Airway Occlusions to Measure Inspiratory Effort, Respiratory Drive, and Lung Mechanics During Noninvasive Ventilation

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Scientific knowledge on the topic

During invasive assisted ventilation, brief occlusion maneuvers allow measurement of Pocc, P0.1, and plateau pressure, providing bedside quantification of inspiratory effort, respiratory drive, and lung mechanics. However, no clinical studies have validated the feasibility of occlusion maneuvers in patients receiving NIV.

What does this study add to the field?

We show that Pocc is feasible during facemask NIV and provides clinically acceptable noninvasive estimates of inspiratory effort, dynamic transpulmonary driving pressure, and lung compliance. Ventilator-derived P0.1 discriminates patients with high respiratory drive, whereas plateau pressure is unreliable.

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ABSTRACT

Rationale: In intubated patients, occlusion maneuvers allow non-invasive assessment of inspiratory effort, respiratory drive and lung mechanics.

Objectives: To assess the feasibility of occlusion maneuvers during noninvasive ventilation (NIV).

Methods: In this multicenter study, 60 hypoxemic patients underwent two randomized 1-hour NIV sessions with oro-nasal and full-face masks after extubation. End-expiratory and end-inspiratory occlusions measured expiratory occlusion pressure (Pocc), 100-ms airway-pressure drop (P0.1), and plateau pressure. Esophageal manometry, calibrated before extubation, provided reference values for inspiratory effort, assessed as esophageal pressure swing (ΔPes), and dynamic transpulmonary driving pressure (ΔPL,dyn = pressure support − ΔPes). Interface-specific conversion factors (K) translating Pocc into predicted ΔPes (K × Pocc) and predicted ΔPL,dyn (pressure support − predicted ΔPes) were derived through 100-interaction cross-validation (20-patient derivation set, 40-patient validation set).

Main Results: Pocc was measurable in all patients. Mean K was 0.71 with the oro-nasal mask and 0.80 with the full-face mask. Predicted ΔPes agreed with observed ΔPes (oro-nasal bias -0.41 cm H_2O, 95% limits of agreement -2.3 to 1.5; full-face 0.09, -2.9 to 3.1), and predicted ΔPL,dyn agreed with observed ΔPL,dyn (oro-nasal bias 0.03, -2.9 to 2.9; full-face -0.04, -4.3 to 4.2). Predicted ΔPes identified observed ΔPes ≤ -10 cm H_2O, with areas under the receiver-operating-characteristic curve of 0.98 (oro-nasal) and 0.97 (full-face). Ventilator-derived P0.1 did not precisely quantify respiratory drive, but values >2.7 cm H_2O with the oro-nasal mask and >3 cm H_2O with the full-face mask identified high drive with specificity >90%. Plateau pressure was unstable in 78% (oro-nasal) and 90% (full-face) of patients. More negative predicted ΔPes, higher predicted ΔPL,dyn, and lower predicted lung compliance (expiratory tidal volume/predicted ΔPL,dyn) were associated with subsequent re-intubation.

Conclusion: During NIV, Pocc-derived parameters provide non-invasive estimates of inspiratory effort, lung stress and mechanics, whereas ventilator P0.1 and plateau pressure are less reliable.

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Keywords: noninvasive ventilation; occlusion maneuver; Pocc; airway occlusion; plateau pressure; inspiratory effort; transpulmonary driving pressure; lung compliance; reintubation

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INTRODUCTION

In hypoxemic patients, noninvasive ventilation (NIV) can improve oxygenation, reduce the work of breathing, and may avert endotracheal intubation (1). However, prolonged NIV with delayed intubation may worsen outcomes, particularly in patients with vigorous inspiratory effort (2–4). Excessive inspiratory effort may lead to high tidal volumes and transpulmonary driving pressure, thereby increasing global and regional lung stress and contributing to self-inflicted lung injury (5).

Esophageal manometry is the gold standard for measuring inspiratory effort and transpulmonary driving pressure (6–8). Physiological studies have demonstrated the value of monitoring inspiratory effort through esophageal manometry for early identification of patients at risk of NIV failure (9–11). However, this technique is invasive and requires dedicated equipment and expertise, limiting its routine use in clinical practice.

To overcome these limitations, noninvasive surrogates have been proposed in intubated patients. An end-expiratory occlusion allows measurement of the negative deflection in airway pressure during the first breath (Pocc), which provides a reliable estimate of inspiratory effort (12). The airway pressure drop 100 ms after the beginning of an occluded breath (P0.1) reflects respiratory drive (13). A brief end-inspiratory hold allows measurement of plateau pressure (Pplat) and calculation of airway driving pressure (14). Whether these metrics are applicable during NIV has not been established yet.

We conducted a multicenter study to assess whether occlusion-derived parameters accurately reflect inspiratory effort, respiratory drive, lung stress and compliance during NIV. Some of the results of these studies have been previously reported in the form of an abstract (15).

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METHODS

Additional details are provided in *Online Supplement*.

Study design

This multicenter physiological study was conducted in five general intensive care units in Italy between November 2023 and September 2025. Ethical approval was obtained in each center (coordinating center: Bari University Hospital, approval No.7748-0049191; ClinicalTrials.gov: NCT06344234). Written informed consent was obtained from all enrolled patients according to committee recommendations.

Study population

Adult intubated patients who had received invasive mechanical ventilation for ≥48 hours and were scheduled for extubation were screened for inclusion. Patients were screened before extubation to allow for correct positioning and calibration of the esophageal catheter, which can only be performed during invasive ventilation (16). Hypoxemic, non-hypercapnic (PaO_2/FiO_2 ratio <300 mmHg and $PaCO_2$ ≤45 mmHg) patients with at least one high-risk factor for re-intubation were included (17, 18). Exclusion criteria were: failure of the spontaneous breathing trial (19, 20), neuromuscular disease, pregnancy, tracheostomy, acute exacerbation of chronic respiratory disease, refusal of consent, and an air leaks >30% during NIV before study initiation.

Study procedure

After a successful spontaneous breathing trial and the decision to extubate, patients were reconnected to mechanical ventilation for 1 hour (21). During this period, an esophageal balloon catheter (Nutrivent, Sidam, Mirandola, Italy) was inserted if not already in place, and esophageal pressure (Pes) was verified using a dynamic occlusion test (16). NIV was immediately initiated after

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extubation using a gas-compressed mechanical ventilator connected through a dual-limb circuit and a heat-and-moisture exchanger. For study purposes, NIV-specific ventilator software was not activated and leak compensation was disabled; NIV was initially set with positive end-expiratory pressure (PEEP) of 5-7 cmH_2O and pressure support of 5 cmH_2O, then titrated to achieve a tidal volume of 6-8 mL/kg predicted body weight; FiO_2 was adjusted to maintain SpO_2 between 92 and 96%. Pressurization time was set at 50-100 ms and expiratory trigger sensitivity at 20-50% of peak inspiratory flow. All patients underwent two 1-hour NIV sessions in randomized order (computer-generated random sequence), using two different interfaces (oro-nasal and full-face masks; HMC GROUP, Mirandola, Italy). During NIV, three non-consecutive end-expiratory and end-inspiratory occlusion maneuvers were performed to measure Pocc and plateau pressure. P0.1 was measured by the ventilator. Between NIV sessions, high-flow nasal oxygen was administered for 1 hour. After completion of the protocol, patients were managed with alternating high-flow nasal oxygen and NIV, for at least 48 hours, and then according to clinical practice (22). The decision to re-intubate the patients in case of post-extubation distress was made by attending physicians, who were blinded to study measurements.

Measurements

Patients' demographics and most relevant clinical characteristics were collected at study entry. During study procedures Pocc, P0.1, and Pplat were collected from the ventilator screen; ventilator-derived Pplat was measured after approximately 1s of inspiratory hold. For offline analysis, airway flow (Fleisch pneumotachograph No. 2, Metabo, Lausanne, Switzerland) was measured at airway opening (Y-piece) together with airway pressure (Paw). Pes and Paw were recorded continuously at 200 Hz and stored for offline analysis (ICU Lab, Kleistek, Bari, Italy). For each patient, 155-222 non-occluded breaths and three end-expiratory and three end-inspiratory occlusions were analyzed. Tidal volume (Vt) was obtained as digital integration of flow signal. When measured offline from data recorded by the pneumotachograph, Pocc and P0.1 were defined as the maximal

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negative Paw deflection and the Paw drop during the first 100 ms, respectively (23), whereas Pplat was measured at 0.3 and 1.0 s after the onset of end-inspiratory occlusion (Pplat,0.3s and Pplat,1s) and its stability was defined as a difference ≤ ±1 cmH_2O between these two values (24) (**Figure 1**). Airway driving pressure was Pplat - PEEP. Inspiratory effort was calculated as the negative Pes swing during non-occluded breaths (actual ΔPes) (25), averaged over 5 min of stable breathing before occlusions. Respiratory drive was referred as Pes drop at 100 ms during end-expiratory occlusion (P0.1,es) (26, 27). As a complementary analysis, respiratory drive was also assessed by the maximal rate of esophageal pressure decrease during inspiration (ΔPes/dt) measured on non-occluded breaths. Transpulmonary pressure was Paw-Pes (16); dynamic transpulmonary driving pressure (ΔPL,dyn) was the positive swing in transpulmonary pressure from the onset of inspiration to its peak value (12, 14); dynamic lung compliance (Clung,dyn) was the ratio between expiratory tidal volume and ΔPL,dyn (26). For all calculations, the beginning of inspiration was identified at the point of initial Pes decay (28). Gas exchange and hemodynamics were recorded at the end of each NIV session.

Objective

The primary objective was to assess the feasibility of occlusion maneuvers, the accuracy of derived metrics in estimating inspiratory effort, respiratory drive, lung stress and mechanics during NIV. The impact of air leaks on these measurements was also assessed. As an exploratory endpoint, we evaluated whether occlusion-derived indices were associated with re-intubation within 7 days from extubation.

Statistical analysis

Data are reported as median [IQR] or n (%). Normality was assessed using the Shapiro-Wilk test. Intra-patient variability was quantified by the coefficient of variation (CV%) and intraclass correlation coefficient (ICC) (Table E1). Between-group and within-group comparisons used the chi-square or Mann-Whitney U tests, and the Wilcoxon signed-rank test, as appropriate. To derive

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inspiratory effort and lung stress from Pocc, we performed 100 repeated internal cross-validations: at each iteration, patients were randomly assigned to a derivation set (one third) and a validation set (two thirds). In the derivation set, we calculated K = actual ΔPes /Pocc and applied it in the validation set to compute predicted ΔPes = K × Pocc and predicted ΔPL,dyn =[Puressure support - (K × Pocc)] (12). Ventilator-derived Pocc was used to compute predicted ΔPes, and predicted ΔPL,dyn. Associations between measurements were evaluated using mixed-effects models to account for repeated measures, with patients included as random effects and time included as a fixed effect, while agreement was assessed using the concordance correlation coefficient (CCC) and Bland-Altman analysis, both adapted for repeated measurements (29, 30). Excessive inspiratory effort and high drive were defined as actual ΔPes ≤-10 cmH_2O (9–11) and P0.1,es >3 cmH_2O (27), respectively. Discriminatory power of predicted ΔPes (for excessive effort) and P0.1 (for high drive), was evaluated by receiver operating characteristic (ROC) curve analysis with bootstrapped 95% CIs. Extubation failure risk was analyzed by univariable logistic regression using patient-level mean values (averaged across three measurements) stratified by NIV interface. Kaplan-Meier analysis for time to reintubation was performed by stratifying patients according to the median value of Predicted ΔPes, PL,dyn and Clung,dyn observed in the extubation failure group; curves were compared using log-rank test. Sample size was determined a priori, yielding a planned total of 60 patients.

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RESULTS

Among 106 screened patients, 46 were excluded per predefined criteria (**Figure E1**). Demographics and most relevant clinical characteristics of the 60 included patients are reported in **Table 1**. Breathing pattern and clinical variables during oronasal and full-face NIV are summarized in **Table 2**.

Pocc and Inspiratory effort

Pocc was available in all patients with both interfaces (**Figure E2**). In the derivation cohort, the conversion factor K (actual ΔPes/Pocc) was 0.71 (95% CI, 0.68 to 0.75) for oro-nasal and 0.80 (95% CI, 0.79 to 0.81) for full-face NIV. In the validation cohort, predicted ΔPes (K×Pocc) showed good agreement with actual ΔPes (oro-nasal: CCC 0.92 [0.90-0.94], bias -0.41 cm H_2O, limits -2.3 to 1.5; full-face: CCC 0.93 [0.91-0.94], bias 0.09 cm H_2O, limits -2.9 to 3.1) (**Figure 2A**); visual inspection of the Bland-Altman plots suggested heteroscedasticity, with lower precision at higher levels of inspiratory effort (**Table E3**). Actual ΔPes was ≤-10 cm H_2O in 19 patients during oro-nasal and 21 during full-face NIV; predicted ΔPes < -9 cmH_2O accurately identified excessive effort (AUC 0.98 [0.97-0.99] and 0.97 [0.96-0.99], respectively) (**Table E2**).

Pocc and lung mechanics

Predicted ΔPL,dyn [pressure support - (K×Pocc)] showed moderate concordance with measured Δ PL,dyn, with minimal bias (oro-nasal: 0.03 cm H_2O, limits -2.9 to 2.9; full-face: -0.04 cm H_2O, limits -4.3 to 4.2). Predicted Clung,dyn also showed moderate concordance with Clung,dyn (oro-nasal: bias 0.003 mL/cm H_2O, limits -7.1 to 7.1; full-face: bias 0.05 mL/cm H_2O, limits -12.0 to 12.1) (**Figure 2, panels B and C**). As for predicted ΔPes, agreement became less precise at higher ΔPL,dyn and lower CLung,dyn values (**Table E3**).

P0.1 and respiratory drive

Ventilator-derived P0.1 had poor concordance with respiratory drive (P0.1,es) (oro-nasal: CCC 0.17 [-0.04 to 0.37]; full-face: CCC 0.03 [-0.11 to 0.17]) (**Figure 2D**). Pneumotachograph-derived P0.1 showed higher concordance with P0.1,es (oro-nasal: CCC 0.84 [0.73-0.89]; full-face:

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CCC 0.86 [0.82-0.90]) but clinically wide limits of agreement (oro-nasal: bias -0.2 cm H_2O, limits -1.7 to 1.2; full-face: bias -0.1 cm H_2O, limits -1.7 to 1.4), indicating low precision at the individual level (**Figure E3**). Ventilator-derived P0.1 thresholds >2.7 cm H_2O (oro-nasal) and >3.0 cm H_2O (full-face) identified high drive with low sensitivity but with good specificity (>90%) (**Table E4**). Complementary analysis also showed no correlation between ventilator-derived P0.1 and ActualΔPes/dt in both interfaces (**Figure E7**).

Plateau pressure and lung mechanics

A stable plateau pressure tracing was obtained in 13 patients (22%) with oronasal and 6 (10%) with full-face NIV. Most occlusions showed incremental Pplat (52% and 55%), whereas decremental patterns were less frequent (26% and 35%) (**Figure E5**). Ventilator- and pneumotachograph-derived Pplat had high concordance (oronasal: CCC 0.95 [0.94-0.96]; full-face: CCC 0.97 [0.96-0.98]) but limits of agreement were wide (oro-nasal: bias 0.01 cm H_2O, limits -1.7 to 1.8; full-face: bias 0.03 cm H_2O, limits -1.6 to 1.8) (**Figure E4**). When Pplat was deemed reliable, static respiratory system driving pressure, neither measured with Pplat 0.3s nor 1s, did not show a robust correlation with ΔPL,dyn (oro-nasal: r=0.17, p=0.06; r=0.03, p=0.75; full-face: r=0.37, p<0.05; r=0.34, p<0.05).

NIV air leaks and occlusion-derived parameters

Median air leaks was 20% [17-22] during oronasal and 21% [17-24] during full-face NIV. Air leaks was not associated with Pocc (oro-nasal r=0.22, p=0.30; full-face r=0.01, p=0.95) and the mean conversion factor K (actual ΔPes/Pocc) remained stable across leaks levels (**Figure 3)**, suggesting that the air-leak did not meaningfully affect Pocc-derived parameters. Air leaks was also not associated with P0.1 or Pplat (**Figure E6**).

Exploratory Outcomes

Fourteen patients (23%) required reintubation. Patients' characteristics according to weaning outcome are shown in **Table E5;** breathing pattern and clinical variables are summarized in **Table 3**. Among occlusion-derived parameters, more negative predicted ΔPes (oro-nasal OR 0.71 [95% CI, 0.57-0.87]; full-face OR 0.66 [0.52-0.84]), higher predicted ΔPL,dyn (oro-nasal OR 1.34 [1.10-1.63];

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full-face OR 1.52 [1.20-1.93]), and lower predicted Clung,dyn (oro-nasal OR 0.87 [0.78-0.96]; full-face OR 0.86 [0.77-0.96]) were associated with subsequent reintubation (**Figure 4**; **Table E6**).

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DISCUSSION

The results of the present multicenter physiological study conducted on patients receiving NIV through a facemask can be summarized as follows:

- End-expiratory occlusion is feasible. Pocc-derived parameters provide high concordance for inspiratory effort and moderate concordance for lung stress and lung compliance, with lower precision at extreme values; air leaks did not meaningfully affect the accuracy of these measures.
- Ventilator-derived P0.1 does not reliably quantify respiratory drive during NIV. This limitation seems partly related to ventilator readouts: pneumotachograph-derived P0.1 showed no systematic bias versus P0.1,es, yet the wide limits of agreement indicate poor precision. Together, these findings suggest that P0.1 has inherent limitations during NIV. Despite low overall accuracy, a high ventilator-derived P0.1 (>2.7 cmH_2O) identifies elevated drive with specificity>90%, whereas low P0.1 values are not informative.
- A stable end-inspiratory plateau pressure is measurable in only a minority of patients, limiting its use for assessing respiratory system static driving pressure.
- Higher inspiratory effort, higher dynamic transpulmonary driving pressure, and lower dynamic lung compliance, all assessed noninvasively by Pocc, are associated with subsequent reintubation.

When used in hypoxemic patients, NIV offers important advantages; however, early recognition of treatment failure is critical because it may substantially affect patient outcomes (31–33). At the bedside, an elevated tidal volume is one of the most recognizable warning signs of NIV failure (34, 35). However, a high tidal volume should be better interpreted as a downstream result of the mechanistic pathway leading to lung injury progression, where excessive inspiratory effort is the primary determinant of increases in global and regional lung stress (36). During assisted ventilation, inspiratory effort and ventilator pressure support add to generate the transpulmonary driving pressure, which represents the elastic load applied and can be viewed as tidal volume normalized to the size of

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the aerated lung (37–39). While tidal volume often tracks this process and therefore retains prognostic value, it is less specific and can be substantially influenced by respiratory system mechanics, ventilator settings, and interface-related factors (40). These considerations provide a robust physiological rationale for directly monitoring inspiratory effort and transpulmonary driving pressure during NIV. Accordingly, physiological studies using esophageal pressure have shown that higher effort and transpulmonary driving pressure may predict subsequent NIV failure earlier and more accurately than absolute tidal volume (9, 41).

Esophageal manometry is the gold standard to quantify inspiratory effort and transpulmonary driving pressure during NIV, but its use is limited in clinical practice, especially in nonintubated patients (42). Accordingly, efforts have focused on identifying simpler, less invasive, bedside-available surrogates. In intubated patients, brief end-expiratory occlusions allow measurement of Pocc and P0.1, and end-inspiratory holds enables assessment of Pplat; these provide clinically accurate estimates of effort, respiratory drive and lung stress without esophageal manometry (43, 44). In our study, Pocc and its derived indices are shown to provide clinically acceptable estimates of inspiratory effort, lung stress, and compliance during NIV, with consistent performance across both oro-nasal and full-face interfaces. Importantly, we derived an interface-specific conversion factor to translate Pocc into predicted ΔPes, and validated this approach in a cohort, suggesting its potential generalizability. Notably, in intubated patients, the conversion factor used to estimate esophageal pressure swing from Pocc is 0.66, implying that Pocc per se overestimates Pes swing by approximately 34%. In our study this overestimation was approximately 30% with the oro-nasal mask (K = 0.71) and 20% with the full-face mask (K = 0.80). One possible explanation is that the facemask and upper airway add compliance to the system. As a result, part of the pressure generated during an occluded inspiratory effort may be absorbed by deformation of the interface and upper airway, rather than being fully transmitted to the airway opening. This may explain both the difference from intubated patients and the higher conversion factor observed with the full-face mask compared with the oro-nasal mask. Overall, these observations suggest that conversion factors derived in

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intubated patients should not be directly applied during NIV, as this may result in systematic underestimation of inspiratory effort.

Ventilator-derived P0.1 did not reliably quantify respiratory drive during NIV. A plausible explanation relates to patient-interface interaction: unlike in intubated patients, the first 100 ms after an occlusion are strongly influenced by mask compliance, as cushion deformability can transiently absorb patient-generated pressure, thereby damping the early airway pressure decay measured by the ventilator. Although ventilator-derived P0.1 is imprecise and not accurate for quantifying drive at the individual level, it may retain some clinical usefulness as a rule-in signal: high values (e.g., >3 cmH_2O) make elevated respiratory drive likely, whereas low values cannot reliably exclude it (45). Limitations in point estimates for P0.1 may be attributable to ventilator readouts, since pneumotachograph-derived P0.1 showed high concordance with respiratory drive. In addition, the finding that P0.1,vent was higher than P0.1,es suggests that, during NIV, the early airway pressure signal may be influenced not only by inspiratory drive itself, but also by patient-interface interaction, mask compliance, and possibly expiratory muscle relaxation at the onset of inspiration. However, the wide limits of agreement indicate limited precision in individual point estimates, which constrains its accuracy for patient-level quantification. Notably, although the absolute dispersion of pneumotachograph-derived P0.1 was comparable to that observed for Pocc-derived estimates, its relative impact was substantially larger: similar absolute limits of agreement translate into a much higher percentage of the expected P0.1, thereby reducing the clinical interpretability of single patient-level measurements despite an overall acceptable mean bias. Overall, our data are consistent with previous reports (46), suggesting that P0.1 may still be informative of respiratory drive when acquired with a high-fidelity technique (e.g. pneumotachograph), whereas the additional measurement error associated with ventilator-derived P0.1 may render it less reliable.

Similarly, an accurate end-inspiratory plateau pressure was obtained only in a minority of patients, limiting the clinical use of static respiratory system driving pressure and compliance during NIV. This limitation is likely multifactorial. During end-inspiratory holds, leaks and instability of the

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patient-interface interaction may compromise the pressure tracing. Moreover, expiratory muscle activity may further distort airway pressure during the hold, even in the presence of an apparently stable plateau (47, 48). By contrast, the better performance of end-expiratory occlusion-derived measurements may be physiologically plausible. During end-expiratory occlusion, expiratory muscle activity may be less relevant to the interpretation of Pocc, whereas inspiratory effort generates a negative pressure deflection within the interface that may transiently improve mask sealing. Consistent with this interpretation, no association was found between the magnitude of air leaks during tidal breathing and the relationship between Pocc and inspiratory effort.

In our study, NIV-specific software was disabled during occlusion maneuvers. We recognize that this approach may limit the clinical applicability of our findings; however, this decision was driven by the need to preserve the physiological assumptions underlying occlusion-derived measurements. Since NIV algorithms are proprietary and may not be fully consistent across manufacturers, we could not rule out the possibility that leak compensation might affect the validity of occlusion-derived metrics to a variable extent depending on the ventilator used. From a practical standpoint, not all ICU ventilators allow occlusion maneuvers while NIV software is active, conversely a temporary switch from NIV mode to invasive mode appears feasible at the bedside without meaningfully altering ventilatory assistance. However, to further address this issue, we performed additional bench experiments using different ventilators and multiple combinations of PEEP and simulated inspiratory effort (Figure E8). Across all tested conditions, no clinically significant differences were observed in Pocc when occlusions were obtained with or without NIV-specific software enabled (Table E7). Although bench experiments cannot replace direct clinical validation, these additional data provide reassuring support for the robustness of our findings

Our results have relevant clinical implications. First, bedside monitoring of inspiratory effort, transpulmonary driving pressure and dynamic compliance may enable earlier recognition of injurious breathing patterns, thereby reducing delays in endotracheal intubation (9). Second, different interfaces and ventilator settings can have markedly different effects on effort and transpulmonary

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driving pressure (49). Their interaction with the individual breathing pattern, which varies across individuals, may explain why a given support strategy is effective in some patients but not in others (50). Pocc-derived estimates of effort and transpulmonary driving pressure may allow clinicians to individualize pressure support and PEEP in a physiology-informed manner, approximating the information that would otherwise require esophageal manometry (51, 52). Third, inspiratory effort, transpulmonary driving pressure and compliance may provide a pragmatic way to assess severity and stratify risk during NIV. Consistent with evidence in intubated patients (39, 53), our exploratory outcome analyses suggest that higher effort and lung stress and lower compliance are associated with subsequent re-intubation, supporting the potential prognostic value of these metrics.

Our study has limitations. First, we estimated inspiratory effort using ΔPes rather than total muscle pressure, as commonly done in intubated patients (12). However, estimating total muscle pressure in non-intubated patients is challenging, as it requires measurement of chest-wall elastance, which in turn relies on accurate inspiratory holds, that are inherently uncertain during NIV. Moreover, ΔPes is the effort-related metric most frequently used during NIV, and has been associated with clinically relevant outcomes in this setting (9–11). Second, the lack of reliability of P0.1 during NIV could theoretically be influenced by ventilator-specific algorithms. Unfortunately, we did not systematically record the ventilator model used for each patient, precluding a ventilator-specific subgroup analysis and limiting our ability to determine whether particular devices or proprietary algorithms contributed differentially to measurement error (46). Third, NIV was delivered using a dual-limb circuit, and NIV-specific software was disabled to avoid automatic leaks compensation; therefore, our findings may not be applicable to dedicated NIV devices that use single-limb circuits with intentional leaks set-ups. Fourth, the number of patients requiring re-intubation was relatively small, which may have limited the statistical power of comparisons between success and failure groups. In this context, the Kaplan-Meier analysis should be interpreted as exploring the prognostic value of early physiological markers measured after extubation in relation to the subsequent risk of NIV failure. Finally, our population consisted of post-extubation patients rather than patients with *de*

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novo acute hypoxemic respiratory failure. This design was necessary because accurate calibration of the esophageal balloon catheter can be reliably performed only during invasive ventilation. Although there is no clear physiological rationale to anticipate that the relationship between Pocc-derived indices and esophageal reference measurements would fundamentally differ in *de novo* patients, we acknowledge that using a threshold of $\Delta Pes \leq -10$ cmH_2O to define excessive inspiratory effort may be relatively conservative. However, several studies have shown that esophageal pressure swings above this threshold are associated with treatment failure, escalation to invasive ventilation, or potentially injurious breathing patterns (9–11). Importantly, our data suggest that precision decreases as inspiratory effort increases. This heteroscedasticity, however, does not preclude the use of Pocc during NIV, but rather mirrors the same pattern previously observed in intubated patients (12). Moreover, responses to different noninvasive supports may not differ substantially between hypoxemic and post-extubation patients (10, 54).

CONCLUSIONS

During NIV, Pocc-derived metrics are a feasible bedside approach to quantify inspiratory effort, lung stress, and lung mechanics; P0.1 and Pplat appear to be of limited utility in this setting, although high P0.1 values may still help identify elevated drive. In our cohort, Pocc-derived indices are associated with subsequent re-intubation, supporting their potential clinical relevance for early risk stratification and clinical decision-making.

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Table 1 Demographics and baseline characteristics of enrolled patients

Demographics Characteristic	All patients (n = 60)
Age, years	64 [57, 72]
Men, nº (%)	43 (71.7)
APACHE II [a],	
At ICU admission	17 [13, 20]
On day of extubation	12 [9, 16]
Length of MV before extubation, days	5 [4, 6]
Body mass index [b]	27 [26, 29]
RASS	1 [0, 2]
Predicted Body Weight, Kg[c]	61 [54, 69]
Diagnosis at admission, n (%)	
Primary respiratory failure	37 (61.7)
Medical	12 (20.0)
Postoperative Care	11 (18.3)
Comorbidities, n (%)	
Arterial hypertension	18 (30.0)
Neurologic disease	12 (20.0)
Diabetes mellitus	17 (28.3)
Renal disease	11 (18.3)
Liver disease	9 (15.0)
Obesity (BMI > 30)	5 (8)
Baseline ventilation, oxygenation and hemodynamics before extubation	
PEEP, cmH_2O	7 [6, 8]
PS, cmH_2O	7 [6, 8]
V_T/PBW	7.15 [6.90, 7.50]
Respiratory rate, bpm	21 [18, 24]
Arterial pH	7.40 [7.38, 7.42]
PaO_2/ FiO_2 mm Hg	183 [167, 222]
$PaCO_2$, mm Hg	41 [37, 42]
Systolic arterial pressure, mmHg	122 [110, 132]
Diastolic arterial pressure, mmHg	76 [68, 82]
Heart rate, bpm	80 [71, 87]

Results are expressed as median [IQR] for continuous variables and number (percentage) for categorical variables. Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; ICU, intensive care unit; MV, mechanical ventilation; RASS, Richmond Agitation and Sedation Scale; PEEP, positive-end expiratory pressure; PS, pressure support delivered by ventilator; V_T, tidal volume; PBW, predicted body weight FiO_2, inspiratory fraction of oxygen; Paw, airways pressure; Pes, esophageal pressure; PaO_2, arterial oxygen partial pressure; $PaCO_2$, arterial carbon dioxide partial pressure.[a] APACHE II score was calculated from 17 variables. Scores range from 0 to 71 points, with higher scores indicating more severe disease. [b]Calculated as weight in kilograms divided by height in meters squared. [c] Calculated as: 50 [or 45.5 for women] +0.91×[Height[cm]-152.4].

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Table 2. Breathing pattern and clinical variables during oro-nasal and full-face NIV.

	NIV INTERFACE		P value
	Oro-nasal	**Full-Face**	
Non-occluded breaths			
PEEP, cmH_2O	5 [5,6]	5 [5,6]	0.83
Ppeak, cmH_2O	11 [11,12]	11 [11,12]	0.71
V_T / PBW, mL/kg	7.8 [7.1,9.5]	8.7 [8.1,9.4]	0.13
Respiratory Rate, breaths/min	15 [12,20]	15 [12,21]	0.91
Air Leaks (%)	20 [17,21]	21 [17,23]	0.71
Actual ΔPes, cmH_2O	-6 [-10,-4]	-7 [-11,-5]	0.48
ΔPL,dyn, cmH_2O	12 [10,16]	12 [10,17]	0.68
Clung,dyn, ml/cmH_2O	35 [28,45]	32 [27,48]	0.24
Occlusion-derived parameters			
Pocc, cmH_2O	-9 [-14,-7]	-9 [-14,-7]	0.65
Pocc, pneumotach cmH_2O	-9 [-14,-7]	-10 [-15,-7]	0.98
P0.1, es cmH_2O	0.8 [0.5,1.2]	0.8 [0.5,1.4]	0.72
P0.1, vent, cmH_2O	2.1 [1.9,2.2]	2.6 [2.5,2.8]	0.08
P0.1, pneumotach, cmH_2O	2.5 [1.6,3.3]	2.6 [1.5,3.4]	0.99
Pplat, vent, cmH_2O	12 [10,14]	12 [10,14]	0.72
Pplat,0.3s cmH_2O	11 [11,12]	11 [10,12]	0.07
Pplat,1s, cmH_2O	12 [9,14]	12 [10,14]	0.60
Gas exchange and hemodynamics collected at the end of NIV session			
Arterial pH	7.41 [7.38,7.44]	7.41 [7.38,7.44]	0.08
PaO_2/ FiO_2 mm Hg	212 [184,260]	223 [188,255]	0.46
$PaCO_2$, mm Hg	42 [37,44]	43 [38,44]	0.35
Systolic arterial pressure, mmHg	123 [112,135]	125 [112,139]	0.15
Diastolic arterial pressure, mmHg	80 [75,86]	81 [73,86]	0.55
Heart rate, bpm	76 [66,82]	73 [68,84]	0.55

Results are expressed as median [IQR].

Abbreviation: NIV: non-invasive ventilation; Paw: airway pressure; PEEP: positive end-expiratory pressure; Ppeak: Peak airway opening pressure; V_T/PBW: inspired tidal volume normalized to predicted body weight; Pes: esophageal pressure; Actual ΔPes: maximal swing in esophageal pressure recorded during non-occluded breath (reference metric for inspiratory effort); P0.1,es: Pes drop 100 ms after the onset of inspiratory effort (reference metric for respiratory drive);PL: transpulmonary pressure; ΔPL,dyn: Dynamic transpulmonary driving pressure; Clung,dyn: Dynamic lung compliance; Pocc: airway occlusion pressure; P0.1: airway occlusion pressure at 100 ms; Pplat : Inspiratory plateau pressure recorded at 0.3 s (Pplat,0.3sec) and 1.0 s (Pplat,1sec) from the start of the end-inspiratory hold. FiO_2, inspiratory fraction of oxygen; PaO_2, arterial oxygen partial pressure; $PaCO_2$, arterial carbon dioxide partial pressure.

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Table 3. Breathing pattern and clinical variables during oro-nasal and full-face NIV in patients who subsequently experienced extubation success or failure.

	Extubation Success (n=46)		Extubation Failure (n=14)	
	Oro-nasal NIV	**Full-face NIV**	**Oro-nasal NIV**	**Full-face NIV**
Non-occluded breaths				
PEEP, cmH_2O	5 [5,6]	5 [5,6]	5 [5,6]	5 [5,6]
Ppeak, cmH_2O	11 [11,12]	11 [9,11]	11 [11,12]	11 [11,12]
V_T / PBW, mL/kg	7.8 [6.9, 9.5]	8.0 [7.3, 9.4]	9.5 [7.9, 10.2]§	9.0 [8.4, 11.5]§
Respiratory Rate, breaths/min	15 [12,20]	15 [13,20]	16 [12,25]	13 [10,19]
Air Leaks (%)	20 [17, 22]	20 [16, 23]	21 [14-24]	22 [19-23]
Actual ΔPes, cmH_2O	-6 [-9,-4]	-6 [-9,-4]	-11 [-14,-9]*	-13 [-13,-9]*
ΔPL Dyn, cmH_2O	11 [10,14]	11 [10,14]	17 [15,20]*	18 [15,19]*
Clung,dyn	33 [29,39]	37 [31,48]§	26 [20,29]*	26 [24,39]*
Occlusion-derived parameters				
Pocc, cmH_2O	-8 [-11,-6]	-8 [-11,-6]	-16 [-18,-12]*	-15 [-18,-12]*
Pocc, pneumotach cmH_2O	-8 [-11,-6]	-9 [-12,-7]	-16 [-17,-12]*	-16 [-17,-14]*
P0.1, es cmH_2O	0.7 [0.5,1.1]	0.7 [0.4,1.1]	1.2 [1.0,1.9]*	1.4 [1.1,1.8]*
P0.1, vent, cmH_2O	2.1 [1.8,2.2]	2.6 [2.5,2.8]	2.2 [2.0,2.3]*	2.5 [2.4,2.6]
P0.1, pneumotach, cmH_2O	2.3 [1.5,3.0]	2.4 [1.5,2.9]	3.4 [2.7,4.1]*	3.7 [3.1,3.9]*
Pplat, vent, cmH_2O	12 [10,14]	11 [9,13]	11 [9,13]	14 [13,14]*
Pplat,0.3s cmH_2O	11 [11,12]	11 [10,12]	11 [11,12]	10 [10,11]
Pplat,1s, cmH_2O	12 [10,14]	12 [10,13]	11 [9,13]	12 [9,13]
Predicted Values derived from occlusion				
PredictedΔPes	-6 [-8,-4]	-7 [-9,-5]	-11 [-12,-9]*	-13 [-13,-11]*
Predicted ΔPLdyn	11 [10,14]	12 [11,14]	17 [14,18]*	18 [17,19]*
Predicted Clung,dyn	33 [29,39]	38 [31,44]	26 [21,29]*	26 [24,31]*
Gas exchange and hemodynamics collected at the end of NIV session				

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Arterial pH	7.41 [7.39,7.44]	7.40 [7.37,7.43]	7.41 [7.39,7.44]	7.39 [7.35,7.43]
PaO_2/ FiO_2 mm Hg	208 [174,215]	187 [154,195]	213 [185,202]	195 [172,211]
$PaCO_2$, mm Hg	42 [37,44]	43 [40,44]	40 [38,44]*	39 [36,42]*
Systolic arterial pressure, mmHg	122 [112,135]	127 [118,134]	122 [112,139]	130 [120,137]
Diastolic arterial pressure, mmHg	80 [75,86]	79 [75,85]	81 [72,86]	79 [73,85]
Heart rate, bpm	73 [64,81]	78 [73,89]	73 [67,82]	77 [71,88]

Results are expressed as median [IQR].

* Significantly different from the success group
§ Significantly different between different interfaces but in the same successful group

Abbreviation: NIV: non-invasive ventilation; Paw: airway pressure; PEEP: positive end-expiratory pressure; Ppeak: Peak airway opening pressure; V_T/PBW: inspired tidal volume normalized to predicted body weight; Pes: esophageal pressure; Actual ΔPes: maximal swing in esophageal pressure recorded during non-occluded breath (reference metric for inspiratory effort); P0.1,es: Pes drop 100 ms after the onset of inspiratory effort (reference metric for respiratory drive);PL: transpulmonary pressure; ΔPL,dyn: Dynamic transpulmonary driving pressure; Clung,dyn: Dynamic lung compliance; Pocc: airway occlusion pressure; P0.1: airway occlusion pressure at 100 ms; Pplat : Inspiratory plateau pressure recorded at 0.3 s (Pplat,0.3sec) and 1.0 s (Pplat,1sec) from the start of the end-inspiratory hold. PredictedΔPes = K x Pocc, where Pocc is airway occlusion pressure; Predicted ΔPL,dyn= Pressure support - (K x Pocc); Predicted Clung, dyn = the ratio between Expiratory tidal volume and Predicted ΔPL,dyn.PaO_2, arterial oxygen partial pressure; FiO_2, inspiratory fraction of oxygen; $PaCO_2$, arterial carbon dioxide partial pressure.

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Figure legend

Figure 1. Representative experimental records of airway flow, airway pressure, esophageal pressure and transpulmonary pressure during end-expiratory and end-inspiratory occlusion maneuvers.

Figure 2. Agreement between Pocc-derived indices and reference metrics of inspiratory effort (*Panel A*), lung stress (*Panel B*), and lung compliance (*Panel C*): Scatterplots (left) show the concordance between paired measurements; the solid line denotes the line of identity (y = x), indicating perfect agreement; each dot represents one paired measurement. Bland-Altman plots (right) were constructed using all individual out-of-sample observations generated during the repeated cross-validation procedure; the solid horizontal line indicates the mean bias and dashed lines the limits of agreement. *Panel (D)*: Concordance between paired measurements: Left panel: P0.1 measured by the ventilator versus P0.1 measured by the pneumotachograph. Middle panel: ventilator-derived P0.1 versus the reference metric of respiratory drive (P0.1,es). Right panel: pneumotachograph-derived P0.1 versus P0.1,es.

Figure 3. Median (IQR) conversion factor K = Actual ΔPes/Pocc across leaks categories: during oro-nasal NIV, ≤15% (n=11), 16-20% (n=20), 21-25% (n=23), and 26-30% (n=6); during full-face NIV, ≤15% (n=14), 16-20% (n=14), 21-25% (n=24), and 26-30% (n=8).

Figure 4. *Upper panels* show the probability of re-intubation as a function of predicted ΔPes, predicted ΔPL,dyn, and predicted Clung,dyn during oro-nasal NIV (red) and full-face NIV (blue): Solid curves represent the fitted logistic regression and shaded bands the 95% confidence intervals. *Lower panels* show the cumulative incidence of successful extubation over 7 days after extubation, stratified according to the median values observed in the failure group; solid lines denote the extubation success group and dashed lines the failure group. Shaded areas indicate 95% confidence intervals

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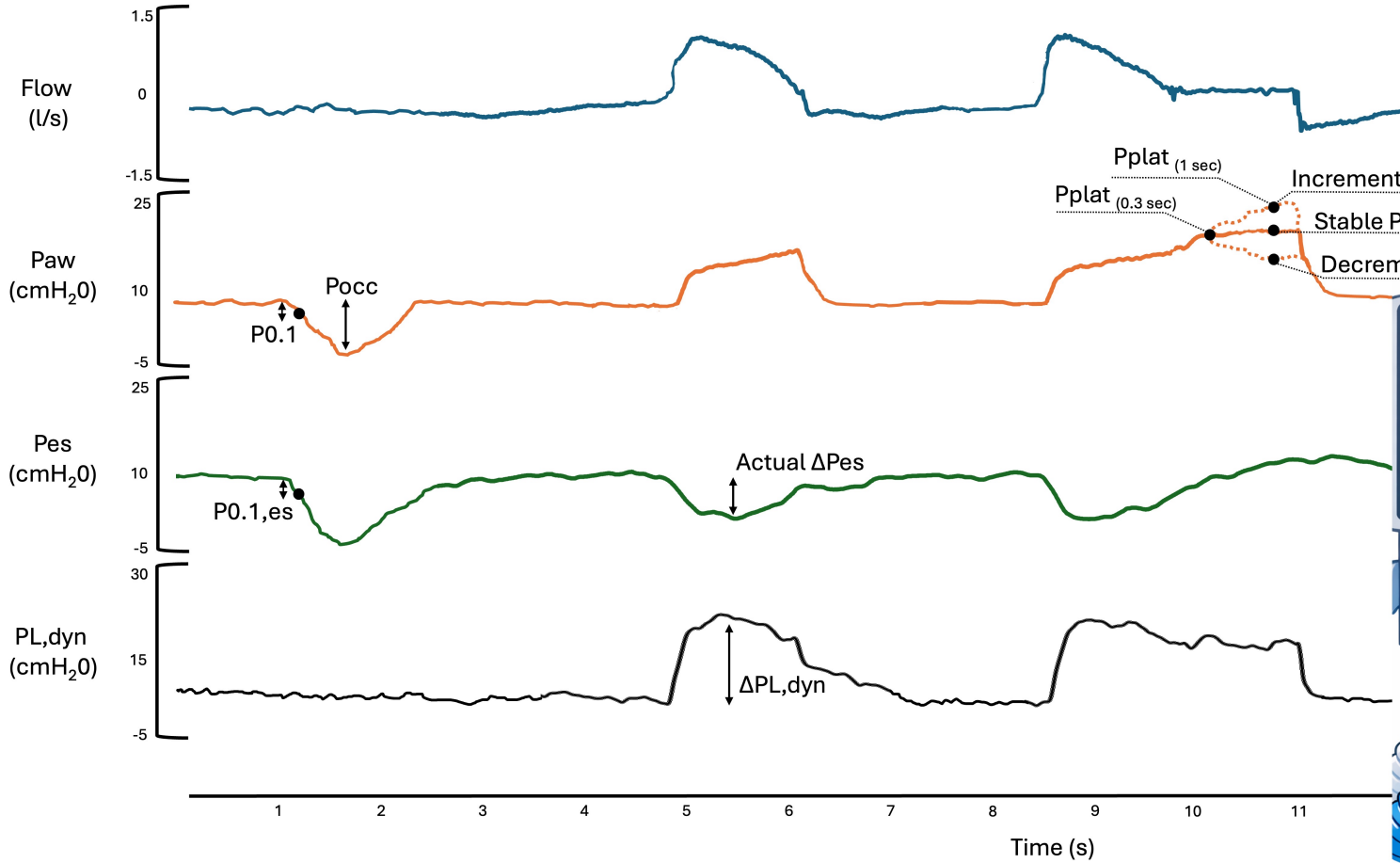
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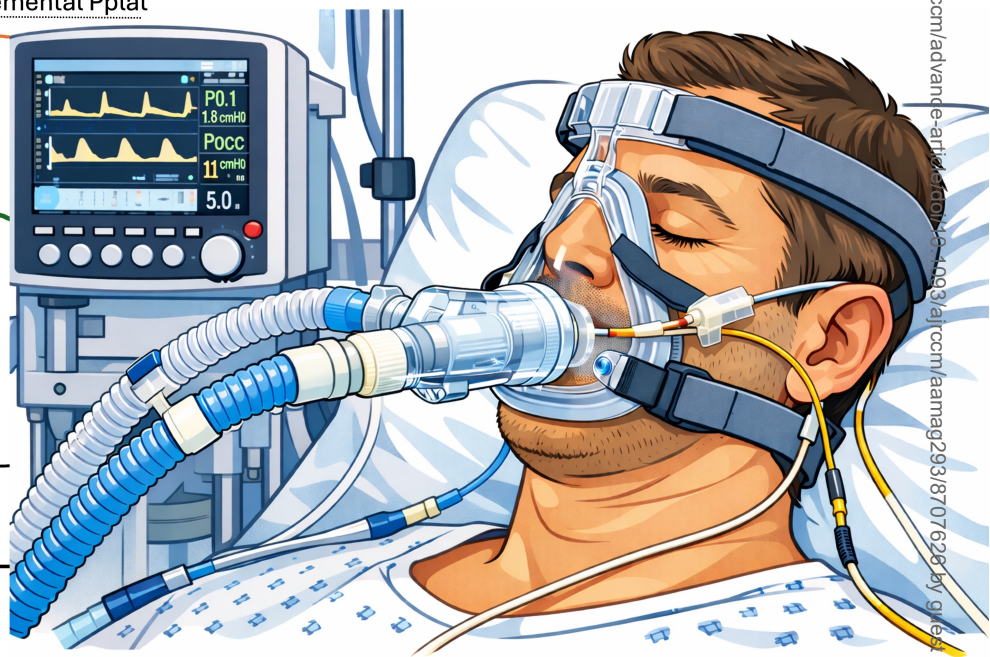
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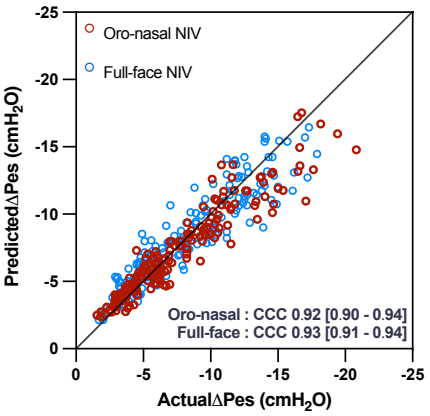
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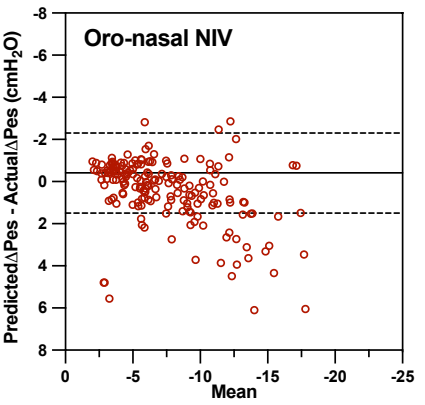


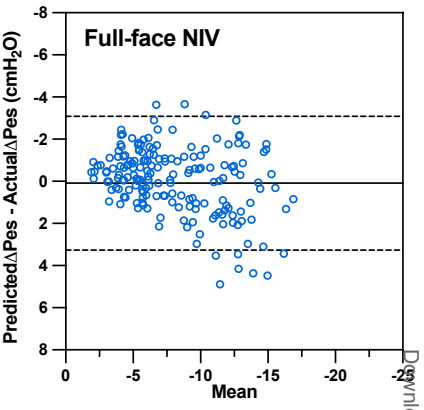


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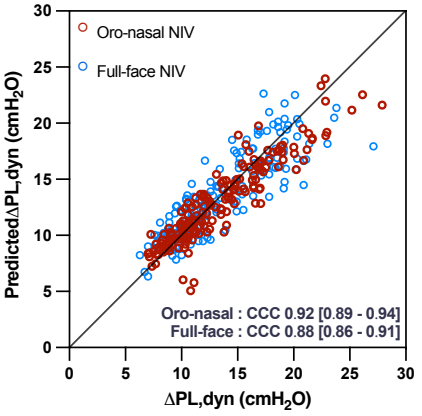
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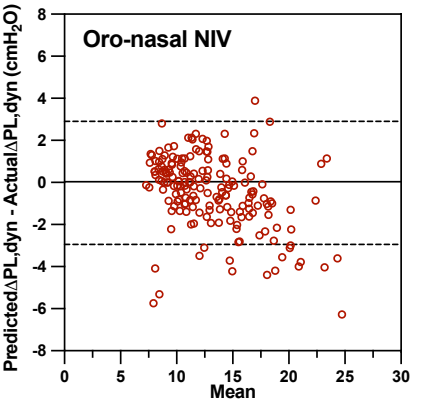


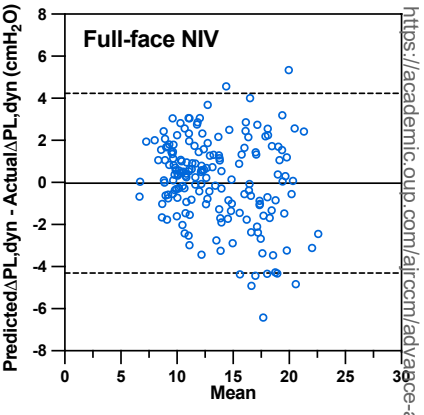




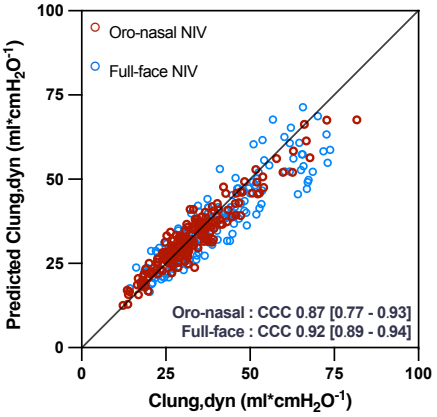
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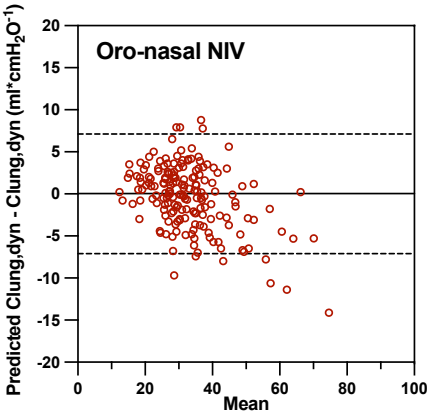


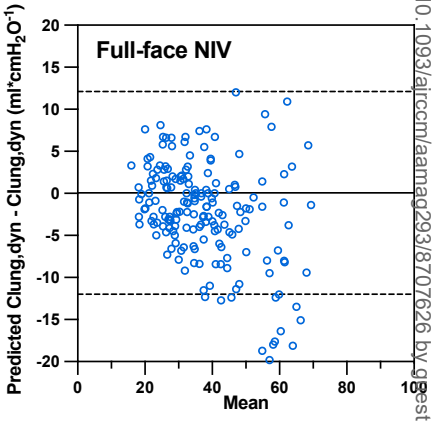




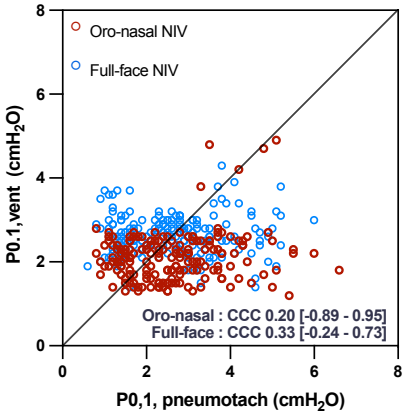
C. Pocc and lung compliance

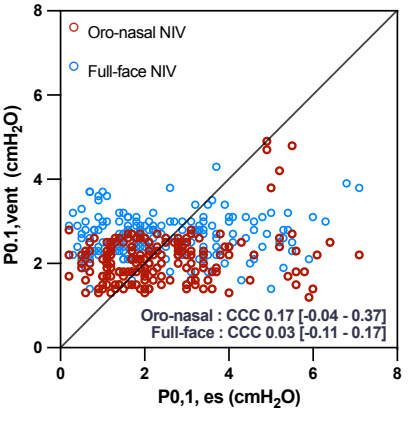


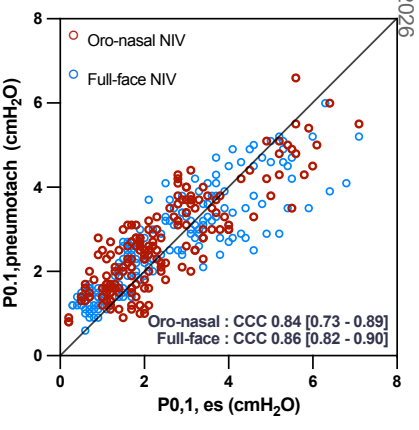




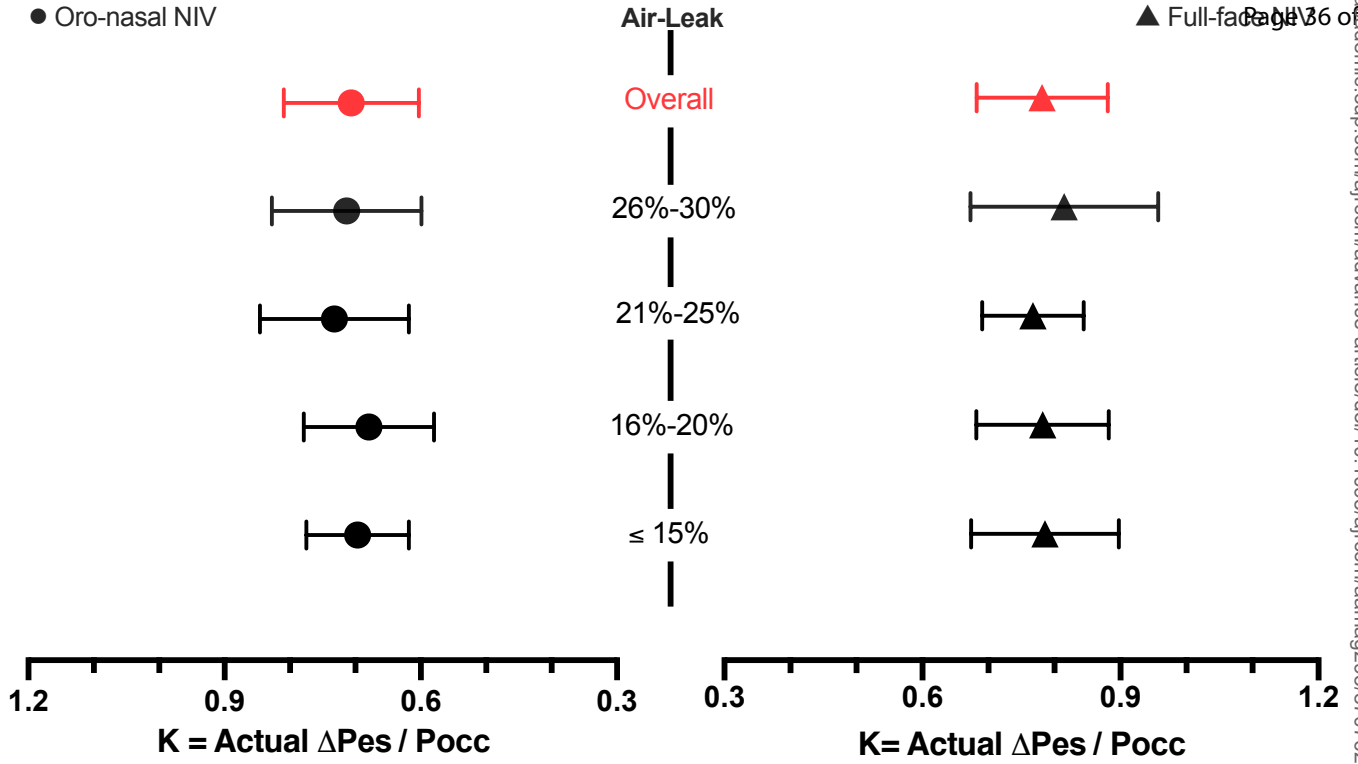
D. P0.1 and respiratory drive



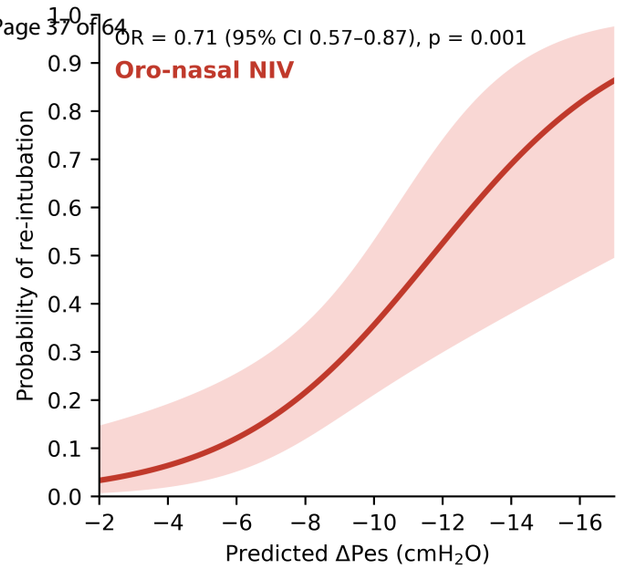


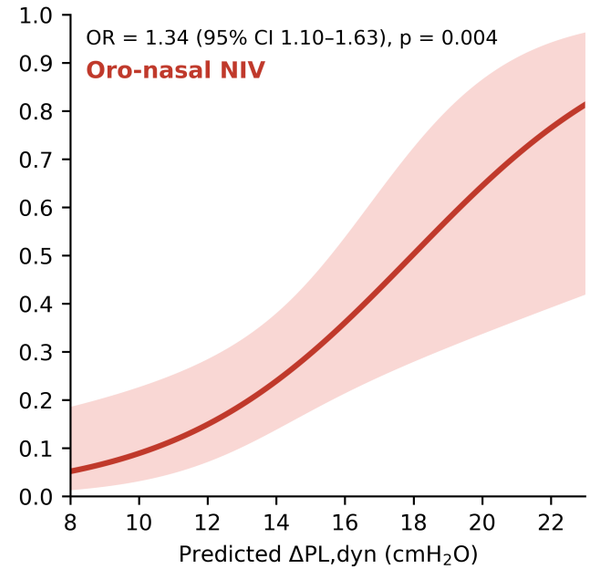


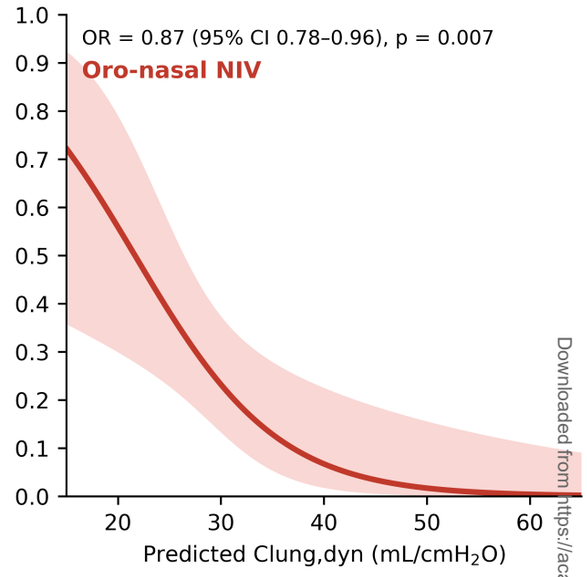
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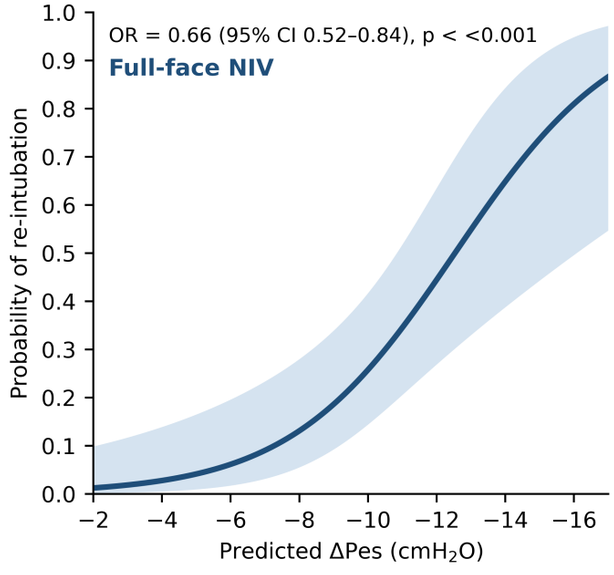


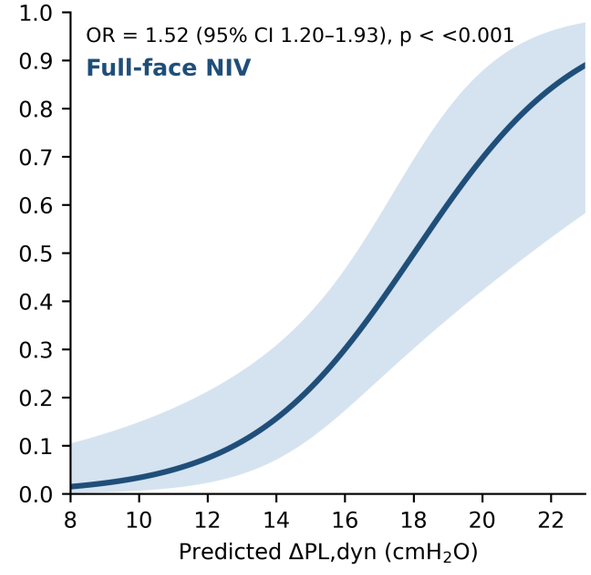
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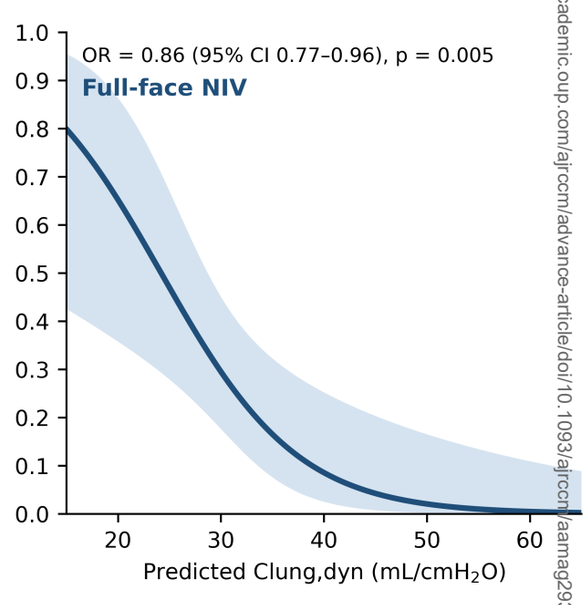


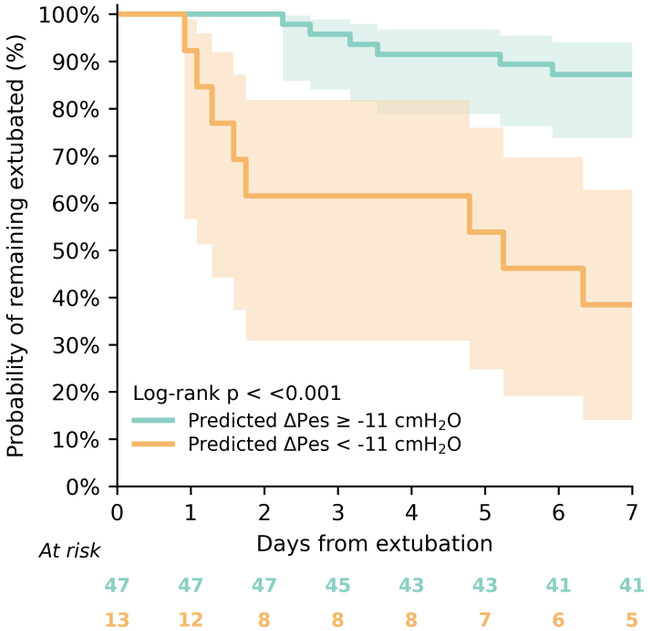


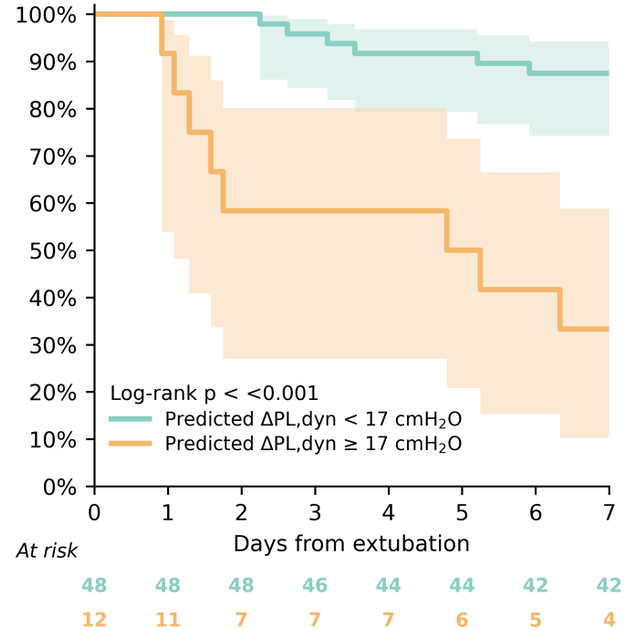


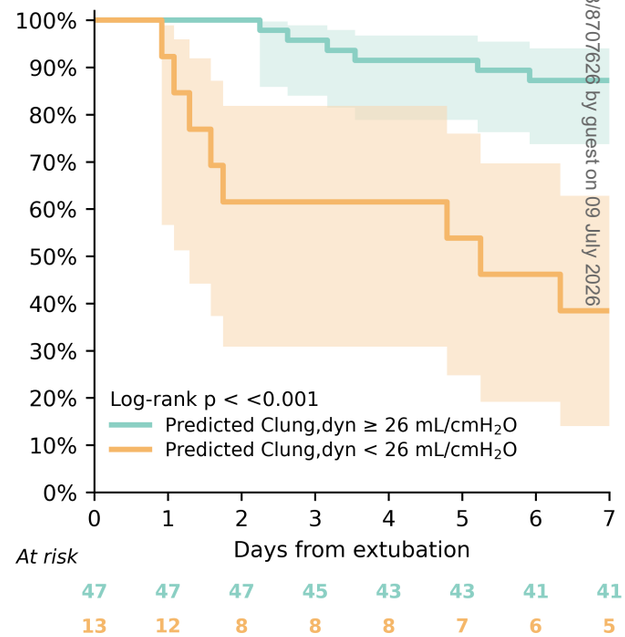












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