V_{TE} in the NIV success group with a significantly lower ΔP_L indicated a higher lung compliance than the failure group. A differential change in ΔPes to ΔP_L (31.5→39.5 cm H_2O [Δ8 cm H_2O] vs. 11→30.5 cm H_2O [Δ19.5 cm H_2O]) with a similar level of pressure support and positive end-expiratory pressure (PEEP), 2 hours after the NIV trial in the failure and the success group, needs further clarification. Interestingly, $V_{TE}/\Delta P_L$ was lower in the NIV success group than the NIV failure group despite having a significantly lower ΔP_L. Even if a similar compliance is assumed for both groups, a persistent higher $\dot{V}_E$ indicates reduced cardiac output or systemic oxygen delivery in the NIV failure group. The success of mechanical ventilation and spontaneous breathing is inherently linked with cardiorespiratory interactions (4). A greater inspiratory drive in the NIV failure group resulted in lower intrapleural pressure, which could have further reduced the cardiac output and systemic oxygen delivery by increasing afterload and reducing the blood flow from the intrathoracic to the extrathoracic part of the aorta (5). In addition, an exaggerated venous return due to a higher negative intrapleural pressure coupled with increased afterload could have led to additional pulmonary congestion and deterioration in chest X-rays in the NIV failure group. Furthermore, a persistent higher inspiratory effort in the NIV failure group despite a nonsignificant difference in HACOR (Heart Rate, Acidosis, Consciousness, Oxygenation, Respiratory Rate) score suggests a different pathophysiology of hypoxemia. A continued higher $\dot{V}_E$ requirement did not allow ΔPes to reduce significantly in the NIV failure group. Therefore, a reduction in $\dot{V}_E$ could also have been a potential predictor of NIV success with reasonable accuracy. Furthermore, titration of pressure support and PEEP during the NIV trial may be guided by a reduction in $\dot{V}_E$ and work of breathing as the majority of the clinical parameters (RR, $P_{O_2}/F_{I_{O_2}}$, and $V_{TE}/\Delta P_L$) did not reach statistical significance to achieve the role of potential predictors. ■

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Reply to Spinelli *et al.* and to Jha

From the Authors:

We read with interest the letters by Dr. Spinelli and colleagues and by Dr. Jha commenting on our work on esophageal manometry and noninvasive ventilation (NIV) in acute *de novo* respiratory failure (ARF) (1). Both of them discussed the potential mechanisms behind the different behavior of lung mechanics in patients who failed NIV compared with those who succeeded.

Spinelli and colleagues pointed out that higher values of pressure support (PS) were allowed to fulfill the ventilation need (without increasing the expired V_T [V_{TE}]) in patients who succeeded the NIV trial, whereas significantly lower PS (at comparable ventilation) in the failure group suggested that higher assistance could have produced a harmful rise in V_{TE}.

In his letter, Jha also argued why in the failure group a persistently higher $\dot{V}_E$ with a higher inspiratory drive but lower intrapleural pressure could have driven an increased fluid afterload with a reduced $\dot{Q}$ and/or systemic oxygen delivery.

These points of discussion give us now the opportunity to further discuss the interplay between respiratory effort, lung mechanics (V_{TE} and dynamic transpulmonary pressure [ΔP_L]), respiratory drive, and the cardiopulmonary interactions.

V_{TE} at 2 hours was higher than the cutoff limit of 9.5 ml/kg of predicted body weight (2) in both groups of patients and started diverging significantly at 12 hours, with considerable reduction in the success group. This suggests that in patients with ARF, protective ventilation is difficult to achieve soon after NIV application and that V_{TE} alone might be an insufficient marker to identify those patients who may benefit from NIV. Moreover, in our patients, the magnitude of inspiratory effort as assessed by esophageal manometry at the time of NIV start correlated inversely with $V_{TE}/\Delta P_L$ (a surrogate measure of lung compliance) but not with the baseline V_{TE} (1). Therefore, V_{TE} did not reflect the intensity of the respiratory effort of our patients, introducing the concept of "baby lung assessment" during NIV that surely deserves further investigation. On the other hand, the values of ΔP_L increased similarly in both groups within the first 2 hours of NIV. However, this increase was due to the elevated values of esophageal pressure (ΔPes) (with low values of PS to avoid excessive V_{TE}) in patients who failed, whereas it was driven by a higher level of the PS set (associated with an unharmful V_{TE}) in those who succeeded. Overall, an average ΔP_L value $>$30 cm H_2O (as observed in our patients) could be harmful, although this is

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not a precise marker of the stress applied to the lung parenchyma (3). Because ΔP_L seems not to represent the local lung stress and overdistension during spontaneous breathing, the underlying mechanism of patient self-inflicted lung injury would not be similar to that of ventilator-induced lung injury. In particular, patients who present higher ΔPes for a given level of ΔP_L, in a heterogeneous "solid-like" injured lung, are those who produce high respiratory effort, with more negative swing in pleural pressure, injurious inflation patterns, more tidal recruitment (Pendelluft phenomenon) in the dependent lung (4), and also might reach a negative alveolar pressure, thus enhancing (inflammatory) alveolar edema (5). Therefore, ΔPes measurement and monitoring would be a more accurate physiological parameter able to discriminate patients at risk for patient self-inflicted lung injury. As a matter of fact, ΔPes correlated with radiographic change on chest X-ray at 2 hours (*see* online supplement of Reference 1), whereas ΔP_L did not (Figure 1).

Finally, we agree with Dr. Jha in that the persistence of elevated $\dot{V}_E$ in the failure group might indicate a reduced $\dot{Q}$ of peripheral oxygen delivery, which in turn might increase the respiratory drive, thus giving room for $\dot{V}_E$ as a parameter to be monitored. Notwithstanding, it seems more likely that ΔPes is a more accurate and easy parameter to monitor to predict the failure under NIV as compared with $\dot{V}_E$ as a surrogate marker of the $\dot{Q}$. This aspect appears more as an effect rather than the cause, and indeed, monitoring $\dot{V}_E$ is clearly inaccurate under NIV, and other methods to monitor hemodynamics are less informative and not easy to set up during ARF, even when this is clinically indicated (6).

When referring to the presence of other nonmechanical determinants of the respiratory drive, we agree with the comments by Spinelli and coworkers. In patients with ARF, the inspiratory effort might be influenced by different stimuli (vagal nerve stimulation, pulmonary stretch receptor inhibition, or pulmonary C-fiber activation) acting on a neuronal-inflammatory basis (7). Because the respiratory drive may be unaffected by the unloading of respiratory muscle through the NIV application, an accurate management of nonmechanical triggers should be welcomed. We strongly agree that a multimodal strategy aimed at taming the respiratory drive is crucial.

Therefore to conclude, we do believe that esophageal manometry may allow researchers to monitor the effects of any "multimodal treatment," regardless of the contributing causes of an increased respiratory effort.

Quoting a famous movie by Wim Wenders, further studies are needed to establish whether self-inflicted lung injury and ventilator-induced lung injury are really "faraway, so close!" (8). ■

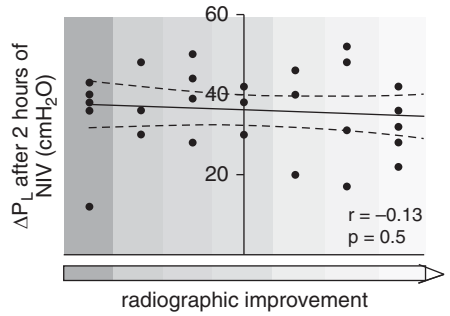

Figure 1. Pearson's correlation coefficient between dynamic transpulmonary pressure (after 2 h of noninvasive ventilation) and radiographic changes on chest X-ray at 24 hours. Each panel corresponds with categories of radiographic change (from left to right: relevant worsening, worsening, mild worsening, unmodified, mild improvement, improvement, and relevant improvement). ΔP_L = dynamic transpulmonary pressure; NIV = noninvasive ventilation.

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Tissue Doppler Imaging of the Diaphragm: A Novel Approach but Too Early for Clinical Implementation?

To the Editor:

Tissue Doppler imaging (TDI) is a robust ultrasound technique used in cardiology to quantify myocardial motion velocity, but the validity and clinical applications of diaphragm TDI are as yet uncertain. We read with great interest the work of Soilemezi and colleagues (1) on TDI to describe diaphragm motion properties of critically ill patients during ventilator weaning. The authors mention that diaphragm pulsed-wave (PW)-TDI is a straightforward method with a fast learning curve. Although we agree that these are essential features for any ultrasound method, we would like to address some important challenges that should be taken into account before implementing this technique in clinical practice.

First, PW-TDI results are very dependent on ultrasound settings and probe position. Doppler signals within a region of interest ("sample volume," or "gate") are converted into an average velocity signal. However, increasing the gain broadens the velocity spectrum and results in higher peak velocities (2, 3). Furthermore, as TDI measures the motion vector that is parallel to the ultrasound beam, the insonation angle must be kept as low as possible and changes in angle will affect both pulse length and spectral width. Angle correction can be applied but only for angles $<60^{\circ}$ because this correction is nonlinear. In addition, reverberation artifacts may occur, resulting in a clutter band along the baseline. This is presented in Figure E1B in the online supplement of Reference 1, where the concept of "smoothing" is introduced. Although smoothing improves visualization of the contour of the velocity signal, peaks are directly affected by the gain and too much smoothing results in signal loss. The authors mentioned that different filters and gains were set to obtain the best velocity images according to the speed of the diaphragmatic motion and the subject under examination. It would be great if they could address how this method was standardized (i.e., quantify "best"), as PW-TDI results can be manipulated easily by adjusting settings on the ultrasound machine.

Furthermore, despite high reliability of results reported in healthy volunteers, it is not entirely clear if PW-TDI results represent what they are intended to. As the velocity–time integral (VTI) reflects diaphragm displacement, VTI should match M-mode displacement (less sensitive to measurement errors compared with PW-TDI), but a large discrepancy was reported in patients (mean 1.27 vs. 0.78 cm for M-mode displacement vs. VTI, respectively; *see* Table 2 of Reference 1). Also, inspiratory and expiratory VTI should be similar over a large number of breaths, as end-expiratory diaphragm position should not change. Based on our own experience with PW-TDI, and in line with the presented examples (1), VTI inspiration is often larger than VTI expiration. Therefore, reporting a direct comparison of M-mode displacement versus VTI, and VTI inspiration versus VTI expiration, would be valuable to address the validity of PW-TDI results. If there is a systematic underestimation of VTI (and thus also of velocity results), it should be explored whether differences can be minimized sufficiently by adapting ultrasound settings or by performing offline correction.

Noninvasive measures to quantify diaphragm mechanics are highly needed, and correlations between transdiaphragmatic pressure (Pdi) and PW-TDI were evaluated. No relationship between VTI and diaphragm pressure–time product (PTPdi) was found. The authors assumed that VTI could possibly represent diaphragmatic work, because it is defined as the area under the inspiratory PW-TDI curve, similarly to PTPdi being the area under the Pdi–time waveform. This lack of relationship is not surprising given the poor correlation between diaphragm displacement and breathing effort (4, 5). A correlation was found between TDI-maximal relaxation rate (MRR) and Pdi-MRR. TDI-MRR was defined as the slope of the steepest part of the PW-TDI signal during expiration. From a physiological perspective, however, TDI-MRR represents diaphragm deceleration as the signal is already a derivative of displacement. Hence, peak relaxation velocity better reflects MRR and it would be of clinical interest to evaluate its relationship with Pdi-MRR.

Undoubtedly, diaphragm TDI is an exciting approach. However, standardization of the method and further understanding of the capabilities and limitations is important before using this technique for clinical decision-making. ■

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