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Estimation of inspiratory muscle effort using three common indices in various respiratory models, a bench study

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Abstract

Background
Liberation from mechanical ventilation is a complex therapeutic challenge in the intensive care unit. Estimating inspiratory effort during mechanical ventilation can mitigate lung and diaphragmatic injury, along with weakness and atrophy. During a spontaneous breathing trial, it can be critical to predict over or under assistance to guide safe liberation. While estimation of the inspiratory effort requires special equipment, many other indices have been developed to estimate patient effort, work, and actual muscle pressure.
In this bench study, we compare three commonly used maneuvers: airway occlusion at 100 msec (P0.1), airway pressure drop during full occlusion (Pocc), and pressure muscle index (PMI) for their accuracy in predicting the actual muscle effort.
Methods
A single active lung compartment using ASL5000 was modeled to simulate three common patient care scenarios, including "normal" (airway resistance 5 cm/l/s; compliance 60 ml/cm/H_2O), "restrictive" (airway resistance 10 cm/l/s; compliance 30 ml/cm/H_2O); and "obstructive" (airway resistance of 20 cm/l/s; compliance of 80 ml/cm/H_2O) with respiratory rate of 15/minute, inspiratory time of 1 second (10 % rise, 0% hold, and 10% release while exhalation is passive). A Bellavista 1000e ventilator was used for pressure support of 5 cmH_2O and positive end-expiratory pressure (PEEP) of 5 cmH_2O.
Each index was measured to the inputted Pmus, which ranged from 1 to 30 cmH_2O and increased by increments of 1. Results were analyzed using Pearson correlation and regression analysis to predict an associated formula. These were compared to the inputted Pmus using single factor ANOVA followed by post Hoc Tukey test. Formulas from the P0.1 and the Pocc were then compared against previously published equations using single factor ANOVA. Statistics were performed using SPSS 20. $P < 0.05$ was considered statistically significant.
Results
All three indices had strong correlations to Pmus, P0.1 [R 0.978, 95% CI 0.97, 0.99, $P < 0.001$], Pocc [R 0.999, 95% CI 1.1, 1.12, $P < 0.001$], and PMI [R 0.722, 95% CI 0.61, 0.81, $P < 0.001$]. The equations to estimate Pmus were: P0.1: 3.95 (P0.1) - 2.05; Pocc: 1.11 (Pocc) + 0.82; and PMI: 1.03 (PMI) + 8.26. A significant difference ($P < 0.001$) was observed when comparing the inputted Pmus with Pmus estimated from P0.1, Pocc, or PMI. Post hoc analysis showed no difference between Pmus to Pmus estimated from P0.1, Pmus to Pmus estimated from Pocc, and Pmus estimated from P0.1 and Pocc; while comparisons of Pmus estimated from PMI to those from the P0.1 and Pocc revealed significant differences ($P < 0.001$ and $P < 0.001$, respectively).
When comparing our formula for P0.1 to the previously published formula and the actual Pmus, no significant difference was observed (P 0.261), with post hoc tests revealing no significant differences between any pair. In contrast, a significant difference was found when comparing the formula for Pocc to the previously published formula and the actual Pmus ($P < 0.001$). Post hoc tests showed no difference between the new formula and Pmus (P 0.99), but a significant difference between Pmus and previous formula ($P < 0.001$).
Conclusions
While overall all three methods tested showed good correlation with the actual set Pmus, only P0.1 and the Pocc had strong correlation with the set Pmus in all three settings, suggesting that derived formulas can be useful to estimate muscle effort. PMI did not prove accurate, especially in obstructive scenarios, and may not be relied upon in practice.

Keywords: Pmus, P0.1, P occlusion, PMI

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Introduction

Liberation from mechanical ventilation is a complex therapeutic challenge in the intensive care unit. Estimating inspiratory effort during mechanical ventilation, and especially during a spontaneous breathing trial, is critical in predicting safe ventilation and liberation.

During inspiration, the global effect of muscle exertion is estimated as peak inspiratory muscle effort (Pmus), which encompasses not only the diaphragm but other accessory muscles. Typically, it is calculated as the difference between esophageal pressure swing and the pressure needed to overcome chest wall elastic recoil. [1] In addition to helping assess appropriate effort during spontaneous breathing trials, Pmus measurement can help guide prevention of excessively high or low effort during mechanical ventilation, allowing for lung and diaphragmatic protective ventilation. [2]

Patient self-inflicted lung injury (P-SILI) is a serious condition that describes damage to already injured lungs by excessive work of breathing in spontaneously breathing patients. This can occur in mechanical ventilation with risk factors including inappropriately elevated transpulmonary stress and strain, ventilator dyssynchrony, or other inherent causes. [3] Conversely, disproportionately low Pmus may signal ventilator-induced diaphragmatic dysfunction (VIDD) and atrophy, which describes reduction in force-generating capacity of the diaphragm. [4] VIDD is prevalent during critical illness and is believed to be a common cause of liberation failure, prolonged mechanical ventilation, ICU stay and even mortality; risk factors surround duration of ventilation, and use of paralytic agents and positive end-expiratory pressure (PEEP). [5-8]

There are multiple methods of estimating the Pmus. Subjectively, this can be approximated through clinical assessments or interpretation of the pressure-flow graphs. [9,10] Objectively, one can also utilize diaphragmatic ultrasound, electrical activity of the diaphragm (EAdi), transdiaphragmatic pressure (Pdi), work of breathing, or the pressure-time product. [11-13] However, the gold standard is via esophageal manometry for measurement of esophageal pressure swings. Yet, likely due to the invasive nature and need for proper placement, it is not routinely implemented in clinical practice. [14] Thus, ventilator indices, such as the rapid shallow breathing index, flow index, and occlusion maneuvers can be applied as non-invasive modalities of estimation of Pmus. [15,16] Three established techniques include airway occlusion pressure at 100 msec (P0.1), airway occlusion method (Pocc), and pressure muscle index (PMI) which can be obtained from the ventilator interface (Figure 1).

P0.1 measures the force generated against an occluded airway during the first 100 msec of inspiration and is an estimate of the neuromuscular drive to breathe. Multiple studies have shown that P0.1 correlates well with muscle effort and can even estimate Pmus when using a derived formula. [17-19]

Pocc represents inspiratory swing and is measured as the difference between the lowest value of pressure drop and PEEP during an expiratory hold; prior work has corroborated its utility assessing elevated inspiratory effort and transpulmonary driving pressure. [20]

PMI is measured by the difference between peak and plateau pressures during an inspiratory pause during pressure support ventilation; previous investigations have also found good correlation with Pmus and the pressure-time product. [21,22]

Our previous work has demonstrated that on a ventilatory simulator, Pmus can be accurately correlated with these three common methods of estimation. [23] However, this has yet to be applied to different respiratory templates that are more common in the patient care setting. This benchmark study aims to compare these three non-invasive methods of estimating Pmus in different common respiratory models to ascertain their correlation.

Methods

Using a single lung compartment simulator ASL5000 (Ingmar medical, PA, USA) three common respiratory scenarios were modeled. These included a "normal" (airway resistance 5 cm/l/s, compliance of 60 ml/cm/H_2O); "restrictive" (airway resistance of 10 cm/l/s, compliance of 30 ml/cm/H_2O); and "obstructive" (airway resistance of 20 cm/l/s, compliance of 80 ml/cm/H_2O).

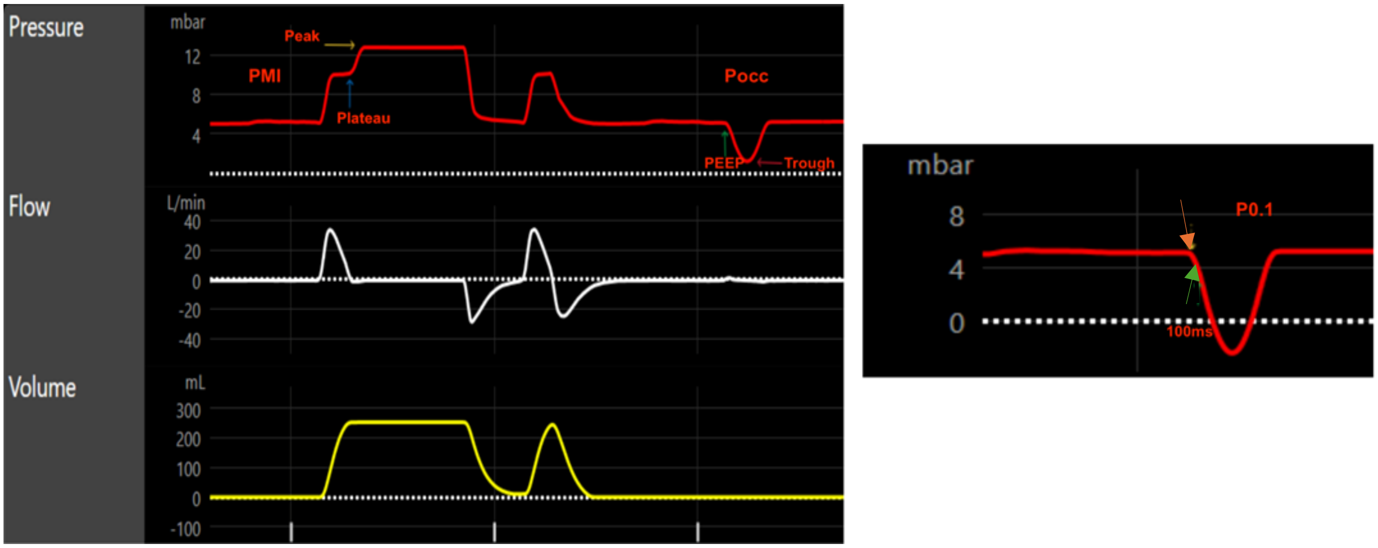

Figure 1: Ventilator interface showing inspiratory effort. Key features are labelled for measurement of PMI (during inspiratory hold), and Pocc and P0.1 (measuring during expiratory hold). Arrows denote the beginning and end of the maneuver.

The compliance and resistance levels for each system were based on expected ranges for their archetype disease. [24] Other baseline parameters included a respiratory rate of 15 and inspiratory time of 1 second (10% rise, 0% hold, 10% release while exhalation is passive). Using a Bellavista 1000e ventilator (Zoll, MA, USA), the ventilator was set to pressure support mode of 5 cmH_2O and PEEP 5 cmH_2O with flow trigger 2 L/min, and expiratory cycling sensitivity at 25%.

Known Pmus was inputted into the simulator and increased by increments of 1. With each subsequent level, an inspiratory and expiratory hold maneuvers for 3 seconds were performed to ascertain P0.1, Pocc, and PMI.

The variables were then analyzed using Pearson correlation and regression analysis to predict a formula for estimating Pmus in each method. All the formulas from the regression analysis were compared to the set Pmus using single factor ANOVA followed by post Hoc Tukey test. We compared our derived formulas from the P0.1 and the Pocc to previously published formulas using single factor ANOVA. Statistics were performed using SPSS 20 software. $P < 0.05$ was considered statistically significant.

Results

All three tests had strong correlation to inputted Pmus on the ventilatory simulator, P0.1 [R 0.978, 95% CI 0.97, 0.99, $P < 0.001$], Pocc [R 0.999, 95% CI 1.1, 1.12, $P < 0.001$], and PMI [R 0.722, 95% CI 0.61, 0.81, $P < 0.001$]. Using regression analysis, the estimated equations are as follows(Table 1):

- (P0.1) Pmus = 3.95 (P0.1) - 2.05
- (Pocc) Pmus = 1.11 (Pocc) + 0.82
- (PMI) Pmus = 1.03 (PMI) + 8.26

Compared to inputted Pmus, the formulas derived from the above analysis showed significant differences overall ($P < 0.001$). Post-hoc analysis revealed that between Pmus and the P0.1 and Pocc formula there was no significant difference (P 0.899 and P 0.219, respectively); however, there was a difference between Pmus and PMI ($P < 0.001$). Between the formulas, there was no significant difference when P0.1 was compared to Pocc (P 0.217); however, there was a difference when comparing P0.1 to PMI, and Pocc to PMI ($P < 0.001$ and $P < 0.001$, respectively). (Table 2)

Comparing the formula for P0.1 to the previously published formula by Hamata and colleagues, and the actual Pmus, there was no significant differences (P 0.261), post hoc test showed no statistical significance between any pair. [17] Comparing the formula for Pocc by Bertoni and colleagues to the previously published formula and the actual Pmus, there was significant difference ($P < 0.001$), post hoc test showed no difference between the new formula and Pmus (P 0.99), and significant difference between Pmus and previous formula ($P < 0.001$). [20]

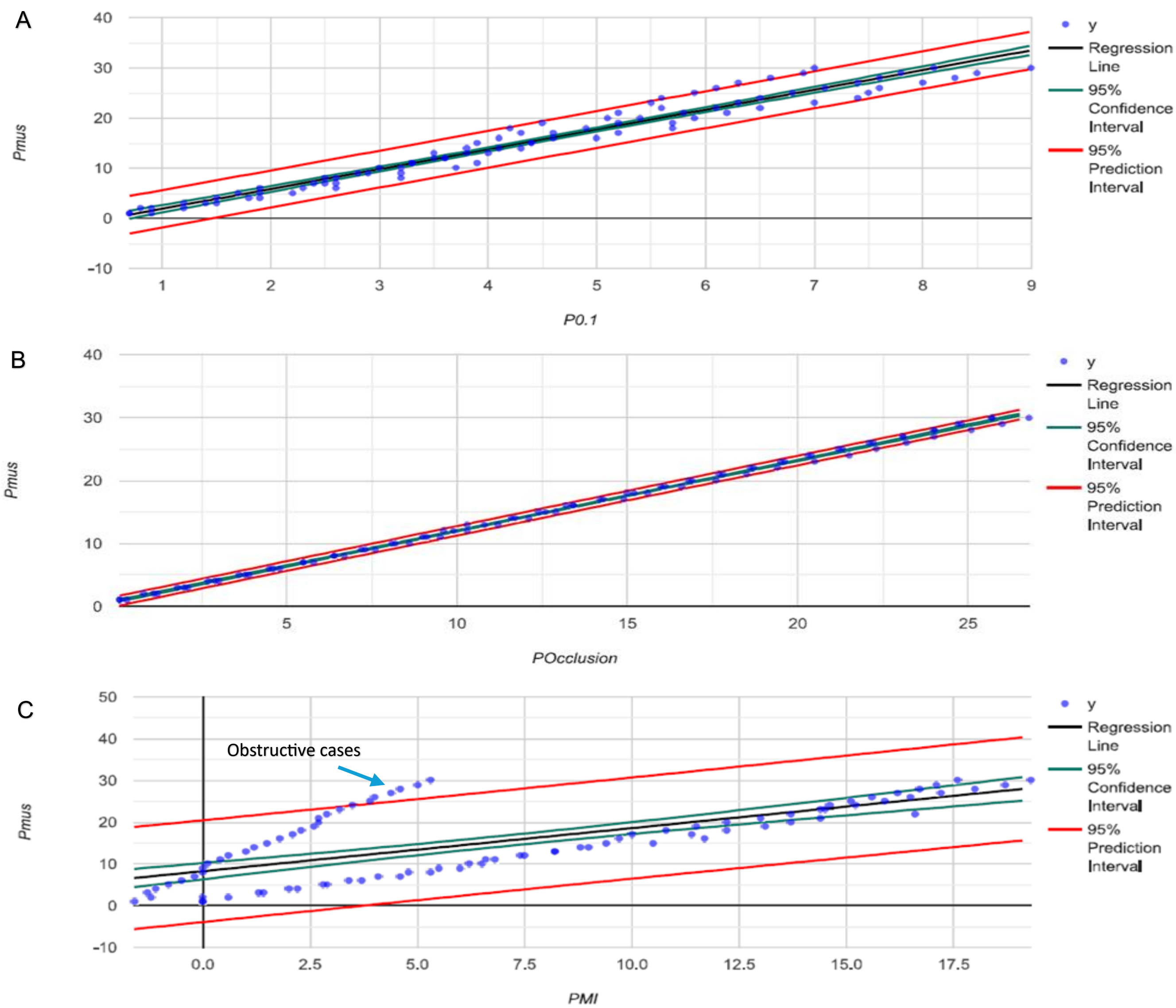

Figure 2: Correlation and linear regression of all the three maneuvers with the Pmus. A: P0.1, B: Pocc, C: PMI. Blue arrow donates obstructive cases

	R	**CI**	**P**	**Equation**
P0.1	0.978	0.97, 0.99	< 0.001	3.95 (P0.1) - 2.05
Pocc	0.999	1.1, 1.12	< 0.001	1.11 (Pocc) + 0.82
PMI	0.722	0.68, 0.81	< 0.001	1.03 (PMI) + 8.26

Table 1: Pearson correlation between Pmus and all the 3 maneuvers, and the corresponding equation based on the regression analysis. R: correlation coefficient, CI: confidence interval, P: P value

	Pmus	**P0.1**	**Pocc**	**PMI**
Pmus		0.899	0.219	0.001
P0.1			0.217	0.001
Pocc				0.001

Table 2: post-hoc Tukey HSD (Honestly Significant Difference) P values comparing Pmus to the estimated Pmus variables from the 3 equations

Discussion

Our findings show that both P0.1 and Pocc are better representatives of the inspiratory effort than PMI, and both are comparable to estimate the muscle effort through surrogate formulas. Measuring peak inspiratory muscle effort can mitigate the risk of over and under ventilatory assistance that can lead to VIDD and myotrauma. Some experts have published potential therapeutic targets for diaphragmatic protection based on commonly used measures of diaphragmatic effort that include the Pmus and all three of the maneuvers we tested, however, they mention that "the specification of ranges for the target values reflects uncertainty on the part of the authors about the safe upper limit for inspiratory effort; values specified represent suggested targets based on available physiological and clinical evidence". [25] Additionally, estimation of the actual muscle effort can be decisive in assisting with determination of a patient's ability to be safely liberated from mechanical ventilation. [26]

P0.1 has been studied extensively, especially as a weaning index to predict successful liberation. [27,28] Prior work has also noted the utility of Pocc and PMI; however, they have not yet garnered sufficient evidence to predict weaning success. [20]

This study also found that PMI was not as accurate in determining Pmus in the "obstructive" model. Overall, the correlation between PMI and Pmus was still strong (R = 0.722), but it was less compared to the P0.1 and Pocc. When excluding the "obstructive" cohort, the correlation was much stronger (R = 0.988). These findings agree with Foti and colleagues who initially suggested that PMI may not be as reliable in obstructed patients. [21] This may be due to the high resistance and the slow flow decay, as the pressure drop reflects the resistive load rather than the muscle effort. Additionally, the estimated formula from regression analysis yielded significantly different numbers from the known Pmus in this setting. Thus, we caution regarding use of PMI to estimate Pmus in patients with obstructive pattern and high resistance, as it may underestimate Pmus.

A recent study by Gao and colleagues [29] studied PMI during PSV and found that PMI could reliably predict the high and low contribution of a patient's effort during assisted ventilation, however their study included diverse patients with respiratory failure and undisclosed respiratory mechanics or number of patients with obstructive physiology.

Hamahata and colleagues also derived a formula to estimate Pmus from the P0.1 in a bench study with four different ventilators using regression analysis, (Pmus = P0.1 x 2.99 + 0.53). [17] When compared to the equation derived from this study there was no significant difference, which reinforces the accuracy of our new formula.

Bertoni and his group also investigated the value of Pocc to estimate the Pmus in a small study showing that it is possible to estimate muscular pressure by multiplying Pocc by 0.75. [20] In comparison, our formula was more accurate, and their formula may underestimate the actual Pmus.

A recent study compared Pocc with P0.1 to assess diaphragmatic activity and found that both maneuvers can reliably identify patients with low or high extremes in diaphragm effort and lung stress, where Pocc outperformed P0.1. [30]

A recent publication by Docci and colleagues also presents a conceptual model for a nonlinear behavior of the interaction between a patient's Pmus and the ventilator during pressure support ventilation. They used the P0.1 and PMI as estimates of Pmus, however, their model assumed only normal resistance below 10 $cmH_2O/L/s$. [31]

Limitations, our study has several limitations. Though bench simulator studies are a valuable tool for evaluating the performance of mechanical ventilators, the results must be interpreted through the context of numerous factors. The spontaneous effort created by the simulator was uniform in shape (descent and relaxation) and timing, and there was no expiratory effort. Our experiment was done with one ventilator while other studies were done with different ventilators which can have some effects on comparison.

Conclusions

While all three methods tested all had strong correlation to the actual set Pmus, only P0.1 and the Pocc correlated well with the set Pmus, and a derived formula could be used to estimate the muscle effort in these settings. PMI did not prove very accurate, especially in obstructive scenarios, and may not be relied upon. Further investigations are needed in the clinical setting to test whether these benchwork findings may be applied to practice.

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