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EXPIRATORY PAUSE MANEUVER TO ASSESS INSPIRATORY MUSCLE PRESSURE DURING ASSISTED MECHANICAL VENTILATION: A BENCH STUDY

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Abstract

Background: The generation of excessive inspiratory muscle pressure (P_{mus}) during assisted mechanical ventilation in patients with respiratory failure may result in acute respiratory muscle injury/fatigue and exacerbate ventilator induced lung injury. A readily available, non-invasive surrogate measure of P_{mus} may help in titrating both mechanical ventilation and sedation to minimize these risks. This bench study explored the feasibility and accuracy of utilizing a ventilator's expiratory pause hold function to measure P_{mus} across multiple operators.

Methods: A standardized technique for executing a brief (< 1s) expiratory pause maneuver (EPM) was used to measure airway occlusion pressure change (ΔP_{aw}) using 3 simulated muscle pressures (ΔP_{mus}: 5, 10, 15 cmH_2O) under: 1) pressure support ventilation (PSV: 0, 10, 15 cmH_2O, 2) volume and pressure-regulated volume ventilation, 3) flow and pressure triggering, 4) varying levels of PEEP, and pressure-rise time. Individual and grouped measurements were made by 4-7 clinicians on 3 different ventilators. Concordance between occlusion ΔP_{aw} and ΔP_{mus} was arbitrarily set at $\leq$ 2 cmH_2O. Data were evaluated by ANOVA and Tukey-Kramer post-test. Correlation was assessed by Pearson R test; bias and precision were assessed by the Bland-Altman method. Alpha was set at 0.05.

Results: Grouped EPM measurements of occlusion ΔP_{aw} across simulated ΔP_{mus}, mode and level of ventilatory support showed reasonable concordance regardless of the ventilator used. Occlusion ΔP_{aw} accuracy frequently decreased by ~3 cmH_2O when both PSV and ΔP_{mus} reached 15 cmH_2O. EPM accuracy was not affected by trigger mechanism/sensitivity, PEEP, or post-trigger pressurization rate. In general only small differences in ΔP_{aw} occurred between individual operators.

Conclusion: EPM generally provided reproducible, stable approximations of ΔP_{mus} across ventilators and ventilator settings and a range of simulated effort. Technique standardization produced relatively consistent results across multiple operators. EPM appears feasible for general use in monitoring inspiratory effort during assisted mechanical ventilation.

Introduction

A major goal of mechanical ventilation is to control patient work of breathing. During critical illness abnormal chest mechanics, in concert with high resting minute ventilation demand, places excessive workloads upon the ventilatory muscles leading to fatigue, acute injury and the potential for overt muscle failure.[1, 2] Although the ventilator is adjusted with the objective of either normalizing or minimizing patient work of breathing, the severity of illness often renders these adjustments alone insufficient. Consequently, deep sedation and sometimes neuromuscular blockade are required to gain adequate control over both the power of breathing and gas exchange. Severe respiratory failure thus presents a management conundrum because most patients are at risk for developing acute ventilatory muscle injury caused by one of two opposing mechanisms: dis-use atrophy from prolonged periods of either passive or over-supported ventilation, and "use-atrophy" from sustained periods excessive workloads.[2]

In the era of lung-protective ventilation even continuous ventilation (ie. "assist-control") modes often result in excessive patient work of breathing. This is largely explained by tidal volume mismatching despite adequate inspiratory flow rates.[3-6] Moreover, excessive negative inspiratory muscle pressure (P_{mus}) transmitted to the pleural space is associated with excessive trans-alveolar stresses that likely potentiate ventilator-induced lung injury, as well as enhance pulmonary edema formation and worsen hypoxemia.[4, 7-10]

A significant clinical problem in these circumstances is the lack of a non-invasive surrogate measure of P_{mus}. that could help titrate both mechanical ventilation and sedation to minimize the risks of both dis-use and use atrophy, and reduce the potential risk for "self-induced lung injury" from the generation of excessive negative transpulmonary pressures.[10] Patient effort during

assisted mechanical ventilation is measured by tidal changes in esophageal pressure (ΔP_{es}) as a signifier of ΔP_{mus} that is used to calculate patient work of breathing. Accurate P_{es} measurements require proper balloon positioning signified by synchronous, and close agreement between ΔP_{es} and occlusive airway pressure change (ΔP_{aw}) during a "Baydur Maneuver" (ie. the standard inspiratory occlusion test).[11]

Because occluded ΔP_{aw} implicitly is the gold standard for estimating ΔP_{mus}, we reasoned that by introducing a brief expiratory pause hold (ie. threshold load) prior to patient-triggered inspiration, the resulting airway occlusion pressure could reasonably be used as a signifier for the "intended" effort emanating from the respiratory centers. Therefore, such an *expiratory pause maneuver* (EPM) might be a practical, expedient method to non-invasively assess inspiratory effort at the bedside.

This bench study investigates whether manually generated EPM estimates of inspiratory effort are reasonably accurate and reproducible as to be incorporated into clinical practice. We assessed two aspects of EPM measurements: 1) its accuracy and reproducibility across multiple operators, intensity of simulated effort, ventilator modes, intensity of mechanical support, and 2) whether its accuracy might be affected by PEEP and trigger sensitivity settings, and differences between how ventilators execute expiratory pause holds. In order to simplify the narrative simulated effort (ie, inspiratory muscle pressure change) is referred to as ΔP_{mus} and occlusive airway pressure change is referred to as ΔP_{aw}.

Methods

Measurement rationale

The intention of EPM is to capture the initial pressure drop during an airway occlusion as an extension of the "pre-trigger phase" (ie. prior to pressurization of the ventilator circuit).[12] EPM is based upon the same assumptions as underlies the 100ms airway occlusion pressure test (P_{100} or $P_{0.1}$) used to signify central respiratory drive; that being to capture the "intended" respiratory motor-neuronal output.[13] The distinction is that EPM is intended to capture *peak inspiratory effort* rather than respiratory drive per-se (**Fig 1**). Based upon available (albeit limited) physiologic evidence we reasoned that peak ΔP_{mus} occurs early in the inspiratory phase, particularly at high levels of respiratory drive.

Assuming a sufficient lag time (ie. trigger delay/circuit re-pressurization), quickly releasing the pause-hold once a deflection in end-expiratory P_{aw} is detected might capture peak ΔP_{mus}. It also might limit potential bias from altered respiratory drive resulting from either proprioceptive feedback or conscious perception of threshold loading.

Ventilators and settings

Three ventilators capable of imposing an expiratory pause (negative inspiratory force or NIF maneuver) were studied: Evita XL (Draeger, Telford PA.), PB-980 (Medtronic, Minneapolis MN.) and Avea (CareFusion, Yorba Linda CA.). Each ventilator first underwent a full device check. EPM accuracy was tested in four modes: continuous positive airway pressure (CPAP), pressure support ventilation (PSV), volume control ventilation (VCV) and pressure-regulated volume control (PRVC).

CPAP was tested at 5 cmH_2O and PSV was tested at driving pressures of 10 and 15 cmH_2O above PEEP of 5 cmH_2O. For both VCV and PRVC the settings were as follows: f of 20, V_T of 500

mL, inspiratory time (Ti) of 0.85s and PEEP of 5 cmH_2O. For PSV a maximum (quickest) pressurization rate was used except for the protocol examining post-trigger pressurization characteristics. For all protocols (except one examining the influence of trigger mechanism and sensitivity level), flow trigger was used and set to a sensitivity of 2 L/m.

Model

Spontaneous breathing was simulated using an Ingmar ASL-5000 (Ingmar, Pittsburgh, PA) set to a *f* of 25 and T_i of 0.85s and time fraction (T_i/T_{tot}) of 0.35. These values fell within the interquartile range of unassisted breathing reported in ARDS subjects.[14] The inspiratory phase was characterized by P_{mus} rise time of 220ms which is consistent with data derived from physiologic studies.[15, 16] P_{mus} sustain and decay times were set at 0.410ms and220ms respectively to achieve the targeted Ti. Mild, moderate, and high ΔP_{mus} of -5, -10, and -15 cmH_2O respectively were used. Simulated chest mechanics consisted of a compliance of 40 mL/cmH_2O and a resistance of 5 cmH_2O per L/s producing inspiratory and expiratory time constants of 0.2s (ie. 95% monoexponential equilibration time of 800ms). An arbitrary *pre hoc* concordance between ΔP_{mus} and ΔP_{aw} of $\leq$ 2 cmH_2O was considered clinically reasonable.

EPM technique

Prior to any experimental run, each investigator ("operator") had a practice session of 1-2 minutes to rehearse their technique. For the Draeger Evita XL the NIF menu was accessed and the pressure scaler waveform formatted to facilitate clear visualization of pressure deflections. The NIF pause hold was activated after peak expiratory flow and released after a negative deflection was noted upon subsequent inspiratory effort. The NIF function also was utilized in

the PB-980. Because scalar waveforms were not available during the NIF maneuver on the PB-980, operators had to respond to the sudden appearance of a negative deflection of the P_{aw} waveform. For the Avea ventilator the expiratory pause function was engaged while monitoring the scalar flow and pressure tracings (again formatted to facilitate clear visualization). The NIF reported on each ventilator was recorded.

Because EPM duration must balance the likelihood of capturing peak effort while also preventing alterations in respiratory drive, we developed a uniform method for timing EPM and tested three release techniques: having operators rapidly count to "1-2-3" before releasing the pause hold, "1,2"-release" and "1"-release. The goal was achieving an EPM duration of ~500 msec. The "1-release" produced the briefest pause duration and was used for all EPM measurements reported in this study (**Supplementary Fig 1**)

Intra- and inter-operator variability and EMP variability between ventilator modes

Between 4-7 investigators performed 12 measurements each at every P_{mus} level tested on each ventilator mode/settings tested. EPM data were analyzed within and between operators. Operator data also were combined to evaluate the overall impact of ΔP_{mus} intensity on ΔP_{aw} accuracy. Data from all modalities were grouped together to calculate the correlation coefficient, bias and precision of ΔP_{aw} measurements on each ventilator compared to ΔP_{mus} on the Ingmar 5000.

Supplementary Protocols

For completeness, we studied whether ventilator settings such as different trigger mechanisms, sensitivity threshold, PEEP, post-trigger pressurization intensity and circuit re-pressurization time

might influence EPM measurements. The methodology and results can be found in the supplementary materials.

Statistical Analysis

Statistical analysis was done using PRISM software 8.3.0 (Graphpad, San Diego CA.). Multiple comparisons were assessed by ANOVA and Tukey-Kramer post-tests and discreet comparisons were made using paired t-tests. Variability of both intra-individual and inter-individual measurements were assessed by the percentage of ΔP_{aw} measurements deviating > 2 cmH_2O from ΔP_{mus}. This was done with groupings of ΔP_{mus} and by mode. Correlation was assessed by Pearson R test; bias and precision were assessed by the Bland-Altman method, and categorical variables compared using Fisher Exact Test. Alpha was set at 0.05.

Results

Measurement accuracy and variability with increasing simulated effort

Grouped ΔP_{aw} measurements across effort intensity, level and mode of ventilatory support demonstrated reasonable concordance with ΔP_{mus} regardless of the ventilator used (**Tables 1, Table 2**). However, ΔP_{aw} accuracy deteriorated when ΔP_{mus} reached 15 cmH_2O and most often occurred when PSV was 15 cmH_2O. Of the 129 instances in 90% the error exceeded pre hoc accuracy criteria by only 1 cmH_2O (ie, 3 vs. $\leq$ 2 cmH_2O) (**Table 3**). Mean ΔP_{aw} underestimated ΔP_{mus} by approximately 1, 2 and 2.5 cmH_2O at simulated efforts of 5, 10 and 15 cmH_2O respectively. By contrast mean ΔP_{aw} measured by the Avea ventilator underestimated ΔP_{mus} by $\leq$ 1.5 cmH_2O under all test conditions. During VCV and PRVC, ΔP_{aw} underestimated ΔP_{mus}

by 0.5 - 1.1 cmH_2O when effort was 5 and 10 cmH_2O and by 1.1- 1.8 cmH_2O when ΔP_{mus} was 15 cmH_2O.

Inter-operator variability and increased simulated effort

Small, statistically significant differences in ΔP_{aw} were found between individual operators across both the intensity of effort and the level of ventilatory support, with notable divergence only when ΔP_{mus} reached 15 cmH_2O (**Supplementary Tables 1-3**).

Differences between ventilators

Grouped operator data revealed no clinically appreciable difference between ventilators in concordance between ΔP_{aw} and ΔP_{mus} (**Fig 2**). Correlation between ΔP_{aw} and ΔP_{mus} was the same for each ventilator (r = 0.99). The bias and precision (95% limit of agreement) were similar but improved marginally from the Draeger XL, to the PB-980 and Avea ventilators: -1.86 ± 0.80 (-3.44 to -0.29), -1.35 ± 0.77 (-2.86 to 0.15) and -1.25 ± 0.56 (-2.36 to -0.15) respectively (**Supplementary Figures 2-4**). The incidence of ΔP_{aw} exceeding the pre hoc accuracy threshold of > 2 cmH_2O was 129 with the distribution across ventilators of 40%, 39% and 21% for the Draeger XL, PB-980 and Avea respectively. Only the incidences between the Draeger XL and Avea were significant: OR: 1.80 (1.12-2.93) P = 0.015.

Discussion

Our primary finding was that manually generated EPM under simulated breathing conditions yielded ΔP_{aw} that was reasonably accurate in reflecting ΔP_{mus} and reproducible across multiple operators and ventilator modes. Thus we believe the technique can reasonably be considered for further evaluation during routine clinical practice. Out of 2412 discreet

measurements made across modes and ventilator brands, ΔP_{aw} underestimated ΔP_{mus} by $\leq$ 2 cmH_2O in ~95% of instances with only 4.9% that deviated by 3 cmH_2O and 0.5% that deviated by $\geq$ 4 cmH_2O. EPM accuracy was reasonably consistent both within and between operators. Deterioration in accuracy occurred mostly when both simulated effort and PSV level reached 15 cmH_2O.And as examined in the supplementary protocols EPM accuracy was unaffected by trigger mechanism, sensitivity level, speed of circuit re-pressurization or PEEP level.

Since we began our study in mid-2018, others have validated EPM clinically compared to invasive techniques with esophageal manometry.[17, 18,19, 20] Bertoni and colleagues randomly applied EPM using a 1-2s pause while simultaneously measuring P_{es} and diaphragmatic electromyography.[17] They found predicted values of P_{mus} and trans-alveolar pressure (based on estimated chest wall elastance using EPM generated ΔP_{aw}) accurately detected excessive levels of measured P_{mus} and trans-alveolar pressure. Moreover, excessive levels of P_{mus} and trans-alveolar pressure were found during the majority of observations, supporting the rationale for EPM in clinical practice. Roesthuis and colleagues also found that EPM generated ΔP_{aw} accurately detected excessive levels of measured P_{mus} and trans-alveolar pressure (ie, > 15 and > 20 cmH_2O respectively).[21] In addition, EPM generated ΔP_{aw} was strongly correlated with both respiratory muscle pressure-time product (a signifier of respiratory muscle oxygen consumption) and power output. Another study found the combination of elevated EPM generated ΔP_{aw} and $P_{0.1}$ was associated with relapse respiratory failure in subjects who failed weaning attempts.[19]

In clinical practice numerous personnel are involved so that the validity of EPM-generated ΔP_{aw} likely depends upon the ability to recognize effort onset and quickly release the expiratory pause prior to either unconscious or conscious recognition of threshold loading. Detection and

response to threshold loading may enhance inspiratory effort, giving the false impression of excessive effort where none exists. In our limited clinical experience we occasionally encountered this phenomenon in lightly sedated or fully conscious patients and in these limited instances it appeared as a secondary negative spike in P_{aw} (**Supplementary Fig 5**). Detection latency associated with threshold loading is discussed in more detail in the **Supplementary Materials**.

It is because of these concerns that we attempted to minimize EMP duration towards a rarely achieved goal of 500 msec. We suspect that excessive measurement discrepancies were caused by a too brief EPM. Although we lack sufficient data to support this, it is notable that the least discrepancies occurred with the Avea ventilator that also had slightly higher EPM duration compared to the other ventilators (**Figure 3**). The overall low incidence of measurement discrepancies may be considered a reasonable trade-off during clinical practice.

It is encouraging, therefore, that EMP durations of 1-2s did not appear to alter inspiratory effort during clinical studies, [17] with some investigators suggesting that EPM duration can be increased to 5s.[22] However, information regarding sedation assessment scores were not reported. Hence, their findings do not exclude the possibility that some patients may perceive sudden threshold loading resulting in inaccurate assessment of patient effort or estimated lung stress. This would be more likely to occur in patients with high respiratory drive and/or light sedation. Therefore, we think it prudent to limit EPM duration to $\leq$ 1s until further information on the impact of sedation and drive on EPM generated ΔP_{aw} becomes available.

The major limitation is that this is a bench study in which we have imputed a spontaneous breathing pattern that *might* reasonably approximate patients with ARDS. To our knowledge the characteristics of inspiratory flow and P_{mus} development have never been comprehensively

explored since the initial studies conducted ~70 years ago.[15, 16, 23] Therefore, repeating this experiment imputing different temporal values for inspiratory pressure rise, sustain and decay might produce different results in terms of intra- and inter-operator accuracy/variability. It is also important to emphasize that the intention of EPM generated ΔP_{aw} is to produce only a clinically useful approximation for either P_{mus} or trans-alveolar pressure during unobstructed breathing. More accurate assessment would require invasive measurement of chest wall elastance with esophageal manometry and also estimating the effects of chest wall motion.[22]

In summary, under simulated breathing conditions when both compliance and airways resistance are low, EPM generated ΔP_{aw} approximates ΔP_{mus} that varies little between multiple operators using the same technique. EPM measurements are relatively stable across ventilation modes, settings and the brand of ventilators tested. However, under the modelling conditions and technique tested accuracy tends to deteriorate when both inspiratory effort and PSV levels reach 15 cmH_2O using an EPM duration < 1 sec. Nonetheless, EPM is an easy to perform, clinically practical, noninvasive technique that may be useful monitoring inspiratory effort during assisted mechanical ventilation.

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Figure Legends

Figure 1. Scalar pressure waveforms of an expiratory pause maneuver (EPM) followed by unobstructed simulated efforts (simulated muscle pressure is depicted in blue and airway pressure in orange)

Figure 2. Change in occlusion airway pressure (ΔP_{aw}) during an expiratory pause maneuver across three ventilators representing three levels of simulated muscle pressure (ΔP_{mus}) depicted as red hash lines. PB = Puritan-Bennett 980 ventilator, XL = Draeger XL ventilator.

Figure 3. Expiratory pause maneuver duration of all operators across ventilators. $P < 0.001$ by ANOVA and *$P = 0.003$ vs. Draeger XL, †$P = 0.002$ vs. Draeger XL.

Supplementary Figure 1. Differences in expiratory pause maneuver duration when using a "quick count". Measurements made during technique standardization.

Supplementary Figure 2. Bland-Altman plot comparing expiratory pause maneuver across occlusion airway pressure (ΔP_{aw}) to simulated muscle pressure (ΔP_{mus}) in the Draeger XL ventilator.

Supplementary Figure 3. Bland-Altman plot comparing expiratory pause maneuver across occlusion airway pressure (ΔP_{aw}) to simulated muscle pressure (ΔP_{mus}) in the PB-980 ventilator.

Supplementary Figure 4. Bland-Altman plot comparing expiratory pause maneuver across occlusion airway pressure (ΔP_{aw}) to simulated muscle pressure (ΔP_{mus}) in the Avea ventilator.

Supplementary Figure 5. Depiction of an airway pressure scalar waveform observed in clinical practice when a patient became aware of threshold loading during an expiratory pause maneuver and responded by increasing his inspiratory effort within the same breath.

Quick Look

Current Knowledge: Preliminary clinical studies suggest that airway pressure deflections during a brief airway occlusion reflect transpulmonary pressure and inspiratory muscle pressure during assisted mechanical ventilation. This maneuver might be useful in detecting inspiratory efforts that may increase the risk for both ventilator-induced lung injury as well as acute inspiratory muscle injury.

What This Paper Contributes to Our Knowledge: This bench study demonstrates that standardization of such an expiratory pause maneuver generally produces consistent, reproducible measurements of airway occlusion pressure both within and between clinician operators as well as across ventilator modes and ventilator brands. Occlusion pressure tends to underestimate simulated muscle pressure by approximately 1-2 cmH_2O, with minor increases to 3 cmH_2O when simulated effort is highest.

EPM Tables

Table 1. Grouped operator comparisons of expiratory pause maneuver across three ventilators and two modes comparing ΔP_{aw} to ΔP_{mus}.

Ventilator	ΔP_{mus} (cmH_2O)	CPAP 5 cmH_2O	PS Δ10/5 cmH_2O	PS Δ15/5 cmH_2O	ANOVA
Drager XL	5	4 ± 0	3.9 ± 0.5	4.0 ± 0.1	P = 0.17
	10	8.5 ± 0.5	8.0 ± 0.1*	8.1 ± 0.6*	P < 0.001
	15	12.6 ± 1.0	12.8 ± 0.6	12.5 ± 0.7	P = 0.25
PB-980	5	4 ± 0	4 ± 0	4.0 ± 0.1	P = 0.37
	10	8.6 ± 0.5	8 ± 0†	8 ± 0†	P < 0.001
	15	13 ± 0‡	12.9 ± 0.3‡	12.3 ± 0.5	P < 0.001
Avea	5	3.9 ± 0.3	4 ± 0§	3.9 ± 0.3	P = 0.013
	10	8.8 ± 0.4	8.8 ± 0.4	8.7 ± 0.6	P = 0.43
	15	13.8 ± 0.4	13.5 ± 0.9‖	13.5 ± 0.9	P < 0.001

Key: ANOVA = analysis of variance, CPAP = continuous positive airway pressure, ΔP_{aw} = occlusive airway pressure change, ΔP_{mus} = simulated inspiratory muscle pressure change.PS = pressure support, *P < 0.001 vs. CPAP 5, †P < 0.001 vs. CPAP, ‡P < 0.001 vs. PS Δ15/5, §P = 0.003 vs. CPAP 5 and PS Δ15/5, ‖ P = 0.002 vs. CPAP 5 and PS Δ15/5.

Table 2. Grouped operator comparisons between ΔP_{aw} to ΔP_{mus} across three ventilators and two continuous ventilation modes comparing.

	Mode	ΔP_{mus}		
Ventilator		5 cmH_2O	10 cmH_2O	15 cmH_2O
Draeger XL	VCV	3.9 ± 0.5	9.0 ± 0.1	13.8 ± 0.4
	PRVC	4.0 ± 0.1	9.0 ± 0.0	13.5 ± 0.5
PB-980	VCV	4.6 ± 0.5	9.0 ± 0.2	13.2 ± 0.6
	PRVC	4.8 ± 0.4*	9.5 ± 0.5†	13.9 ± 0.3†
Avea	VCV	4.1 ± 0.4	8.9 ± 0.2	13.8 ± 0.2
	PRVC	4.1 ± 0.3*	9.0 ± 0.1†	13.9 ± 0.2†

Key: ΔP_{aw} = occlusive airway pressure change, ΔP_{mus} = simulated inspiratory muscle pressure change, PRVC = pressure-regulated volume control, VCV = volume control ventilation, $^{*}P = 0.03$ vs. VCV, $^{\dagger}P < 0.001$ vs. VCV

Table 3. Incidence of ΔP_{aw} underestimating simulated ΔP_{mus} by > 2 cmH_2O across both intensity of inspiratory effort and ventilatory support (denominator: total number of measurements).

Mode	ΔP_{mus} 5 cmH_2O	ΔP_{mus} 10 cmH_2O	ΔP_{mus} 15 cmH_2O	% High Aberrancy*
		Drager XL		
CPAP	0/48	1/48 (2%)	10/48 (21%)	3/144 (2%)
PS-10	1/48 (2.1%)	1/48 (2%)	8/48 (17%)	2/144 (1%)
PS-15	0/48	2/48 (4%)	17/48 (35%)	4/144 (3%)
VCV	2/60 (3%)	0/60	0/60	2/180 (1%)
PRVC	0/60	0/60	0/60	NA
		PB-980		
CPAP	0/60	0/60	0/60	NA
PS-10	0/60	0/60	7/60 (11.7%)	0/180
Ps-15	0/60	0/60	40/60 (66.6%)	0/180
VCV	0/60	0/60	1/60 (1.6%)	1/180 (<1%)
PRVC	0/60	0/60	0/60	NA
		Avea		
CPAP	0/48	0/48	0/48	NA
PS-10	0/48	0/48	12/48 (25%)	0/144
PS-15	0/48	3/48 (6%)	12/48 (25%)	0/144
VCV	0/48	0/48	0/48	0/144
PRVC	0/48	0/48	0/48	0/144

Key: CPAP = continuous positive airway pressure, NA = not applicable (no data), ΔP_{aw} = occlusive airway pressure change, P_{mus} = simulated inspiratory muscle pressure change, PS = pressure support, PRVC = pressure-regulated volume control, VCV = volume control ventilation, *Most errors were only 1 cmH_2O greater than *pre hoc* cut-off of 2 cmH_2O for precision (ie, 3 cmH_2O). High aberrancy was added to describe the incidence of measurements deemed as excessively underestimating ΔP_{mus} (ie. $\geq$ 4 cmH_2O)

Supplementary Table 1 Drager XL ventilator: individual operator measurements of ΔP_{aw}

P_{mus} (cmH_2O)	Opr-1	Opr-2	Opr-3	Opr-4	ANOVA
			CPAP 5 cmH_2O		
5	4 ± 0	4 ± 0	4 ± 0	4 ± 0	*
10	8.3 ± 0.6	8.6 ± 0.5	8.6 ± 0.5	8.5 ± 0.5	P = 0.25
15	14 ± 0	14 ± 0	14 ± 0	13 ± 0	P = 0.09
			PS Δ10/5 cmH_2O		
5	3.9 ± 0.3	3.9 ± 0.3	4 ± 0	3.8 ± 0.9	P = 0.63
10	8 ± 0	8 ± 0	8 ± 0	7.9 ± 0.3	P = 0.40
15	12.8 ± 0.4	12.5 ± 0.9	13 ± 0	12.8 ± 0.6	P = 0.22
			PS Δ15/5 cmH_2O		
5	3.9 ± 0.3	4 ± 0	4 ± 0	4 ± 0	P = 0.40
10	7.9 ± 0.7	8 ± 0	8.3 ± 0.5	8.1 ± 0.3	P = 0.52
15	12.3 ± 1.2	12.7 ± 0.5	12.6 ± 0.5	12.4 ± 0.5	P = 0.53

Key: CPAP = continuous positive airway pressure, Opr = operator, ΔP_{aw} = occlusive airway pressure change, P_{mus} = simulated inspiratory muscle pressure change, PS = pressure support. *unable to perform analysis of variance: standard deviation of zero.

Supplementary Table 2. PB-980 Ventilator: individual operator measurements of ΔP_{aw}

P_{mus} (cmH_2O)	Opr-1	Opr-2	Opr-3	Opr-4	Opr-5	ANOVA
			CPAP 5 cmH_2O			
5	4 ± 0	4 ± 0	4 ± 0	4 ± 0	4 ± 0	*
10	8.8 ± 0.5	8.5 ± 0.5	8.5 ± 0.5	8.8 ± 0.5	8.6 ± 0.5	P = 0.54
15	13 ± 0	13 ± 0	13 ± 0	13 ± 0	13 ± 0	*
			PS Δ10/5 cmH_2O			
5	4 ± 0	4 ± 0	4 ± 0	3.9 ± 0.3	4 ± 0	*
10	8 ± 0	8 ± 0	8 ± 0	8 ± 0	8 ± 0	*
15	12.8 ± 0.4	13 ± 0	12.9 ± 0.3	12.8 ± 0.4	12.8 ± 0.4	P = 0.65
			PS Δ15/5 cmH_2O			
5	4 ± 0	4 ± 0	4 ± 0	3.9 ± 0.3	4 ± 0	*
10	8 ± 0	8 ± 0	8 ± 0	8 ± 0	8 ± 0	*
15	12.4 ± 0.5	12.4 ± 0.5	12.4 ± 0.5	12.3 ± 0.5	12.1 ± 0.3	P = 0.36

Key: CPAP = continuous positive airway pressure, Opr = operator, ΔP_{aw} = occlusive airway pressure change, P_{mus} = simulated inspiratory muscle pressure change, PS = pressure support, *unable to perform analysis of variance: standard deviation of zero.

Supplementary Table 3 Avea ventilator: individual operator measurements of ΔP_{aw}

P_{mus} (cmH_2O)	Opr-1	Opr-2	Opr-3	Opr-4	ANOVA
			CPAP 5 cmH_2O		
5	3.7 ± 0.5	3.8 ± 0.5	4 ± 0	4 ± 0	P = 0.036
10	9 ± 0*	9 ± 0*	9 ± 0*	8.2 ± 0.4	P < 0.001
15	14 ± 0	14 ± 0	14 ± 0	13 ± 0	†
			PS Δ10/5 cmH_2O		
5	4 ± 0	4 ± 0	4 ± 0	4 ± 0	†
10	9 ± 0	9 ± 0	9 ± 0	8 ± 0	†
15	14 ± 0	14 ± 0	14 ± 0	12 ± 0	†
			PS Δ15/5 cmH_2O		
5	3.7 ± 0.5	3.8 ± 0.4	4 ± 0	4 ± 0	P = 0.036
10	9 ± 0*	9 ± 0*	8.9* ± 0.3	7.8 ± 0.5	P < 0.001
15	14 ± 0	14 ± 0	13.9 ± 0.3	12 ± 0	†

Key: ANOVA = analysis of variance, CPAP = continuous positive airway pressure, Opr = operator, ΔP_{aw} = occlusive airway pressure change, P_{mus} = simulated inspiratory muscle pressure change, PS = pressure support,*P< 0.001 vs. Opr-4, †unable to perform analysis of variance: standard deviation of zero.

Supplementary Table 4. Comparisons of ΔP_{aw} with ΔP_{mus} between flow and pressure triggering mechanisms at different trigger levels (Drager XL ventilator) during an expiratory pause maneuver.

Ventilator	ΔP_{mus} (cmH_2O)	Trigger Sensitivity		P
Drager XL		2L/m	5 L/min	
	5	4.7 ± 0.5	4.4 ± 0.5	0.002
	10	8.9 ± 0.8	8.9 ± 0.6	0.89
	15	13.1 ± 0.4	13.1 ± 0.4	0.77
Avea		-2 cmH_2O	-5 cmH_2O	
	5	4.3 ± 0.5	4.5 ± 0.5	0.44
	10	9.0 ± 0.0	9.2 ± 0.4	0.16
	15	13.4 ± 0.7	13.0 ± 0	0.10

Key: CPAP = continuous positive airway pressure, ΔP_{aw} = occlusive airway pressure change, P_{mus} = simulated inspiratory muscle pressure change.

Supplementary Table 5. Comparisons of ΔP_{aw} at different levels of post-trigger pressure rise time during high level pressure support ventilation and simulated effort.

PS Δ15/PEEP 5 cmH_2O (FT 2L/m)				
ΔP_{mus} (cmH_2O)	PRT 0s	PRT 0.5s	PRT 0.75s	ANOVA
15	12.5 ± 0.7	12.3 ± 0.4	12.2 ± 0.4*	0.009

Key: FT = flow trigger, ΔP_{mus} = simulated inspiratory muscle pressure change, ΔP_{aw} = occlusive airway pressure change, PRT = pressure rise time, PS = pressure support *P = 0.007 vs. PRT of 0s.

Supplementary Table 6. Individual operator EPM durations across ventilators*

Operator†	Drager XL	PB-980	Avea
1	557 ± 67	633 ± 61	670 ± 37
2	608 ± 70	580 ± 0	689 ± 117
3	563 ± 98	690 ± 72	592 ± 113
4	695 ± 108	737 ± 58	759 ± 104
5	545 ± 154	680 ± 67	
6	603 ± 62		
7	498 ± 95		
Max mean difference	197	157	167

Key: EPM = expiratory pause maneuver. *all measurements expressed in milliseconds, †operators are assigned numbers according to their participation during specific sessions in which EPM duration was assessed for each ventilator tested. Hence, the numeric value does not necessarily correspond to the same operator across different ventilators.

Supplementary Table 7 Trigger phase re-pressurization time between normal ("unobstructed") trigger conditions compared to EPM conditions (measurements in milliseconds).

	Drager XL	PB-980	AVEA	P
Normal Triggering	200 ± 20[*]	190 ± 20[†]	170 ± 10	<0.001
EPM	190 ± 10[‡§]	160 ± 10[II]	160 ± 30	<0.001

Key: EPM = expiratory pause maneuver, [*]P < 0.001 vs. Avea, [†]P = 0.02 vs. Avea, [‡]P < 0.001 vs. PB-980, [§]P < 0.001 vs. Avea. II P < 0.001 vs. PB-980 during normal triggering.

Fig 1

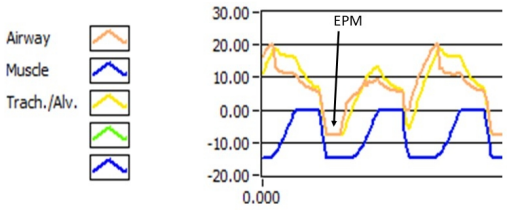

Figure 1. Scalar pressure waveforms of an expiratory pause maneuver (EPM) followed by unobstructed simulated efforts (simulated muscle pressure is depicted in blue and airway pressure in orange)

338x190mm (96 x 96 DPI)

Fig 2

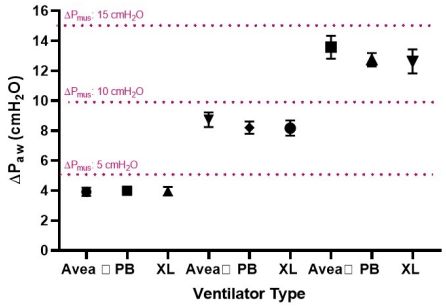

Figure 2. Change in occlusion airway pressure (ΔPaw) during an expiratory pause maneuver across three ventilators representing three levels of simulated muscle pressure (ΔPmus) depicted as red hash lines. PB = Puritan-Bennett 980 ventilator, XL = Draeger XL ventilator.

338x190mm (96 x 96 DPI)

Fig 3

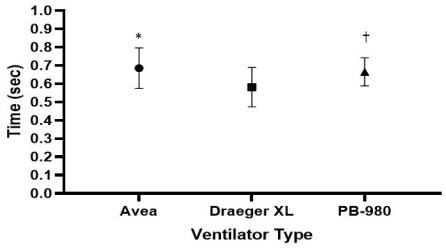

Figure 3. Expiratory pause maneuver duration of all operators across ventilators. P < 0.001 by ANOVA and *P = 0.003 vs. Draeger XL, †P = 0.002 vs. Draeger XL.

338x190mm (96 x 96 DPI)