Expiratory Pause Maneuver to Assess Inspiratory Muscle Pressure During Assisted Mechanical Ventilation: A Bench Study

Richard H Kallet, Justin S Phillips, Travis J Summers, Gregory Burns, Lance Pangilinan, Logan Carothers, Earl R Mangalindan, and Michael S Lipnick

BACKGROUND: The generation of excessive inspiratory muscle pressure (P\text{mus}) during assisted mechanical ventilation in patients with respiratory failure may result in acute respiratory muscle injury and/or fatigue, and exacerbate ventilator-induced lung injury. A readily available noninvasive surrogate measure of P\text{mus} may help in titrating both mechanical ventilation and sedation to minimize these risks. This bench study explored the feasibility and accuracy of using a ventilator’s expiratory pause hold function to measure P\text{mus} across multiple operators. METHODS: A standardized technique for executing a brief (<1 s) expiratory pause maneuver was used to measure the airway occlusion pressure change (ΔP\text{aw}) by using 3 simulated P\text{mus} (ΔP\text{mus}: 5, 10, 15 cm H\text{2}O) under (1) pressure support ventilation (0, 10, 15 cm H\text{2}O), (2) volume and pressure-regulated volume ventilation, (3) flow and pressure-triggering, and (4) varying levels of PEEP and pressure-rise time. Individual and grouped measurements were made by 4 – 7 clinicians on 3 different ventilators. The concordance between occlusion ΔP\text{aw} and ΔP\text{mus} was arbitrarily set at ≤ 2 cm H\text{2}O. Data were evaluated by using analysis of variance and the Tukey-Kramer posttest. Correlation was assessed by using the Pearson R test; bias and precision were assessed by using the Bland-Altman method. Alpha was set at 0.05. RESULTS: Grouped expiratory pause maneuver measurements of occlusion ΔP\text{aw} across simulated ΔP\text{mus}, mode and level of ventilatory support showed reasonable concordance, regardless of the ventilator used. Occlusion ΔP\text{aw} accuracy frequently decreased by ~3 cm H\text{2}O when both pressure support ventilation and ΔP\text{mus} reached 15 cm H\text{2}O. Expiratory pause maneuver accuracy was not affected by trigger mechanism and/or sensitivity, PEEP, or the post-trigger pressurization rate. In general, only small differences in ΔP\text{aw} occurred among the individual operators. CONCLUSIONS: The expiratory pause maneuver generally provided reproducible, stable approximations of ΔP\text{mus} across ventilators and ventilator settings, and a range of simulated effort. Technique standardization produced relatively consistent results across multiple operators. The expiratory pause maneuver seemed feasible for general use in monitoring inspiratory effort during assisted mechanical ventilation. Key words: expiratory pause maneuver; assisted mechanical ventilation; inspiratory effort. [Respir Care 0;0(0):1–C15. © 0 Daedalus Enterprises]

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 place excessive workloads on the ventilatory muscles, which lead to fatigue, acute injury, and the potential for overt muscle failure.\textsuperscript{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 1 of 2 opposing mechanisms: disuse atrophy from prolonged periods of either passive or oversupported ventilation, and “use atrophy” from sustained periods of excessive workloads.\textsuperscript{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
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A significant clinical problem in these circumstances is the lack of a noninvasive surrogate measure of $P_{mus}$ that could help titrate both mechanical ventilation and sedation to minimize the risks of both disuse and atrophy, and reduce the potential risk for self-induced lung injury from the generation of excessive negative transpulmonary pressures. Patient effort during assisted mechanical ventilation is measured by tidal changes in esophageal pressure as a signifier of $\Delta P_{mus}$ that is used to calculate patient work of breathing. Accurate changes in esophageal pressure measurements require proper balloon positioning, signified by synchronous and close agreement between changes in esophageal pressure and occlusive airway pressure change ($\Delta P_{aw}$) during a Baydur maneuver (ie, the standard inspiratory occlusion test). Because occluded $\Delta P_{aw}$ implicitly is the accepted standard for estimating $\Delta P_{mus}$, we reasoned that, by introducing a brief expiratory pause hold (ie, threshold load) before patient-triggered inspiration, the resulting airway occlusion pressure could reasonably be used as a signifier for the “intended” effort that emanates from the respiratory centers. Therefore, such an expiratory pause maneuver might be a practical, expedient method to noninvasively assess inspiratory effort at the bedside.

This bench study investigated whether manually generated expiratory pause maneuver estimates of inspiratory effort are reasonably accurate and reproducible to be incorporated into clinical practice. We assessed 2 aspects of expiratory pause maneuver 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 among how ventilators execute expiratory pause holds. To simplify the narrative simulated effort (ie, inspiratory $P_{mus}$ change) is referred to as $\Delta P_{mus}$ and occlusive airway pressure change is referred to as $\Delta P_{aw}$.

Methods

Measurement Rationale

The intention of the expiratory pause maneuver is to capture the initial pressure drop during an airway occlusion as an extension of the “pre-trigger phase” (ie, before pressurization of the ventilator circuit). The expiratory pause maneuver is based on the same assumptions that underlie the 100-ms 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. The distinction is that the expiratory pause maneuver is intended to capture peak inspiratory effort rather than respiratory drive per se (Fig. 1). Based on available (albeit limited) physiologic evidence, we reasoned that peak $\Delta P_{mus}$ occurs early in the inspiratory phase, particularly at high levels of respiratory drive. When assuming a sufficient lag time (ie, trigger delay and/or circuit re-pressurization), quickly releasing the pause hold once a deflection in end-expiratory $P_{aw}$ is detected might capture the peak $\Delta P_{mus}$. It also might limit a potential bias from altered respiratory drive, which results from either

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Supplementary material related to this paper is available at http://www.rcjournal.com.

Mr Kallet discloses relationships with Nihon Kohden and ContinuED. The other authors have disclosed no conflicts of interest.

Mr Pangilinan and Mr Summers presented a version of this study at AARC Congress 2018, held December 4th-7th, 2018, in Las Vegas, Nevada.

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Current knowledge

Results of 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 demonstrated that standardization of such an expiratory pause maneuver generally produced 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 ~1 – 2 cm H$_2$O, with minor increases to 3 cm H$_2$O when simulated effort is highest.
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The inspiratory phase was characterized by a \( P_{\text{mus}} \) rise time of 220 ms, which was consistent with data derived from physiologic studies. \( P_{\text{mus}} \) sustain and decay times were set at 0.410 ms and 220 ms, respectively, to achieve the targeted inspiratory time. Mild, moderate, and high \( \Delta P_{\text{mus}} \), of −5, −10, and −15 cm H\(_2\)O, respectively, were used. Simulated chest mechanics consisted of a compliance of 40 mL/cm H\(_2\)O and a resistance of 5 cm H\(_2\)O/L/s, producing inspiratory and expiratory time constants of 0.2 s (ie, 95% monoexponential equilibration time of 800 ms). An arbitrary pre hoc concordance between \( \Delta P_{\text{mus}} \) and \( \Delta P_{\text{aw}} \) of \( \pm 2 \) cm H\(_2\)O was considered clinically reasonable.

Expiratory Pause Maneuver Technique

Before any experimental run, each author/investigator (hereafter referred to as “operator”) had a practice session of 1 – 2 min to rehearse his technique. For the Dräger Evita XL ventilator, the negative inspiratory force menu was accessed and the pressure scaler waveform was formatted to facilitate clear visualization of pressure deflections. The negative inspiratory force pause hold was activated after the peak expiratory flow and was released after a negative deflection was noted on subsequent inspiratory effort. The negative inspiratory force function also was used in the PB-980 ventilator. Because scalar waveforms were not available during the negative inspiratory force maneuver on the PB-980 ventilator, the operators had to respond to the sudden appearance of a negative deflection of the \( P_{\text{aw}} \) 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 negative inspiratory force reported on each ventilator was recorded.

Because the expiratory pause maneuver duration must balance the likelihood of capturing peak effort while also preventing alterations in respiratory drive, we developed a uniform method for timing the expiratory pause maneuver and tested 3 release techniques: having the operators rapidly count “1, 2, 3” before releasing the pause hold; “1, 2” release; and “1” release. The goal was to achieve an expiratory pause maneuver duration of \( \sim 500 \) ms. The “1” release produced the briefest pause duration and was used for all expiratory pause maneuver measurements reported in this study (Supplementary Fig. 1 [see the supplementary materials at http://www.rcjournal.com])

Intra- and Inter-Operator Variability and Expiratory Pause Maneuver Variability Between Ventilator Modes

Between 4 and 7 operators performed 12 measurements each at every \( P_{\text{mus}} \) level tested on each ventilator mode and/or settings tested. Expiratory pause maneuver data were analyzed within and between operators. Operator data also were combined to evaluate the overall impact of \( \Delta P_{\text{mus}} \) intensity on \( \Delta P_{\text{aw}} \) accuracy. Data from all the modalities were grouped together to calculate the correlation.

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Table 1. Grouped Operator Comparisons of Expiratory Pause Maneuver Across Three Ventilators and Two Modes That Compare ΔP<sub>aw</sub> With ΔP<sub>mus</sub>

<table>
<thead>
<tr>
<th>ΔP&lt;sub&gt;mus&lt;/sub&gt;</th>
<th>CPAP, 5 cm H&lt;sub&gt;2&lt;/sub&gt;O</th>
<th>PS, Δ10 / 5 cm H&lt;sub&gt;2&lt;/sub&gt;O</th>
<th>PS, Δ15 / 5 cm H&lt;sub&gt;2&lt;/sub&gt;O</th>
<th>P&lt;sub&gt;1&lt;/sub&gt;, ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dräger XL ventilator</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 cm H&lt;sub&gt;2&lt;/sub&gt;O</td>
<td>4 ± 0</td>
<td>3.9 ± 0.5</td>
<td>4.0 ± 0.1</td>
<td>.17</td>
</tr>
<tr>
<td>10 cm H&lt;sub&gt;2&lt;/sub&gt;O</td>
<td>8.5 ± 0.5</td>
<td>8.0 ± 0.1&lt;sup&gt;†&lt;/sup&gt;</td>
<td>8.1 ± 0.6&lt;sup&gt;**&lt;/sup&gt;</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>15 cm H&lt;sub&gt;2&lt;/sub&gt;O</td>
<td>12.6 ± 1.0</td>
<td>12.8 ± 0.6</td>
<td>12.5 ± 0.7</td>
<td>.25</td>
</tr>
<tr>
<td>PB-980 ventilator</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 cm H&lt;sub&gt;2&lt;/sub&gt;O</td>
<td>4 ± 0</td>
<td>4 ± 0</td>
<td>4.0 ± 0.1</td>
<td>.37</td>
</tr>
<tr>
<td>10 cm H&lt;sub&gt;2&lt;/sub&gt;O</td>
<td>8.6 ± 0.5</td>
<td>8 ± 0&lt;sup&gt;†&lt;/sup&gt;</td>
<td>8 ± 0&lt;sup&gt;†&lt;/sup&gt;</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>15 cm H&lt;sub&gt;2&lt;/sub&gt;O</td>
<td>13 ± 0&lt;sup&gt;†&lt;/sup&gt;</td>
<td>12.9 ± 0.3&lt;sup&gt;†&lt;/sup&gt;</td>
<td>12.3 ± 0.5</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Avea ventilator</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 cm H&lt;sub&gt;2&lt;/sub&gt;O</td>
<td>3.9 ± 0.3</td>
<td>4 ± 0&lt;sup&gt;†&lt;/sup&gt;</td>
<td>3.9 ± 0.3</td>
<td>.01</td>
</tr>
<tr>
<td>10 cm H&lt;sub&gt;2&lt;/sub&gt;O</td>
<td>8.8 ± 0.4</td>
<td>8.8 ± 0.4</td>
<td>8.7 ± 0.6</td>
<td>.43</td>
</tr>
<tr>
<td>15 cm H&lt;sub&gt;2&lt;/sub&gt;O</td>
<td>13.8 ± 0.4</td>
<td>13.5 ± 0.9&lt;sup&gt;†&lt;/sup&gt;</td>
<td>13.5 ± 0.9</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD

<sup>*P < .001 vs CPAP 5.</sup>

<sup>†P < .001 vs CPAP.</sup>

<sup>‡P < .003 vs CPAP 5 and PS Δ15/5.</sup>

<sup>§P < .002 vs CPAP 5 and PS Δ15/5.</sup>

ΔP<sub>aw</sub> = occlusive airway pressure change

ΔP<sub>mus</sub> = simulated inspiratory muscle pressure change

PS = pressure support

ANOVA = analysis of variance

coefficient, bias, and precision of ΔP<sub>aw</sub> measurements on each ventilator compared with ΔP<sub>mus</sub> on the IngMar ASL5000 breathing simulator.

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 expiratory pause maneuver measurements. The methodology and results can be found in the supplementary materials (see the supplementary materials at http://www.rcjournal.com).

Statistical Analysis

Statistical analysis was done by using Prism software 8.3.0 (GraphPad, San Diego, California). Multiple comparisons were assessed by using analysis of variance and Tukey-Kramer posttests, and discreet comparisons were made by using paired t tests. Variability of both intra-individual and inter-individual measurements were assessed by the percentage of ΔP<sub>aw</sub> measurements deviating > 2 cm H<sub>2</sub>O from ΔP<sub>mus</sub>. This was done with groupings of ΔP<sub>mus</sub> and by mode. Correlation was assessed by using the Pearson r test, bias and precision were assessed by the Bland-Altman method, and categorical variables were compared by using the Fisher exact test. Alpha was set at .05.

Results

Measurement Accuracy and Variability with Increasing Simulated Effort

Grouped ΔP<sub>aw</sub> measurements across effort intensity, level, and mode of ventilatory support demonstrated reasonable concordance with ΔP<sub>mus</sub> regardless of the ventilator used (Tables 1 and 2). However, ΔP<sub>aw</sub> accuracy deteriorated when ΔP<sub>mus</sub> reached 15 cm H<sub>2</sub>O, and most often occurred when PSV was 15 cm H<sub>2</sub>O. Of the 129 instances in 90%, the error exceeded pre hoc accuracy criteria by only 1 cm H<sub>2</sub>O (ie, 3 vs ≤2 cm H<sub>2</sub>O) (Table 3). The mean ΔP<sub>aw</sub> underestimated ΔP<sub>mus</sub> by ~1.2, and 2.5 cm H<sub>2</sub>O at simulated efforts of 5, 10, and 15 cm H<sub>2</sub>O, respectively. By contrast, the mean ΔP<sub>aw</sub> measured by the Avea ventilator underestimated ΔP<sub>mus</sub> by ≤1.5 cm H<sub>2</sub>O under all test conditions. During volume control ventilation and pressure-regulated volume control, ΔP<sub>aw</sub> underestimated ΔP<sub>mus</sub> by 0.5 – 1.1 cm H<sub>2</sub>O when effort was 5 and 10 cm H<sub>2</sub>O and by 1.1 – 1.8 cm H<sub>2</sub>O when ΔP<sub>mus</sub> was 15 cm H<sub>2</sub>O.

Inter-Operator Variability and Increased Simulated Effort

Small, statistically significant differences in ΔP<sub>aw</sub> were found among the individual operators across both the intensity of effort and the level of ventilatory support, with notable divergence only when ΔP<sub>mus</sub> reached 15 cm H<sub>2</sub>O.
Differences Among Ventilators

Grouped operator data revealed no clinically appreciable difference among the ventilators in concordance between $\Delta P_{aw}$ and $\Delta P_{mus}$ (Fig. 2). The correlation between $\Delta P_{aw}$ and $\Delta P_{mus}$ was the same for each ventilator ($r = 0.99$). The mean bias (standard deviation) and precision (95% limit of agreement) were similar but improved marginally from the Dra¨ger XL to the PB-980 and Avea ventilators: $–1.86 \pm 0.80$ ($–3.44$ to $–0.29$), $–1.35 \pm 0.77$ ($–2.86$ to $0.15$), and $–1.25 \pm 0.56$ ($–2.36$ to $–0.15$), respectively (Supplementary Figs. 2 - 4 [see the supplementary materials at http://www.rcjournal.com]). The number of incidences of when $\Delta P_{aw}$ exceeded the pre hoc accuracy threshold of $>2c$ mH$_2$O was 129, with the distribution across ventilators of 40, 39, and 21% for the Dra¨ger XL, PB-980, and Avea ventilators, respectively. Only the incidences between the Dra¨ger XL and Avea ventilators were significant: odds ratio $1.80 \; 95\% \; CI \; (1.12–2.93); P = .02$.

Discussion

Our primary finding was that a manually generated expiratory pause maneuver under simulated breathing

Table 2. Grouped Operator Comparisons Between $\Delta P_{aw}$ at Each Level of $\Delta P_{mus}$ Across Three Ventilators and Two Continuous Ventilation Modes

<table>
<thead>
<tr>
<th>Mode</th>
<th>$\Delta P_{mus}, 5$ cm H$_2$O</th>
<th>$\Delta P_{mus}, 10$ cm H$_2$O</th>
<th>$\Delta P_{mus}, 15$ cm H$_2$O</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dra¨ger XL ventilator</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VCV</td>
<td>$3.9 \pm 0.5$</td>
<td>$9.0 \pm 0.1$</td>
<td>$13.8 \pm 0.4$</td>
</tr>
<tr>
<td>PRVC</td>
<td>$4.0 \pm 0.1$</td>
<td>$9.0 \pm 0.0$</td>
<td>$13.5 \pm 0.5$</td>
</tr>
<tr>
<td>PB-980 ventilator</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VCV</td>
<td>$4.6 \pm 0.5$</td>
<td>$9.0 \pm 0.2$</td>
<td>$13.2 \pm 0.6$</td>
</tr>
<tr>
<td>PRVC</td>
<td>$4.8 \pm 0.4^*$</td>
<td>$9.5 \pm 0.5^*$</td>
<td>$13.9 \pm 0.3^*$</td>
</tr>
<tr>
<td>Avea ventilator</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VCV</td>
<td>$4.1 \pm 0.4$</td>
<td>$8.9 \pm 0.2$</td>
<td>$13.8 \pm 0.2$</td>
</tr>
<tr>
<td>PRVC</td>
<td>$4.1 \pm 0.3^*$</td>
<td>$9.0 \pm 0.1^*$</td>
<td>$13.9 \pm 0.2^*$</td>
</tr>
</tbody>
</table>

Data are presented as mean $\pm$ SD

$^*P = .03$ vs VCV.

$^1P < .001$ vs VCV.

$\Delta P_{aw}$ = occlusive airway pressure change

$\Delta P_{mus}$ = simulated inspiratory muscle pressure change

VCV = volume control ventilation

PRVC = pressure-regulated volume control

Table 3. The incidence of $\Delta P_{aw}$ Underestimating Simulated $\Delta P_{mus}$ by $>2$ cm H$_2$O Across Both Intensity of Inspiratory Effort and Ventilatory Support

<table>
<thead>
<tr>
<th>Mode</th>
<th>$\Delta P_{mus}, 5$ cm H$_2$O</th>
<th>$\Delta P_{mus}, 10$ cm H$_2$O</th>
<th>$\Delta P_{mus}, 15$ cm H$_2$O</th>
<th>High Aberrancy$^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dra¨ger XL ventilator</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPAP</td>
<td>0/48</td>
<td>1/48 (2)</td>
<td>10/48 (21)</td>
<td>3/144 (2)</td>
</tr>
<tr>
<td>PS-10</td>
<td>1/48 (2.1)</td>
<td>1/48 (2)</td>
<td>8/48 (17)</td>
<td>2/144 (1)</td>
</tr>
<tr>
<td>PS-15</td>
<td>0/48</td>
<td>2/48 (4)</td>
<td>17/48 (35)</td>
<td>4/144 (3)</td>
</tr>
<tr>
<td>VCV</td>
<td>2/60 (3)</td>
<td>0/60</td>
<td>0/60</td>
<td>2/180 (1)</td>
</tr>
<tr>
<td>PRVC</td>
<td>0/60</td>
<td>0/60</td>
<td>0/60</td>
<td>NA</td>
</tr>
<tr>
<td>PB-980 ventilator</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPAP</td>
<td>0/60</td>
<td>0/60</td>
<td>0/60</td>
<td>NA</td>
</tr>
<tr>
<td>PS-10</td>
<td>0/60</td>
<td>0/60</td>
<td>7/60 (11.7)</td>
<td>0/180</td>
</tr>
<tr>
<td>PS-15</td>
<td>0/60</td>
<td>0/60</td>
<td>40/60 (66.6)</td>
<td>0/180</td>
</tr>
<tr>
<td>VCV</td>
<td>0/60</td>
<td>0/60</td>
<td>1/60 (1.6)</td>
<td>1/180 (&lt;1)</td>
</tr>
<tr>
<td>PRVC</td>
<td>0/60</td>
<td>0/60</td>
<td>0/60</td>
<td>NA</td>
</tr>
<tr>
<td>Avea ventilator</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPAP</td>
<td>0/48</td>
<td>0/48</td>
<td>0/48</td>
<td>NA</td>
</tr>
<tr>
<td>PS-10</td>
<td>0/48</td>
<td>0/48</td>
<td>12/48 (25)</td>
<td>0/144</td>
</tr>
<tr>
<td>PS-15</td>
<td>0/48</td>
<td>3/48 (6)</td>
<td>12/48 (25)</td>
<td>0/144</td>
</tr>
<tr>
<td>VCV</td>
<td>0/48</td>
<td>0/48</td>
<td>0/48</td>
<td>0/144</td>
</tr>
<tr>
<td>PRVC</td>
<td>0/48</td>
<td>0/48</td>
<td>0/48</td>
<td>0/144</td>
</tr>
</tbody>
</table>

Data are presented as no./total no. measurements (%).

$^*Most$ $errors$ $were$ $only$ $1 \: cm \: H_2O$ $greater$ $than$ $the$ $pre$ $hoc$ $cutoff$ $of$ $2 \: cm \: H_2O$ $for$ $precision$ $(ie. \: 3 \: cm \: H_2O)$.

$^1High$ $aberrancy$ $was$ $added$ $to$ $describe$ $the$ $incidence$ $of$ $measurements$ $deemed$ $as$ $excessively$ $underestimating$ $\Delta P_{mus}$ $(ie. \: \geq 4 \: cm \: H_2O)$.

$\Delta P_{aw}$ = occlusive airway pressure change

$\Delta P_{mus}$ = simulated inspiratory muscle pressure change

PS = pressure support

VCV = volume control ventilation

PRVC = pressure-regulated volume control

NA = not applicable (no data)
conditions yielded a $\Delta P_{aw}$ that was reasonably accurate in reflecting $\Delta P_{mus}$ and reproducible across multiple operators and ventilator modes. Thus, we believe that the technique can reasonably be considered for further evaluation during routine clinical practice. Of 2,412 discreet measurements made across the modes and ventilator brands, $\Delta P_{aw}$ underestimated $\Delta P_{mus}$ by $\leq 2 \text{ cm H}_2\text{O}$ in $\sim 95\%$ of instances, with only $4.9\%$ that deviated by $3 \text{ cm H}_2\text{O}$ and $0.5\%$ that deviated by $\geq 4 \text{ cm H}_2\text{O}$. Expiratory pause maneuver accuracy was reasonably consistent both within and between the operators. Deterioration in accuracy occurred mostly when both simulated effort and PSV level reached $15 \text{ cm H}_2\text{O}$ and, as examined in the supplementary protocols (see the supplementary materials at http://www.rcjournal.com), expiratory pause maneuver accuracy was unaffected by the trigger mechanism, sensitivity level, speed of circuit repressurization, or PEEP level.

Since we began our study in mid 2018, other investigators have validated the expiratory pause maneuver clinically compared with invasive techniques by using esophageal manometry. Bertoni et al.\textsuperscript{17} randomly applied the expiratory pause maneuver by using a 1–2 s pause while simultaneously measuring the changes in esophageal pressure and diaphragmatic electromyography. They found predicted values of $P_{mus}$ and transalveolar pressure (based on estimated chest wall elastance when using the expiratory pause maneuver–generated $\Delta P_{aw}$) accurately detected excessive levels of measured $P_{mus}$ and transalveolar pressure.

Moreover, excessive levels of $P_{mus}$ and transalveolar pressure were found during most observations; this supports the rationale for the expiratory pause maneuver in clinical practice. Roesthuis et al.\textsuperscript{20} also found that the expiratory pause maneuver–generated $\Delta P_{aw}$ accurately detected excessive levels of measured $P_{mus}$ and trans-alveolar pressure (ie, $>15$ and $>20 \text{ cm H}_2\text{O}$, respectively). In addition, expiratory pause maneuver generated $\Delta P_{aw}$ was strongly correlated with both respiratory $P_{mus}$-time product (a signifier of respiratory muscle oxygen consumption) and power output. Another study found that the combination of elevated expiratory pause maneuver–generated $\Delta P_{aw}$ and $P_{0.1}$ was associated with relapse respiratory failure in subjects for whom weaning attempts failed.\textsuperscript{19}

In clinical practice, numerous personnel are involved so that the validity of expiratory pause maneuver–generated $\Delta P_{aw}$ likely depends on the ability to recognize effort onset and to quickly release the expiratory pause before either unconscious or conscious recognition of threshold loading. The detection and response to threshold loading may enhance the inspiratory effort, which gives the false impression of excessive effort when none exists. In our limited clinical experience, we occasionally encountered this phenomenon in patients who were lightly sedated or fully conscious and, in these limited instances, it appeared as a secondary negative spike in $P_{aw}$ (Supplementary Fig. 5 [see the supplementary materials at http://www.rcjournal.com]). Detection latency associated with threshold loading is discussed in more detail in the supplementary materials (see the supplementary materials at http://www.rcjournal.com).

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

Therefore, it is encouraging that expiratory pause maneuver durations of 1–2 s did not seem to alter inspiratory effort during clinical studies,\textsuperscript{17} with some investigators suggesting that the expiratory pause maneuver duration can be increased to 5 s.\textsuperscript{22} However, information with regard to sedation assessment scores was not
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reported. Hence, their findings do not exclude the possibility that some patients may perceive sudden threshold loading that results 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 the expiratory pause maneuver duration to \( \leq 1 \) s until further information on the impact of sedation and drive on expiratory pause maneuver-generated \( \Delta P_{aw} \) becomes available.

The major limitation is that this was a bench study in which we 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 \( \sim 70 \) years ago.\(^{15,16,23}\) Therefore, repeating this experiment by imputing different temporal values for inspiratory pressure rise, sustain, and decay might produce different results in terms of intra- and inter-operator accuracy and/or variability. It is also important to emphasize that the intention of expiratory pause maneuver-generated \( \Delta P_{aw} \) is to produce only a clinically useful approximation for either \( P_{mus} \) or trans-alveolar pressure during unobstructed breathing. A more accurate assessment would require invasive measurement of chest wall elastance with esophageal manometry and also in estimating the effects of chest wall motion.\(^{22}\)

Conclusions

Under simulated breathing conditions, when both compliance and airways resistance are low, expiratory pause maneuver-generated \( \Delta P_{aw} \) approximates \( \Delta P_{mus} \) that varied little among multiple operators when using the same technique. Expiratory pause maneuver measurements are relatively stable across ventilation modes, settings, and the brand of ventilators tested. However, under the modeling conditions and technique tested accuracy tends to deteriorate when both inspiratory effort and PSV levels reach \( 15 \) cm H\(_2\)O by using an expiratory pause maneuver duration of \(<1\) s. Nonetheless, the expiratory pause maneuver is an easy-to-perform, clinically practical, noninvasive technique that may be useful in monitoring inspiratory effort during assisted mechanical ventilation.

REFERENCES

20. Roesthuis L, van den Berg M, van der Hoeven H. Non-invasive method to detect high respiratory effort and transpulmonary driving

