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Ventilatory ratio: a simple bedside measure of ventilation

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Background. Measures of oxygenation are traditionally used to monitor the progress of patients on positive pressure ventilation. Although CO_2 elimination depends on fewer variables, measures of CO_2 elimination are comparatively overlooked except when monitoring patients who are difficult to ventilate. CO_2 elimination is dependent upon CO_2 production and alveolar ventilation, which together determine Pa_{CO_2}. Alveolar ventilation is the efficient portion of minute ventilation ('*E*'). In the clinical setting, problems with CO_2 elimination are observed as increasing Pa_{CO_2}, increasing minute ventilation, or both. In conventional tests of respiratory function, actual measurements are frequently compared with predicted measurements. However, this approach has rarely been applied to the measurement of ventilatory efficiency.

Methods. We have developed a ratio, called the ventilatory ratio (VR), which compares actual measurements and predicted values of minute ventilation and Pa_{CO_2}.

$$VR = \frac{\dot{V}_{E_{measured}} \times Pa_{CO_{2measured}}}{\dot{V}_{E_{predicted}} \times Pa_{CO_{2predicted}}}$$

$\dot{V}_{E_{predicted}}$ is taken to be 100 (ml kg^{-1} min^{-1}) based on predicted body weight, and $Pa_{CO_{2predicted}}$ is taken to be 5 kPa.

Results. Inspection shows VR to be a unitless ratio that can be easily calculated at the bedside. VR is governed by carbon dioxide production and ventilatory efficiency in a logically intuitive way. We suggest that VR provides a simple guide to changes in ventilatory efficiency. A value close to 1 is predicted for normal individuals and an increasing value would correspond with worsening ventilation, increased CO_2 production, or both.

Conclusions. VR is a new tool providing additional information for clinicians managing ventilated patients.

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Over the last five decades, emphasis in mechanical ventilation has increasingly focused on improving oxygenation, while avoiding iatrogenic complications. Although carbon dioxide measurements are used to guide ventilatory adequacy, most ventilatory strategies are aimed primarily at adequate oxygenation. Measurements and indices of oxygenation, such as Pa_{O_2}, Sp_{O_2}, and Pa_{O_2}/FI_{O_2} or A–a (alveolar–arterial) gradients are frequently utilized to adjust ventilatory settings and aid in clinical decision-making.[1–4] Although attention is paid to minute ventilation, ventilatory frequency, tidal volumes, and Pa_{CO_2}, there is no common unifying index that can be easily used to assess the efficacy of CO_2 elimination at the bedside. Especially in an era where permissive hypercapnia is widely practiced,[5] the development of such an index becomes evermore crucial.

Clinical problems with CO_2 elimination will be manifest as an elevation in Pa_{CO_2}, a requirement for increased minute ventilation, or a combination of both. The ideal index reflecting CO_2 elimination would need to be simple to use and easily repeatable. We use the ratio of the product of

measured $\dot{V}_E$ and Pa_{CO_2} to predicted values of the same parameters to derive a novel index called ventilatory ratio (VR). We present the physiological analysis of VR, followed by a description of the calculation and rationale of the predicted values. Outlined below is the theoretical description of VR, an index we believe in time will be shown to have a wide range of clinical applications.

Methods

Physiological analysis

We define the VR as

$$\mathrm{VR} = \frac{\dot{V}_{E_{\mathrm{measured}}} \times Pa_{CO_{2\mathrm{measured}}}}{\dot{V}_{E_{\mathrm{predicted}}} \times Pa_{CO_{2\mathrm{predicted}}}} \quad (1)$$

At steady state, carbon dioxide production and alveolar ventilation are the determinants of Pa_{CO_2}. Alveolar ventilation is a variable fraction of minute ventilation (about two-thirds in fit unanaesthetized individuals), the remaining fraction being physiological deadspace ventilation.

VR can be analysed in terms of carbon dioxide production and the fraction of minute ventilation that is alveolar ventilation, as follows.

First

$$\dot{V}CO_2 = \dot{V}_A \times FA_{CO_2} \quad (2)$$

and

$$FA_{CO_2} = \frac{PA_{CO_2}}{P_B} \quad (3)$$

Therefore, equation (3) may be substituted into equation (2) and rearranged as

$$PA_{CO_2} = \frac{\dot{V}CO_2}{\dot{V}_A} \times P_B \quad (4)$$

Assuming,

$$Pa_{CO_2} \approx PA_{CO_2} \quad (5)$$

Equation (5) may be restated for Pa_{CO_2}

$$Pa_{CO_2} = \frac{\dot{V}CO_2}{\dot{V}_A} \times P_B \quad (6)$$

This is a restatement of standard concepts in respiratory physiology. [We will discuss the validity of the assumption in equation (5) later.]

Secondly, it is helpful to have a way of speaking about alveolar ventilation as a fraction of minute ventilation. We call this the 'ventilatory efficiency', E

$$E = \frac{\dot{V}_A}{\dot{V}_E} \quad (7)$$

From which

$$\dot{V}_E = \frac{\dot{V}_A}{E} \quad (8)$$

Equation (9) demonstrates the relationship of ventilatory efficiency to the more usually considered deadspace ventilation

$$E = \frac{\dot{V}_A}{\dot{V}_E} = \frac{\dot{V}_E - \dot{V}_D}{\dot{V}_E} = 1 - \frac{\dot{V}_D}{\dot{V}_E} \quad (9)$$

although the right-hand side of equation (9) is not required for our purposes.

Thirdly, the concept of 'actual' and 'predicted' carbon dioxide production and ventilatory efficiency is required. Measured minute ventilation and arterial carbon dioxide will be dependent upon actual carbon dioxide production and ventilatory efficiency. Equations (6) and (8) can be applied to these concepts as follows

$$Pa_{CO_{2\mathrm{measured}}} = \frac{\dot{V}CO_{2_{\mathrm{actual}}}}{\dot{V}_{A_{\mathrm{actual}}}} \times P_B \quad \text{and} \quad \dot{V}_{E_{\mathrm{measured}}} = \frac{\dot{V}_{A_{\mathrm{actual}}}}{E_{\mathrm{actual}}} \quad (10)$$

and

$$Pa_{CO_{2\mathrm{predicted}}} = \frac{\dot{V}CO_{2_{\mathrm{predicted}}}}{\dot{V}_{A_{\mathrm{predicted}}}} \times P_B \quad \text{and} \quad \dot{V}_{E_{\mathrm{predicted}}} = \frac{\dot{V}_{A_{\mathrm{predicted}}}}{E_{\mathrm{predicted}}} \quad (11)$$

Finally, the right-hand sides of the two pairs of equations (10) and (11) are substituted into equation (1), the definition of VR, which results

$$\mathrm{VR} = \frac{\dot{V}CO_{2_{\mathrm{actual}}}}{E_{\mathrm{actual}}} \times \frac{E_{\mathrm{predicted}}}{\dot{V}CO_{2_{\mathrm{predicted}}}} \quad (12)$$

.

This is more conveniently rearranged to give

$$\mathrm{VR} = \frac{\dot{V}CO_{2_{\mathrm{actual}}}}{\dot{V}CO_{2_{\mathrm{predicted}}}} \times \frac{E_{\mathrm{predicted}}}{E_{\mathrm{actual}}} \quad (13)$$

Calculation of predicted values

In order to calculate VR, we must first calculate the predicted values.

For the predicted value of minute ventilation, we are using 100 ml kg^{-1} min^{-1}. This value is extracted from population nomograms from anaesthesic practice.[6 7]

For predicted body weight (PBW), we have used the ARDSnet PBW calculator. PBW (kg) is calculated using the formula 50+0.91 (centimetres of height−152.4) for males, and 45.5+0.91 (centimetres of height−152.4) for females.[8]

The predicted value used for Pa_{CO_2} is 5 kPa. Because the range of Pa_{CO_2} values in healthy individuals is narrow, we have used a value that lies close to the mean to represent the predicted Pa_{CO_2}.

For clinical application at the bedside, VR can be restated in a user-friendly form by the insertion of the above-mentioned predicted values into equation (1)

$$\mathrm{VR} = \frac{\dot{V}_{E_{\mathrm{measured}}}(\mathrm{ml\,min^{-1}}) \times Pa_{CO_2}(\mathrm{kPa})}{100 \times \mathrm{PBW} \times 5} \qquad (14)$$

VR in the clinical setting

In order to derive an impression of the range of values of VR, a retrospective analysis of intensive care unit (ICU) and anaesthetic charts was carried out to calculate the VR in 100 mechanically ventilated patients. Ninety-two of the patients were admitted to the ICU and eight patients were perioperative patients. For ICU patients, VR was calculated twice a day during the course of ICU admission, and for perioperative patients, a single VR value was calculated. For the purposes of analysis, we have used a single value of VR per patient, this was the highest recorded VR value.

Co-variate analysis was carried out using the Mann–Whitney *U*-test.

Results

Inspection of equation (13) shows that VR is governed by carbon dioxide production and ventilatory efficiency in a logically intuitive way. VR is a dimensionless numerical value. Where predicted values match actual values, as in normal individuals, the range of VR will be distributed around unity. When considering dynamic changes, an increasing VR represents increasing carbon dioxide production, decreasing ventilatory efficiency, or both. Conversely a decreasing VR represents decreasing carbon dioxide production, increasing ventilatory efficiency, or both. Provided the other variable remains constant, VR has a linear relationship with both Pa_{CO_2} and $\dot{V}_E$. Similarly, VR would have a linear relationship to ventilatory frequency and tidal volume, provided the other variable remains constant. As the ratio is dependent on minute ventilation and Pa_{CO_2}, any alterations in ventilatory settings that result in a change in VR would either be due to changes in alveolar ventilation or a significant change in the CO_2 production. Figure 1 shows the hyperbolic relationship of minute ventilation and Pa_{CO_2}, for given values of VR.

Outlined below is a brief summary of the findings from the patients. As anticipated, there is a wide range of values of VR in ICU patients.

The range of VR was 0.536–5.222 [median 1.674, inter-quartile range (IQR) 1.277–2.364] for all patients.

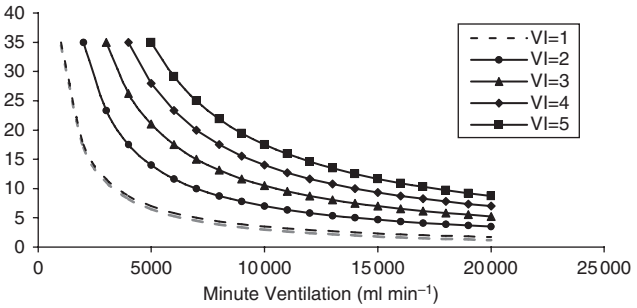

Fig 1 Relationship of Pa_{CO_2} to minute ventilation for given values of VR.

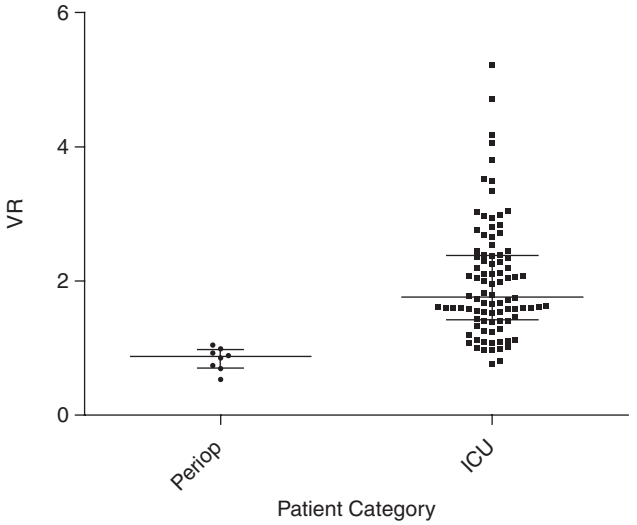

Fig 2 Comparison of VR values between perioperative and ICU patients. Horizontal bars represent median values and IQRs.

For ICU patients, the range was 0.776–5.222 (median 1.762, IQR 1.438–2.382). The range for perioperative patients was 0.54–1.04 (median 0.84, IQR 0.73–0.945). The differences between the two groups are illustrated in Figure 2; it is anticipated that the VR values of the perioperative group represent 'normal values'.

As shown in Table 1, there was no significant difference in VR between age, sex, and smokers. Patients with a respiratory cause for their admission or those patients who developed ventilator-associated pneumonia had a significantly higher VR (n=31, median 2.192, P=0.0004). Patients with known chronic obstructive lung disease also had significantly higher VR (n=18, median 2.883, $P<0.0001$).

Discussion

Factors influencing VR

Ventilatory efficiency

In equation (13), if the ratio $\dot{V}CO_{2\mathrm{actual}}/\dot{V}CO_{2\mathrm{predicted}}$ remains constant, that is, an individual in a steady state of

Table 1 Comparison of median values of ventilatory ratio (VR), IQ, inter-quartile; †*P*-values calculated using Mann–Whitney *U*-test; *denotes significant values

Characteristic (*n*)	Median values of VR (IQR)	*P*-value†
Sex		0.172
Male (61)	1.60 (1.12–2.12)	
Female (39)	2.06 (1.53–2.69)	
Age		0.663
>62 yr (46)	1.63 (1.40–2.36)	
≤62 yr (49)	1.71 (1.09–2.70)	
Diagnosis		0.0004*
Pulmonary (31)	2.19 (1.68–2.98)	
Non-pulmonary (69)	1.60 (1.22–2.23)	
Lung disease		<0.0001*
COPD (16)	2.88 (2.07–3.88)	
No known COPD (84)	1.62 (1.32–2.29)	
Smoking history		0.205
Smokers (37)	2.05 (1.46–2.88)	
Non-smokers (55)	1.67 (1.41–2.35)	

CO_2 production, then any changes in VR would directly represent changing ventilatory efficiency or, stated otherwise, a change in the physiological deadspace ventilation. Limited data are available on the respective contributions of ventilatory efficiency and CO_2 production on changes in minute ventilation and Pa_{CO_2}. Ravenscraft and colleagues[9] have demonstrated that changes in ventilatory efficiency had a greater impact on 'excess' minute ventilation than changes in $\dot{V}CO_2$ in critically unwell mechanically ventilated patients. In clinical practice, it is anticipated that variation in alveolar ventilation is greater than $\dot{V}CO_2$; therefore, changes in VR would foremost represent ventilatory efficiency.

CO_2 production ($\dot{V}CO_2$)

CO_2 production is a measure of metabolic activity.[10 11] Factors influencing cellular metabolism, for example, sepsis, exercise, routine ICU interventions, altering levels of sedation, or temperature, changes would result in a change in $\dot{V}CO_2$.[11–13] Extrinsic factors such as increased nutritional load[14] and drug administration[15] can also influence $\dot{V}CO_2$. In spontaneously breathing patients, an elevation in $\dot{V}CO_2$ will manifest itself as an increase in $\dot{V}_E$ or an increase in Pa_{CO_2}, or both, whereas in patients with fixed minute ventilation, elevation in $\dot{V}CO_2$ levels will lead to an increase in Pa_{CO_2}. Both spontaneously ventilating and fixed minute ventilation groups have been shown to have reduced ventilatory efficiency and an increase in measured deadspace ventilation.[13] The full extent and impact of variation in CO_2 production in ICU patients, and the influence on VR, requires further investigation. In the absence of an obvious ventilatory cause, the evaluation of changing VR should incorporate a consideration of altered metabolism. From the mathematical model described above, it can be stated that in a patient where the ventilatory efficiency remains constant, a doubling of $\dot{V}CO_2$ would result in the doubling of VR. Similarly, in a patient with constant $\dot{V}CO_2$, a halving of the alveolar ventilation would result in doubling of VR. In mechanically ventilated patients, studies have shown that although metabolically stimulating interventions can result in $\dot{V}CO_2$ elevations of up to 35%, they tend to be short-lived and return to baseline levels rapidly.[12 16] Therefore, it is expected that sustained changes in VR are most likely to represent changes in ventilatory efficiency.

Right-to-left shunt

In respiratory physiology, it is widely assumed that Pa_{CO_2} approximates to $P_{A_{CO_2}}$.[17] However, with this assumption, the additional effect of true shunt cannot be extracted from VR. Additionally, in critically unwell patients, $P_{E'_{CO_2}}$ frequently misrepresents $P_{A_{CO_2}}$;[18] therefore, the use of Pa_{CO_2} reduces the associated unquantifiable variation and having practical simplicity. The predicted effect of the right-to-left shunt is thought to be small under most circumstances. Diseases such as ARDS where there is likely to be massive ventilation–perfusion mismatch, the combined impact of deadspace ventilation and shunt on CO_2 elimination will be reflected by the ratio.

Further research is being undertaken to establish the proportional impact that each of the above-mentioned factors will exert on a changing value of VR in the critically unwell patients.

Future applications of VR

VR provides clinicians with an easily calculated numerical value that reflects changes in ventilatory efficiency, or $\dot{V}CO_2$, or both. Minute ventilation and Pa_{CO_2} can be measured at the bedside, and this information is currently recorded by most ICUs. Single calculations of VR will provide information on the degree of variation from the predicted values. However, the most useful application as a monitoring tool in the critical care setting would be to observe trends in VR. In particular, in patients with permissive hypercapnia, VR may be used to monitor changing underlying ventilatory efficiency. VR would also provide useful information while assessing therapeutic procedures carried out to improve alveolar ventilation. Currently, success of manoeuvres such as recruitment, bronchoscopy, and prone positioning in mechanically ventilated patients is judged on improvement in oxygenation.[19 20] Although calculation of deadspace ventilation has been shown to be a useful tool,[21] this is often difficult to carry out at the bedside. VR offers information about changes in alveolar ventilation, a parameter at the heart of the manoeuvres, and it is easy to calculate.

The value of Pa_{CO_2} as a prognostic indicator in ARDS has been elegantly demonstrated by Gattinoni and colleagues.[22] Physiological deadspace is also known to predict the outcome in ARDS.[23] As VR incorporates both these variables, it may be a useful prognostic indicator. We expect the $Pa_{O_2}/F_{I_{O_2}}$ ratio and VR to behave largely independently of one another, especially in patients who

are difficult to oxygenate. VR should, therefore, further subdivide these patients according to the level of associated ventilatory inefficiency. Thus, a further application of VR could be for diagnostic categorization, especially in patients with ARDS.

Previous indices and markers of ventilation

Radford[10] outlined the use of preset ventilatory standards for measuring adequacy of mechanical ventilation, but in general the comparison of 'measured' and 'predicted' parameter values is seldom used in current critical care practice. In contrast, in respiratory medicine, particularly in lung function testing, such methods of comparison are well established.[24] VR revisits this concept to reflect ventilation in the critically ill.

VR can be calculated by measuring tidal volume, ventilatory frequency, and $P\mathrm{a}_{\mathrm{CO}_2}$. Previous attempts have been made to analyse these variables either individually or in combination, to develop indices to facilitate decision-making in mechanically ventilated patients. However, it has proved difficult to develop an objective ratio of ventilatory function that combines all three variables while being simple to calculate at the bedside. Jabour and colleagues[25] proposed a weaning ratio that combines ventilatory endurance with efficiency of gas exchange. They have defined the term 'VE40' as the predicted minute ventilation (normalized to body weight) required to bring $P\mathrm{a}_{\mathrm{CO}_2}$ to 40 mm Hg. They used VE40 to calculate the efficiency of gas exchange for the purpose of weaning. Although conceptually similar, VR produces a simple numerical value, offering broader applications. Other investigators have looked at minute ventilation as an aid both to managing and to weaning ventilated patients. Adaptive support ventilation (Hamilton Galileo) utilizes Otis and colleagues'[26] minimal work of breathing calculations to adjust ventilatory frequency and tidal volume to produce a target minute ventilation of 100 ml kg^{-1} in adult patients.[27] Although Martinez and colleagues[28] have proposed monitoring minute ventilation recovery time as a parameter for predicting successful weaning.

Yang and Tobin[29] have defined a weaning index that uses frequency/tidal volume to quantitate rapid shallow breathing. Similar to VR, f/V_t is an easy to calculate index, but offers little insight into CO_2 elimination. In a study elsewhere Jubran and Tobin[30] have demonstrated that impaired CO_2 elimination results in an increase in failure to extubate in chronic obstructive pulmonary disease (COPD) patients. The product of $P\mathrm{a}_{\mathrm{CO}_2}$ and inspiratory pressure–time product was utilized as an index of inefficient CO_2 clearance.

In contrast to the above-mentioned studies, VR is unique because changes in its value reflect changes in both $\dot{V}_E$ and $P\mathrm{a}_{\mathrm{CO}_2}$ and can be easily calculated from measured values at the bedside. In conjunction with indices that reflect work of breathing, such as f/V_t, VR may be a useful tool in predicting weaning.

In summary, the VR is a novel measure of ventilatory function. By comparing measured with predicted values, VR is normalized to the individual. Changes in VR reflect changes in ventilatory efficiency and changes in $\dot{V}\mathrm{CO}_2$. VR has a wide range of exciting potential applications in clinical practice, enhanced by the simplicity of its calculation at the bedside.

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