SMART Phones and the Acute Respiratory Patient

Abstract:
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Definition of Respiratory Failure using PaO2 alone is confounded when patients are commenced on oxygen therapy prior to arterial blood gas (ABG) measurement. Furthermore, classification of Respiratory Failure as Type 1 or Type 2 using PaCO2 alone can give an inaccurate account of events as both types can co-exist. 100 consecutive presentations of acute respiratory distress were assessed initially using PaCO2, and subsequently PaO2/FiO2 ratio, to diagnose Respiratory Failure. Respiratory Failure cases were classified as Type 1 or Type 2 initially using PaCO2, and subsequently arterial-alveolar (A-a) gradient. Any resultant change in management was documented. Of 100 presentations, an additional 16 cases were diagnosed as Respiratory Failure using PaO2/FiO2 ratio in place of PaCO2 alone (p=0.0038). Of 57 cases of Respiratory Failure, 22 cases classified as Type 2 using PaCO2 alone were reclassified as Type 1 using A-a gradient (p=0.0031). Of these 22 cases, management changed in 18.

Introduction
Traditionally, Respiratory Failure is defined as arterial oxygen tension (PaO2) less than 8 kilopascals (kPa) on room air at sea level, a value obtained through performance of arterial blood gas (ABG) 
. In practice, however, patients are often commenced on oxygen therapy prior to ABG being performed, thus PaO2 value obtained is confounded by an alteration in the fraction of inspired oxygen (FiO2). The PaO2/FiO2 ratio, however, aids to discount a rise in PaO2 secondary to oxygen therapy and thus can assist diagnosis of Respiratory Failure. Respiratory Failure occurs by two primary pathophysiologic mechanisms, giving rise to its classification into Type 1 (hypoxaemic) Failure and Type 2 (ventilatory) Failure. Hypoxaemic Failure occurs when disease processes, such as pneumonia or pulmonary embolus, cause an increase in physiologic dead space resulting in increased mismatching between ventilation and perfusion (V/Q mismatch). In Type 1 failure PaCO2 is typically normal or low. In contrast, Type 2 (ventilatory) Failure, results from inadequate minute ventilation of the alveoli, in conditions such as chest wall deformity, neuromuscular diseases affecting the thoracic cage and end stage structural lung disease, particularly chronic obstructive pulmonary disease (COPD). This results in primary hypercapnia, usually > 6kPa, with secondary hypoxaemia. Thus, hypoxaemic respiratory failure is synonymous with ventilatory failure. In clinical practice, distinction between Type 1 and Type 2 Respiratory Failure leads to divergent clinical management. Management of Type 1 failure involves inter alia administration of high concentration oxygen therapy, whereas Type 2 failure requires limitation of oxygen therapy concentration to prevent respiratory suppression in patients reliant on a hypoxaemic respiratory drive. Classification also dictates inter alia modes of non-invasive ventilation (NIV), with continuous positive airway pressure (CPAP) the typical choice in the treatment of severe hypoxaemic failure and bi-level positive airway pressure (BiPAP) favoured in cases of ventilatory failure.

Traditionally, classification of Respiratory Failure (PaO2 < 8kPa) relies on ABG indices, with arterial carbon dioxide tension (PaCO2) greater than 6kPa representative of Type 2 failure and normal or low PaCO2 representative of Type 2 failure. This classification directs clinical management, it oversimplifies the pathophysiology underlying an acute respiratory presentation. Both hypoxaemic and ventilatory failure frequently co-exist and reliance on a single parameter in order to establish which mechanism predominates can result in suboptimal therapeutic decisions. A more accurate account of events at alveolar level is offered by calculation of alveolar-arterial oxygen tension gradient (A-a gradient) which represents the difference between alveolar oxygen tension and arterial oxygen tension. Hypoxaemia in the presence of increased A-a gradient indicates impaired oxygenation of capillary blood at alveolar level, suggesting a Type 1 Failure component. Conversely, hypoxaemia in the setting of normal or low A-a gradient implying the low alveolar oxygen tension mirrors a low alveolar oxygen tension is typical of Type 2 or ventilatory failure. Previously, derivation of the A-a gradient involved complex and time-consuming calculations, however, with the advent of medical internet applications available on mobile phones in recent years, this has become a readily available tool to assist the clinician at the bedside. This paper seeks to address the following hypotheses: (1) that Respiratory Failure is underestimated when defined by PaO2 < 8kPa alone and that incorporation of the PaO2/FiO2 ratio into diagnostic criteria increases identification of cases; (2) that in cases classified as Type 2 failure using PaCO2-related criteria, use of the A-a gradient allows greater insight into the relative components of Type 1 and Type 2 Failure that results in changes in clinical management.

Methods
This study compared diagnosis and classification of Acute Respiratory Failure based on ABG indices (PaO2 and PaCO2) with indices derived from ABG-based clinical equations (PaO2/FiO2 and A-a gradient). kPa units were used throughout. Data were collected prospectively for 100 consecutive cases of acute respiratory distress presenting to a dedicated Respiratory service in a Dublin Teaching hospital. An acute respiratory presentation was defined as that in which the primary presenting complaint was that of shortage of breath. Patient age, gender, past medical history, and working diagnosis were recorded, PaO2 and PaCO2 values, and the FiO2 value at which the ABG was performed were recorded. Using medical SMART phone applications the PaO2/FiO2 ratio and the A-a gradient were calculated in accordance with the formulae:

PaO2/FiO2 ratio = (PaO2 x FiO2) x 100
A-a gradient = (FiO2 x [Patm - PH2O]) - PaCO2 - PaO2

Each case of acute respiratory distress was initially assessed using the PaO2, and then reassessed using the PaO2/FiO2 ratio to identify cases of respiratory failure. PaO2 levels less than 6kPa and PaO2/FiO2 ratio less than 38 were diagnostic of Respiratory Failure. Each confirmed case of Respiratory Failure was then classified as Type 1 or Type 2 Failure based on PaCO2, and subsequently, each case was subjected to calculation of A-a gradient to identify presence of significant Type 1 or Type 2 failure components. PaCO2 less than 6kPa indicated Type 1 Failure and greater than 6kPa indicated Type 2 Failure. A-a gradient greater than 3 indicated a significant Type 1 component. Management plan initiated following initial classification as Type 1 or Type 2 Failure based on PaCO2 was documented for each case. Any change in this plan resulting from calculation of the A-a gradient was recorded. Data were entered into the Statistical Package for Social Sciences (SPSS Inc. Chicago, USA: Windows Version 16®) and results were analysed using the Chi-squared test with Yates correction. Statistical significance was set at p < 0.05.

Results
Data were collected for 100 consecutive acute respiratory presentations, including 86
patients (with 14 patients presenting twice). 45 subjects were male and 41 were female. Median age was 68 years (range 30 to 85 years). Of 100 cases, underlying diagnosis was COPD in 34 cases, pneumonia in 16 cases, congestive cardiac failure in seven cases, asthma in six cases, bronchiectasis in six cases, pulmonary fibrosis in four cases, Pickwickian syndrome in four cases, pulmonary embolus in two cases, and pulmonary arteriovenous malformation in one case.

Identification of Respiratory Failure
Using the PaO2 alone to define it, 41 of 100 cases assessed were diagnosed as Respiratory Failure (Figure 1). When reassessed using the PaO2/FiO2 ratio-based definition, 57 of 100 cases met the criteria for diagnosis. This represents an additional 16 cases of Respiratory Failure identified using the PaO2/FiO2 ratio, which was statistically significant (p=0.0338).

Classification of Respiratory Failure as a Type 1 or Type 2 Picture
Using PaCO2 criteria alone, 27 of these 57 cases were classified as Type 1 Failure and 30 of 57 cases classified as Type 2 Failure (Figure 2). On further bedside analysis, it was found that 49 of 57 cases had a significant Type 1 component with A-a gradient greater than 3, A-a gradient less than or equal to 3, indicating a predominantly Type 2 picture, was recorded in only 8 of 57 cases. This represents a highly statistically significant alteration in classification of Respiratory Failure using A-a gradient (p<0.001). All 27 patients originally classified as Type 1 Failure using PaCO2 subsequently had high A-a gradient. Of 30 cases originally classified as Type 2 Failure, mean PaCO2 of cases with high A-a gradient was 7.6-4.97 (range 6.3-10.1) and mean PaCO2 of cases with normal or low A-a gradient was 10.6-2.50 (range 7.5-16.0) (Figure 3).

Figure 2: Number of identified cases of respiratory failure (n) classified as Type 1 Failure (white) and Type 2 Failure (black) using PaCO2 (a) and A-a gradient (b).

Figure 3: Mean PaCO2 for 30 cases originally classified as Type 2 Failure using PaCO2 alone, with (a) representing cases reclassified as Type 1 Failure and (b) cases confirmed as Type 2 Failure, using A-a gradient.

Impact of A-a Gradient Calculation on Clinical Management
For all 27 patients classified as Type 1 Failure using both PaCO2 and A-a gradient, initial management remained unchanged (Figure 4). Of 22 patients classified as Type 2 Failure using PaCO2 but subsequently found to have a significant Type 1 component using A-a gradient, change from initial management was initiated in 18. For all 8 patients classified as Type 2 failure using both PaCO2 and A-a gradient, initial management remained unchanged.

Figure 4: Number of cases (n) in which a change in clinical management was initiated following calculation of the A-a gradient, with (a) representing cases reclassified as Type 1 Failure using both PaCO2 and A-a gradient; (b) representing cases classified as Type 2 Failure using both PaCO2 and A-a gradient; and (c) representing cases classified as Type 2 Failure using PaCO2 but reclassified as Type 1 Failure using A-a gradient.

Discussion
Respiratory Failure occurs when PaO2 falls below 8kPa when breathing room air. Room air comprises 21% O2 (i.e. 2.1kPa) or FiO2 of 0.21. A common medical problem in the Emergency Department is establishing the presence or absence of Respiratory Failure in patients requiring additional oxygen, as many are. Simple calculation of the PaO2/FiO2 ratio circumvents this problem. As PaO2 of 8kPa on 21% O2 (room air) gives a PaO2/FiO2 of 38 (i.e. 8kPa/0.21 = 38), a PaO2/FiO2 value less than 38 was considered diagnostic of Respiratory Failure in this study. 16 additional cases of Respiratory Failure were identified when PaO2/FiO2 ratio was utilised in place of PaO2, and this was statistically significant (p=0.0338). This supports the hypothesis that Respiratory Failure is underdiagnosed when PaO2 alone is used.

Use of A-a gradient enables further insight beyond that provided by PaCO2 alone into the relative components of Type 1 and Type 2 Failure contributing to the acute respiratory presentation. Ideally, the normal A-a gradient should approach unity, representative of perfect unimpaired transfer of oxygen from alveolus to bloodstream. In reality, A-a gradient varies due to physiological inequalities in ventilation and perfusion and a normal value is approximated to be 2-6kPa. Thus, in this study, A-a gradient greater than 3 was considered representative of a substantial Type 1/hypoxemic component while A-a gradient less than or equal to 3 represented a hypoventilated alveolus, a predominantly Type 2 Failure. Of the 57 cases of Respiratory Failure identified in the first part of the study, 27 were classified as Type 1 Failure and 30 as Type 2 Failure using PaCO2 alone. When A-a gradient was calculated for each case, however, an additional 22 presentations i.e. 49 cases in total, were found to have a substantial Type 1 component. Only 8 cases demonstrated true predominantly Type 2 Failure. This represents a highly statistically significant change in classification when A-a gradient is utilised (p<0.001). All 27 patients originally classified as Type 1 Failure by means of PaCO2-related criteria were found to have A-a gradient greater than 3, thus A-a gradient calculation may not contribute great additional information in cases initially classified as Type 1 Failure.

Of the 30 cases initially classified as Type 2 Failure using PaCO2, 22 cases demonstrated a substantial Type 1 component when A-a gradient was calculated. Mean initial PaCO2 in these cases was 7.6kPa. 8 cases initially classified as Type 2 Failure using PaCO2-related criteria were confirmed as predominantly Type 2 Failure using A-a gradient, with mean initial PaCO2 of 10.6kPa. These data imply that calculation of A-a gradient can contribute significant additional information in cases initially classified as Type 2 Failure using PaCO2-related criteria. Furthermore,
calculation of A-a gradient may be of greater benefit in cases where PaCO2 is closer to the diagnostic cut-off point. Limitations to the use of A-a gradient in Respiratory Failure classification exist. The calculation has been shown to be unreliable in the setting of high inspired oxygen concentration due to a disproportional rise in alveolar oxygen tension compared to rise in arterial oxygen tension. The value has also been shown to rise with increasing age, with exercise and in the setting of hyperventilation.

Of 22 cases of Type 2 Respiratory Failure found to have a significant Type 1 component, a change in clinical management was initiated on the basis of this additional information in 18. In 12 of 22 cases, concentration of oxygen therapy was increased. Of 22 patients the initial management plan remained unchanged following demonstration of a Type 1 component. This demonstrates that enhanced understanding of the relative components of Type 1 and Type 2 Failure in the clinical setting can result in changes to patient management. Assessment of impact on patient outcomes resultant from the change to management initiated by calculation of the A-a gradient was beyond the scope of this preliminary study, but further research in this area is warranted, particularly in determining the clinical implications of the limitations to the use of A-a gradient mentioned above.

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References