Official Title:
Assessment of Inspiratory Effort and Diaphragmatic Function Across Pressure Support Levels in Surgical ICU Patients: A Prospective Physiological Study

ClinicalTrials.gov Identifier (NCT Number):
NCTXXXXXXXX

Document Date:
17th September 2025

Title Assessment of Respiratory Drive and Inspiratory Effort Across Pressure Support Levels in Patients After Major Abdominal Surgery: A Physiological Observational Study

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Background

Pressure support ventilation (PSV) is one of the most used modes of partial ventilatory assistance in critically ill patients, such as those recovering from acute respiratory failure, major surgery, or during weaning from mechanical ventilation [1,2]. In PSV, tidal volume (Vt) is the result of a dynamic interaction between patient-generated inspiratory effort and ventilator-delivered pressure. While this mode aims to unload respiratory muscles and preserve spontaneous breathing, inappropriate levels of support—whether too low or too high—may contribute to patient harm[3].

Patients undergoing major abdominal surgery[4] often experience significant physiological changes that impair respiratory function, including reduced diaphragmatic excursion, decreased lung compliance, and impaired cough and secretion clearance due to postoperative pain, abdominal splinting, and the effects of anesthesia. These changes can persist for days, increasing the risk of atelectasis, ventilator-associated complications, and delayed weaning[5,6]. In this context, carefully titrated PSV is essential to provide sufficient support while avoiding over-assistance that may promote diaphragm disuse [3,7,8] or under-assistance that may lead to excessive respiratory effort and patient self-inflicted lung injury (P-SILI).[3,9,10]

Traditional parameters such as Vt and respiratory rate alone are insufficient to evaluate the patient's contribution to breathing effort. The gold standard for measuring inspiratory effort remains esophageal pressure (Pes) monitoring, which allows estimation of the work of breathing and transpulmonary pressure [1,11,12]. Alternatively, the electrical activity of the crural diaphragm (EAdi) has been proposed as a surrogate for respiratory drive and effort [13]. However, both methods are limited by their invasiveness, cost, and technical complexity, which limits their feasibility in routine practice.

Given these limitations, several simpler bedside tools have emerged, including occlusion pressure at 0.1 seconds (P0.1), maximum negative occlusion pressure (Pocc), and the pressure muscle index (PMI). P0.1 (airway occlusion pressure measured during the first 100 milliseconds of inspiration) is a useful screening tool for assessing respiratory drive, whereas Pocc (the maximum negative pressure during an inspiratory occlusion) and PMI (a derived measure estimating inspiratory effort) may better reflect inspiratory effort [1,3,14,15]. Low PMI or a lack of inspiratory pressure plateau may indicate over-assistance, while high Pocc values suggest excessive effort and under-assistance[1,3,14].

Importantly, no prior studies have specifically investigated how respiratory parameters change in response to pressure support level adjustments in the postoperative setting following major abdominal surgery. To date, only two relevant studies exist: Docci et al. (2023)[7] conducted a physiological study in patients recovering from acute respiratory failure, examining the impact of PSV level changes on PMI, Vt, and related variables. Another earlier study by Umbrello et al. (2015) [16] included a broader population of post-major elective surgery patients (10 of whom had undergone abdominal surgery), evaluating the correlation between diaphragm ultrasound and traditional effort indices during varying PSV levels. Neither study focused exclusively on the unique postoperative physiology of major abdominal surgery patients requiring prolonged mechanical ventilation, leaving an important knowledge gap.

Despite these developments, no consensus exists on the optimal PSV level that ensures sufficient ventilatory support while preserving respiratory muscle activity. Docci et al. [7] introduced a conceptual model suggesting a patient-specific "adequate PSV window," wherein patients modulate their effort to maintain a target Vt across a range of support levels. However, data supporting precise bedside criteria or cutoff values for over- or under-assistance remain limited

This study has two primary objectives. First, to evaluate changes in respiratory drive and inspiratory effort—measured by Pocc, PMI, and P0.1—and corresponding Vt across varying levels of pressure support in surgical ICU patients after major abdominal surgery who require prolonged mechanical ventilation (>48 hours)[17]. Second, we aim to determine the incidence of inadequate assistance (active, quasipassive)[7] in patients receiving PSV and explore its association with relevant clinical outcomes.

Study Design

This is a prospective, single-center, observational physiological study conducted in the surgical intensive care unit (ICU). A repeated-measures design is employed to systematically evaluate the effects of pressure support (PS) level adjustments on respiratory effort, drive, and diaphragmatic function in mechanically ventilated patients.

Study Population

Inclusion Criteria

- Adult patients (age ≥18 years) admitted to the surgical ICU.
- Recent major abdominal surgery requiring postoperative ICU care
- Receiving invasive mechanical ventilation for more than 48 hours
- Clinically stable, with no plan for extubation within 6 hours of study enrollment.

- Able to tolerate short-term adjustments in pressure support (PS) level as per protocol.

Exclusion Criteria

- Known neuromuscular diseases affecting respiratory muscle function.
- Hemodynamic instability requiring escalation of vasopressor support.
- Severe hypoxemic respiratory failure requiring PEEP >10 cmH_2O or FiO_2 >60%.
- Deep sedation (Richmond Agitation-Sedation Scale [RASS] score < –3) or ongoing neuromuscular blockade.
- History of chronic obstructive pulmonary disease (COPD) or other obstructive lung diseases.

Intervention / Protocol

After confirming eligibility and obtaining informed consent (from patients or legally authorized representative), enrolled patients will undergo a standardized stepwise adjustment of pressure support (PS) levels while remaining in pressure support ventilation mode. During the protocol, Automatic Tube Compensation (ATC) will be turned off to avoid interference with respiratory measurements. This protocol was adapted from Docci et al. [7]. Measurements will be performed once daily for up to three consecutive days or until the patient is extubated—whichever occurs first.

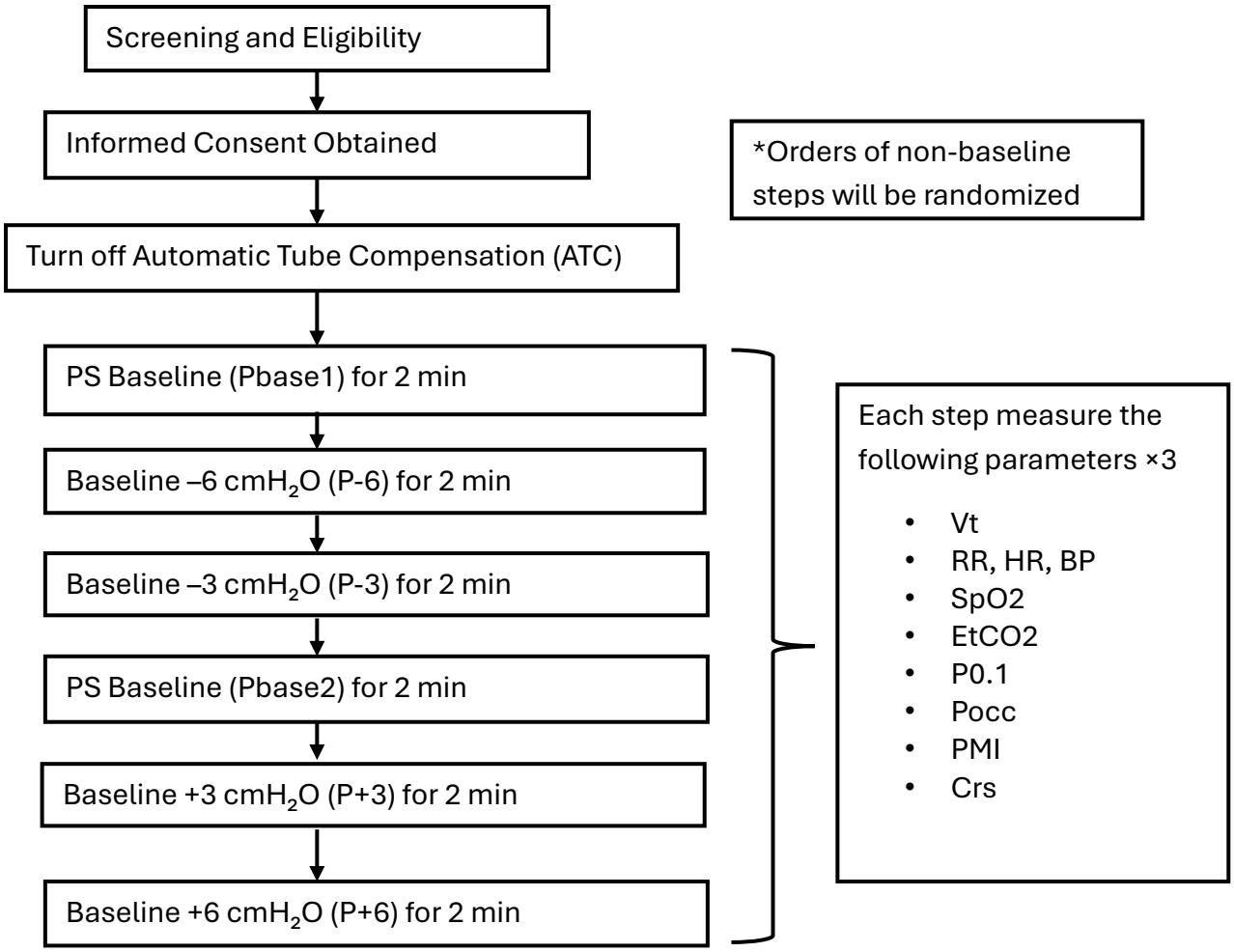
Pressure Support Steps
Patients will be studied at six PS levels in the following sequence:

- Baseline PS (clinically set level)
- Baseline −6 cmH_2O
- Baseline −3 cmH_2O
- Return to baseline PS
- Baseline +3 cmH_2O
- Baseline +6 cmH_2O

The order of the four non-baseline steps will be randomized for each patient using sealed envelopes, while the baseline PS step will be performed first and repeated last to assess measurement reproducibility.

At each pressure support (PS) level, a 2-minute stabilization period will be followed by three consecutive measurements of the following parameters: tidal volume (Vt), respiratory rate, P0.1, Pocc, pressure muscle index (PMI), static compliance of the

respiratory system (Crs), and peripheral oxygen saturation (SpO_2). Vt, RR, P0.1, Pocc, PMI, and Crs will be obtained from the ventilator, while SpO_2 will be recorded from the ICU monitor. PMI will be calculated as PMI = Pplat − (PEEP + PS), and Crs as Crs = Vt / (Pplat − PEEP). All values will be averaged across the three readings. **Figure 1. Study Protocol Flowchart**



Measurements and Outcomes

Primary Outcome

- To evaluate changes in respiratory drive and inspiratory effort—quantified using P0.1, maximum negative occlusion pressure (Pocc), and pressure muscle index (PMI)—across varying levels of pressure support in adult surgical ICU patients after major abdominal surgery.

Secondary Outcomes

- To quantify the incidence of quasi-passive and active response patterns during pressure support ventilation, based on physiological criteria derived from patient responses.
- To assess the relationship between these ventilatory response patterns and clinical outcomes, including duration of mechanical ventilation, ICU length of stay, reintubation or non-invasive ventilation use, and ICU/hospital discharge disposition.

Definition of ventilatory response patterns:

- An active pattern is characterized by relatively stable Vt and plateau pressure despite reductions in pressure support, accompanied by a compensatory increase in PMI—indicating greater patient-driven effort. In contrast, a quasi-passive pattern is marked by a progressive decline in Vt and plateau pressure with little or no change in PMI, suggesting limited patient contribution to ventilation. [7]
- As no standardized thresholds currently exist, these classifications will be determined post hoc based on individual response trends observed in the study dataset.

Data Collection

All data will be prospectively collected during each predefined pressure support (PS) level (baseline, ±3 cmH_2O, ±6 cmH_2O), following a 2-minute stabilization period at each step. The following variables will be recorded:

1. <u>Demographics and Baseline Clinical Data</u>
- Age, sex, height, weight, BMI
- Primary diagnosis and operation
- APACHE II or SOFA score at ICU admission
- Time from intubation to enrollment (hours)
- Baseline ventilator settings (PEEP, FiO_2, baseline PS)
- Baseline arterial blood gas (ABG): pH, $PaCO_2$, PaO_2, HCO_3^-, SaO_2

2. Ventilatory and Physiological Parameters (at each PS level)
- Tidal volume (Vt) – measured from ventilator display
- Respiratory rate– measured from ventilator
- Minute ventilation (MV) – calculated
- P0.1 – occlusion pressure at 0.1 seconds
- Pocc – airway pressure drop during inspiratory hold
- PMI – pressure muscle index calculated as Pplat − (PEEP + PS)
- Pplat – plateau pressure (via inspiratory hold)
- Ppeak – peak inspiratory pressure
- Crs – static compliance: Vt / (Pplat − PEEP)
- SpO_2 – peripheral oxygen saturation (pulse oximetry)
- $EtCO_2$ – end-tidal CO_2 if available
- HR and MAP – heart rate and mean arterial pressure (non-invasive or arterial line)
- Use of accessory muscles – observational note
- Signs of distress or dyssynchrony – e.g., paradoxical breathing, anxiety, diaphoresis

4. Post-Protocol Clinical Follow-up
- Duration of mechanical ventilation after study (in hours)
- Need for reintubation or non-invasive ventilation within 48 h
- Total ICU length of stay (LOS)
- ICU and hospital discharge status
- Complications: VAP, barotrauma, unexpected weaning failure

Safety and Tolerability

The protocol allows immediate cessation of PS level changes and return to baseline settings if any of the following occur:

- Respiratory rate >35 breaths/min
- SpO2 < 90%
- HR > 140 bpm or >30% change from baseline
- Signs of distress: diaphoresis, agitation, anxiety
- Hemodynamic instability

Sample Size

This is an exploratory physiological study using a repeated-measures design. Based on prior literature (Docci et al., 2023; Umbrello et al., 2015), a within-subject difference in

the pressure muscle index (PMI) of approximately 2.0 cmH_2O (standard deviation ~2.5) between pressure support (PS) levels is considered clinically meaningful.

Using a two-sided paired t-test with the following assumptions:

- Alpha (α) = 0.05
- Power (1 − β) = 0.90
- Effect size = 0.8

The calculated minimum required sample size is 20 patients. To improve the precision of subgroup analyses, enhance generalizability, and account for possible dropouts or incomplete data, we plan to enroll a total of 40 patients.

Statistical Analysis

Descriptive statistics will be used to summarize baseline characteristics. Continuous variables will be presented as mean ± standard deviation or median (IQR), depending on distribution. Categorical variables will be summarized as counts and percentages.

Primary analysis:

- Repeated-measures ANOVA or Friedman test (non-parametric) will be used to assess changes in PMI, Pocc, and P0.1 across PS levels.
- Post-hoc pairwise comparisons will be performed with Bonferroni correction.

Secondary analysis:

- Pearson or Spearman correlation will be used to evaluate relationships between effort indices (PMI, Pocc, P0.1).
- Linear mixed models will explore associations between PS levels and effort parameters, accounting for intra-patient variability.
- The incidence of under- and over-assistance will be described, and logistic regression may be used to assess their associations with clinical outcomes (e.g., prolonged ventilation).

A p-value <0.05 will be considered statistically significant. Statistical analyses will be performed using R.

Ethical Considerations

- Study protocol to be approved by institutional ethics board.
- Written informed consent obtained from patient or surrogate.
- Minimal risk as PS level adjustments are brief and within clinically accepted ranges.

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