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Comparison of Inspiratory Effort, Workload and Cycling Synchronization Between Non-Invasive Proportional-Assist Ventilation and Pressure-Support Ventilation Using Different Models of Respiratory Mechanics

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Background: This study assessed lung models for the influence of respiratory mechanics and inspiratory effort on breathing pattern and simulator-ventilator cycling synchronization in non-invasive ventilation.

Material/Methods: A Respironics V60 ventilator was connected to an active lung simulator modeling mildly restrictive, severely restrictive, obstructive and mixed obstructive/restrictive profiles. Pressure-support ventilation (PSV) and proportional-assist ventilation (PAV) were set to obtain similar tidal volume (V_T). PAV was applied at flow assist (FA) 40–90% of resistance (Rrs) and volume assist (VA) 40–90% of elastance (Ers). Measurements were performed with system air leak of 25–28 L/minute. Ventilator performance and simulator-ventilator asynchrony were evaluated.

Results: At comparable V_T, PAV had slightly lower peak inspiratory flow and higher driving pressure compared with PSV. Premature cycling occurred in the obstructive, severely restrictive and mildly restrictive models. During PAV, time for airway pressure to achieve 90% of maximum during inspiration (T90) in the severely restrictive model was shorter than those of the obstructive and mixed obstructive/restrictive models and close to that measured in the PSV mode. Increasing FA level reduced inspiratory trigger workload (PTP_{300}) in obstructive and mixed obstructive/restrictive models. Increasing FA level decreased inspiratory time (T_I) and tended to aggravate premature cycling, whereas increasing VA level attenuated this effect.

Conclusions: PAV with an appropriate combination of FA and VA decreases work of breathing during the inspiratory phase and improves simulator-ventilator cycling synchrony. FA has greater impact than VA in the adaptation to inspiratory effort demand. High VA level might help improve cycling synchrony.

MeSH Keywords: **Pulmonary Medicine • Recycling • Ventilation**

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Background

Patient-ventilator synchrony is an important goal of assisted mechanical ventilation that reduces a patient's inspiratory workload. Meanwhile, patient-ventilator asynchrony is associated with complications such as prolonged mechanical ventilation, deterioration of tolerance, and increased mortality [1–3]. Proportional-assist ventilation (PAV), a ventilation mode reported by Younes in 1992, first introduced the notion of "positive-feedback" ventilation [4]. In principle, PAV can generate assistance proportional to the patient's effort, thereby decreasing respiratory muscle burden, improving ventilation and oxygenation, reducing the symptoms of dyspnea, and achieving better patient-machine synchronization. The concept underlying PAV is that the characteristics of mechanical ventilation are adapted to those of the patient's respiratory center drive, including tidal volume (V_T), inspiratory flow, and durations of inspiration and expiration [5–9].

Achieving optimal PAV is challenging. Evidence indicates that the level of PAV affects inspiratory cycling [7,10,11]. Moreover, widespread clinical application of PAV, especially during non-invasive ventilation, has been limited by the necessity to perform regular measurements of respiratory mechanics (resistance and elastance) and timely adjustments in the level of assistance when the patient's demand is altered. Excessive compensation results in run-away and hyperinflation, whereas under-compensation leads to insufficient inspiratory support [12]. Recently, a new software was developed (PAV+, Covidien) that automatically estimates the mechanics of the respiratory system by the mini-occlusion technology and provides a constant level of assistance after measurements of resistant and elastic elements [13]. Nonetheless, respiratory mechanics cannot be monitored precisely during non-invasive ventilation because air leak always exists and dynamically changes. Meanwhile, how changes in airway resistance, static compliance of the patient's respiratory system and PAV assist level affect the degree of patient-ventilator cycling synchrony in the PAV mode remains unclear [14–17].

The aim of this bench study was to investigate how different levels of PAV assistance affected the workload and synchrony in a mechanical model of patients with respiratory failure. Changes in respiratory mechanics to mimic disease states, such as restrictive and obstructive conditions, and the level of assistance provided by PAV are likely to alter the breathing pattern and simulator-ventilator synchronization. Another important aim was to compare ventilation and synchronization variables between PAV and pressure-support ventilation (PSV) at a similar level of V_T.

Material and Methods

Lung models

The present bench study employed different lung models to assess the influences of respiratory mechanics and inspiratory effort on breathing pattern and simulator-ventilator cycling synchronization in PSV and PAV. The ASL 5000 Breathing Simulator (IngMar Medical Ltd., USA) features a computerized lung simulator comprising a piston moving in a cylinder. The simulator was a single compartment according to the work of Beloncle and colleagues [15]. Respiratory mechanics conditions were adjusted to simulate an adult patient placed in the semi-recumbent position (inclination of 45°). Four respiratory mechanics conditions were preset: mildly restrictive (Rrs [resistance]=5 $cmH_2O/L/s$, Crs [compliance]=50 mL/cmH_2O and rate=15 breaths/min); obstructive (Rrs=20 $cmH_2O/L/s$, Crs=50 mL/cmH_2O and rate=15 breaths/min); severely restrictive (Rrs=5 $cmH_2O/L/s$, Crs=25 mL/cmH_2O and rate = 30 breaths/min); mixed obstructive and restrictive (Rrs=20 $cmH_2O/L/s$, Crs=25 mL/cmH_2O and rate=15 breaths/min). The inspiratory time was set at 0.8 seconds for the severely restrictive condition and 1.6 seconds for the remaining 3 conditions [18–20]. The simulator's inspiratory effort was –5 cmH_2O for the mildly restrictive, obstructive and mixed obstructive/restrictive conditions and –10 cmH_2O for the severely restrictive condition. Pressure reduction produced 300 ms following initiation of an obstructed inspiratory effort was –5 cmH_2O. A semi-sinusoidal inspiratory waveform was chosen with rise and release times each of 50% and an inspiratory hold time of 0%. The simulator integrates user-controlled leaks using a plateau exhalation valve (PEV). In the current study, leak flow was controlled between 25 L/min and 28 L/min with 20 cmH_2O peak airway pressure. Inspired oxygen fraction (F_IO_2) was maintained at 0.21 for various measurements.

The patient-mask interface was simulated by a mannequin head. Endotracheal tubes (inner diameter, 22 mm) placed in mouth and nostrils directed the gas from facemask to simulator. An oro-nasal facemask without exhalation ports (BestFit™; Curative Medical Inc., USA) was fastened firmly to the mannequin head by means of standard straps. A leak flow below 2–3 L/min was obtained at 20 cmH_2O positive pressure after PEV removal (Figure 1).

Ventilator settings

A Respironics V60 Bilevel Ventilator (Philips, USA) was linked to the lung simulator via a 2.0-m long single-use, single limb, corrugated circuit with an expiratory valve. This bench study was performed using a dry circuit.

The ventilator was calibrated and configured in the PSV mode. The ventilator's parameters were set according to respiratory

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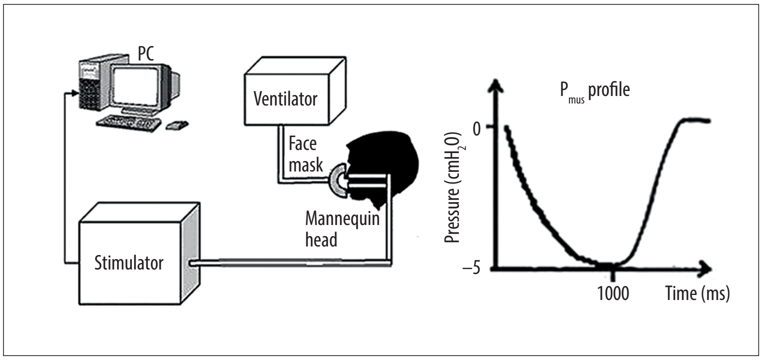

Figure 1. Experimental setup. The patient-mask interface was simulated by a mannequin head. The ventilator, facemask, simulator and computer are depicted. P_{mus} – pressure applied by the respiratory muscles.

mechanics profiles: positive end-expiratory pressure (PEEP) and pressure support levels were 5 cmH_2O and 10 cmH_2O, respectively, for the obstructive and severely restrictive profiles; 5 cmH_2O and 5 cmH_2O, respectively, for the mildly restrictive profile; and 5 cmH_2O and 15 cmH_2O, respectively, for the mixed obstructive/restrictive profile. The back-up respiratory rate was 10 breaths/min, and the maximal duration of the inspiratory phase was 2.0 second. The fastest value was selected for inspiratory rise time, and trigger sensitivity and cycling criteria were auto-adjusted (digital Auto-Trak™) [21].

The parameters of the PAV mode were adjusted as follows. First, volume assist (VA) level was set at 75% of the elastance (Ers=1/Crs), and flow assist (FA) level varied between 40% and 90% of Rrs. Then, FA level was set at 50% of Rrs and VA level varied from 40% to 90% of Ers. The PEEP, back-up respiratory rate and maximal inspiratory time were as described for the PSV mode. The high V_T alarm level was 1000 mL, with the high airway pressure alarm at 40 cmH_2O.

Protocol description

After baseline pressure stabilization, air leaks from the PEV were supplemented to the system, with ≥5 min allowed for ventilator/simulator synchronization. In case of synchronization failure, sensitivity and/or inspiratory effort were changed. If synchronization remained unachievable, the ventilator was regarded as not fit for assisted ventilation at that level of leak. Upon stabilization, 10 breaths were recorded at 1-minute intervals. Asynchrony (auto- or inefficient triggering) was not recorded in this study. When run-away occurs during mechanical ventilation, the ventilator may not provide normal and stable ventilation support. Normal ventilation is interrupted after frequent alarms. At this time, the data of each parameter is abnormal and cannot be used for statistical analysis.

Data collection

After each setting adjustment, 10 measurements were recorded, resulting in 10 measurements/cases. Offline assessment of all breaths was carried out with the software provided with the ASL 5000 Breathing Simulator. The inspiratory triggering workload and cycling delay were assessed, as major determinants of the interaction between the simulator and ventilator. The parameters measured included work of breathing (WOB) and inspiratory pressure-time product at 300 ms (PTP_{300}). The V_T was monitored by the simulator. The mean inspiratory flow rate was calculated as the ratio between V_T and inspiratory time (T_I). The driving pressure (ΔP) was calculated as: PIP – PEEP. In the inspiratory phase, peak inspiratory flow (PIF), peak inspiratory pressure (PIP), T_I and time between ventilator and airway pressure achieving 90% of its peak during inspiration (T90) were measured by the simulator. The pressure of respiratory muscles (P_{mus}) during PAV can be estimated by the following equation: P_{mus}=(PIP–PEEP)×[(100–proportion)/proportion], where "proportion" is the percentage of assistance [22].

Definitions

V_T was the volume of air displaced between normal inhalation and exhalation. PTP_{300} was determined as the area under the pressure-time curve from the beginning of inspiratory effort to return to atmospheric pressure or the preset PEEP. WOBp/tot was the percentage of inspiratory workload in the total workload of respiration. The total workload of respiration includes the inspiratory workload of the simulator and the workload of the ventilator from overcoming the resistance of the respiratory system during assisted ventilation. Cycling delay time (Cdelay) was the time from inspiratory effort completion (simulator) to the ventilator cycling from inspiration to expiration. Negative Cdelay indicates premature cycling, while a positive value indicates that pressurization lasts more than inspiratory effort (cycling delay) [23].

Statistical analysis

Data are presented as mean±standard deviation (SD). SPSS 19.0 (IBM Corp., USA) was employed for all statistical analyses. Variables obtained at various cycling sensitivities were evaluated by one-way ANOVA. The Student's *t*-test was used to compare 2 groups of data. *P*<0.05 indicated statistical significance.

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Table 1. Ventilation and synchronization variables in the obstructive profile in the presence of system leaks.

	V_T (mL)	T_I (ms)	T90 (ms)	PIF (L/min)	V_T/T_I (L/min)	Cdelay (L/min)	ΔPaw (cmH_2O)	PTP_{300} ($cmH_2O\cdot ms$)	WOBp/tot (%)
PSV	**488±3.8**	**1394±15.1**	**354±7.6**	**46±0.4**	**21±0.2**	**−101±7.3**	**11±0.2**	**17±0.9**	**31±0.2**
40%FA+75%VA	294±6.5	1273±28.7	660±11.6	22±0.6	14±0.5	−293±3.0	7±0.12	17±0.9	48±1.5
50%FA+75%VA	363±7.0	1321±18.5	644±18.3	27±0.5	17±0.5	−203±7.6	9±0.3	16±0.8	41±0.9
60%FA+75%VA	434±13.9	1247±28.3	522±34.4	43±1.6	21±0.9	−248±6.9	15±0.9	12±0.6	36±2.9
65%FA+75%VA	473±16.6	1102±19.3	481±15.9	46±1.1	26±0.4	−375±7.8	15±0.6	11±0.7	33±1.4
50%FA+40%VA	232±5.9	1224±12.9	448±23.3	19±0.5	11±0.3	−322±23.4	5±0.2	32±2.8	62±2.5
50%FA+50%VA	288±4.6	1259±15.6	524±12.6	24±0.6	14±0.2	−290±11.1	6±0.1	21±0.9	49±1.5
50%FA+60%VA	296±4.9	1263±18.9	547±10.3	23±0.3	14±0.3	−249±11.1	6±0.2	21±1.7	47±1.9
50%FA+70%VA	339±4.9	1292±16.9	592±17.7	26±0.3	16±0.3	−210±13.9	8±0.1	21±1.5	41±1.1
50%FA+80%VA	399±5.0	1368±19.3	516±13.9	28±0.6	17±0.3	−118±6.1	10±0.2	15±0.9	40±1.4
50%FA+90%VA	**472±4.2**	**1445±20.7**	**473±16.3**	**32±0.3**	**20±0.3**	**−61.5±8.0**	**13±0.3**	**14±0.4**	**31±1.1**
*P**	N.S.	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Cdelay – cycling delay time; FA – flow assist; N.S. – not significant; ΔPa – driving pressure (peak inspiratory pressure minus positive end-expiratory pressure); PIF – peak inspiratory flow; PSV – pressure-support ventilation; PTP_{300} – inspiratory pressure-time product at 300 ms; T90 – time for airway pressure to achieve 90% of maximum during inspiration; T_I – inspiratory time; VA – volume assist; V_T – tidal volume; WOBp/tot – simulator's inspiratory workload as percentage of total work of breathing. * *P*-values (Student *t*-test) are for comparisons between the PSV group and the 50%FA+90%VA group. Data are shown as mean±standard deviation and are the results of 10 measurements/cases.

Results

General performance of PAV

The Respironics V60 ventilator could cope with air leaks (25–28 L/min) without requiring the triggering settings to be adjusted. When the ventilator was used according to the preset FA and VA values, run-away occurred frequently. In all cases, failure to synchronize resulted in rapid auto-triggering or an ineffective triggering. As run-away occurred during the severely restrictive and mixed obstructive/restrictive profiles despite FA level adjustments this data is not provided for comparison.

Ventilation and synchronization variables in PAV and PSV at the same level of V_T

An important aim of this study was to compare ventilation and synchronization variables between PAV and PSV at a similar level of V_T (i.e., with no significant difference in V_T between PAV and PSV). Ventilation and synchronization variables for the obstructive, severely restrictive, mixed obstructive/restrictive and mildly restrictive profiles are shown in Tables 1–4, respectively. At a similar level of V_T, the driving pressure was significantly higher for PAV compared with PSV in the obstructive (13.47±0.34 versus 10.67±0.16 cmH_2O, *P*<0.001), severely restrictive (13.35±0.23 versus 10.32±0.17 cmH_2O, *P*<0.001) and mildly restrictive (6.32±0.16 versus 5.32±0.04 cmH_2O, *P*<0.001) profiles, but lower in the mixed obstructive/restrictive profile (15.51±0.63 versus 15.89±0.33 cmH_2O, *P*<0.001). At a similar V_T level, PIF was significantly lower for PAV compared with PSV in all 4 respiratory mechanics profiles (obstructive, 32.08±0.34 versus 46.38±0.38 L/min; severely restrictive, 65.26±0.67 versus 96.74±1.41 L/min; mixed obstructive/restrictive, 34.12±1.03 versus 51.74±0.62 L/min; mildly restrictive, 45.96±0.87 versus 58.94±0.46 L/min; all *P*<0.001). T_I was significantly prolonged for PAV in comparison with PSV (at similar V_T) in the obstructive (1445.0±20.7 versus 1394.0±15.1 ms, *P*<0.001) and severely restrictive (647.7±7.0 versus 563.8±5.1 ms, *P*<0.001) profiles, but shorter in the mixed obstructive/restrictive (961.3±15.5 versus 982.5±21.4 ms, *P*<0.001) and mildly restrictive (949.7±16.8 versus 1012.8±11.7 ms, *P*<0.001) profiles. T90 was significantly prolonged for PAV compared with PSV (at comparable V_T) in the obstructive (473.1±16.3 versus 353.5±7.6 ms, *P*<0.001), mixed obstructive/restrictive (404.0±12.3 versus 387.2±17.8 ms, *P*<0.001) and mildly restrictive (366.6±7.5 versus 294.1±6.5 ms, *P*<0.001) profiles, but shorter in the severely restrictive profile (205.0±2.2 versus 234.4±4.8 ms, *P*<0.001). PTP_{300} was significantly lower for PAV

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Table 2. Ventilation and synchronization variables in the severely restrictive profile in the presence of system leaks.

	V_T (mL)	T_I (ms)	T90 (ms)	PIF (L/min)	V_T/T_I (L/min)	Cdelay (L/min)	ΔPaw (cmH_2O)	PTP_{300} (cmH_2O·ms)	WOBp/tot (%)
PSV	**484±3.3**	**564±5.1**	**234±4.8**	**97±1.4**	**52±0.5**	**−240±5.3**	**10±0.2**	**1237±33**	**47±0.7**
50%FA+40%VA	**500±5.1**	**648±7.0**	**205±2.2**	**65±0.7**	**46±0.8**	**−179±8.6**	**13±0.2**	**208±6.9**	**56±1.3**
50%FA+50%VA	528±3.5	649±3.3	214±2.1	75±0.9	49±0.4	−143±6.6	15±0.3	309±8.1	54±1.0
50%FA+60%VA	601±12.3	719±8.7	226±3.7	85±1.1	50±1.4	−67±4.5	20±0.5	381±7.8	44±0.9
*P**	N.S.	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Cdelay – cycling delay time; FA – flow assist; N.S. – not significant; ΔPaw – driving pressure (peak inspiratory pressure minus positive end-expiratory pressure); PIF – peak inspiratory flow; PSV – pressure-support ventilation; PTP_{300} – inspiratory pressure-time product at 300 ms; T90 – time for airway pressure to achieve 90% of maximum during inspiration; T_I – inspiratory time; VA – volume assist; V_T – tidal volume; WOBp/tot – simulator's inspiratory workload as percentage of total work of breathing. * *P*-values (Student *t*-test) are for comparisons between the PSV group and the 50%FA+40%VA group. Data are shown as mean±standard deviation and are the results of 10 measurements/cases.

Table 3. Ventilation and synchronization variables in the mixed obstructive/restrictive profile in the presence of system leaks.

	V_T (mL)	T_I (ms)	T90 (ms)	PIF (L/min)	V_T/T_I (L/min)	Cdelay (L/min)	ΔPaw (cmH_2O)	PTP_{300} (cmH_2O·ms)	WOBp/tot (%)
PSV	**372±3.7**	**983±21.4**	**387±17.8**	**52±0.6**	**21±0.5**	**185±9.0**	**16±0.3**	**13±1.3**	**24±0.3**
40%FA+75%VA	233±8.5	986±11.3	400±10.0	27±3.7	14±0.6	−63±17.6	10±0.4	17±2.3	39±2.6
50%FA+75%VA	**281±8.8**	**961±15.5**	**404±12.3**	**34±1.0**	**18±0.5**	**−99±9.7**	**16±0.6**	**12±0.9**	**36±1.8**
50%FA+40%VA	176±2.5	872±16.5	454±11.0	23±0.6	12±0.2	−147±910.0	6±0.2	21±3.3	50±0.9
50%FA+50%VA	191±3.6	912±16.7	458±5.8	24±0.5	13±0.5	−112±12.1	7±0.3	20±1.7	45±2.3
50%FA+60%VA	224±2.9	942±15.9	540±8.4	27±0.6	14±0.2	−74±12.0	10±0.5	16±0.8	36±1.1
50%FA+70%VA	279±4.9	966±32.3	560±13.2	31±0.62	17±0.7	−26±10	13±0.4	14±0.5	37±2.5
*P**	N.S.	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Cdelay – cycling delay time; FA – flow assist; N.S. – not significant; ΔPaw – driving pressure (peak inspiratory pressure minus positive end-expiratory pressure); PIF – peak inspiratory flow; PSV – pressure-support ventilation; PTP_{300} – inspiratory pressure-time product at 300 ms; T90 – time for airway pressure to achieve 90% of maximum during inspiration; T_I – inspiratory time; VA – volume assist; V_T – tidal volume; WOBp/tot – simulator's inspiratory workload as percentage of total work of breathing. * *P*-values (Student *t*-test) are for comparisons between the PSV group and the 50%FA+40%VA group. Data are shown as mean±standard deviation and are the results of 10 measurements/cases. * *P*-values (Student *t*-test) are for comparisons between the PSV group and the 50%FA+75%VA group. Data are shown as mean±standard deviation and are the results of 10 measurements/cases.

compared with PSV in all 4 profiles (obstructive, 15.42±0.86 versus 16.54±0.91 cmH_2O·ms; severely restrictive, 208.34±6.86 versus 1236.91±32.58 cmH_2O·ms; mixed obstructive/restrictive, 11.53±0.86 versus 13.15±1.28 cmH_2O·ms; mildly restrictive, 33.75±3.17 versus 320.10±13.00 cmH_2O·ms; all $P<0.001$). There were also significant differences between PAV and PSV for Cdelay and WOB (Tables 1, 3, 4).

Premature cycling

During PSV, premature cycling (i.e., a negative Cdelay) was observed in the obstructive, severely restrictive and mildly restrictive models but not in the mixed obstructive/restrictive profile (Tables 1–4). PAV was associated with premature cycling in all 4 profiles. Premature cycling could be minimized by adjusting FA and/or VA values (Tables 1–4). Optimal cycling synchrony during PAV was observed at FA=50% and VA=90% in the obstructive profile, FA=50% and VA=60% in the severely

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Table 4. Ventilation and synchronization variables in the mildly restrictive profile in the presence of system leaks.

	V_T (mL)	T_I (ms)	T90 (ms)	PIF (L/min)	V_T/T_I (L/min)	Cdelay (L/min)	ΔPaw (cmH_2O)	PTP_{300} (cmH_2O·ms)	WOBp/tot (%)
PSV	**476±1.4**	**1013±11.7**	**294±6.6**	**59±0.5**	**28±0.3**	**–556±11.9**	**5±0.04**	**320±13.0**	**45±0.3**
40%FA+75%VA	818±11.5	1229±22.1	464±11.1	60±0.6	40±1.4	–240±27	15±0.6	59±4.1	33±1.1
50%FA+75%VA	834±8.8	1128±25.8	509±13.7	67±0.8	44±1.0	–208±11.3	17±0.5	82±3.3	33±1.4
60%FA+75%VA	905±18.6	1015±19.3	504±9.4	73±1.3	54±1.2	–366±19.9	18±0.3	153±7.9	30±0.4
70%FA+75%VA	970±10.8	1027±21.4	494±9.2	79±1.3	57±1.4	–576±11.2	20±0.5	191±7.8	27±0.8
80%FA+75%VA	1265±38.6	1003±21.8	470±7.6	121±3.9	76±3.0	–569±10.2	27±1.4	304±13.1	22±1.7
50%FA+40%VA	432±5.8	873±6.6	349±5.6	43±0.4	30±0.4	–703±9.2	6±0.2	26±1.0	56±0.5
50%FA+50%VA	**452±7.6**	**950±16.8**	**367±7.5**	**46±0.9**	**29±0.6**	**–633±16.7**	**6±0.2**	**34±3.2**	**55±0.8**
50%FA+60%VA	588±8.6	1045±20.8	420±7.4	50±1.7	34±1.0	–553±7.4	10±0.2	51±3.3	45±1.1
50%FA+70%VA	805±15.9	1175±20.2	461±7.8	60±0.7	41±1.7	–467±7.1	15±0.5	69±3.7	34±1.8
50%FA+80%VA	929±13.0	1119±13.2	548±6.4	75±1.5	50±0.9	–447±9.0	19±0.4	115±4.4	30±0.8
50%FA+90%VA	1187±47	1162±18.4	593±5.9	97±1.2	61±2.9	–378±16.2	25±1.0	177±5.5	21±1.5
P*	N.S.	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Cdelay – cycling delay time; FA – flow assist; N.S. – not significant; ΔPaw – driving pressure (peak inspiratory pressure minus positive end-expiratory pressure); PIF – peak inspiratory flow; PSV – pressure-support ventilation; PTP_{300} – inspiratory pressure-time product at 300 ms; T90 – time for airway pressure to achieve 90% of maximum during inspiration; T_I – inspiratory time; VA – volume assist; V_T – tidal volume; WOBp/tot – simulator's inspiratory workload as percentage of total work of breathing. * *P*-values (Student *t*-test) are for comparisons between the PSV group and the 50%FA+40%VA group. Data are shown as mean±standard deviation and are the results of 10 measurements/cases. * *P*-values (Student *t*-test) are for comparisons between the PSV group and the 50%FA+50%VA group. Data are shown as mean ± standard deviation and are the results of 10 measurements/cases.

restrictive profile, FA=50% and VA=70% in the mixed obstructive/restrictive profile, and FA=50% and VA=75% in the mildly restrictive profile (Figure 2).

Comparison of ventilation and synchronization variables for PAV between different respiratory mechanics models

During PAV, inspiratory T90 in the severely restrictive model was shorter than those of the obstructive and mixed obstructive/restrictive models, and close to that measured in the PSV mode (Tables 1–4). Increasing FA level reduced inspiratory trigger workload (PTP_{300}) in the obstructive and mixed obstructive/restrictive profiles but enhanced it in the mildly restrictive profile (Tables 1–4). The simulator's inspiratory workload as a proportion of total ventilator inspiratory workload was decreased in all models when PAV assistance level was increased (Tables 1–4). Increasing FA level in the PAV mode was associated with gradually decreased T_I and a tendency to aggravate premature cycling, although this was attenuated by VA level increase.

Discussion

An important finding of the present bench study was that ventilator output performance, cycling synchrony, and inspiratory workload were influenced by the respiratory mechanics profile and level of assistance provided by PAV. Moreover, breathing pattern variability was greater for PAV compared with PSV. Notably, PAV reduced simulator-ventilator cycling asynchrony and trigger workload compared with PSV when an appropriate combination of FA and VA was used for each respiratory mechanics profile. In all 4 respiratory mechanics models, cycling asynchrony during PAV was improved by increasing VA level (≥60% of Ers) and using a moderate FA level (50% of Rrs).

There is a paucity of bench studies employing different respiratory mechanics models to specifically compare ventilator performance and simulator-ventilator cycling synchrony between PSV and PAV using the Auto-Trak™ technology. A small number of clinical studies have evaluated patient-ventilator asynchrony in chronic obstructive pulmonary disease (COPD) and cases undergoing resolution for acute respiratory distress syndrome (ARDS), representing clinical scenarios that might correspond

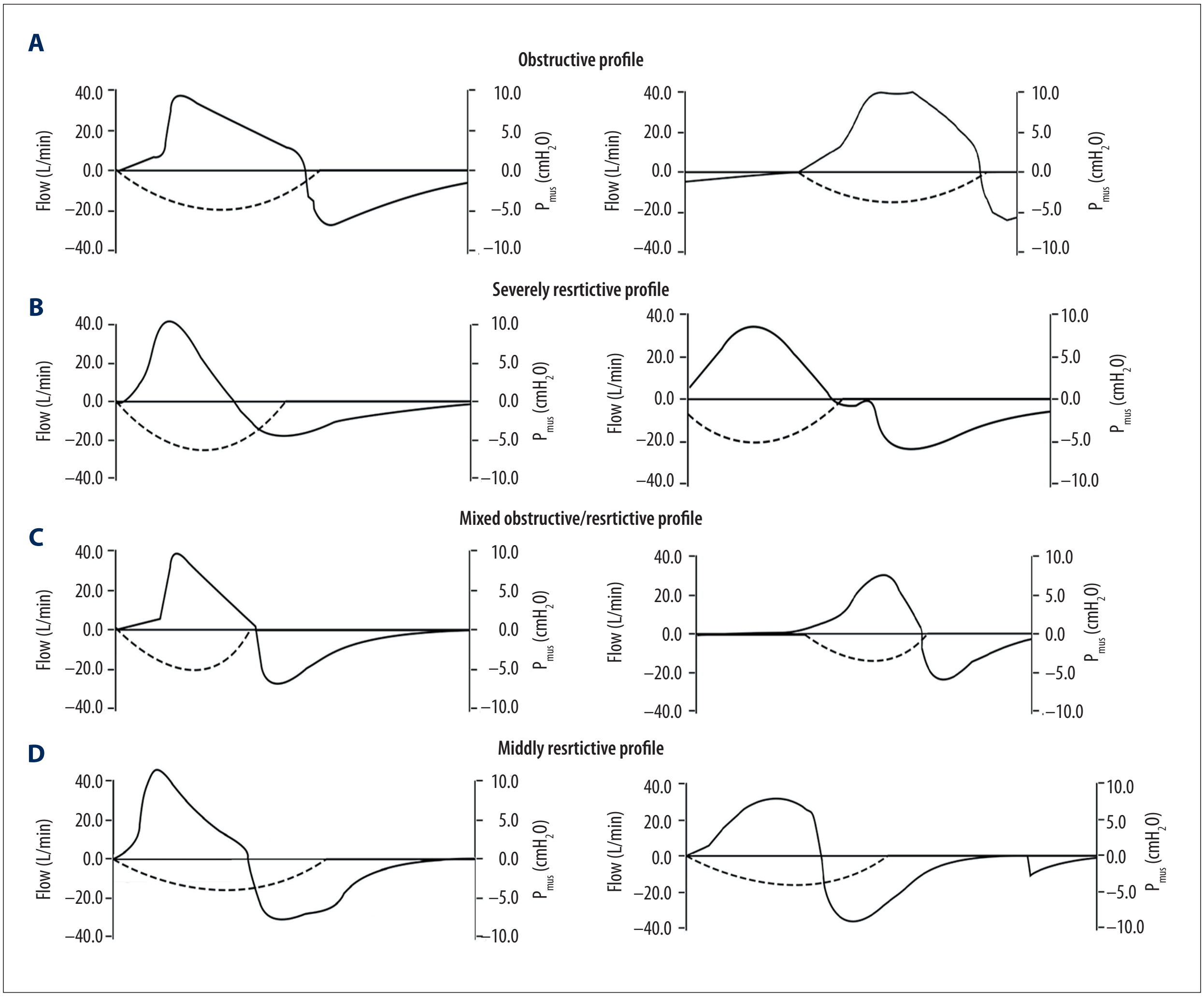

Figure 2. Representative flow waveforms (L/min, solid line, left axis) and respiratory muscle pressure (P_{mus}, cmH_2O, dashed line, right axis) over time for pressure-support ventilation (PSV, **left**) and proportional-assist ventilation (PAV, **right**) in the different respiratory mechanics profiles. (**A**) Obstructive profile; (**B**) severely restrictive profile; (**C**) mixed obstructive/restrictive profile; (**D**) Mildly restrictive profile.

to the obstructive and severely restrictive models used in the present bench study [24–26]. Cycling delay and ineffective efforts are common during PSV in patients with COPD, and premature cycling occurs frequently in patients with ARDS, especially at a threshold of 30% of PIF [25–28]. The current findings do not corroborate the aforementioned observational data, since delay cycling, and ineffective efforts were not observed for PSV in the obstructive or severely restrictive model. It is noteworthy that delay cycling occurred only in the mixed obstructive/restrictive model during PSV, as the cycling threshold was auto adjusted by the instrument's inherent algorithm.

Clinical comparisons of PSV and PAV have shown that PAV with appropriate assistance improves inspiratory trigger workload and cycling synchrony [23]. In addition, previous findings suggest that the level of PAV influences inspiratory cycling [7,10,11]. These previous findings agree with our results that although cycling asynchrony and premature cycling occurred in the PAV mode, they could be eliminated by adjusting the assist proportion. In the present study, PAV could deliver inspiratory flow that matched the inspiratory effort when FA and VA proportions were set appropriately, which improved cycling synchrony. Vasconcelo et al. found that the V_T value for PAV is lower than that of PSV for the same mean airway pressure [29]. Comparable results were obtained in this bench study, i.e., V_T tended to be lower for PAV compared with PSV for a similar driving pressure (see Tables 1–4), irrespective of the respiratory mechanics profile. A potential benefit of lower V_T is that it could reduce the risk of air trapping and ventilatory over-assistance (run-away).

Evaluating respiratory mechanics can enable individualized mechanical ventilation therapy [15], but most mathematical lung

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models developed to date are only suitable for fully sedated patients and/or too complex for use at the bedside [30–32]. Respiratory models of spontaneously breathing patients should simulate the intermittent inspiratory effort by modifying pressure and flow. Patients show spontaneous breathing efforts continuously during non-invasive mechanical ventilation [33]. To individualize ventilatory therapy, it is essential to establish a lung model that simulates the respiratory system mechanics in spontaneously breathing patients and is suitable for real-time use at the bedside. The IngMar ASL 5000 lung simulator was selected in the present investigation. Previous bench studies of mechanical ventilators used mechanical lung simulators [24,34], which better mimic the elastic recoil recorded during exhalation compared with ASL 5000 that seems to display more passive exhalation [35]. This bench study selected a semi-sinusoidal inspiratory waveform, with rise and release times of 50% each, and an inspiratory hold time of 0%.

The aim of this bench study was to evaluate workload and synchrony in a mechanical model of patients with respiratory failure at different levels of PAV assistance. To this end, different respiratory mechanics profiles were designed to simulate conditions such as severe COPD, ARDS and mixed ventilatory dysfunction. The Rrs and Crs values used for the four respiratory mechanics profiles (obstructive, mildly restrictive, severely restrictive and mixed obstructive/restrictive) in this study were based on previously published data. For example, Salihoglu et al. reported dynamic respiratory compliance (Cdyn) and airway resistance (Raw) of 40±8 mL/cmH_2O and 19±4 cmH_2O/L/s, respectively, in intubated patients with COPD in the supine position [36]. In 10 mechanically ventilated patients with acute exacerbations of COPD, Chen et al. determined Raw and Crs to be 17.4±7.6 cmH_2O/L/s and 46.0±23.6 mL/cmH_2O, respectively [37]. Frantzeskaki et al. found an expiratory Ers of 50.16±7.31 cmH_2O/mL in 9 intubated patients with ARDS for only 20.85±3.73 cmH_2O/mL in healthy individuals [38]. Moreover, a study by Razazi et al. reported Crs and Raw values of 32±13 mL/cmH_2O and 22±7 cmH_2O/L/s, respectively, in patients with pleural effusion before drainage [39].

Respiratory system impedance may vary from time to time in mechanically ventilated patients, and Ers and Rrs values change dynamically during inspiration and expiration cycles. PAV was designed to overcome the patient's inspiratory workload by delivering ventilator assistance in proportion to the individual's instantaneous flow and volume, thereby amplifying their actual efforts and overcoming elastic and resistive pressures. During spontaneous breathing, the muscle workload at the initial phase of inspiration is used mainly to overcome Rrs. Ers gradually increases as the alveoli expand; thus, muscle workload is used to overcome Ers particularly at the end of inspiration. When PAV is used, FA mainly compensates for Rrs at the early stage of inspiration to alleviate dyspnea, while VA compensates for Ers and improves alveolar inflation [4–6]. Theoretically, a patient's respiratory muscle load can be reduced to zero when proportional assist level is close to 100%, but run-away (excessive compensation) can easily occur if spontaneous breathing is unstable and/or in case of ventilator tube vibration. Therefore, FA and VA levels usually do not exceed 95%, but there is some debate as to optimal settings. Luo et al. investigated the effects of different assist levels during PAV in cases with acute exacerbations of COPD and found that the level comfortably tolerated by patients is 57±11%; this assist level decreased the trans-diaphragmatic pressure, PTP and WOB by 72%, 65%, and 57%, respectively, and improved dyspnea [40]. Costa et al. observed that a PAV assistance level of 59±10% achieves the same mean airway pressure as PSV [41], while Su et al. found that a PAV assistance level of 60% results in an appropriate muscular effort (5–10 cmH_2O) [42]. Thus, previous clinical studies have suggested that a PAV assist level of 60% may be appropriate. However, the present study has refined this analysis by identifying optimal combinations of FA and VA levels for different respiratory mechanics profiles. This bench study was designed to adjust the PAV assist level to achieve a similar V_T to that obtained in PSV. The P_{mus} during PAV can be estimated by the following equation: P_{mus}=(PIP–PEEP)×[(100–proportion)/proportion], where "proportion" is the percentage of assistance [22]. Carteaux et al. utilized this equation to perform bedside adjustment of PAV assist level to maintain a reasonable respiratory effort [22]. In the present lung model study, the PEEP value was maintained constant regardless of ventilatory mode changes. FA level increase was associated with elevated V_T, PIP, and PIF but decreased T90 and T_I. Moreover, run-away occurred frequently with FA level reaching 70%, which did not benefit synchrony. However, a higher VA level (≥60%) in combination with a FA level of 50% resulted in prolonged T_I and alleviated premature cycling, which would be beneficial to gas distribution and exchange. These findings suggest that FA and VA at the same level provide adequate ventilatory support only in the severely restrictive profile; an FA level of 50–60% Rrs and a higher VA level (≥60% Ers) may be more suitable for the other respiratory mechanics profiles.

Patient-ventilator asynchrony is frequently encountered in invasive and non-invasive mechanical ventilation modes [43]. Auto-triggering as well as severe premature/delayed cycling are promoted by air leaks surrounding the mask and are more reflective of the ventilator's capacity to manage leaks compared with the clinician's settings. This bench study demonstrated that the inherent non-invasive ventilation algorithm of the V60 ventilator (digital Auto-Trak™) achieved stable leak compensation. Previous studies revealed that adjusting auto-adaptive triggering, cycling and leaks might help clinicians spend less time on threshold adjustment and mask refitting [21,23]. However, only one level of air leak was assessed, which may not reproduce the conditions encountered in the clinical setting.

Costa et al. found that mechanical inspiratory time in PSV is significantly longer compared with inspiratory time in a patient with COPD [41]. Notably, Cdelay was reduced during PAV, with the time of synchrony being significantly longer during PAV compared with PSV [41]. In contrast, the present bench study found that mechanical inspiratory time was always shorter than simulator inspiratory time during PSV in the obstructive and restrictive profiles; this might be attributable to the Auto-Trak™ algorithm and simulator settings. Although premature cycling was a potential issue during PAV, it could be eliminated by appropriate adjustment of FA and VA levels. Improved cycling synchrony during PAV could be attained with a higher VA level (≥60%) and a moderate FA level (50%) in the obstructive lung mechanics profile.

This study had some limitations. We used a mechanical model of the respiratory system that might not simulate a real clinical case perfectly; hence, the present results should be confirmed in the clinical setting. Nonetheless, important advantages of the lung simulator are the ability to carry out evaluations under various conditions with good reproducibility and reliability, and avoidance of risks to patients, which are inherent in clinical investigations [43]. In addition, we assessed only pressure triggering (not flow triggering). Pressurization (rise time), which is known to influence mechanical ventilation synchrony [43], was set at the fastest level in PSV. The aim of this study was to compare the ventilation parameters between 2 ventilation models, especially between the different proportional assist strategies of PAV and PSV, in the cases of different mechanical model disease conditions where the ventilator provided the same tidal volume. On the other hand, we did not seek to use 10 cmH_2O of PSV as the standard. The experiments were carried out "at a similar level of V_T, i.e., when there is no significant difference in V_T between PAV and PSV."

Finally, the experimental settings did not include simulation of cardiogenic oscillation, which could cause auto-triggering.

Conclusions

Overall, the present bench study highlights PSV and PAV limitations regarding the prevention of patient-ventilator cycling asynchrony using a mechanical model. The findings of this research have several practical implications. PAV was superior to PSV in that it offered inspiratory support proportional to respiratory muscle effort, avoiding premature cycling and hypoventilation with appropriately adjusted assistance. Appropriate adjustment of FA and VA levels achieved improved simulator-ventilator cycling synchronization and similar ventilatory support compared to PSV. Furthermore, optimal PAV settings reduced the workload in simulated patients with different respiratory mechanics, improved ventilator management and minimized asynchrony. Because PAV needs to provide proportional assistance to the patient's respiratory mechanics parameters, and the patient's respiratory mechanics characteristics change with the disease condition, the lack of assistance can cause insufficient ventilation support, which results in an increase in the patient's respiratory muscle work and respiratory muscle fatigue. On the other hand, excessive assistance causes runaway, leading to ventilation support failure. Therefore, new respiratory mechanics measurement techniques are needed to dynamically, continuously and accurately monitor the patient's respiratory mechanics parameters.

Conflict of interest

None.

References:

1. Thille AW, Rodriguez P, Cabello B et al: Patient-ventilator asynchrony during assisted mechanical ventilation. Intensive Care Med, 2006; 32: 1515–22
2. Kondili E, Prinianakis G, Georgopoulos D: Patient-ventilator interaction. Br J Anaesth, 2003; 91: 106–19
3. Pierson DJ: Patient-ventilator interaction. Respir Care, 2011; 56: 214–28
4. Younes M: Proportional assist ventilation, a new approach to ventilatory support. Theory Am Rev Respir Dis, 1992; 145: 114–20
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. Wrigge H, Golisch W, Zinserling J et al: 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: 790–98
7. 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
8. Hawkins P, Johnson LC, Nikoletou D et al: Proportional assist ventilation as an aid to exercise training in severe chronic obstructive pulmonary disease. Thorax, 2002; 57: 853–59
9. Xirouchaki N, Kondili E, Vaporidi K et al: Proportional assist ventilation with load-adjustable gain factors in critically ill patients: Comparison with pressure support. Intensive Care Med, 2008; 34: 2026–34
10. Ranieri VM, Giuliani R, Mascia L et al: Patient-ventilator interaction during acute hypercapnia: Pressure-support *vs.* proportional-assist ventilation. J Appl Physiol (1985), 1996; 81: 426–36
11. Giannouli E, Webster K, Roberts D, Younes M: Response of ventilator-dependent patients to different levels of pressure support and proportional assist. Am J Respir Crit Care Med, 1999; 159: 1716–25
12. Delaere S, Roeseler J, D'Hoore W et al: Respiratory muscle workload in intubated, spontaneously breathing patients without COPD: Pressure support *vs.* proportional assist ventilation. Intensive Care Med, 2003; 29: 949–54
13. Teixeira SN, Osaku EF, Costa CR et al: Comparison of proportional assist ventilation plus, T-tube ventilation, and pressure support ventilation as spontaneous breathing trials for extubation: A randomized study. Respir Care, 2015; 60: 1527–35
14. Beloncle F, Akoumianaki E, Rittayamai N et al: Accuracy of delivered airway pressure and work of breathing estimation during proportional assist ventilation: A bench study. Ann Intensive Care, 2016; 6: 30

15. Lauzon AM, Bates JH: Estimation of time-varying respiratory mechanical parameters by recursive least squares. J Appl Physiol (1985), 1991; 71: 1159–65
16. Hickling KG: The pressure-volume curve is greatly modified by recruitment. A mathematical model of ARDS lungs. Am J Respir Crit Care Med, 1998; 158: 194–202
17. Donovan GM: Multiscale mathematical models of airway constriction and disease. Pulm Pharmacol Ther, 2011; 24: 533–39
18. Tawhai MH, Bates JH: Multi-scale lung modeling. J Appl Physiol (1985), 2011; 110: 1466–72
19. Grinnan DC, Truwit JD: Clinical review: Respiratory mechanics in spontaneous and assisted ventilation. Crit Care, 2005; 9: 472–84
20. Chen Y, Cheng K, Zhou X: Effectiveness of inspiratory termination synchrony with automatic cycling during noninvasive pressure support ventilation. Med Sci Monit, 2016; 22: 1694–701
21. Carteaux G, Mancebo J, Mercat A et al: Bedside adjustment of proportional assist ventilation to target a predefined range of respiratory effort. Crit Care Med, 2013; 41: 2125–32
22. Vasconcelos Rdos S, Melo LH, Sales RP et al: Effect of an automatic triggering and cycling system on comfort and patient-ventilator synchrony during pressure support ventilation. Respiration, 2013; 86: 497–503
23. Bunburaphong T, Imanaka H, Nishimura M et al: Performance characteristics of bilevel pressure ventilators: A lung model study. Chest, 1997; 111: 1050–60
24. 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: 1283–89
25. Hoff FC, Tucci MR, Amato MB et al: Cycling-off modes during pressure support ventilation: Effects on breathing pattern, patient effort, and comfort. J Crit Care, 2014; 29: 380–85
26. Tokioka H, Tanaka T, Ishizu T et al: The effect of breath termination criterion on breathing patterns and the work of breathing during pressure support ventilation. Anesth Analg, 2001; 92: 161–65
27. Costa R, Navalesi P, Spinazzola G et al: Influence of ventilator settings on patient-ventilator synchrony during pressure support ventilation with different interfaces. Intensive Care Med, 2010; 36: 1363–70
28. Vasconcelos RS, Sales RP, Melo LHP et al: Influences of duration of inspiratory effort, respiratory mechanics, and ventilator type on asynchrony with pressure support and proportional assist ventilation. Respir Care, 2017; 62: 550–57
29. Murata S, Yokoyama K, Sakamoto Y et al: Effects of inspiratory rise time on triggering workload during pressure-support ventilation: A lung model study. Respir Care, 2010; 55: 878–84
30. Ferreira JC, Chipman DW, Kacmarek RM: Trigger performance of mid-level ICU mechanical ventilators during assisted ventilation: A bench study. Intensive Care Med, 2008; 34: 1669–75
31. Marini JJ, Crooke PS 3rd, Truwit JD: Determinants and limits of pressure-preset ventilation: A mathematical model of pressure control. J Appl Physiol (1985), 1989; 67: 1081–92
32. Chiew YS, Pretty C, Docherty PD et al: Time-varying respiratory system elastance: A physiological model for patients who are spontaneously breathing. PLoS One, 2015; 10: e0114847
33. Vignaux L, Tassaux D, Jolliet P: Performance of noninvasive ventilation modes on ICU ventilators during pressure support: A bench model study. Intensive Care Med, 2007; 33: 1444–51
34. Medical I: ASL5000 Active Servo Lung Computerized Breathing Simulator and Ventilator Test Instrument user's manual. 2006
35. Salihoglu Z, Demiroluk S, Baca B et al: Effects of pneumoperitoneum and positioning on respiratory mechanics in chronic obstructive pulmonary disease patients during Nissen fundoplication. Surg Laparosc Endosc Percutan Tech, 2008; 18: 437–40
36. Chen WC, Chen HH, Chiang CH et al: Effect of salmeterol/fluticasone combination on the dynamic changes of lung mechanics in mechanically ventilated COPD patients: A prospective pilot study. Int J Chron Obstruct Pulmon Dis, 2016; 11: 167–74
37. Frantzeskaki F, Amygdalou A, Rasmussen TR et al: Effects of PEEP on inspiratory and expiratory mechanics in adult respiratory distress syndrome. Respir Med, 2003; 97: 159–66
38. Razazi K, Thille AW, Carteaux G et al: Effects of pleural effusion drainage on oxygenation, respiratory mechanics, and hemodynamics in mechanically ventilated patients. Ann Am Thorac Soc, 2014; 11: 1018–24
39. Luo Q, Li Y, Chen RC et al: [Physiologic response to proportional assist ventilation in patients with acute exacerbation of chronic obstructive pulmonary disease]. Zhonghua Jie He He Hu Xi Za Zhi, 2004; 27: 743–47 [in Chinese]
40. Costa R, Spinazzola G, Cipriani F et al: A physiologic comparison of proportional assist ventilation with load-adjustable gain factors (PAV+) versus pressure support ventilation (PSV). Intensive Care Med, 2011; 37: 1494–500
41. Su PL, Kao PS, Lin WC et al: Limited predictability of maximal muscular pressure using the difference between peak airway pressure and positive end-expiratory pressure during proportional assist ventilation (PAV). Crit Care, 2016; 20: 382
42. Vignaux L, Tassaux D, Carteaux G et al: Performance of noninvasive ventilation algorithms on ICU ventilators during pressure support: A clinical study. Intensive Care Med, 2010; 36: 2053–59
43. 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

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