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Transpulmonary Pressure as a Predictor of Successful Lung Recruitment: Reanalysis of a Multicenter International Randomized Clinical Trial

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The study was performed at the Department of Anesthesia, Critical Care and Pain Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts.

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Abstract

Background:

Recruitment maneuvers are used in patients with ARDS to enhance oxygenation and lung mechanics. Heterogeneous lung and chest-wall mechanics lead to unpredictable transpulmonary pressures and could impact recruitment maneuver success. Tailoring care based on individualized transpulmonary pressure might optimize recruitment, preventing overdistention. This study aimed to identify the optimal transpulmonary pressure for effective recruitment and to explore its association with baseline characteristics.

Methods:

We performed post hoc analysis on the Esophageal Pressure Guided Ventilation (EpVent2) trial. We estimated the dose-response relationship between end-recruitment end-inspiratory transpulmonary pressure and the change in lung elastance after a recruitment maneuver by using logistic regression weighted by a generalized propensity score. A positive change in lung elastance was indicative of overdistention. We examined how patient characteristics, disease severity markers, and respiratory parameters predict transpulmonary pressure by using multivariate linear regression models and dominance analyses.

Results:

Of 121 subjects, 43.8% had a positive change in lung elastance. Subjects with a positive change in lung elastance had a mean – SD transpulmonary pressure of 15.1 – 4.9 cm H₂O, compared with 13.9 – 3.9 cm H₂O in those with a negative change in lung elastance. Higher transpulmonary pressure was associated with increased probability of a positive change in lung elastance (adjusted odds ratio 1.35 per 1 cm H₂O of transpulmonary pressure, 95% CI 1.13–1.61; $P = .001$), which indicated an S-shaped dose-response curve, with overdistention probability > 50% at transpulmonary pressure values > 18.3 cm H₂O. The volume of recruitment was transpulmonary pressure–dependent ($P < .001$; $R^2 = 0.49$) and inversely related to a change in lung elastance after adjusting for baseline lung elastance ($P < .001$; $R^2 = 0.43$). Negative correlations were observed between transpulmonary pressure and body mass index, PEEP, Sequential Organ Failure Assessment score, and PaO₂/FIO₂, whereas baseline lung elastance showed a positive correlation. The body mass index emerged as the dominant negative predictor of transpulmonary pressure (ranking 1; contribution to $R^2 = 0.08$), whereas pre-recruitment elastance was the sole positive predictor (contribution to $R^2 = 0.06$).

Conclusions:

Higher end-recruitment transpulmonary pressure increases the volume of recruitment but raises the risk of overdistention, providing the rationale for transpulmonary pressure to be used as a clinical target. Predictors, for example, body mass index, could guide recruitment maneuver individualization to balance adequate volume gain with overdistention.

QUICK LOOK

Current knowledge

The role of recruitment maneuvers in patients with ARDS has been controversial, with equivocal evidence that suggests benefits in oxygenation and ventilation in some patients and overdistention in others. The esophageal pressure measurement to predict transpulmonary pressure serves as the ideal way to individualize recruitment maneuvers by using sufficient transpulmonary pressure for beneficial volume gain while preventing harmful overdistention. A previous study suggested a safety threshold for transpulmonary pressure.

What this paper contributes to our knowledge

Higher transpulmonary pressure was associated with a higher probability of overdistention and harmful volume gain. Subjects' baseline characteristics including body mass index, PEEP, SOFA score, P_{aO_2}/F_{IO_2} , and baseline lung elastance were significantly correlated to transpulmonary pressure. Body mass index had the strongest dominance of negative prediction. These findings may enhance individualization of recruitment maneuvers, avoiding the harmful gain in transpulmonary pressure and lung overdistention.

Introduction

ARDS results in severe lung injury and hypoxemia secondary to inflammation and loss of aerated lung.¹ Recruitment maneuvers are commonly used in ARDS settings to open collapsed lung tissue and to improve oxygenation and pulmonary mechanics, yet their roles are still controversial, with equivocal evidence that suggests benefit in some patients and harm in others.^{2–11} Typical recruitment maneuvers are achieved by applying CPAP of nearly 40 cm H₂O for 10 to 30 s. There is not a standardized approach however, and recruitment can be attained via any prolonged exposure to high airway pressures (P_{aw}), which aims to overcome the critical opening pressures of airways and alveoli, and increase the functional ventilated lung volume.^{2,12}

Whereas many factors contribute to the success or failure of the recruitment maneuver, the heterogeneity in chest-wall mechanics of patients with ARDS may impact the response to the maneuver.¹³ Fifty percent of patients may not respond to the recruitment maneuver due to high chest-wall elastance, which can decrease the applied pressure to the lungs (transpulmonary pressure) and hence limit the recruitment.¹⁴ Conversely, overly high applied transpulmonary pressure during the recruitment maneuver may result in harm from barotrauma or hemodynamic compromise. Direct measurement of the esophageal pressure (Pes) allows for estimating transpulmonary pressure, in which the transpulmonary pressure is $P_{aw} - P_{es}$ at any time point during mechanical ventilation.¹⁵

We previously hypothesized that individualized recruitment maneuvers could be ideal because they could serve to assure both sufficient transpulmonary pressure for sufficient volume gain while also preventing the application of overly high pressures, which could result in overdistention or hemodynamic effects. We hypothesized that the change in lung elastance after recruitment maneuvers when compared with baseline elastance before the maneuvers could be used to determine if patients were having successful recruitment with improved elastance due to opening of previously closed lung units (a negative change in lung elastance) or overdistention (a positive change in lung elastance) with a maneuver. In addition, our previous findings from 28 subjects with ARDS suggest that, although adequate transpulmonary pressure is needed to recruit the lung and improve lung volume (volume of recruitment), there may be a safety cutoff point (which we initially postulated to be roughly 20 cm H₂O) above, which there was a high likelihood for overdistention.¹⁶

In this study, our aim was to determine a possible safety threshold indicative of overdistention by investigating the relationship between increased transpulmonary pressure and changes in elastance. In addition, we investigated the association between the transpulmonary pressure and the subject's baseline characteristics to identify patient characteristics that may serve as reliable predictors of transpulmonary pressure, thereby facilitating the precise application of recruitment maneuvers in patients with ARDS.

Methods

Study design

In this study, we reanalyzed data from the multi-center international EPVent2 trial,¹⁷ which enrolled adult subjects with ARDS who were undergoing mechanical ventilation at 14 North American hospitals between October 31, 2012, and September 14, 2017. All procedures were

followed in accordance with the ethics standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975. Data from the trial were approved for extensive use of waveform analysis (Beth Israel Deaconess Medical Center Institution Review Board, FWA00003245, approved the EPVent2 trial 17 under institutional review board protocol 2009P000374; date of approval: February 23, 2010) and a waiver of informed consent was issued. The trial registration identifier at ClinicalTrials.gov is NCT01681225. See the original study for full details of enrollment and study protocol.¹⁸ Our study was conducted at the Center for Anesthesia Research Excellence, Harvard Medical School, Beth Israel Deaconess Medical Center, Boston, Massachusetts, the coordinating center for EPvent2.

Study population

We included adult subjects who met the Berlin Criteria of moderate-to-severe ARDS and who received a recruitment maneuver within 48 h of mechanical ventilation initiation in the ICU and had flow, pressure, and volume waveforms recorded before, during, and after the recruitment maneuver. Patients with missing or poor quality waveforms due to channel drifting, artifacts, and evidence of multiple spontaneous breaths that interfered with the plateauing needed in pressure waveforms during recruitment maneuver, were excluded (Supplementary Fig. S1). Per the EPvent2 trial protocol¹⁷, all the subjects had an initial alveolar recruitment maneuver performed by raising P_{aw} to 35 cm H₂O for 30 s to standardize the lung volume history. If blood pressure fell during the recruitment maneuver to <90 mm Hg systolic, then the recruitment maneuver should have been terminated and fluid resuscitation considered.¹⁷

Exposure and outcome measures

The primary exposure was the transpulmonary pressure recorded at the end of the recruitment maneuver, as the resulting value of P_{aw} minus P_{es} . The primary outcome was the change in lung elastance at the end of the recruitment maneuver, in which a negative change was a marker of successful recruitment and a positive change was a marker of overdistention, calculated as the difference between the lung elastance at end of recruitment minus the baseline lung elastance. This calculation technique was used in a previous research letter to assess the effect of the recruitment maneuver during the maneuver itself.¹⁶ Our choice was driven by data quality considerations because post-recruitment maneuver measures are often compromised by missing post-recruitment breath holds data. Measuring elastance during the recruitment maneuver, particularly at its end point, provides critical insight. However, measuring elastance after the recruitment maneuver (as opposed to during the recruitment maneuver) could be of interest, but this value may vary significantly, depending on how clinicians set the ventilator post-recruitment maneuver (Supplementary Fig. S2).

Confounder model

In our model, we integrated multiple a priori defined confounding variables, which were selected based on clinical plausibility and previous literature. Age, sex, race, height, weight, body mass index (BMI), both APACHE III and Sequential Organ Failure Assessment scores, tidal volume, set PEEP, plateau pressure, F_{IO_2} , P_{aO_2} , P_{aO_2}/F_{IO_2} , ARDS severity,¹⁹ and baseline lung elastance were included.

Primary analysis

In the primary analysis, we created a generalized propensity score that incorporated a priori defined confounders. We then estimated a dose-response relationship between the transpulmonary pressure and the change in lung elastance through a logistic regression analysis weighted by the generalized propensity score within a Bayesian framework. This approach was chosen due to its precedence in inferring causality and flexibility in accommodating several confounding variables with respect to the small number of degrees of freedom.^{20,21} In addition, we defined a possible cutoff of transpulmonary pressure above which there was a > 50% chance for causing alveolar overdistention (a positive change in lung elastance) to identify a possible upper safety threshold.

Secondary analysis

Multivariable linear regression models were used in our secondary analysis, which studied the association between the transpulmonary pressure and volume of recruitment controlling for lung elastance, and the change in lung elastance and volume of recruitment confounding for baseline lung elastance. The volume of recruitment was calculated by using the following equation: volume of recruitment = volume at end recruitment maneuver minus volume at the start of recruitment maneuver.

Exploratory analysis

In an exploratory attempt, we investigated the relative importance of multiple patient characteristics, clinical and respiratory variables in predicting transpulmonary pressure by using dominance analysis of predictors. Height, BMI, both APACHE III and SOFA scores, tidal volume, PEEP, plateau pressure, F_{IO_2} , P_{aO_2}/F_{IO_2} , Berlin ARDS severity,¹⁹ and baseline lung elastance (before recruitment maneuver) were all also investigated as potential predictors of transpulmonary pressure through a multivariable linear regression model. As additional exploratory analysis, we mirrored our previous paper, which used the proposed safety cutoff defined in the primary analysis to divide the cohort by a transpulmonary pressure above and below this value to isolate patients we thought would be at high risk for overdistention.¹⁶ We used these new cohorts to compare key demographic and mechanics values above and below this cutoff.

Sensitivity analysis

To support the robustness of our results, a sensitivity analysis by using multivariate adjusted logistic regression and the locally weighted scatterplot smoothing model that investigates the association between transpulmonary pressure and the change in lung elastance was conducted.

Statistical analyses

Data quality was assessed by investigating the continuous variables and their components and the number of patients per category of each confounding variable. Potential collinearity with the primary exposure variable and between confounding variables themselves was addressed by using variance inflation factors and Pearson correlation coefficients. Results are reported as estimated marginal means and odds ratios with 95% CIs. Alpha was set to .05. All analyses were performed in Stata (Version SE 16.0, StataCorp, College Station, Texas).

Results

Study cohort and characteristics

All 200 adult subjects with ARDS enrolled in the EPvent2 were considered for inclusion. The final study cohort consisted of 121 subjects. We excluded patients with poor quality waveforms due to channel drifting, artifacts, or evidence of multiple spontaneous breaths that interfered with the plateauing needed in pressure waveforms during the recruitment maneuver (Supplementary Fig. S3). The mean \pm SD of end-recruitment end-inspiratory transpulmonary pressure was 14.4 \pm 4.4 cm H₂O. The baseline characteristics and distribution of variables per mean end-recruitment end-inspiratory transpulmonary pressure are summarized in Table 1. The baseline characteristics and distribution of variables per the results-derived cutoff of transpulmonary pressure and change in elastance are summarized in Supplementary Tables S1 and S2. End-recruitment end- inspiratory transpulmonary pressure values widely varied between 2.9 and 25.5 cm H₂O, at roughly the same airway recruitment pressure (ranging from 30 to 40 cm H₂O [Fig. 1]).

Primary analysis

Fifty-three subjects (43.8%) had a positive change in lung elastance. The mean \pm SD end-recruitment end-inspiratory transpulmonary pressure was 15.1 \pm 4.9 cm H₂O in the subjects who had a positive change in lung elastance compared with 13.9 \pm 3.9 cm H₂O in the subjects who had a negative change in lung elastance. In a generalized propensity score-weighted analysis, a higher end-recruitment end-inspiratory transpulmonary pressure was associated with a higher probability of positive change in lung elastance (adjusted odds ratio 1.35 per 1 cm H₂O transpulmonary pressure, 95% CI 1.13–1.61; $P = .001$) and predicted an S-shaped dose-response curve, in which the probability of a positive change in lung elastance was $> 50\%$ when transpulmonary pressure values were > 18.3 cm H₂O (Fig. 2).

Secondary analyses

Multivariate linear regression showed that the volume of recruitment was dependent on end-recruitment end-inspiratory transpulmonary pressure when confounding for lung elastance ($P < .001$; $R^2 = 0.49$), however, it was inversely dependent on a change in lung elastance ($P < .001$; $R^2 = 0.43$).

Exploratory analyses

By using a multivariate linear regression, BMI, PEEP, SOFA score, P_{aO_2}/F_{IO_2} , and baseline lung elastance were significantly associated with end-recruitment end-inspiratory transpulmonary pressure with coefficients of -0.11 , -0.25 , -0.31 , -0.04 , and 0.1 and with $P = .005$, $P = .031$, $P = .045$, $P = .039$, $P = .02$, respectively. Dominance analyses of predictors showed that BMI had the strongest dominance, as determined by its contribution to transpulmonary pressure prediction (ranking 1; contribution to $R^2 = 0.08$) (Fig. 3). Therefore, thin body habitus predicted high end-recruitment end-inspiratory transpulmonary pressure, hence over-distention. Baseline lung elastance was the only positive predictor, which suggests that higher baseline elastance predicts higher transpulmonary pressure during the recruitment maneuver (ranking 2, contribution to $R^2 = 0.06$).

By using the data-defined cutoff of 18.3 cm H₂O suggested from the primary analysis (Supplementary Table S1), we found that the subjects above the cutoff had on median a positive change in lung elastance (1.7 [−0.6 to 5.3, interquartile range] cm H₂O/L), whereas patients below this cutoff had a negative change in lung elastance (−1.7 [−6.2 to 2.2, interquartile range] cm H₂O/L; *P* = .006). In addition, the subjects at higher risk for overdistention based on this cutoff had a lower PEEP versus the subjects with a lower risk (10 [10–14, interquartile range] cm H₂O vs 14 [10–17, interquartile range] cm H₂O; *P* = .02) and significantly lower BMI versus the low-risk group (25.5 [23.5–29, interquartile range] kg/m² vs 30.9 [26.4–39.1, inter-quartile range] kg/m²; *P* < .001).

Table 1. Subject characteristics and distribution of variables per median end-recruitment transpulmonary pressure

	<i>Low end-recruitment transpulmonary pressure (<14.4 cm H₂O) (n = 59)</i>	<i>High end-recruitment transpulmonary pressure (≥ 14.4 cm H₂O) (n = 62)</i>	<i>P</i>
Age, y	58.0 (47.0–67.0)	57.0 (43.0–66.0)	.78
Sex, n (%)			.66
Men	30 (51)	34 (55)	
Women	29 (49)	28 (45)	
Race, n (%)			.95
White	46 (78)	47 (76)	
Black	6 (10)	8 (13)	
Asian, Middle Eastern, Indian	1 (2)	2 (3)	
Other	4 (7)	3 (5)	
Unknown	2 (3)	2 (3)	
Height, cm	168.0 (160.0–178.0)	168.0 (158.0–175.0)	.56
Actual body weight, kg	90.6 (74.7–105.0)	77.0 (65.4–95.7)	.008
Predicted body weight, kg	59.6 (51.9–73.2)	61.2 (50.1–70.5)	.68
Body mass index, kg/m ²	31.1 (26.5–40.2)	27.2 (24.2–33.2)	.004
Clinical characteristics			
APACHE III score	25.0 (21.0–30.5)	27.5 (21.5–31.5)	.82
SOFA score	9.0 (5.0–11.0)	7.0 (4.0–9.0)	.07
Primary cause of lung injury, n (%)			.25
Pulmonary	23 (39)	25 (42)	
Abdominal	2 (3)	0 (0)	
Trauma	0 (0)	2 (3)	
Sepsis	34 (58)	32 (54)	
Respiratory characteristics			
Tidal volume, mL	400.0 (328.0–450.0)	400.0 (350.0–425.0)	.25
Tidal volume, mL/kg predicted body weight	6.1 (5.9–6.8)	6.3 (6.0–6.8)	.66
PEEP	15.0 (12.0–18.0)	12.0 (10.0–14.0)	<.001
F _{IO₂}	0.6 (0.5–0.8)	0.6 (0.5–0.7)	.57
P _{aO₂} /F _{IO₂} , mm Hg	90.0 (68.8–129.0)	103.3 (77.0–123.6)	.37
Berlin ARDS severity, n (%)			.034
Moderate, P _{aO₂} /F _{IO₂} 100–200 mm Hg	21 (36)	34 (55)	
Severe, P _{aO₂} /F _{IO₂} ≤ 100 mm Hg	38 (64)	28 (45)	
Plateau pressure, cm H ₂ O	28.0 (25.0–31.0)	25.0 (22.0–29.0)	.002
Driving pressure, cm H ₂ O	11.0 (10.0–14.0)	12.0 (10.0–14.0)	.59
Volume of recruitment maneuver, mL	756.8 (534.8–1037.8)	807.8 (604.2–1059.0)	.29
Recruitment maneuver transpulmonary elastance, cm H ₂ O/L	19.0 (13.7–24.3)	20.7 (15.9–31.3)	.03
Pre-recruitment maneuver transpulmonary elastance, cm H ₂ O/L	18.8 (14.3–25.3)	23.2 (19.0–32.5)	.004

Data are presented as median (interquartile range) for continuous, and frequencies (prevalence in percentage) for categorical variables.

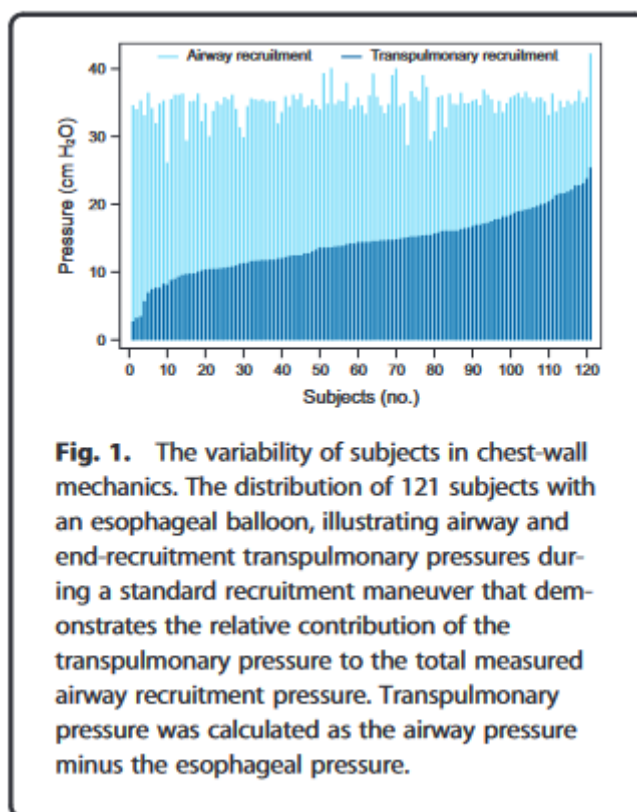
Sensitivity analyses

In a multivariate adjusted logistic regression, the results were consistent, which showed that higher end-recruitment end-inspiratory transpulmonary pressure was associated with a higher risk of a positive change in lung elastance (adjusted odds ratio 1.24 per 1 cm H₂O transpulmonary pressure, 95% CI 1.10–1.45; *P* = .001). A locally weighted scatterplot model was consistent with the weighted logistic regression, and an end-recruitment end-inspiratory

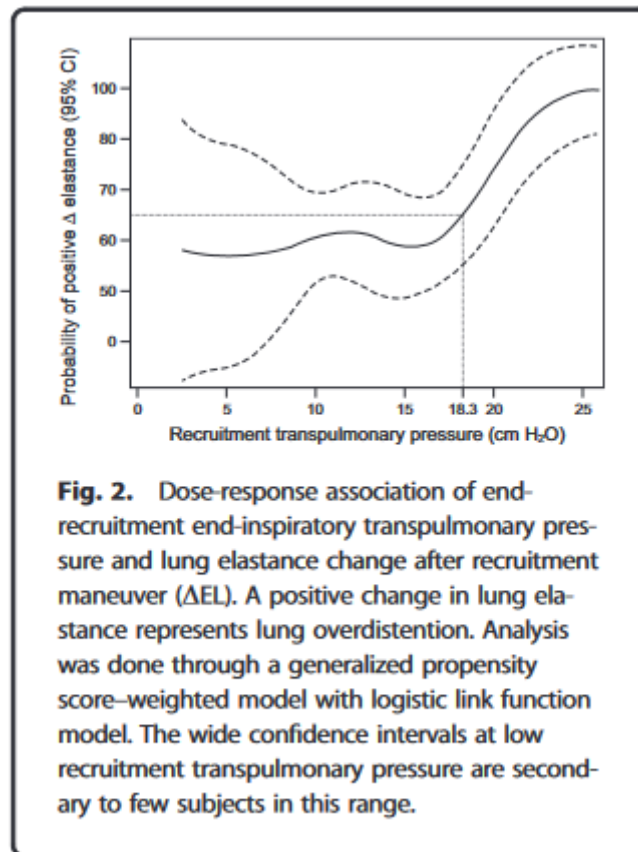
transpulmonary pressure value of >19.3 cm H₂O was associated with increased risk of a positive change in lung elastance (Fig. 4).

Discussion

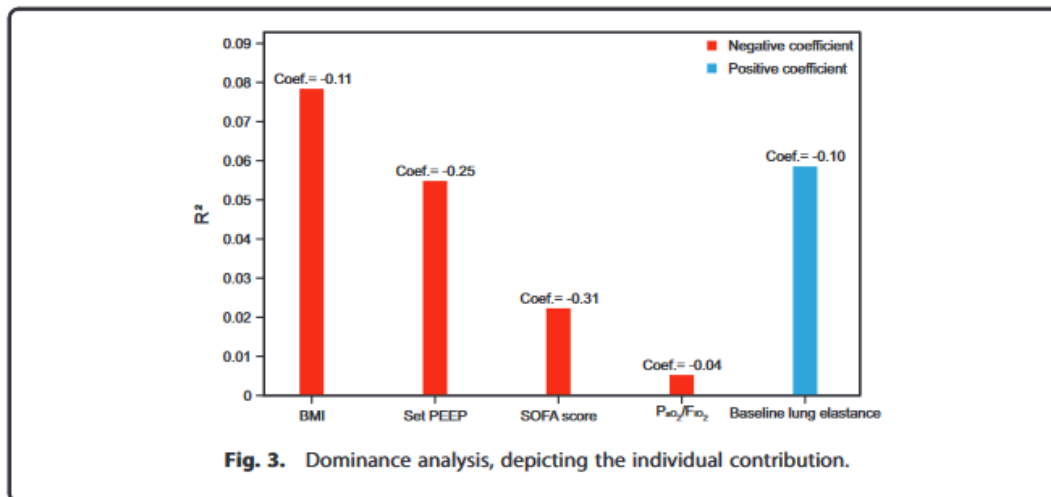
In this multi-center retrospective cohort of 121 subjects with ARDS who received recruitment maneuver in their first 2 d of ICU stay at 14 medical centers in North America, we found that higher levels of transpulmonary pressure were associated with lung overdistention (a positive change in lung elastance), with a transpulmonary pressure > 18.3 cm H₂O serving as a potential cutoff, which predicts a high likelihood for overdistention. We also observed that the volume of recruitment was dependent on transpulmonary pressure and inversely dependent on a change in lung elastance when controlling for recruitment and baseline lung elastance, respectively. There also was a stronger contribution of BMI over other patient characteristics in predicting transpulmonary pressure, in which the subjects with thinner body habitus had a higher risk of having high transpulmonary pressure, hence potential recruitment failure and overdistention. Our findings remained consistent across the sensitivity analysis, which supported the significant aforementioned association between transpulmonary pressure and a change in lung elastance, and these are overall consistent with our previous findings in the initial research letter.¹⁶



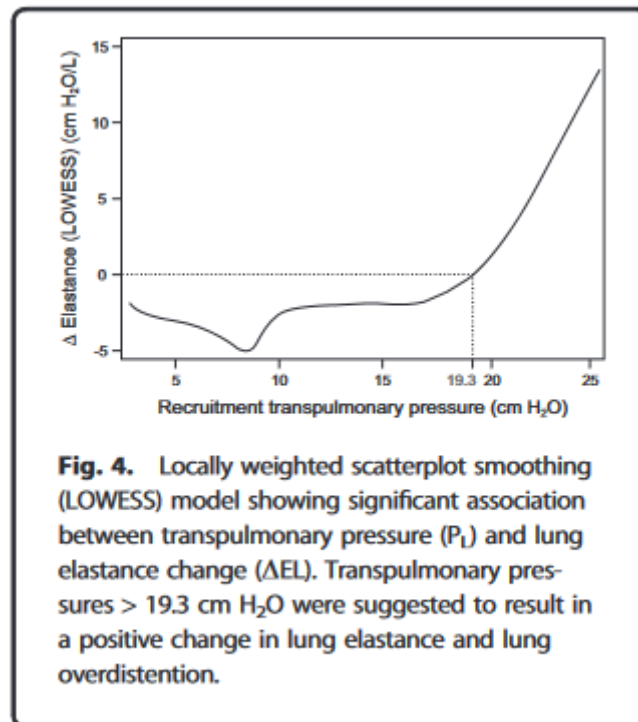
As our previous work demonstrated, and further emphasized in Figure 1, there seemed to be wide variability between the subjects in chest-wall mechanics.¹⁶ This chest-wall variability leads to dramatic differences between patients in the resulting lung stress (transpulmonary pressures) despite similar applied P_{aw} .²² Without the use of esophageal manometry and transpulmonary pressure measurements, these differences in end-inspiratory stress would be difficult to differentiate. Because the chest wall can dissipate applied energy and pressure, the total P_{aw} should be of much less importance when considering the potential for lung injury than the pressure across the lungs independent from the chest wall.^{16,23,24} Indeed, previous studies support the use of P_{es} to improve the physicians' understanding of the pathophysiology of acute lung injury²⁵ and patient-ventilator interaction.^{13,17} Its use in PEEP titration could also optimize oxygenation and lung compliance in patients with ARDS.^{14,15} To date, however, there have been no studies that prospectively targeted transpulmonary pressure to guide recruitment maneuvers, and this remains an intriguing area of investigation.



In our previous study, which included 28 independent subjects with ARDS, we hypothesized that there was a possible optimal window of transpulmonary pressure between 10 and 20 cm H₂O that would be sufficient to expand the lung, optimize lung elastance, and prevent overdistention.¹⁶ The findings from our new analysis have made us reassess this initial hypothesis. Because higher transpulmonary pressure correlates with both a higher volume of recruitment and an increased risk of overdistention, our interpretation of these findings for clinical care would be to aim for the highest transpulmonary pressure that does not cause significant overdistention, thereby balancing the potentially competing effects. As such, rather than a “window” of optimal transpulmonary pressure, analysis of our data would suggest more of an upper limit to not exceed. Furthermore, the initial hypothesis that suggests 20 cm H₂O as the cutoff seems to have been close; however, based on our new data from this study, the cutoff may be slightly lower (at *18 cm H₂O). Although we must be careful to not overly extrapolate clinical management from this retrospective analysis, this threshold provides an intriguing target cutoff for future prospective work when using transpulmonary pressure, and this cut-off could, in theory, be a safety threshold for both recruitment maneuvers and tidal breathing; however, this requires further investigation.



In addition to the potential value that these data may have for defining clinical targets, these data have other potentially important interpretations when considering the physiologic and clinical response to recruitment maneuvers. Whereas recruitment maneuvers have been used extensively in the past as part of the open lung strategy, their use has become more controversial.^{8,26–28} Multiple previous systematic reviews and meta-analyses of 10 trials, including > 6,000 subjects with ARDS, found that recruitment maneuvers do not decrease the mortality rate but may improve oxygenation and reduce the length of hospital stay.^{12,29} Another systematic review also concluded that, in subjects with moderate-to-severe ARDS, higher PEEP without a recruitment maneuver was associated with a lower risk of death when compared with lower PEEP; however, a higher PEEP with a prolonged recruitment maneuver strategy was associated with an increased risk of death when compared with higher PEEP without recruitment maneuver.³⁰ In contrast, results of a larger meta-analysis suggest, with limited confidence, that recruitment maneuver in combination with a higher PEEP ventilation strategy can reduce mortality.³¹ In addition, in the ART study,¹¹ a large randomized controlled trial that used recruitment maneuvers as part of the open lung strategy, worsened mortality was found in the recruitment maneuver–open lung arm, which may have been related, in part, to the very high applied pressures used and resulting hemodynamic effects. In agreement with this hypothesis were the findings from our re-analysis of the EPVent2 data, which found that the best predictor for shock-free days was a lower end-inspiratory transpulmonary pressure.³² As such, although recruitment maneuvers in the right patients seem to improve oxygenation, may re-open the lung and even improve outcomes, it also seems that overly high applied end-inspiratory pressures during recruitment maneuver may result in patient harm, which further emphasized the importance of our findings in this study and the potential clinical importance of using esophageal manometry to measure transpulmonary pressure during recruitment maneuvers.



Although our findings clearly demonstrate that trans- pulmonary pressure is widely variable and unpredictable at a given P_{aw} , importantly, this study is also the first, to our knowledge, to identify potential predictors of trans- pulmonary pressure in patients with ARDS during recruitment maneuvers, which may help in the future to guide decision making on who could be considered for balloon placement. Our results show that subjects' BMI was the dominant predictor of transpulmonary pressure. The effect of recruitment maneuvers on patients who were obese has been previously discussed, including in relation to postoperative pulmonary complications,³³ postoperative pain, and quality of recovery, particularly in patients undergoing laparoscopic sleeve gastrectomy,³⁴ and in improving respiratory mechanics and blood gas values.³⁵ In addition, the value of esophageal manometry and monitoring of transpulmonary pressure has been well documented in patients who were obese because patients with obesity may be particularly prone to lung collapse and atelectrauma.^{36,37} Furthermore, lung collapse due to high P_{aw} required for recruitment maneuver and high resultant pleural pressures in patients with ARDS and with a high BMI may make them less prone to overdistention after recruitment maneuver.³⁷ When measuring lung volumes by integrating advanced imaging modalities, such as electrical impedance tomography or computed tomography, into future research endeavors will be instrumental in advancing the comprehension between the transpulmonary pressure predictors and lung volume, collapse, and overdistention. As such, these exploratory findings could suggest, in the context of previous work¹⁴, that patients with obesity in particular would receive value from transpulmonary pressure-guided recruitment maneuvers.

Our results can also gain significance when interpreted within the framework of the stress-strain relationship, as proposed by the Hooke law. This relationship posits that pressure results from the ratio of volume to the compliance of the relaxed respiratory system. Numerous studies have emphasized the variability of the risk associated with volume, contingent on compliance.^{38,39} Compliance serves as a vital indicator of disease severity, correlating with the quantity of aerated and recruitable lung units, reminiscent of the concept elucidated by the Gattinoni “baby lung” theory. Consequently, diminished compliance or heightened elastance, characteristic of individuals with higher BMIs and with collapsed lung, could identify some patients with more recruitable alveoli, which rendered them less susceptible to alveolar overdistention. Airway titration that matches pleural pressure has improved lung function and oxygenation, maintained hemodynamic stability without impairing right-ventricular function.³⁶ These findings were contradictory to the ART trial¹¹, in which similar transpulmonary pressure resulted in significant lung overdistention, and need further studying.

The strength of the study includes the high level of data granularity, with the largest cohort of patients we are aware of who have had recruitment maneuvers while monitoring transpulmonary pressure. Other strengths include building multivariate models to determine the impact of transpulmonary pressure on overdistention during recruitment maneuvers because many factors other than transpulmonary pressure alone likely contribute to the “success” or “failure” of a recruitment maneuver.

Limitations arise from the retrospective study design, in which sample selection and the choice of confounding variables are restrained to data availability. Further research is needed on the impact of the findings on post-recruitment maneuver elastance values, which was beyond the scope of this study, in part, due to the lack of data. Post-recruitment maneuver values, although of clinical interest, may also be significantly impacted by the PEEP and tidal volume settings potentially masking success or failure of the recruitment maneuver itself, which provides a rationale for the approach taken in this study. Despite the limitation in the sample size, the primary model has allowed adjustments for multiple clinically relevant confounders and the sensitivity analysis was used to corroborate our primary findings. However, we acknowledge that our findings are too preliminary to use as definitive cutoff points during clinical care, and this is not the purpose of presenting them in this study. We agree that a clinical cutoff that involves calculating the risk at the bedside is not a useful tool. This, however, is an excellent starting point to use for future studies as a safety cutoff to test the hypotheses generated from this small study.

Conclusions

Subjects with high transpulmonary pressure had a lower probability of successful recruitment, marked by the positive change in lung elastance, which can predict harmful volume gain and lung overdistention. BMI was the best predictor of transpulmonary pressure. Clinicians may benefit from using dominant predictors of transpulmonary pressure to improve recruitment maneuver and idealize recruitment volume.

Author Disclosure Statement

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