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Effect of Training on Inspiratory Load Compensation in Weaned and Unweaned Mechanically Ventilated ICU Patients

Running title: Load compensation in ventilated ICU patients

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Conflict of Interest Statement: Drs. Smith and Davenport have no conflicts of interest to disclose. The University of Florida and Drs Martin and Gabrielli have applied for a patent to modify clinical mechanical ventilators to provide threshold inspiratory muscle training to patients receiving mechanical ventilation support.

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Abstract

Background: While inspiratory muscle weakness is common in prolonged mechanical ventilation, inspiratory muscle strength training (IMST) can facilitate strengthening and ventilator weaning. However, the inspiratory load compensation (ILC) responses to threshold loads are not well-characterized in patients. The purpose of this study was to retrospectively compare ILC responses according to the clinical outcomes of IMST (i.e. maximal inspiratory pressure (MIP), weaning outcome), in difficult to wean ICU patients.

Methods: Sixteen tracheostomized patients (weaned = 10, unweaned = 6) from a previous clinical trial underwent IMST 5 days/week at the highest tolerated load, in conjunction with daily, progressive spontaneous breathing trials. MIP and ILC of a 10 cm H_2O load were compared in the subjects before and after IMST, using repeated measures ANOVA. Changes in ILC performance were further characterized (5, 10, 15 cm H_2O loads) in the trained patients who weaned. Pearson correlation identified relationships between MIP and ILC.

Results: Demographics, respiratory mechanics and initial MIP (52±26 vs. 42±13 cm H_2O) did not significantly differ between groups. Upon enrollment, MIP significantly correlated with flow ILC responses to the 10 cm H_2O load ($r=0.638$, $p<0.01$). After IMST, MIP significantly increased in the entire sample ($p<0.05$). Both before and after IMST, subjects who weaned generated greater flow and volume ILC than patients who failed to wean. Additionally, ILC flow, volume and duty cycle increased upon ventilator weaning, at loads of 5, 10 and 15 cm H_2O.

Conclusions: Flow ILC at a threshold load of 10 cm H_2O in ventilated, tracheostomized patients positively correlated with MIP. Although MIP improved in both groups, flow and volume ILC responses of weaned subjects were more robust, both before and after IMST. The results suggest

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ILC responses are different in weaned and unweaned patients, reflecting dynamic inspiratory muscular efforts that could be influential to weaning. Further study is needed.

Key Words

Respiratory failure (C08.618.846)

Respiratory muscle training (E02.779.474.124)

Respiratory muscles (A02.633.567.900)

Ventilator weaning (E02.041.625.950)

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Introduction

Prolonged mechanical ventilation (MV) has been associated with an imbalance between the respiratory loads that must be overcome to produce airflow and the capacity of the inspiratory muscles to generate pressure.[1, 2] Patients who require mechanical ventilation (MV) assistance may experience excessive ventilatory loads that perturb breathing. Resistive ventilatory loads may occur due to airway obstruction by edema, bronchoconstriction, or mucus plugging, while pulmonary congestion, effusion, ascites, or skeletal injury can create elastic loads. Additionally, chronic co-morbidities such as COPD and obesity compound the acute resistive and elastic ventilatory loads.[3, 4]Patients with repeated weaning failure may experience tidal pressure loads that exceed 40% of maximal transdiaphragmatic pressure.[1]

Both increased tidal breathing loads and an insufficient muscular capacity contribute to difficult weaning. Ventilatory muscle weakness impedes a patient's ability to compensate for unexpected breathing loads, such as an airway obstructed by mucus. [5] Inspiratory weakness is prevalent yet potentially treatable in difficult-to-wean patients [6, 7] and may influence the breathing pattern response to pulmonary intrinsic loads. [2, 6, 8] Inspiratory muscle strength training (IMST) has shown promise to counteract inspiratory muscle weakness. [9, 10] A controlled clinical trial from our laboratory demonstrated that IMST increased static maximal inspiratory pressure (MIP) and facilitated ventilator weaning in MV-dependent adults. [11] A recent systematic review of IMST also found higher-intensity training with pressure-threshold devices conferred greater strengthening benefits. [12]

During IMST, the applied inspiratory loads elicit inspiratory load compensation (ILC) responses, in an effort to maintain minute ventilation during the exercise sets. ILC is a term used

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to describe changes in ventilatory timing, flow, pressure, and volume in response to mechanical disturbances in breathing. The diaphragm and accessory muscles execute ILC motor responses. Healthy adults typically increase inspiratory flow and volume during repeated, moderate pressure-threshold loading, but inspiratory flow decreases with high-magnitude loads.[13-15] However, ILC responses and the effect of training are not well-understood in ventilated patients.

Therefore, the purpose of this study was to determine the ILC responses to pressure-threshold loads in difficult to wean, ventilated ICU patients who underwent IMST. We hypothesized that (1) ILC volume and flow responses would be greater in patients who weaned, and (2) weaned patients would utilize significantly different ILC strategies after IMST.

Methods

This retrospective cohort study was conducted in a subset of patients from a larger, randomized, single-blind clinical trial of IMST and ventilator weaning (NCT00419458, University of Florida IRB #420-1998).[11] In the randomized trial, patients were randomly assigned to either IMST or SHAM training. An initial spontaneous breathing trial to failure was conducted and baseline MIP was measured. On subsequent days, patients received daily, protocolized ventilator weaning trials as well as their assigned training exercises, five days per week. The experimental period lasted up to 28 consecutive days or until weaning occurred.

Subject recruitment and screening:

Subjects were adults with acute, prolonged MV dependence[16] in the adult medical, surgical, and burn ICUs of a University teaching hospital. After resolution of the acute factors contributing to respiratory failure, tracheostomized patients who failed to wean from MV with usual care were identified. The entry and exclusionary criteria for the clinical trial have been detailed elsewhere[11] and include: (1) age 18 years or older, (2) stabilization of the underlying cause of respiratory failure, (3) no evidence of hemodynamic deterioration with low doses of

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intravenous vasopressors, (4) awake, spontaneously triggering the ventilator, and able to follow one-step motor commands, (5) requirement for MV support by continuous spontaneous ventilation mode or pressure- or volume-controlled intermittent mandatory ventilation ($\leq$ 6 breaths / minute) mode, with requirements for pressure support $\leq$ 15 cm H_2O and PEEP $\leq$ 10 cm H_2O, (6) 3 or more previous failed attempts to breathe without MV support for 72 consecutive hours, (7) no radiological evidence of hemidiaphragm elevation, (8) no progressive neuromuscular disease, (9) anticipated life expectancy of at least 12 months, (10) no musculoskeletal pathology that impeded chest wall movement, (11) no pre-existing MV dependence, (12) body mass index $\leq$ 40. Patients or their designees consented to participate in the clinical trial.

We studied a subset of patients from a previous clinical trial of IMST and ventilator weaning. [11] Of the 35 clinical trial participants randomized to receive IMST, we retrospectively examined all patients who completed ILC performance testing with standardized pressure threshold loads on their first and last training sessions. In 19 patients, breath-by-breath ILC respiratory parameters were not available for at least one session. In the remaining 16 patients, MIP and ILC responses of the subjects who subsequently weaned from MV (n=10) were compared to IMST subjects who failed to wean (n=6). We separately compared the demographic characteristics from all 35 IMST participants to the 16-patient subset and did not find significant differences between groups.

Inspiratory muscle strength training:

Patients trained five days per week until they weaned from MV, for up to 28 calendar days. IMST sessions were implemented by physical and respiratory therapists and consisted of four sets of 6-10 best-effort breaths, using a Threshold® PEP device (Phillips-Respironics,

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Murraysville, PA) inverted to deliver inspiratory threshold training loads (**Fig. 1**). Patients were encouraged to take very deep and rapid breaths, but they self-selected the respiratory rate of the training breaths. IMST sets lasted <1 minute. Between sets, subjects rested on their baseline MV settings for 2-3 minutes. The IMST load was set at the highest setting that allowed inspiratory valve opening on every breath, with stable vital signs, and ≥50% of the V_{TI} achieved on resting MV settings.

Ventilator weaning activities:

Physicians, nurses and therapists coordinated concomitant, protocolized ventilator weaning trials for patients, seven days per week. An initial unsupported spontaneous breathing trial (SBT) confirmed the diagnosis of failure to wean and determined time goals for subsequent SBTs. The SBT protocol was used to standardize decision-making for daily weaning activities. The rate of progression for the prescribed daily SBT duration was developed to provide progressive respiratory muscle endurance conditioning (**Fig. 2**). Each morning, the attending physician determined whether the subject was medically stable for SBT trials. Respiratory care initiated each SBT. The patient was disconnected from MV and attached to supplemental oxygen via t-piece ($F_iO_2 \geq 0.4$ to maintain $SpO_2 \geq 92\%$). Heart and respiratory rate, blood pressure, EKG and SpO_2 were continuously monitored during the SBT. The SBT continued until patients exhibited one or more physiological signs of weaning failure (**Table 1**), or when patients could not subjectively tolerate further unassisted breathing and requested to resume MV.

The duration of subsequent trials was based upon the performance of the most recently completed SBT. Subjects who completed the assigned SBT were advanced to the next, longer scheduled time. Subjects who could not tolerate the assigned SBT duration attempted a shorter duration for the subsequent SBT. Occasionally, patients could not complete an SBT without MV

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support. These patients underwent trials with reduced MV support (**Fig. 2**). Patients were considered successfully weaned when they could tolerate 72 continuous hours of breathing without ventilatory support (invasive or noninvasive). Patients who could not complete the SBT protocol and achieve 72 ventilator-free hours at Day 28 were considered unweaned.

Maximal Inspiratory Pressure:

MIP was a primary clinical endpoint and was measured using a 20-second inspiratory occlusion method previously validated for ventilated patients. [17] Briefly, the patient was removed from the ventilator and connected to a manometer and one-way valve that blocked inspiration. Between 20-second efforts, subjects rested on their baseline MV settings between MIP attempts. MIP measurements were repeated three times, and the most negative value was recorded.

Inspiratory Load Compensation:

ILC responses were evaluated to determine their role in strengthening and weaning outcome. With the tracheostomy cuff inflated, subjects took 10-12 best-effort breaths using a threshold training device. Tests were first conducted during the initial IMST session (*pre*). Weaned subjects were tested again the morning prior to the protocolized liberation from MV (*post*). This corresponded to the day a 12-hour SBT trial was completed (**Fig. 2**). ILC was not tested on the morning of liberation, in order to remove the risk that the performance tests could acutely fatigue patients. If patients did not reach 72 ventilator-free hours after liberation, they were not yet considered weaned, and resumed IMST and protocolized weaning trials. For patients who could not breathe without MV for 72 continuous hours by day 28 (unweaned patients), their final IMST session was treated as the “post” condition.

A 10 cm H_2O load was used to determine whether ILC strategies differed between patients who weaned and those who failed to wean. This load was selected because it was systematically

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administered to most subjects on their first IMST session, and all of the unweaned subjects used the 10 cm H_2O pressure threshold load during their final training session. To further discern how the ILC responses to loads of different magnitude changed with IMST in weaned patients, ILC performance was characterized using 5, 10, and 15 cm H_2O threshold loads.

Data Analysis:

Respiratory mechanics, MIP, and ILC performance were recorded with a respiratory monitor (Capnostat® and CO_2SMO®, Philips-Respironics, Murrysville, PA) placed in series with the training equipment. Respiratory mechanics were obtained for at least 15 minutes while in a rested state in the morning, prior to any respiratory testing or training. For ILC, we recorded inspired tidal volume (V_{TI}), peak inspiratory flow (PIF), and inspiratory (T_I) and expiratory (T_E) times. For each 10-12 breath ILC set, the six breaths with the highest combined inspiratory pressure and volume were averaged for statistical analysis.

The data were first tested to determine whether assumptions of normality were met. Based upon these results, group demographics and respiratory mechanics were either compared with independent t-tests or with Mann-Whitney *U* tests. Relationships between MIP and ILC responses were assessed using Pearson correlations. Two-way repeated measures ANOVA for training (pre, post), and weaning outcome (unweaned, weaned) was used to examine group differences in MIP and ILC. To specifically evaluate the effect of the load magnitude on ILC responses of weaned patients, we conducted 2-way repeated measures ANOVA for training (pre-post) and load (5, 10, 15 cm H_2O). Cell means contrasts were used to explore differences when significant interactions were present in ANOVA (SPSS 17.0, Chicago, IL). Normally-distributed data are reported as mean (SD). Median (IQR) is reported for demographic data that did not meet

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the assumption of normality. To illustrate the spread of the ILC responses, box and whisker plots in Figures 5 and 6 show median, IQR, 95 percentile. Statistical significance was $p<0.05$.

Results

Subject Demographics:

Group characteristics are summarized on **Table 2**. Individual causes leading to prolonged MV can be found in **Table S1**. There were no significant group differences in the demographics, respiratory mechanics, number of completed IMST sessions, or total days of study participation. Unweaned patients were ultimately discharged (n=1), underwent surgery (n=2), or experienced unrelated medical complications (n=3).

Initial MIP was comparable between weaned (52.3 ±25.8 cm H_2O) and unweaned (41.8 ±13.2 cm H_2O) patients, and MIP increased after training for both groups (weaned: 61.9 ±23.0 cm H_2O, unweaned: 46.3 ±13.8 cm H_2O, $p<0.05$) (**Fig. 3**).

Relationship between MIP and ILC responses:

To investigate the relationship between MIP and ILC in difficult to wean patients separately from the influence of training, we conducted correlations in the 16-group sample (**Fig. 4**) in the untrained state. With prolonged MV and prior to any training intervention, MIP significantly correlated only to PIF ($r=0.638$, $p<0.01$), indicating that baseline flow ILC responses were greater in stronger patients.

Load compensation differences between weaned and unweaned patients:

Next, we looked at the influences of training and weaning outcome on ILC performance variables. An imposed 10 cm H_2O ILC load represented a similar proportion of the average MIP at the outset of training (weaned group: 25 (15)%, unweaned group: 27 (11)% of MIP) as well as its conclusion (weaned group: 18 (6)%, unweaned group: 24 (8)% of MIP). However, patients

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who ultimately weaned from MV employed a larger PIF both before and after the IMST interventional period (*weaned:* pre: 46.7±16.1 L/min, post: 54.9±28.7 L/min, *unweaned:* pre: 28.5±13.4 L/min, post: 25.9±5.9 L/min, $p<0.05$). Likewise, the V_{TI} response was larger in the weaned group before and after IMST (*weaned:* pre: 5.0±1.7 mL/kg, post: 5.7±1.9 mL/kg, *unweaned:* pre: 3.1±1.4 mL/kg, post: 4.2±1.7 mL/kg, $p<0.05$) than patients who failed to wean. There were no group or training differences in the ILC timing responses (T_I, T_E, T_I/T_{TOT}) against the 10 cm H_2O load (**Fig. 5**).

After IMST, the off-ventilator minute ventilation was similar between groups (weaned: 7.3 (1.2) L/min, unweaned: 7.9 (1.3) L/min), but respiratory rate trended slower in weaned patients (25 (4) breaths, unweaned: 30 (4) breaths, p=0.07).

Inspiratory Load Compensation upon Ventilator Weaning:

For the ten subjects who weaned, we evaluated whether the size of the inspiratory load was a significant influence on the magnitude of ILC training responses (**Fig 6**). The average IMST training load of the 10 weaned patients started at 10.2 (2.5) cm H_2O and improved to 13.7 (3.0) cm H_2O by the time of weaning. In the post-trained state, weaned patients generated significantly greater PIF at the different load magnitudes (*pre:* 5 cm load: 45.7±14.4 L/min, 10 cm load: 46.7±16.1 L/min, 15 cm load: 41.6±15.4 L/min; *post:* 5 cm load: 54.1±25.6 L/min, 10 cm load: 54.9±28.7 L/min, 15 cm load: 48.3±23.1 L/min, $p<0.05$). The V_{TI} ILC responses were also larger after IMST (*pre:* 5 cm load: 5.3±1.7 mL/kg, 10 cm load: 5.0±1.7 mL/kg, 15 cm load: 4.8±1.7 mL/kg; *post:* 5 cm load: 7.5±3.3 mL/kg, 10 cm load: 5.7±1.9 mL/kg, 15 cm load: 5.7±2.2 L/min, $p<0.05$), against the three different pressure threshold loads. Before and after the IMST intervention period, T_I/T_{TOT} was consistently greater with the highest threshold load

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($p<0.05$). Further, T_I/T_{TOT} increased in the post-trained state ($p<0.05$). There were no individual differences in T_I or T_E.

Discussion

Summary of New Findings:

This study identified the characteristics of ILC responses to threshold loads, as a method to assess inspiratory muscle performance. Although we failed to find distinctions in MIP between weaned and unweaned patients, we found that the flow and volume ILC responses were greater in patients who ultimately weaned. There was a positive significant relationship between MIP and flow ILC. In patients who weaned, IMST increased the flow, volume and duty cycle of ILC responses increased across a range of different threshold load magnitudes.

ILC responses and MIP:

A methodological issue with MIP is it measures static "strength" of the breathing pump. MIP is roughly analogous to a maximal voluntary contraction in the limb muscles. [18]While this practical and non-invasive bedside technique is validated to estimate inspiratory muscle strength in clinical research and practice, the maneuver does not generate inspiratory airflow. Therefore, it does not measure dynamic motor performance (i.e. muscle force-velocity) or take into account the effect of airway and pulmonary mechanics. Further, MIP is influenced by the lung volume and diaphragmatic conformation, which could make it more prone to measurement error.

In contrast to static MIP maneuvers, ILC specifically examines the capacity to generate repeated, dynamic muscle contractions. Although the flow response to inspiratory threshold loads was positively correlated to MIP, ILC tests may provide additional useful information beyond MIP about a patient's ability to detect breathing loads and generate pressure. This characteristic of ILC is related to the pressure-threshold load provided by the valve. In ILC, he

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initial phase of a threshold-loaded inspiratory effort is occlusive, until sufficient pressure has been generated to open the inspiratory valve.[19] The inspiratory timing of pressure-threshold ILC is relatively constant, because pressure-threshold loads are flow-independent,[20, 21] unlike inspiratory resistive loads.

ILC and Weaning Success:

While this study was not specifically designed to examine predictors of ventilator weaning, significantly larger flow and volume ILC responses were apparent in weaned patients, even prior to IMST. ILC performance data in healthy adults indicated that the inspiratory and expiratory times are preserved during loaded breaths, while V_{TI} increases.[13, 15] Although the absolute flow and volume ILC of weaned patients remained well-below the values reported in healthy subjects,[14, 15, 19] the results indicated that that weaned patients were able to generate greater inspiratory muscle tension for ILC, producing larger inspired flows and volumes within the same T_I. These findings may reflect a greater ability of weaned patients to produce appropriate motor responses during an elevated work of breathing. Further study is required before we can determine whether specific ILC loads can best differentiate weaning outcomes.

Since strength and respiratory mechanics were similar for both weaning outcomes, other aspects of critical illness may have affected ILC performance of the unweaned patients, such as cardiac insufficiency. In a similar group of patients selected for weaning, the presence of left ventricular diastolic dysfunction during SBT has been associated with weaning failure.[22] The unweaned patients did not have significantly different other organ failure during their period of MV-dependence (**Tables 2, S1**). Alternatively, the unweaned patients may have developed more extensive skeletal muscle cachexia as a result of their prolonged critical illness. The MRC sumscores revealed widespread ICU-acquired muscle weakness in both groups.[23] While there were no group differences in the BMI or MRC sumscore, we cannot rule out the possibility that unweaned patients had less overall muscle mass.

Relationship between IMST and ILC performance:

This study was not designed to measure the training effectiveness of IMST. Since training did not significantly change ILC with 10 cmH_2O threshold loads for either weaning outcome, it is possible IMST only identifies patients with the available reserve needed to wean from MV. However, weaned subjects generated greater flow, volume, and duty cycle ILC responses across a range of load magnitudes (5-15 cm H_2O) after training. A recent systematic review indicated IMST increased inspiratory muscle strength in patients weaning from MV. [12] There is evidence that, much like strength training in limb muscles, IMST induces a multitude of compensatory neuromuscular responses that can be improved with repetition (training).[3, 24-28] A broader range of test loads may be needed to identify whether changes in ILC can help make disctinctions in the effectiveness of IMST.

Besides the changes in the ILC response curve, weaned subjects improved their unassisted breathing pattern during SBTs. After IMST, the weaned patients tended to have a lower respiratory rate, suggesting patients sustained ventilation with a slower breathing pattern. The precise mechanisms by which IMST potentiates chronic ventilatory motor responses require future study.

Limitations of the study method:

The magnitude of the findings could be limited by the small sample size available for analysis and therefore IMST and weaning may yield additional differences in ILC that were not detected by this report. Additionally, the dependent variables were conscious, maximal-effort motor behaviors. Transdiaphragmatic pressure responses to evoked contractions provide the

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most specific assessment of diaphragm activation.[18] However, the equipment and specialized training required for these non-volitional techniques are not available in many clinical weaning settings. The MIP occlusion test has been validated for ventilated adults,[17] and we provided strong encouragement to standardize maximal patient efforts. We cannot rule out a familiarization effect in the patients. However, threshold loading performance appears less susceptible to learning among patients with existing lung disease than in healthy adults.[29] Patient-generated, dynamic inspiratory muscle contraction is the primary method to reliably achieve ventilator independence. Consequently, ILC performance tests may provide additional information for determining what patients will actually be able to accomplish during unassisted breathing trials for progressing ventilator weaning.

Conclusions

In tracheostomized patients undergoing a clinical trial of IMST effects on liberation from MV,[11] flow and volume ILC responses started significantly higher in weaned subjects and remained significantly greater after IMST. In contrast, MIP measurements were similar between weaned and unweaned patients. ILC required patients to generate dynamic contractions against inspiratory loads that differed from static MIP maneuvers to estimate strength. Among patients who weaned, increased volume and flow ILC responses across a range of load magnitudes after IMST suggest a carryover effect. Thus flow and volume ILC measurements may provide additional insights when testing the muscular capacity of difficult to wean patients, including their eligibility for IMST. Future research is needed to determine whether ILC could offer any predictive value for weaning.

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Figure Legends

Figure 1. For ILC testing, a Threshold® PEP training device was inverted and connected to a Capnostat® respiratory sensor (black arrow). The patient was briefly disconnected from the ventilator, and the sensor connected directly to the tracheostomy tube. The valve of the training device remained closed until sufficient inspiratory pressure was generated to overcome the 10 cm H_2O load. Once the threshold pressure was reached, the valve opened, permitting inspiratory airflow (denoted by white arrow). Expiration was unimpeded by the training device.

Figure 2. Progression of spontaneous breathing trials administered during IMST study interventions. Patients who could not initially tolerate at least one hour of spontaneous, unassisted breathing (right) underwent trials of reduced pressure support or CPAP (left).

Figure 3. MIP did not significantly differ between the weaned (gray bars) and unweaned (unfilled bars) groups (p=0.24). In both groups, pressure increased after IMST (* ANOVA main effect, P<0.05). Box and whisker plots show the median, IQR, and 95 percentile of dataset.

Figure 4. Correlations between MIP and ILC ventilatory variables. ILC flow and volume responses to a 10 cm H_2O load are shown in the 16 difficult to wean subjects, prior to institution of IMST. Before IMST, MIP in the weaned subjects was significantly correlated with (**A**) PIF (r=0.638, p<0.01), with a trend in (**B**) V_{TI} (r=0.45, p=0.08). The gray markers represent patients who ultimately weaned from MV after IMST, and unfilled markers delineate patients who failed to wean. In contrast, no linear relationship was found between MIP and inspiratory or expiratory timing during ILC.

Figure 5. Inspiratory load compensation responses before and after IMST in unweaned and weaned patients. ILC responses to a 10 cm H_2O load differed between weaned (unfilled markers) and unweaned (gray markers) subjects. In weaned subjects, (**A**) PIF was significantly greater (p<.05) and (**B**) V_{TI} was significantly larger (p<.05), than unweaned subjects, both before and after implementing IMST. The duty cycle (**C**) and inspiratory (**D**) and expiratory (not shown) times were similar between groups. (* main effect for weaning outcome, p<.05) Box and whisker plots show the median, IQR, and 95th percentile of dataset.

Figure 6. Detailed inspiratory load compensation performance before and after IMST in weaned patients. The ILC responses to 5, 10, and 15 cm H2O loads differed between the pre- and post-trained state in weaned patients. Compared to the pre-IMST state, (**A**) peak inspiratory flow was significantly larger (*p<.05), (**B**) tidal volumes of all breaths were significantly larger (#p<.01), (**C**) and duty cycle was significantly longer (# main effect for training, p<.01) after IMST. Duty cycle was also significantly longer with greater loads (†, p<.05). In contrast, (**D**) inspired time did not change with training. Box and whisker plots show the median, IQR, and 95th percentile of dataset.

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Table 1. Criteria used to conclude a spontaneous breathing trial.

Physiological Signs of Spontaneous Breathing Trial Failure
Increase in heart rate ≥ 30 bpm from resting, or HR 80% of age-predicted maximum
Systolic blood pressure >180 mm Hg or <90 mm Hg
SpO_2 sustained <90% for at least 5 minutes
Respiratory rate >35 bpm sustained for 5 minutes
Serious dysrhythmias
Evidence of impeding fatigue: accessory muscle use, substernal retraction, sternomastoid activation, paradoxical breathing, nasal flaring
Diaphoresis, pallor changes
Patient felt unable to continue, requested assisted ventilation

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Table 2. Demographic characteristics of the sample

	Weaned	Unweaned	P-value
Age	66 (16)	68 (9)	0.77
Gender (% male)	4 of 10	3 of 6	
Prior MV (days)	44 (23)	48 (32)	0.77
MRC sumscore	31 (10)	25 (10)	0.23
SAPS II score	35 (8)	33 (6)	0.56
Organ Failure	3 (2, 3)	3 (3, 5)	0.18[#]
Smokers (%, pk-yr)	50%, 57 (6)	67%, 63 (36)	0.78
Dynamic compliance (ml/cm H_2O)	52.9 (18.1)	55.9 (19.8)	0.76
Dynamic inspiratory resistance (cm H_2O/L/min)	7.4 (3.4)	8.3 (2.3)	0.55
Dynamic expiratory resistance (cm H_2O/L/min)	7.7 (3.5)	8.8 (2.5)	0.51
Days of IMST	9.4 (4.2)	9.2 (3.0)	0.91
Days IMST deferred	2 (1, 3)	8 (3, 9)	0.13[#]
Days of study participation	18 (11, 23)	25 (16, 28)	0.16[#]

Mean (SD)
[#] Mann-Whitney *U* test

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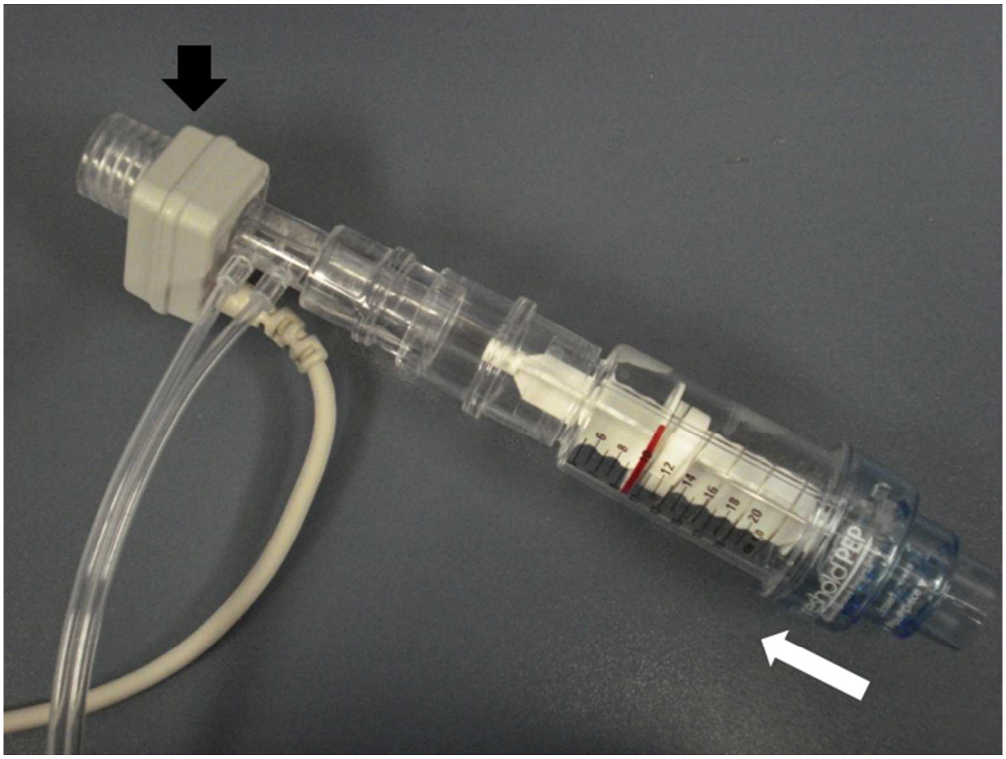

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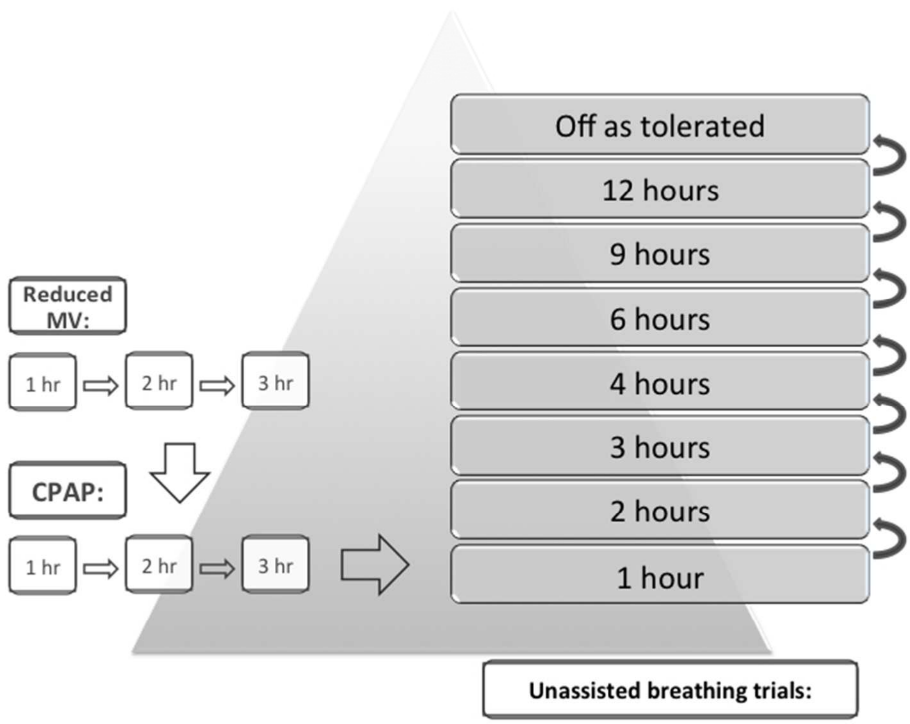

Progression of spontaneous breathing trials administered during IMST study interventions. Patients who could not initially tolerate at least one hour of spontaneous, unassisted breathing (right) underwent trials of reduced pressure support or CPAP (left).
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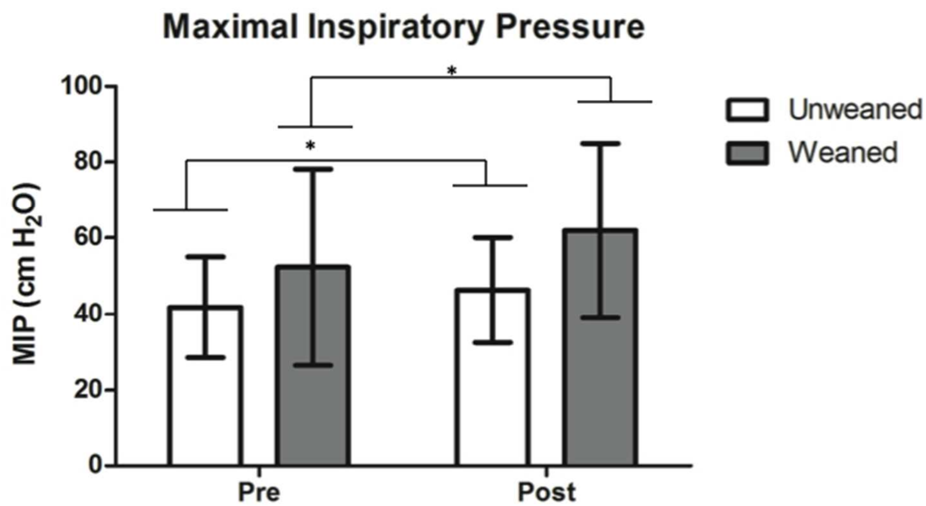
Fig 3



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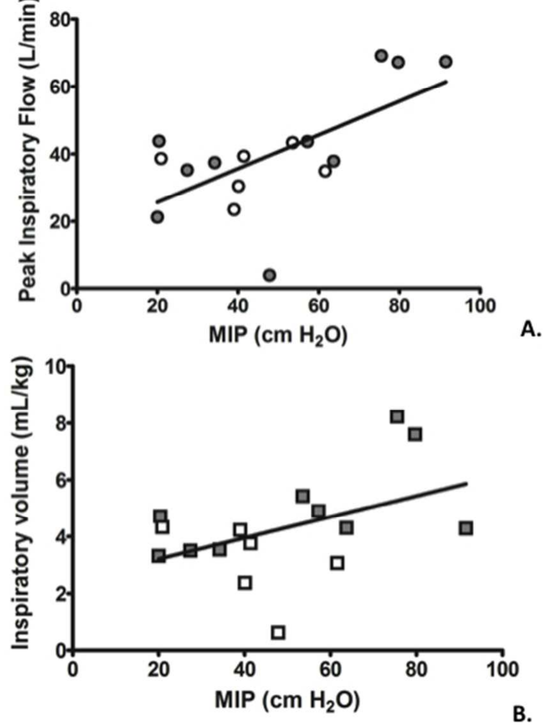

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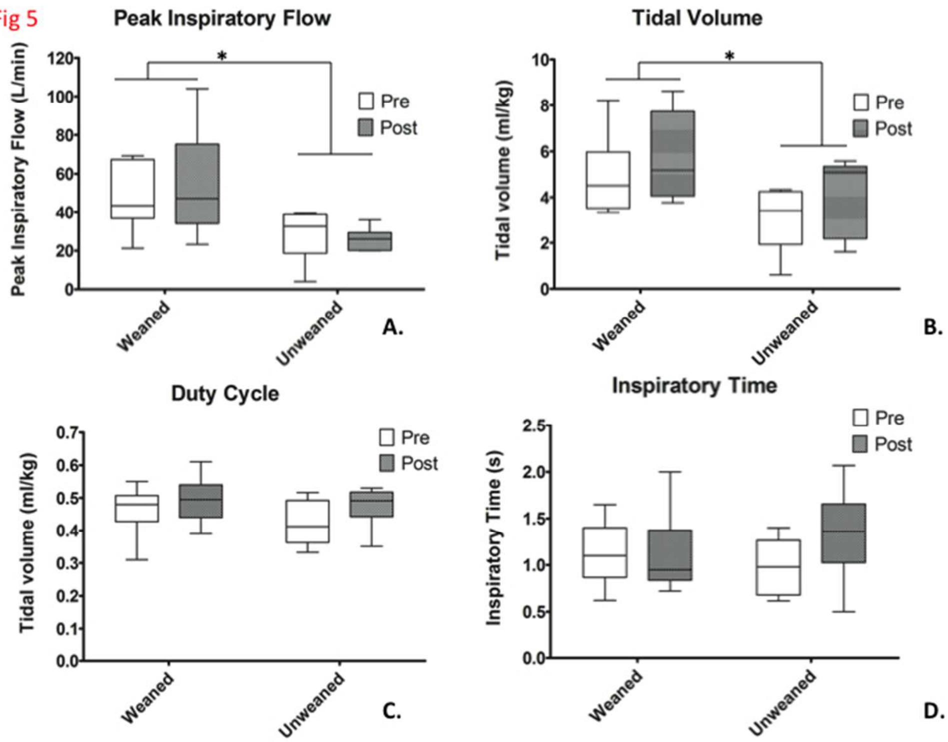
Fig 5



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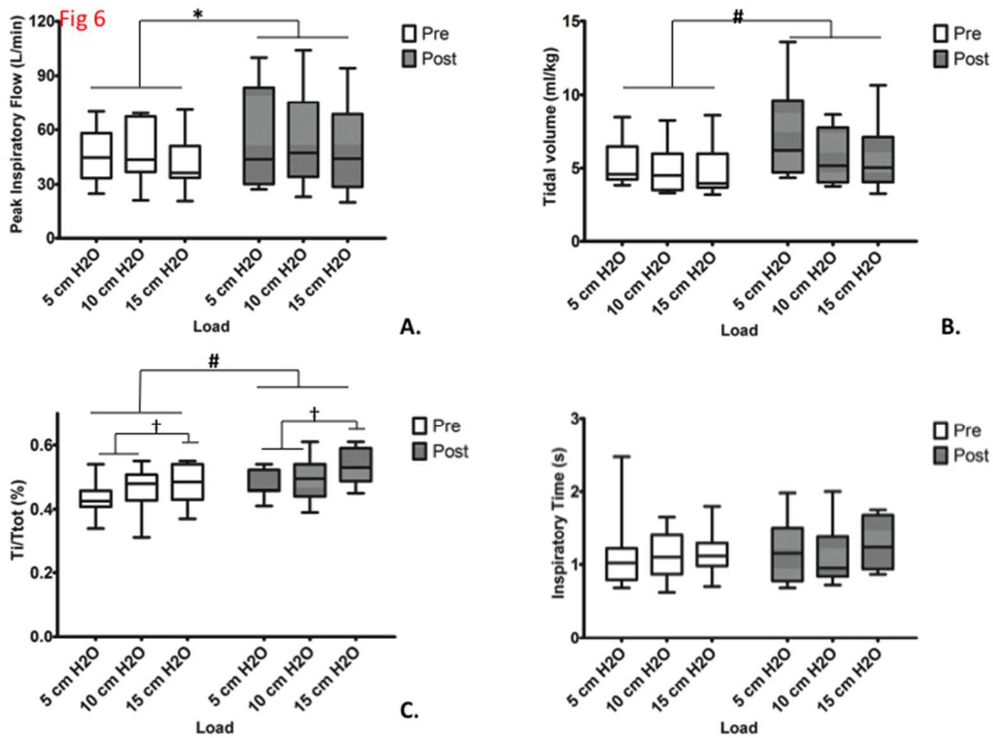

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