this error of the minus sign would be confusing only for non-expert readers. Second, the figures demonstrated what they were designed for: the worse the lung function, the worse the diaphragmatic function. Further, it is clearly stated in the sixth paragraph of the methods section that the correlations were made with measurements from the healthy group ($n = 16$) and the patients with COPD who ended the rehabilitation ($n = 30$), for a total of 46 subjects, not 45 as written in the text.

Regarding the abstract, we agree and thank Rutka et al for highlighting that the text was confusing: the wording of ". . . 52 subjects with moderate to very severe COPD who underwent pulmonary rehabilitation and 16 healthy subjects" should be written as ". . . 52 subjects (ie, 46 subjects with moderate to very severe COPD who underwent pulmonary rehabilitation and 16 healthy subjects)." In any case, I strongly disagree that this information may confound the reader to understand the overall findings of this paper. To conclude, it seems evident that the percent of predicted FEV_1 was used to determine the COPD severity. Still, in any case, if the authors Rutka and colleagues know another way to classify airway obstruction in patients with COPD, we will be happy to be enlightened. The author will update the information regarding the sample size registered at ClinicalTrials.gov. The assessments were concluded as we saw that the research goals were reached with 46 subjects.

As a physiotherapist, researcher, and lecturer, I have always encouraged my peers, colleagues, and students to discuss the meaning of the information related to medical science. It is undeniable that the information related to methods and results must be clear and precise, but, as I see it, to improve the debate's quality we must avoid reducing the critical analyses to simply pointing out typographical errors.

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REFERENCE

1. Corbellini C, Boussuges A, Villafañe JH, Zocchi L. Diaphragmatic mobility loss in subjects with moderate to very severe COPD may improve after in-patient pulmonary rehabilitation. Respir Care 2018;63(10):1271-1280.
2. Schober P, Boer C, Schwarte LA. Correlation coefficients: appropriate use and interpretation. Anesth Analg 2018;126(5):1763-1768.

Fragility Index in Randomized Controlled Trials on Noninvasive Ventilation as a Weaning Strategy in Subjects With Acute Hypoxemic Respiratory Failure

To the Editor:

Optimal ventilation and weaning strategies in patients with acute hypoxemic respiratory failure are far to be assessed.[1] We applaud the systematic review by Shan et al[2] aiming to evaluate the efficacy of noninvasive ventilation (NIV) weaning on hospital and ICU mortalities. In a review of 6 randomized controlled trials (RCTs) with moderate-to-high risk of bias, the authors stated that there was no effect of NIV weaning on hospital and ICU mortality even if it reduced the length of ICU stay and adverse events compared with invasive weaning in acute hypoxemic respiratory failure.[2]

The fragility index (FI), an intuitive measure of the robustness of RCTs, was recently introduced in critical care medicine and has been used in several different systematic reviews.[3-5] The FI is achieved by using a 2-by-2 contingency table and *P* values produced with the Fisher exact test.[3] We calculated the FI of RCTs included in the systematic review by Shan et al[2] and that all of the included studies had a FI of zero (FI = 0 and $P > .05$). This FI score means that the RCTs evaluating the use of NIV weaning on mortality are very fragile and the evidence from these studies is very weak. The FI may be an easy additional index to aid the interpretation of studies and may assist clinicians in appropriate and optimal decision-making on critically ill patients.[6] Our findings support the author's conclusion that stronger evidence is needed to definitively assess whether NIV weaning may reduce hospital and ICU mortality rates. We further suggest that Shan et al[2] include the FI of zero for the included RCTs as a fourth limitation of their systematic review.

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REFERENCES

1. Pelosi P, Vargas M. Mechanical ventilation and intraabdominal hypertension: be-yond good and evil. Crit Care 2012;16(6):187.
2. Shan M, Pang X, Wang W, Lan C, Chen R, Zhu C, et al. Noninvasive ventilation as a weaning strategy in subjects with acute hypoxemic respiratory failure. Respir Care 2020; 65(10):1574-1584.
3. Vargas M, Servillo G. The end of corticosteroid in sepsis: fragile results from fragile trials. Crit Care Med 2018;46(12):e1228.
4. Vargas M, Servillo G. Liberal versus conservative oxygen therapy in critically ill patients: using the fragility index to determine robust results. Crit Care 2019;23(1):132.
5. Vargas M, Buonanno P, Iacovazzo C, Servillo G. Epinephrine for out of hospital cardiac arrest: a systematic review and meta-

analysis of randomized controlled trials. Resuscitation 2019;136:54-56.
6. Ridgeon EE, Young PJ, Bellomo R, Mucchetti M, Lembo R, Landoni G, et al. The fragility index in multicenter randomized controlled critical care trials. Crit Care Med 2016;44(7):1278-1284.

The authors respond

Reply:

We thank Vargas et al very much for their comments[1] on our newly published research[2] in RESPIRATORY CARE. They calculated the fragility index of randomized controlled trials (RCTs) included in the systematic review and found that all RCTs had a fragility index of zero, which suggests that the RCTs evaluating the effect of noninvasive ventilation weaning on mortality were very fragile and the evidence was very weak. These comments were reasonable according to the rules of the fragility index, namely that the larger the fragility index score, the more robust the evidence, and vice versa.[3] We agree completely with the view that the fragility index is an important aid to a reader's interpretation of the results of RCTs and serves to make a correct judement,[3] especially when the *P* value is above or below the threshold value (eg, $P = .051$ or $P = .049$).[4]

However, it is important to note that the benefit of the fragility index might be limited when fragility index scores are used to estimate the secondary outcomes of RCTs, given that the primary outcomes are the core detected effects in RCTs.[3] All of the included studies in our meta-analysis[5-9] reported mortality as the secondary outcome, which might diminish the value of the fragility index to a certain extent, although it was a good recommendation to report the fragility index score of zero as an additional limitation. It is well known that only a few RCTs with small sample sizes have been performed to explore the effect of noninvasive ventilation weaning in subjects with acute hypoxemic respiratory failure,[2] which weakens the evidence from the pooled results. This might inspire more large RCTs to be performed, especially ones focused on mortality.

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REFERENCES

1. Vargas M, Buonanno P, Servillo G. Fragility index in randomized controlled trials on noninvasive ventilation as a weaning strategy in subjects with acute hypoxemic respiratory failure. Respir Care 2021;66(2):355.
2. Shan M, Pang X, Wang W, Lan C, Chen R, Zhu C, et al. Noninvasive ventilation as a weaning strategy in subjects with acute hyp oxemic respiratory failure. Respir Care 2020;65(10):1574-1584.
3. Tignanelli CJ, Napolitano LM. The fragility index in randomized clinical trials as a means of optimizing patient care. JAMA Surg 2019;154(1):74-79.
4. Walsh M, Srinathan SK, McAuley DF, Mrkobrada M, Levine O, Ribic C, et al. The statistical significance of randomized controlled trial results is frequently fragile: a case for a fragility index. J Clin Epidemiol 2014;67(6):622-628.
5. Laiq N, Khan RA, Malik A. Non-invasive positive pressure ventilation facilitates early extubation in post operative cardiac patients. J Postgrad Med Inst 2013;27(4):361-365.
6. Perkins GD, Mistry D, Gates S, Gao F, Snelson C, Hart N, et al. Effect of protocolized weaning with early extubation to noninvasive ventilation vs invasive weaning on time to liberation from mechanical ventilation among patients with respiratory failure: the Breathe randomized clinical trial. JAMA 2018;320(18):1881-1888.
7. Vaschetto R, Longhini F, Persona P, Ori C, Stefani G, Liu S, et al. Early extubation followed by immediate noninvasive ventilation vs. standard extubation in hypoxemic patients: a randomized clinical trial. Intensive Care Med 2019;45(1):62-71.
8. Vaschetto R, Turucz E, Dellapiazza F, Guido S, Colombo D, Cammarota G, et al. Noninvasive ventilation after early extubation in patients recovering from hypoxemic acute respiratory failure: a single-centre feasibility study. Intensive Care Med 2012;38(10):1599-1606.
9. Wang X, Xu S, Liu G, Caikai S. [Study of timing of invasive and noninvasive sequential ventilation in patients with acute respiratory distress syndrome]. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue 2014;26(5):330-334.