Guérin et al[1] compared the diagnostic performance of the Stewart approach and the physiological approach in acid-base disorders in patients with chronic respiratory failure, in stable or unstable respiratory condition. They concluded that the Stewart approach is superior to the physiological approach in its diagnostic ability. This conclusion may be premature, because the comparison of different acid-base assessment methods is fraught with pitfalls.

First, unfortunately, there is no accepted standard to compare the methods with. As a surrogate, interestingly, many advocates of the Stewart method take the superiority of this approach as a matter of fact. Guérin et al[1] mentioned that the Stewart approach found acid-base abnormalities in 23 patients who had normal standardized base excess (16%), in 41 patients with non-elevated bicarbonate (28%), and in 44 patients with normal anion gap (30%).[1] This does not mean, however, that the physiological method or the base-excess method cannot diagnose these disorders. The bicarbonate level can be normal in combined metabolic acidosis and alkalosis: a situation frequently seen in patients with chronic respiratory disorders, due to the use of diuretics, and metabolic acidosis as a result of numerous disorders (eg, sepsis, hypoxemia). These mixed disorders can be assessed by evaluating the difference in increase in anion gap with the decrease in bicarbonate: the so-called "delta-delta."[2] An important general limitation, that the individual anion gap and bicarbonate levels are not known in acutely ill patients, would not have been an issue in this study, because basic acid-base parameters were tested before the deterioration of the pulmonary function.

Considering the base-excess method, a patient with a P_{aCO_2} of 40 mm Hg, bicarbonate of 24 mEq/L, and a pH of 7.4 will have a base excess of zero, by definition. This can, of course, be found in a healthy individual, but it is also found in a patient with chronic respiratory acidosis who develops sepsis, as acute hyperventilation superimposed on chronic hypoventilation and lactic acidosis may have normalized the elevated P_{aCO_2} and bicarbonate levels. The base-excess method can still give a correct diagnosis, but only after partitioning of the base excess.[3]

Second, the Stewart method is considered the accepted standard by some clinicians, perhaps because it gives the false impression of increased accuracy, as many acid-base parameters are included in the evaluation. Paradoxically, however, it is the number of parameters that limits its accuracy. Chloride is one of the key electrolytes in the Stewart method. Even today, unfortunately, significant laboratory analyzer differences exist, in particular in detecting chloride concentrations, with analyzer-related differences of up to 7 mEq/L.[4] Such inaccuracy may lead to erroneous calculation of the strong ion difference, the strong ion gap, and the anion gap. These differences may have a major impact on acid-base parameters, and diagnosis may sometimes be based on technology rather than pathophysiology. Moreover, the large number of parameters increases the magnitude of variability and error. One study found large differences in the limits of agreement for strong ion gap (−5.1 to +6.6 mEq/L).[4] Also, even when biochemical analyzers are accurate, the Stewart method can still cumulate measurement errors, because small analytical differences can become clinically important when the differences are exaggerated via mathematical summation.

Third, Guérin et al included patients in the study when they were admitted for acute respiratory failure, defined as dyspnea increased above baseline and/or respiratory rate > 25 breaths/min, use of accessory respiratory muscles, and/or P_{aCO_2} > 45 mm Hg with arterial pH < 7.36, and some other parameters. Many patients with severe COPD probably have a baseline P_{aCO_2} above 45 mm Hg. Because the baseline values were measured in the routine evaluation, the increase of P_{aCO_2} to a certain percentage or a defined amount rather than an absolute value of > 45 mm Hg would give a better impression of acute respiratory failure. Furthermore, it is also questionable if one can define acidosis when the pH is below 7.36, instead of below 7.39. None of the 8 patients in the control group had a pH below 7.39 (range 7.39–7.45).[5] Studies on the reference range of arterial pH have been scarce in the past few decades. The largest recent study was by Crapo et al,[6] in 1999, in 96 healthy subjects: not a single arterial pH was below 7.39.

Fourth, Guérin et al also concluded that the diagnostic performance of the Stewart approach was better than that of the conventional approach, even when the albumin correction of the anion gap was taken into account. Even if that were true, it would only be applicable to the metabolic component of the acid-base disorder, because, in contrast to the physiological approach and the base-excess approach, the Stewart approach does not define the secondary response in nonrespiratory acidosis and alkalosis. The single examination of the metabolic component, regardless of P_{aCO_2} values, might lead to incorrect diagnosis in 15% of the patients with respiratory alkalosis.[7]

Fifth, although the secondary response can be calculated in metabolic acidosis and alkalosis with the physiological method,[8] unfortunately, these rules are adapted from very old studies in dogs, in non-physiological circumstances, with older equipment, and recent studies have questioned the reliability of those rules in chronic respiratory acidosis. There is a hypothesis that an elevated P_{aCO_2} directly stimulates the proximal tubule of the kidney to increase bicarbonate reabsorption as long as the P_{aCO_2} remains elevated, and that this mechanism increases the bicarbonate level to a higher concentration than previously acknowledged.[9] If that theory is valid, the finding of Guérin et al that the presence of metabolic alkalosis in some chronic-respiratory-failure patients, of about 12% (in 8 of the 67 patients), may not be an additional metabolic alkalosis, but merely a normal physiological response.

Hence, there is no ideal approach for determination of acid-base balance, and comparisons in clinical situations will face many difficulties.

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The author responds:

I was very interested in the comments from Drs Bruno, Berend, and Engels about our recent report.[1] Dr Bruno pointed out that in our report the fact that the significantly higher mean bicarbonate value in group 3 (unstable patients) than in group 1 (stable patients) suggests the presence of a concomitant metabolic alkalosis in many of those patients, whereas the normal bicarbonate in groups 2 and 4 does not exclude the presence of a metabolic disorder. We should say that higher bicarbonate value in group 3 than in group 1 might also reflect that chronic hypercapnia was greater and ongoing for a longer period than in patients in group 3.

Furthermore, Dr Bruno proposed using a slightly modified traditional approach to detect mixed acid-base disorders. It is true that we did not use the approach suggested by Dr Bruno. The traditional approach we used in groups 1 and 3 (Table 1) was clearly unable to detect any single disturbance. We agree that this is too simplistic and a more complex approach would have been of value. Therefore, the comparison between the Stewart approach and the approach proposed by Dr Bruno should be done, since apparently it has not been done. It is likely, however, that the stepwise approach that relies on different measurements, namely biological and clinical, has first to be assessed in terms of diagnostic performance, with pretest odds, positive and negative likelihood ratios, and post-test odds measurements. Dr Bruno also asked for additional data from our patients, which, unfortunately, were not collected in our case report form. Dr Bruno's conclusion that "I think their conclusion of better performance with the Stewart method is not justified. The traditional approach, with only minor adjustments, can provide the same practical information." is, however, not supported by data, as outlined above.

Drs Berend and Engels pointed out 5 issues in our report.[1] I do agree with their first comment, that there is no accepted standard to compare when assessing acid-base abnormalities. Second, to try to circumvent the lack of agreement between laboratories regarding the computation of the contributing variables in the Stewart approach, as suggested by Berend and Engels, we determined normal ranges locally.

I don't yet understand the third issue Berend and Engels raised. Setting the pH threshold below 7.36 to define acute respiratory failure is all but conservative. In a randomized controlled trial in COPD patients admitted for acute respiratory failure in the pneumology ward, Plant et al[2] enrolled COPD patients in acute respiratory failure with pH range 7.25–7.35. The definition we used was composite and centered around dyspnea. Furthermore, we enrolled not only COPD patients but also any patient with chronic respiratory failure, defined with a priori criteria.

Fourth, Fencl et al[3] separated respiratory and non-respiratory acid-base disorders. We enrolled a prospective cohort of patients who were thought by definition to have a respiratory disorder.

I also agree with Berend and Engels' fifth comment, on the hypothesis by Martinu et al,[4] a study we quoted in our report.[1] There is obviously the need for further pathophysiological investigations to better understand the complex acid-base derangements in the setting of chronic respiratory failure.

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