV in a randomized controlled study in a group of 208 critically ill patients, recovering from controlled MV [19]. The patients were randomized to receive PAV+ or PSV for 48 h, unless they met failure criteria or were able to breathe without ventilator assistance. The main result of their study was that the failure rate (patient switched back to controlled mode) during the 48 h of trial was significantly lower in the PAV+ group compared to the PSV group (11.1 vs. 22.0%,  $p = 0.04$ ). The authors concluded that with a significantly lower percentage of major patient–ventilator asynchronies ( $p < 0.001$ ) during PAV+ than during PSV, PAV+ increases the probability of remaining on assisted breathing by reducing the incidence of major patient–ventilator asynchronies. Unfortunately, the authors evaluated patient ventilator asynchronies only noninvasively on the ventilator flow tracings, and not systematically on esophageal pressure tracings. As a consequence, they probably under-reported the major asynchronies, and did not evaluate minor but important asynchronies such as inspiratory and expiratory delays.

In this study we have systematically investigated the incidence of both minor and major patient–ventilator asynchronies during PAV+ and PSV. It has been frequently reported that the prolongation of the mechanical insufflation is likely to occur during PSV and it can, especially at high level of assistance, worsen patient–ventilator interaction by increasing the risk of hyperinflation and of subsequent wasted efforts [6, 7, 11]. In our patients PSV prolonged  $\text{delay}_{\text{trexp}}$  and, as a result, half of mechanical VT on PSV was delivered during patient exhalation without expiratory muscles recruitment (i.e., passive inflation). During PAV+ we did not find significant differences in terms of the size of mechanical VT

delivered to the patients compared to PSV1 and 2; however, the significant reduction of the delay<sub>tr<sub>exp</sub></sub> during PAV+ reduced the portion of VT delivered during passive inflation. These results can explain the trend toward an increase in inspiratory effort during PAV+, compared to PSV1 and 2, related to the increase in VT generated by the patients, as shown by the reduction of the PTPdi/L.

values of inspiratory rise time and cycling off: however, it is important to note that this level of inspiratory rise time has been demonstrated as being optimal by Chiumello et al. in a group of patients with similar clinical conditions at similar values of applied PEEP and PSV. Finally, being a short-term study, few assumptions can be made in terms of medium- and long-term clinical results.

### Limitations of the study

This is a physiologic study, performed in a relatively small sample of selected patients with specific clinical characteristics (difficult to wean surgical patients). We decided to exclude patients with COPD, in whom the presence of intrinsic PEEP may additionally alter patient-ventilator interaction both during PSV and PAV+. Moreover PSV has been set in all patients with similar

### Conclusion

The results of this physiologic study suggest that when PSV is optimized and PAV+ is set at the same mean Paw, similar values of gas exchange, respiratory pattern, and inspiratory effort are obtained, but PAV+ improves patient-ventilator interaction, significantly reducing the incidence of end-expiratory asynchrony, increasing the time of assistance, and reducing the AI.

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