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Effectiveness of Inspiratory Termination Synchrony with Automatic Cycling During Noninvasive Pressure Support Ventilation

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEF 1 **Yuqing Chen**
BCDE 2 **Kewen Cheng**
BCDE 1 **Xin Zhou**

1 Department of Respiratory Medicine, Shanghai First People's Hospital, Shanghai Jiao Tong University, Shanghai, China
2 Department of Respiratory Medicine, Huashan Hospital Baoshan Branch, Fudan University, Shanghai, China

Corresponding Author: Yuqing Chen, e-mail: yqchen1002@sina.com
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Background: Pressure support ventilation (PSV) is a standard method for non-invasive home ventilation. A bench study was designed to compare the effectiveness of patient-ventilator inspiratory termination synchronization with automated and conventional triggering in various respiratory mechanics models.

Material/Methods: Two ventilators, the Respironics V60 and Curative Flexo ST 30, connected to a Hans Rudolph Series 1101 lung simulator, were evaluated using settings that simulate lung mechanics in patients with chronic obstructive pulmonary disease (COPD), acute respiratory distress syndrome (ARDS), or normal lungs. Ventilators were operated with automated (Auto-Trak) or conventional high-, moderate-, and low-sensitivity flow-cycling software algorithms, 5 cmH_2O or 15 cmH_2O pressure support, 5 cmH_2O positive end-expiratory pressure (PEEP), and an air leak of 25–28 L/min.

Results: Both ventilators adapted to the system leak without requiring adjustment of triggering settings. In all simulated lung conditions, automated cycling resulted in shorter triggering delay times (<100 ms) and lower triggering pressure-time product (PTPt) values. Tidal volumes (V_T) increased with lower conventional cycling sensitivity level. In the COPD model, automated cycling had higher leak volumes and shorter cycling delay times than in conventional cycling. Asynchronous events were rare. Inspiratory time (Tinsp), peak expiratory flow (PEF), and cycling off delay time (Cdelay) increased as a result of reduction in conventional cycling sensitivity level. In the ARDS and normal adult lung models, premature cycling was frequent at the high-sensitive cycling level.

Conclusions: Overall, the Auto-Trak protocol showed better patient-machine cycling synchronization than conventional triggering. This was evident by shorter triggering time delays and lower PTPt.

MeSH Keywords: **Lung • Noninvasive Ventilation • Pressure • Ventilators, Mechanical**

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Background

Noninvasive pressure support ventilation (PSV), delivered via a nose- or a face-mask, is widely used because it reduces patient work of breathing (WOB) [1–3]. This is critical for patients with impaired lung mechanics resulting from lung diseases such as COPD or ARDS. The effectiveness of PSV depends on the ability of the ventilator to adjust breath-by-breath inspiratory flow to match the patient's inspiratory demand. Juban et al. reported that some COPD patients recruit their expiratory muscles to terminate inspiration when the ventilator was still inflating the lungs [4]. However, Chiumello et al. observed that the breathing rate and tidal volume could be modified by regulating the flow-cycling criteria in patients recovering from acute lung injury (ALI) [5]. Breathing rate, tidal volume, and inspiratory time depend on the level of pressure support (PS) and the individual patient's lung mechanical properties (impedance and muscle effort) [6]. Each PSV breath is flow-cycled and termination criteria can be either a fixed flow value (e.g., 5 L/min), or a percentage of the peak inspiratory flow (e.g., 25%) [7], referred to as conventional cycling. The ability to adjust flow-cycling criteria to use either conventional or automated regulation software algorithms is now available in many devices [4,8,9].

Patient-ventilator asynchrony, a misalignment between the timing of the ventilator cycle and the patient's respiratory cycle, is very common during assisted ventilation. High levels of asynchrony may prolong the time required for ventilator support and subsequently result in further complications and prolonged weaning from mechanical ventilation [10–12]. Approaches to auto-adjust triggering and cycling have been developed to minimize these problems [13,14]. The aim of this bench study was to evaluate and compare the effects on breathing pattern and patient-ventilator cycling synchronization between automated cycling and conventional flow-cycling protocols during PSV.

Material and Methods

Stimulator settings

The stimulator settings used in this study are consistent with the protocol published by Ferreira et al., with some modifications [15]. The Series 1101 Lung Simulator (Hans Rudolph Inc., Shawnee, KS, USA) is a computerized lung simulator that consists of a piston that moves inside a cylinder. Compliance, resistance, and inspiratory muscle pressure profile (negative pressure created by the respiratory muscles) may be set by the user. The simulator was adjusted to simulate a patient or a healthy adult placed in a semi-reclined position (incline 45°). Three combinations of inspiratory resistance (Rins), expiratory resistance (Rexp), respiratory compliance (Crs), and breathing rate (BR) were set to simulate lung mechanics in a patient with COPD (Rins=20 $cmH_2O/L{\cdot}s^{-1}$, Rexp=20 $cmH_2O/L{\cdot}s^{-1}$, Crs=50 mL/cmH_2O, BR=15 bpm), a patient with ARDS (Rins=5 $cmH_2O/L{\cdot}s^{-1}$, Rexp=5 $cmH_2O/L{\cdot}s^{-1}$, Crs=25 mL/cmH_2O, BR=30 bpm), and normal adult lungs (Rins=5 $cmH_2O/L{\cdot}s^{-1}$, Rexp=5 $cmH_2O/L{\cdot}s^{-1}$, Crs=100 mL/cmH_2O, BR=15 bpm) [16–18]. The inspiratory times of the 3 types of respiratory mechanics (1.0 s for COPD, 0.8 s for ARDS, and 1.5 s for normal adult) were chosen to assess the effect of inspiratory time on triggering and cycling synchronization [19]. Patient inspiratory effort was set at –5 cmH_2O in the 3 patterns of respiratory mechanics, and pressure reduction generated 300 ms after the onset of an occluded inspiratory effort was –3.6 cmH_2O. The simulator incorporates user-controlled leaks by a plateau exhalation valve (PEV). For this experiment, the leak flow was maintained at 25–28 L/min during a peak airway pressure of 20 cmH_2O [20,21]. All measurements were performed at an inspired oxygen fraction of 0.21 (F_IO_2=0.21).

A mannequin head was used to simulate the patient-mask interface. An endotracheal tubes (ID, 22 mm) inserted through the mouth was used to direct gas coming from the facemask to the simulator. A medium-sized oronasal facemask without an exhalation port (BestFit™; Curative Medical Inc., Santa Clara, CA, USA) was affixed tightly to the head of the mannequin with standard straps. A leak of <1–2 L/min was measured at 20 cmH_2O of positive pressure when the PEV was removed.

Ventilator settings

Two bilevel ventilators were compared using the lung simulator with a system leak: V60 (Respironics; Murrysville, PA, USA) and Flexo ST 30 (Curative Medical Inc., Santa Clara, CA, USA). Each ventilator was connected to the lung simulator by a standard disposable corrugated circuit (length, 2.0 m). All the ventilators were studied with a dry circuit. Humidifiers and heat and moisture exchangers were removed.

Both of the ventilators were set in PSV mode, as follows: positive end-expiratory pressure (PEEP), 5 cm H_2O; pressure support (PS) level, 5 cmH_2O (normal adult) and 15 cmH_2O (COPD and ARDS); back-up respiratory rate, 10 breaths/min; maximal duration of the inspiratory phase, 4.0 s. The trigger sensitivity was set to be as sensitive as possible while avoiding auto-triggering. The inspiratory rise time was set to 100 ms.

Data collection

Air leaks generated by the PEV were added sequentially to the system. Once the baseline pressure had stabilized, at least 5 min was allowed for the ventilator to synchronize with the simulator. If synchronization did not occur, changes in sensitivity, inspiratory effort, or both were made and recorded. If

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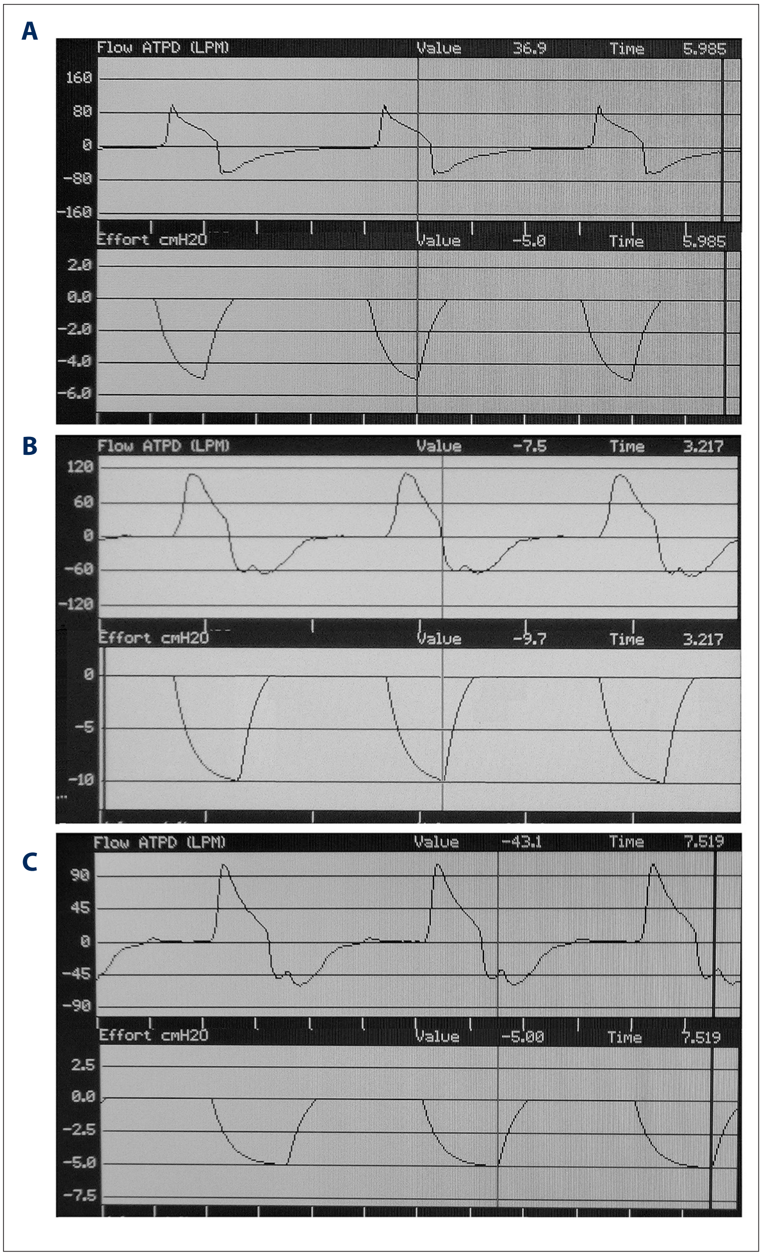

Figure 1. Representative breathing cycles during Auto-Trak protocols in the 3 models. (**A**) Obstructive pattern (COPD). (**B**) Restrictive pattern (ARDS). (**C**) Normal adult pattern.

synchronization was not finally achieved, the ventilator was considered to be unable to provide assisted ventilation at the level of the leak. In all cases, failure to synchronize resulted in rapid auto-triggering or an inability to trigger. After stabilization, 10 representative breaths were collected with a sampling interval of 1 min. Offline analysis of each breath was performed by the Series 1101 lung simulator software.

Inspiratory triggering synchronization was assessed using the triggering delay (Td), the triggering pressure-time product (PTPt). Inspiratory time included ventilator insufflation time (T_I vent), the time between the beginning of the simulated inspiratory effort and the end of the ventilator's insufflation, and T_I simu, the simulated active inspiration time. Cycling delay time (Cdelay) was measured as the time from the end of the inspiratory effort of the simulator to the moment when the ventilator cycled from inspiration to expiration. A negative value reflects premature interruption of pressurization (premature cycling), and a positive value reflects a pressurization time that exceeds the patient's inspiratory effort (delayed cycling) [22].

The peak inspiratory flow (PIF), the peak expiratory flow (PEF), and the inspiratory tidal volume (V_T insp) were monitored by the simulator. The expiratory tidal volume was measured by the ventilator (V_T exp), and the leak volume (V_T leak) was calculated from the difference of V_T insp and V_T exp.

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Table 1. Ventilation and synchronization variables in the COPD patient model with conventional and Auto-Trak protocols ($\bar{\chi}$±s).

Cycling criteria	V_T insp (ml)	V_T exp (ml)	V_T leak (ml)	Breathing rate (bpm)	PIF (L/min)	PEF (L/min)	Tinsp (ms)	Td (ms)	Cdelay (ms)	Insp. flow at cycling/ PIF (%)
Auto-Trak	882.70 ±14.11	670.50 ±28.67	212.20 ±29.06	15	105.66 ±0.42	65.30 ±1.23	944.90 ±21.64	86.90 ±13.76	88.00 ±17.35	14.51 ±2.65
High	857.10 ±13.60	750.70 ±26.65**	106.40 ±27.35**	15	83.76 ±0.44**	58.88 ±0.49**	896.50 ±23.81**	48.00 ±15.49**	51.30 ±12.63**	34.52 ±3.36**
Moderate	879.40 ±14.43	816.00 ±15.71**	63.40 ±17.48** (*t*=4.190) (*P*=0.265)	15	84.11 ±1.00**	65.07 ±0.51	1010.30 ±25.14 (*t*=12.755) (*P*=0.195)	57.00 ±22.14**	162.40 ±15.59*,** (*t*=17.5726) (*P*=0.082)	16.04 ±2.58
Low	962.60 ±17.99* (*t*=38.066) (*P*=0.046)	937.40 ±12.17*,** (*t*=22.077) (*P*=0.001)	25.20 ±7.16*,** (*t*=9.083) (*P*=0.008)	15	83.86 ±0.76**	72.81 ±0.44*,** (*t*=66.535) (*P*=0.056)	3399.70 ±63.12*,** (*t*=117.337) (*P*<0.0001)	57.00 ±22.14**	2522.80 ±55.92*,** (*t*=136.319) (*P*<0.001)	0
F	753.090	285.326	133.731	–	2435.983	585.903	11444.817	8.191	15336.913	320.623
P	<0.001	<0.001	<0.001	–		<0.001	<0.001	<0.001	<0.001	<0.001

Data are plotted as the mean ±SD. * *P*<0.05 *vs.* the highest sensitive level of cycling criteria. ** *P*<0.05 *vs.* the Auto-Trak protocols.

Table 2. Ventilation and synchronization variables in the ARDS patient model with conventional and Auto-Trak protocols ($\bar{\chi}$±s).

Cycling criteria	V_T insp (ml)	V_T exp (ml)	V_T leak (ml)	Breathing rate (bpm)	PIF (L/min)	PEF (L/min)	Tinsp (ms)	Td (ms)	Cdelay (ms)	Insp. flow at cycling/ PIF (%)
Auto-Trak	598.20 ±16.30	480.60 ±14.74	117.60 ±18.64	30	133.32 ±0.83	113.55 ±1.36	717.40 ±25.95	66.00 ±7.75	15.00 ±0.10	4.60 ±0.74
High	548.50 ±14.43**	491.60 ±6.50	56.90 ±8.39**	30	114.21 ±0.77**	62.84 ±1.04**	467.60 ±31.02**	51.00 ±7.75**	-231.70 ±14.50**	34.12 ±4.38**
Moderate	591.40 ±13.13	534.90 ±5.71*,** (*t*=15.831) (*P*<0.001)	56.50 ±7.82**	30	114.29 ±0.67**	90.47 ±1.02*,** (*t*=59.969) (*P*<0.001)	642.00 ±26.87*,** (*t*=13.436) (*P*<0.001)	51.00 ±12.65**	-69.20 ±17.40*,** (*t*=22.686) (*P*<0.001)	15.72 ±2.39*,** (*t*=11.662) (*P*<0.001)
Low	609.90 ±12.85*,** (*t*=36.884) (*P*<0.001)	557.80 ±10.79*,** (*t*=16.619) (*P*<0.001)	52.10 ±11.76**	30	115.29 ±0.54**	110.18 ±1.35* (*t*=136.786) (*P*<0.001)	715.20 ±14.76* (*t*=22.791) (*P*<0.001)	54.00 ±10.49**	15.20 ±0.42*,** (*t*=53.825) (*P*<0.001)	4.26 ±0.78* (*t*=21.228) (*P*<0.001)
F	371.261	246.624	113.689	–	1734.232	9138.618	284.115	5.231	1054.964	301.606
P	<0.001	<0.001	0.465	–	0.02	<0.001	<0.001	0.004	<0.001	<0.001

Data are plotted as the mean ±SD. * *P*<0.05 *vs.* the highest sensitive level of cycling criteria. ** *P*<0.05 *vs.* the Auto-Trak protocols.

Statistical analysis

Data are presented as the mean±standard deviation (SD). Statistical analyses were carried out using the statistical software package, SPSS version 11.0 (SPSS; Chicago, IL, USA). Comparisons of variables at different cycling sensitivity settings were made using the *t* test. A value of *P*<0.05 was considered as statistically significant.

Results

The Respironics V60 and Curative Flexo ST 30 ventilators were able to adapt to the system leak (25–28 L/min) without requiring adjustment of the triggering settings. Representative breathing cycles with Auto-Track setting in the 3 models are shown in Figure 1. As shown in Table 1, the V_T leak differed under the cycling criteria in the COPD model (p<0.001), which was the highest with the Auto-Trak cycling criteria (212.2±29.06 ml) and

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Table 3. Ventilation and synchronization variables in the normal adult model with conventional and Auto-Trak protocols ($\bar{\chi}$±s).

Cycling criteria	V_T insp (ml)	V_T exp (ml)	V_T leak (ml)	Breathing rate (bpm)	PIF (L/min)	PEF (L/min)	Tinsp (ms)	Td (ms)	Cdelay (ms)	Insp. flow at cycling/ PIF (%)
Auto-Trak	930.60 ±13.95	624.80 ±15.39	305.80 ±14.21	15	105.41 ±1.66	58.09 ±1.16	1091.80 ±24.51	48.00 ±13.78	-271.00 ±28.28	15.71 ±1.63
High	852.50 ±14.6**	527.00 ±14.45**	325.50 ±16.04**	15	94.54 ±1.96**	49.34 ±0.87**	878.40 ±19.02**	45.00 ±15.81	-496.00 ±15.81**	37.62 ±2.88
Moderate	948.60 ±15.2* (*t*=43.617) (*P*<0.001)	595.40 ±10.36*,** (*t*=19.182) (*P*=0.037)	353.20 ±12.74*,**	15	93.40 ±1.90**	61.65 ±1.17* (*t*=26.715) (*P*<0.001)	1122.00 ±24.70* (*t*=24.713) (*P*<0.001)	45.00 ±15.81	-225.00 ±15.89* (*t*=38.325) (*P*<0.001)	15.88 ±2.24* (*t*=18.834) (*P*=0.031)
Low	983.20 ±14.96*,** (*t*=60.932) (*P*<0.001)	620.50 ±24.80* (*t*=11.736) (*P*=0.001)	362.70 ±27.01*,**	15	93.82 ±1.86**	96.92 ±1.05*,** (*t*=110.192) (*P*<0.001)	1455.80 ±20.95*,** (*t*=64.537) (*P*<0.001)	60.00 ±20.04	105.10 ±15.82*,** (*t*=84.994) (*P*<0.001)	5.16 ±1.01* (*t*=33.595) (*P*=0.027)
F	1378.341	105.894	28.591	–	376.004	5087.795	1132.113	1.872	1586.363	438.261
P	<0.001	<0.001	<0.001	–	0.056	<0.001	<0.001	0.152	<0.001	<0.001

Data are plotted as the mean ±SD. * *P*<0.05 *vs.* the highest sensitive level of cycling criteria. ** *P*<0.05 *vs.* the Auto-Trak protocols.

decreased with sensitivity level using conventional triggering (high: 106.4±27.35, moderate: 63.4±17.48, low: 25.2 v 7.16). There were few asynchrony events defined as auto-triggering or ineffective triggering. No significant change in breathing rate was observed under any of the experimental conditions.

Inspiratory triggering and flow

The Td was <100 ms for the 2 ventilators in all respiratory mechanics models. For an inspiratory effort of –5 cmH_2O, the PTPt was similar despite the modification of cycling criteria. Higher values for PIF were found during the Auto-Trak protocol than for conventional cycling criteria in COPD and ARDS models (*P*<0.05 Tables 1, 2).

Patient ventilator synchrony in automated and conventional cycling criteria

At 5 and 15 cmH_2O of pressure support, the V_T increased at lower cycling criteria sensitivity levels with conventional PSV settings in all conditions. In the COPD model, delayed cycling always existed during both conventional and Auto-Trak protocols. Tinsp, PEF and Cdelay were also increased as a result of reducing the sensitivity level of the conventional cycling criteria (Table 1).

In the ARDS model, similar outcomes were observed (Table 2). Premature cycling was found during conventional protocols when cycling criteria was preset at the high and moderate levels. Cycling delays only occurred at the lowest sensitivity level of the conventional cycling criteria (15.0±0.10 ms) and during Auto-Trak protocol (15.2±0.42 ms).

In the normal adult model (Table 3), Tinsp was raised from 878.40±19.02 ms to 1455.80±20.95 ms after the cycling criteria was set at the lowest sensitivity level (*P*<0.05). Premature cycling was also eliminated and a small delay in cycling (105.1±15.82) was found. Premature cycling occurred during PSV with the Auto-Trak system.

Inspiratory flow with cycling criteria

According to the 3 respiratory mechanics models, the value of the inspiratory flow at the end of inspiration with the high, moderate, and low sensitivity levels for the cycling criteria during conventional protocols were approximately 35% PIF, 15% PIF, and 5% PIF (Figure 2).

Discussion

During noninvasive positive pressure ventilation, air leak around the mask is unavoidable, and this can interfere with patient-ventilator synchrony and aggravate intolerance [23,24]. Asynchronous events include ineffective triggering, double-triggering, auto-triggering, premature cycling, and delay cycling. Vignaux et al. observed patient-ventilator asynchrony incidents in 60 patients with acute hypercapnic or non-hypercapnic respiratory failure during noninvasive PSV [25]. These asynchronous events occurred frequently and were severe in 26 patients (43%) [25]. Calderni et al. evaluated the effects on patient-ventilator synchrony with 2 different expiratory cycling mechanisms (flow-cycling and time-cycling) in the recovery of patients with acute lung injury. In the presence of air leak, the

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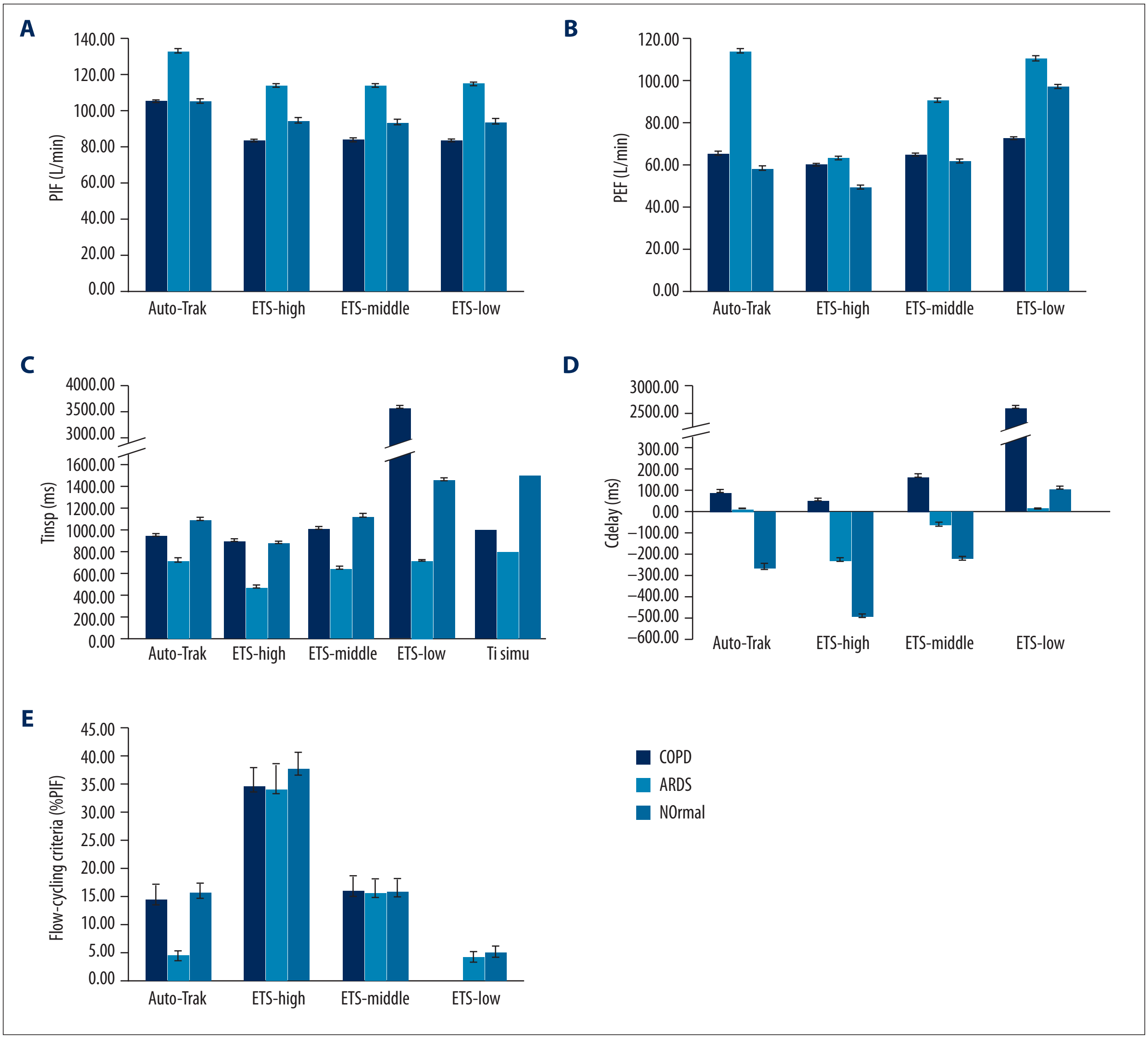

Figure 2. Comparisons of effectiveness of patient-ventilator inspiratory termination synchronization in the 3 patient models with conventional and Auto-Trak protocols. (**A**) Peak inspiratory flow (PIF) values. (**B**) Peak expiratory flow (PEF). (**C**) Inspiratory time (Tinsp) values. (**D**) Cycling-off delay time (Cdelay). (**E**) Inspiratory flow at the end of inspiration (expressed as percentage of PIF).

time-cycling mechanism provided a better patient-machine interaction than the flow-cycling mechanism (25% of PIF) [26]. Nevertheless, Tikioka et al. found that in ARDS or ALI patients the patient-ventilator interaction could be adjusted by modifying the conventional flow-cycling criteria. Premature cycling with double-triggering appeared when the flow-cycling criteria sensitivity was set at a high level (≥35% of PIF). Delayed cycling was often observed with the lowest sensitivity flow-cycling level (1%) [27].

In the present study of simulated obstructive, restrictive, and normal respiratory mechanics, automated triggering and conventional cycling at different flow sensitivities had significant effects on patient-ventilator cycling synchrony. Independent of the cycling criteria, delayed cycling was always observed in the COPD model. Improved cycling synchrony was found with high-level cycling criteria, in which the cut-off point for inspiratory flow was about 35% of PIF. However, the selection of high-level cycling criteria could result in severe premature cycling in restrictive and normal lung conditions. These data suggest that modification of cycling criteria may be able to improve patient-ventilator synchrony.

Optimal patient-ventilator synchrony, especially during noninvasive ventilation (NIV), can be very difficult to achieve due to the presence of air leaks. Although several intensive care

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units (ICU) and transport ventilators are now designed specifically to provide NIV, algorithms, inherent in the design of a mechanical ventilator, are the most critical element for providing automated ventilator adjustments to compensate for leaks [28]. The absence or deficiency of leak compensation can increase the risk of asynchrony and lead to an increase in WOB and patient discomfort. Vignaux et al. found that different NIV algorithms provided by ICU ventilators could result in various cycling patterns. Some of NIV algorithms generated premature cycling, but others led to delayed cycling [29]. A recent study compared the performance and patient-ventilator synchrony between different kinds of ventilators during NIV. By using a lung model that simulated obstructive disease with spontaneous breathing effort, the authors observed that auto-triggering and delayed cycling occurred with ICU and transport ventilators [30]. Dedicated NIV devices that use an NIV algorithm demonstrated better performance and fewer asynchrony events [31]. Some dedicated NIV machines, such as the Respironics BiPAP Vision, required no adjustment of triggering and cycling sensitivity because it can adapt to air leaks ranging from 0 to 37 L/min [15]. Poor performance was observed at the preset PS and PEEP levels in the Respironics BiPAP Vision and Drager Carina bi-level ventilators when the leakage was increased to 52 L/min [32].

The algorithm inherent with BiPAP Vision, registered name "digital Auto-Trak™", is referred to as a shape signal technique. This is a pattern of the actual airflow of the patient, offset by 15 L/min and delayed by 300 ms. When the inspiratory flow of the patient crosses the shape signal, the ventilator terminates inspiration and cycles to exhalation [13,14]. The Auto-Trak system improves patient-ventilator synchrony by adjusting to changing breathing patterns and dynamic leaks. The auto-adaptive triggering, cycling, and leak adjustments may help reduce the time that clinicians spend adjusting thresholds and re-fitting masks.

Previous studies have shown that a triggering delay times between 100 and 120 ms do not generate adverse clinical effects [33,34]. Vasconcelos et al. compared the Auto-Trak software algorithm with conventional settings in terms of patient-ventilator synchrony and discomfort in 12 healthy volunteers who underwent PSV via an endotracheal tube (6 mm) positioned with a mouthpiece [35]. The asynchrony index (AI) and discomfort scores were not significantly different between the 2 protocols. However, in the present study, the use of the Auto-Trak system was associated with a greater triggering delay (169 ms) in the COPD model and premature cycling in the ARDS model. No asynchronous events were observed under either condition. The limitations of the Vasconcelos et al. study are that the tests were performed by an ICU ventilator with conventional settings and the performance of the Auto-Trak system was evaluated with a 6-mm endotracheal tube, not a mask [35].

In the present bench model study, the use of automatic triggering and cycling systems with a facemask demonstrated different inspiratory termination characteristics than the conventional flow-cycling setting used for PSV. However, triggering delay times were similar and shorter (about 60 ms). The benefit of an automatic cycling setting is better patient-machine cycling synchronization in patients with respiratory failure, simplified ventilator management, and fewer errors caused by individual manipulations.

Conclusions

In conclusion, the use of automatic triggering during PSV has a better effect on patient-ventilator cycling synchrony, as evident by shorter triggering time delays and lower PTPt, than conventional flow-cycling settings in respiratory failure patients. The advantage of conventional flow-cycling criteria settings was found to be the avoidance of serious asynchronous events when respiratory mechanics are extremely unstable.

Conflict of interest

The authors declare that they have no conflict of interest.

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