

criteria using $\text{PaO}_2/\text{FiO}_2$ in patients with different severity of respiratory failure will further help researchers in the future. ■

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Predicting the Outcome of Nasal High-Flow Therapy: A Proposed Representation of the Data and a Supplemental Analysis

To the Editor:

I read with interest the paper by Roca and colleagues that followed up on their initial publication in 2016 (1, 2). One aspect of the report that makes interpreting the results difficult is that the authors did not provide graphs with the individual data points for the respiratory rate, the oxygen saturation as measured by pulse oximetry (SpO_2)/ FiO_2 , and the ROX to compare successes and failures, and only provided comparisons of summary data in the tables. In a manner similar to the graph used by Yang and Tobin when they validated the frequency-to- V_T ratio to predict extubation success (3), I suggest that Roca and colleagues

provide a graph with the respiratory rate on the x -axis and the $\text{SpO}_2/\text{FiO}_2$ on the y -axis, plot the failures and the successes in different symbols, and mark the isopleth with a slope of 4.88. Such a graph allows the reader to see the positions of successes and failures in relation to the cut point of 4.88 and the role that tachypnea and hypoxemia played in those positions. I also suggest to the authors testing the index with the respiratory rate squared. The range of the respiratory rate is narrow. This transformation increases the range of the denominator and might create clearer separation between the successes and the failures. ■

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Reply to Tatkov, to Karim and Esquinas, and to Tulaimat

From the Authors:

We read with great interest the letter by Stanislav Tatkov and thank him for his interest in our work. Dr. Tatkov's thoughts are interesting, and the figure he provides is insightful.

The figure shows that two distinct combinations of respiratory rate and FiO_2 (which may reflect two different clinical situations in terms of disease severity)—a respiratory rate of 20 with FiO_2 of 0.8, and a respiratory rate of 40 with FiO_2 of 0.5—provide the same ROX index. The figure further shows that the ROX index is unlikely to drop

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below 4.88 with $F_{I_{O_2}}$ up to 0.5. Although the construction of the curves is unquestionable, the combination Dr. Tatkov highlights is more than unlikely. It is indeed quite exceptional to encounter a patient with a respiratory rate of 40 breaths/min 12 hours after admission to an ICU for acute respiratory failure (which is the time at which the ROX yielded the best value). For example, in the FLORALI (Clinical Effect of the Association of Noninvasive Ventilation and High Flow Nasal Oxygen Therapy in Resuscitation of Patients with Acute Lung Injury) study, the mean respiratory rate of patients under high-flow nasal cannula (HFNC) treatment at 12 hours was only 27 breaths/min. In addition, only 6.5% of the patients had a respiratory rate ≥ 40 (minimum, 40; maximum, 44). Similarly, in the ROX validation cohort, only one patient had a respiratory rate of 40 breaths/min at 12 hours of HFNC, and the mean respiratory rate at this time point was 24 breaths/min. The second component of the combination is the $F_{I_{O_2}}$. Once again, it is rare to encounter a patient with $F_{I_{O_2}}$ below 0.5 within the first 12 hours of treatment. This observation is supported by solid data. For example, in the validation cohort, only 5.2%, 9.2%, and 21.3% of the patients after HFNC onset needed a $F_{I_{O_2}} < 0.5$ after 2 hours, 6 hours, and 12 hours of treatment, respectively (1). Even lower percentages were observed in the FLORALI cohort: 3.9%, 7.1%, and 15.8% at 1 hour, 6 hours, and 12 hours, respectively (2).

The second point raised by Dr. Tatkov is the fact that the ROX index would get under 4.88 when the $F_{I_{O_2}}$ was > 0.8 for respiratory rates of ≥ 20 breaths/min. It is our opinion that the initial settings should favor high levels of $F_{I_{O_2}}$ in patients with more severe disease. However, most of the patients who needed $F_{I_{O_2}} > 0.8$ presented respiratory rates of ≥ 20 breaths/min (83.1%, 79.6%, and 85.7% after 2 hours, 6 hours, and 12 hours of treatment in the validation cohort). It should also be noted that the ROX index measured after 12 hours of treatment predicted better HFNC outcomes than the $F_{I_{O_2}}$ value (area under the receiver operating characteristic curve [AUROC], 0.752 [0.664–0.840] vs. 0.672 [0.574–0.770]; $P = 0.008$). Therefore, even though mathematically the figure is totally valid, from a practical standpoint, most patients may benefit from ROX estimation rather than direct use of the set $F_{I_{O_2}}$.

On the other hand, we also provided other cutoff points for predicting HFNC failure: 2.85, 3.47, and 3.85 at 2 hours, 6 hours, and 12 hours after initiation of HFNC therapy. We suggest that the ROX index should be monitored over time. In fact, if the value of the ROX index is between 3.85 and 4.88 after 12 hours of treatment, the ROX index could be reassessed in 1 or 2 hours. Then, if the score has increased, the patient may have a greater likelihood of success. In contrast, if it has decreased, the patient may be more likely to fail. Finally, if the score is unchanged, another reassessment could be performed after one more hour.

We also thank Drs. Karim and Esquinas for their interest in our paper. We fully agree that oxygen saturation as measured by pulse oximetry (Sp_{O_2})/ $F_{I_{O_2}}$ does not always correlate well with Pa_{O_2} / $F_{I_{O_2}}$. In fact, when this correlation was assessed in patients with acute respiratory distress syndrome, measurements with Sp_{O_2} values $> 97\%$ were excluded from the analysis because the oxyhemoglobin dissociation curve is flat above these levels (3). Therefore, as the authors pointed out, theoretically, one

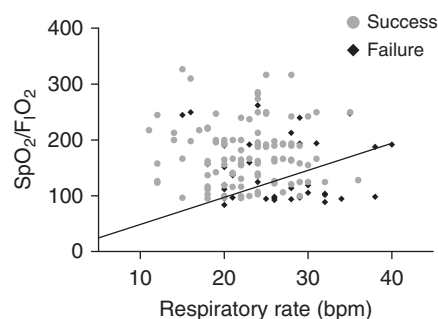


Figure 1. Scatterplot of respiratory rate and $Sp_{O_2}/F_{I_{O_2}}$ with the isopleth corresponding to a ROX index value of 4.88. Sp_{O_2} = oxygen saturation as measured by pulse oximetry.

might expect that the diagnostic accuracy of the ROX index using $Pa_{O_2}/F_{I_{O_2}}$ in predicting HFNC outcomes would be better than the one observed with $Sp_{O_2}/F_{I_{O_2}}$. However, two important issues should be taken into account. First, in the validation cohort, less than half of the patients had a Pa_{O_2} value available, which suggests that patients undergoing HFNC treatment are mainly monitored noninvasively using Sp_{O_2} . Second, no significant differences were observed when the diagnostic accuracy of the ROX index constructed with $Pa_{O_2}/F_{I_{O_2}}$ was compared with the same index constructed with $Sp_{O_2}/F_{I_{O_2}}$ at any time point ($P = 0.652$, $P = 0.122$, and $P = 0.407$ at 2 hours, 6 hours, and 12 hours of HFNC treatment, respectively). Thus, according to these data, it seems that a more practical and feasible approach for measuring the ROX index would be to use the Sp_{O_2} , as it will be available in all patients treated with HFNC at the bedside and it does not predict worse than the modified ROX index using the Pa_{O_2} .

Finally, we thank Dr. Tulimat for his interest in our manuscript. As he suggested, we provided the scatterplot with the respiratory rate on the x-axis and the $Sp_{O_2}/F_{I_{O_2}}$ on the y-axis, with the successes and failures in different colors and the isopleth with a slope of 4.88 marked in black (Figure 1). As the range of the respiratory rate is narrow, we have also tested the diagnostic accuracy of the ROX index with the respiratory rate squared. However, no differences in the AUROC values between the ROX index and the squared ROX index were observed (AUROC, 0.752 [0.664–0.840] vs. 0.753 [0.665–0.840]; $P = 0.968$). Therefore, as the use of a squared respiratory rate for the calculation of the ROX index does not provide any additional benefit in terms of prediction of HFNC success or failure, the use of the normal ROX index may be recommended. ■

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Erratum: Healing Pulmonary Rehabilitation in the United States: A Call to Action for ATS Members



There is an error in the editorial by Garvey and colleagues (1), published in the April 15 issue of the *Journal*. The third sentence of the third paragraph lists a group of advocacy organizations; the American Thoracic Society was incorrectly omitted from this list. ■

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