a single threshold in the b-ALSFRS-R score (<6/12) to exclude a patient from mouthpiece ventilation, but we would rely on an adequate clinical trial, particularly in the absence of prospective studies establishing a more discriminative threshold in a larger population of individuals with ALS. Hence, a small number of subjects were included whose b-ALSFRS-R score was low but who seemed at least initially to be capable and motivated enough to grip the mouthpiece. Even prospective trials may not be able to adequately address the question of sufficient bulbar function for mouthpiece ventilation in given individuals. In the same way that clinically, individuals with severe bulbar ALS with low cough peak flows may not be expected to tolerate NIV or mechanical in-exsufflation based on objective evaluation and published experience,[3-6] much to our surprise, many do. As a result, we suspect that even prospectively established, objective cutoffs will not replace adequate clinical trials of mask NIV, mechanical in-exsufflation, or mouthpiece ventilation.

While we also agree that cough peak flow is an excellent assessment of bulbar function, we would not suggest that it "is the only test that reflects bulbar function." Although glottic function is clearly necessary to enhance expiratory flows above those observed with forced exhalation alone, in our experience, the difference between the maximum insufflation capacity and vital capacity is an equally robust measure of glottic and bulbar function. In fact, the difference between the maximum insufflation capacity and vital capacity has been demonstrated to correlate highly with cough peak flow in a population with Duchenne muscular dystrophy.[7] Clinically, some individuals may fail to demonstrate an enhanced cough peak flow greater than the peak expiratory flow but may still demonstrate a considerable difference between maximum insufflation capacity and vital capacity. As such, we would prefer to rely on either measure or both to help define those who are more likely to manage mouthpiece ventilation effectively.

Further discussion would also be appropriate with regard to the suggestion that mouthpiece ventilation is "particularly useful when there are problems with conventional masks." Rather, mouthpiece ventilation is introduced precisely to replace even perfectly comfortable and effective masks and expressly to provide independence from them. Indeed, mouthpiece ventilation facilitates speech, swallowing, and, perhaps most importantly, the ability to autonomously perform regular lung volume recruitment to increase cough peak flow, maintain airway clearance, and possibly improve respiratory mechanics, all critical activities that cannot be performed with mask NIV. Furthermore, the suggestion that "other aspects [*besides quality of life*] need to be taken into account," if implying that the symptom of dyspnea and/or prolonged use of mask NIV is not a legitimate, sole indication for mouthpiece ventilation and that more objective measure are required, is to suggest that ALS patients experiencing daytime dyspnea need to remain on a confining mask and not be relieved or permitted the ability to perform autonomous lung volume recruitment until more objective signs, such as, presumably, daytime hypercapnia, are identified. To establish definitively the survival benefit of mouthpiece ventilation in ALS, hypercapnia might be necessary, but to provide independence and quality of life in breathing, communicating, and taking nutrition by mouth, it is not. We would continue to advocate that, in those capable of retaining and using a mouthpiece, the introduction of mouthpiece ventilation should occur as soon as the daily amount of mask ventilation exceeds 12 h or whatever time threshold will provide the patient with comfort, relief of dyspnea, and effective daytime ventilation as well as autonomous airway clearance.

We join you in the anticipation of future trials that will better define optimum candidates and the role of mouthpiece ventilation in the respiratory management of individuals with ALS.

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P_{aO_2}/F_{IO_2} Is Not a Guesstimation

To the Editor:

I read with great interest and with some concern the paper by Cao et al[1] that compared volume-controlled and pressure-limited noninvasive ventilation (NIV) in subjects with acute hypercapnic respiratory failure. The authors reported on P_{aO_2}/F_{IO_2} rather than P_{aO_2} as part of their baseline demographics in Table 1 and in their results in Figure 5. The methods for NIV described that supplemental oxygen was delivered through a port in the mask with flow adjusted to maintain oxygen saturation using a specific machine (FLEXO ST30, Curative Medical Technology, Suzhou, China). They used a formula to determine F_{IO_2} delivered to each subject and reported results as P_{aO_2}/F_{IO_2}, which causes me some concern. The authors did state that the conversion factor provided an approximation of F_{IO_2}, which was influenced by minute ventilation, breathing pattern, and gas leakage. I feel that an approximation of F_{IO_2} cannot accurately predict P_{aO_2}/F_{IO_2} where a completely closed system and accurate F_{IO_2} is not provided. I found one abstract[2] that used the formula to help rapidly predict correlation of S_{pO_2}/F_{IO_2} in non-intubated patients as a surrogate to arterial blood gas for determining P_{aO_2}/F_{IO_2} in emergency room patients, which may be a novel noninvasive way to assess respiratory failure.[3-5]

I could not find any reference to the formula to validate and verify an F_{IO_2} via a port for NIV. I have used REMstar NIV machines (Philips Respironics, Murrysville, Pennsylvania) for several decades, and the

general procedure limits oxygen to no more than 10 L for F_{IO_2} approximately 0.4–0.5. I would need a machine that has a blender that would guarantee a delivered F_{IO_2} for higher concentrations to obtain an accurate P_{aO_2}/F_{IO_2}. Examples of calculated flows based on the formula would be as follows: 5 L = 36%, 10 L = 51%, 15 L = 66%, or 20 L = 81%.

I recently cared for a patient with acute hypoxemic respiratory failure and an S_{pO_2} of 89% on 6 L nasal cannula. The patient was placed on a CPAP device without an oxygen blender as I waited for a different machine with a blender. No matter what flow, based on the limitations of that machine, the saturation did not change. The patient required an F_{IO_2} of >0.6 before the S_{pO_2} began to increase. At 8, 10, 15, and 20 L bled into the mask port, S_{pO_2} remained doggedly fixed at 89–90%. Indeed, the limitations on this device did not agree with the formula for F_{IO_2} described in the paper.

The use of this equation may represent some false acceptance that the F_{IO_2} is truly delivered to the patient and may lead to false assumptions regarding the seriousness of the subject's condition. Although the paper has merit with regard to volume or pressure targeting, the authors should have reported flow and P_{aO_2} so that readers could make their own assumptions about oxygenation.

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Ms Couture has disclosed a relationship with Philips Respironics.

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P_{aO_2}/F_{IO_2} Is Not a Guestimation—Reply

In Reply:

We thank Ms Couture for her interest and for commenting on our work.[1] We agree that P_{aO_2}/F_{IO_2} could not be accurately calculated in our study, because supplemental oxygen was delivered through a port in the mask, and the noninvasive ventilator that we used did not provide accurate F_{IO_2}.

According to the protocols of Mehta et al[2] and Bellone et al[3] to determine P_{aO_2}/F_{IO_2} ratios while subjects are receiving noninvasive ventilation, F_{IO_2} is calculated using the following conversion factor: (21% + [3% × oxygen flow in L/min of supplemental oxygen]). This conversion factor is influenced by minute ventilation, breathing patterns, and air leakage. We agree that S_{pO_2}/F_{IO_2}, as an alternative to P_{aO_2}/F_{IO_2}, may be a novel and noninvasive way to rapidly assess respiratory failure. However, the determination of F_{IO_2} remains inaccurate and is influenced by minute ventilation, breathing patterns, and air leakage.

Ms Couture found that a patient with acute hypoxemic respiratory failure had an S_{pO_2} of 89% on 6 L/min of supplemental oxygen, and S_{pO_2} remained unchanged when the supplemental oxygen was increased to 20 L/min. Two possible reasons deserve attention. First, the increment of F_{IO_2} was indeed less than the increment of supplemental oxygen. Second, if acute hypoxemic respiratory failure is caused by serious intrapulmonary shunt, it might be difficult to improve S_{pO_2} by increasing F_{IO_2}.

Finally, the main purpose of the present study was to verify whether, compared with pressure-controlled mode, volume-controlled mode would be more effective in correcting hypercapnia, hence reducing the need for intubation and improving survival in subjects with acute hypercapnic respiratory failure. P_{aO_2}/F_{IO_2} was not the primary end point of the present study and was not the primary issue in our subjects. Hence, despite the inaccurate determination, the P_{aO_2}/F_{IO_2} values from the 2 groups remained comparable, and changes in their values could be used to demonstrate changes in subjects' oxygenation, because F_{IO_2} was determined using an identical formulation.

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