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SHORT REPORT

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Unmasking hypoxemia: the role of standard PaO_2 in interpreting Arterial blood gas analysis

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ABSTRACT

Background: In the assessment of acute respiratory failure (ARF), PaO_2/FIO_2 ratio is widely used, but may be misleading in the presence of hyperventilation-induced hypocapnia. The standard PaO_2 ($_{st}PaO_2$), a theoretical value corrected for $PaCO_2$, may improve clinical interpretation of gas exchange severity.
Methods: We conducted an online survey among Italian physicians using a case vignette of three hypothetical patients with identical PaO_2 values but differing $PaCO_2$ levels. Participants were asked to rank the severity of the cases based solely on arterial blood gas analysis (ABG). A second round was offered after introducing the concept of $_{st}PaO_2$ and providing corresponding values.
Results: A total of 2,241 (8.9%) physicians (median age 53 years, 54.1% male) completed the first round and 1,324 (59%) completed the second one of the survey. Initially, only 9.2% correctly identified the clinical severity pattern–this increased significantly to 16.1% after introducing $_{st}PaO_2$ ($p < 0.01$). The improvement rate was higher among physicians with less than 10 years of clinical experience. Performance improved across all specialties, particularly in emergency and intensive care medicine.
Conclusions: The introduction of $_{st}PaO_2$ significantly enhanced physicians' ability to interpret ABG results in ARF. Although its calculation assumes ideal physiological conditions, $_{st}PaO_2$ remains a useful tool for unmasking hypoxemia in hyperventilating patients. Including $_{st}PaO_2$ in ABG reports may support more accurate clinical decision-making, particularly in emergency and critical care settings.

Key words list: acute respiratory failure (ARF), arterial blood gas analysis (ABG), patient self-inflicted lung injury (P-SILI), PaO_2.

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Authors' contributions: F.D.M., F.R., and L.N. conceived the study, developed the questionnaire, and analyzed the results. C.M., S.P., and S.V., under the supervision of F.R. and L.N., collected the data and compiled the database. F.D.M., L.N., C.M., and S.V. prepared the informational material attached to the survey. F.D.M., F.R., L.N., and M.C. wrote the final version of the manuscript. S.P., G.L., J.C.S, P.S. and D.R. contributed to the interpretation of the results and participated in the preparation of the final version of the manuscript. All authors have read and approved the final manuscript. All co-authors read approved the final version of the manuscript.

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Introduction

Acute respiratory failure (ARF) is a life-threatening complication of numerous lung disorders. Severity of respiratory failure is often graded using the ratio between arterial pressure of oxygen (PaO_2) and inspired oxygen fraction (FIO_2), particularly in intensive care settings [1]. However, this index has several limitations: FIO_2 estimation can be inaccurate, especially during non-invasive support, and the PaO_2/FIO_2 relationship is inherently non-linear across different ranges of Va/Q imbalance and shunt fraction [2-4]. Additionally, PaO_2 is influenced by arterial pressure of carbon dioxide ($PaCO_2$) via the alveolar gas equation, meaning that hyperventilation-induced hypocapnia may elevate PaO_2 and may artifactually mask underlying gas exchange abnormalities [3-6]. To address this, in 1973 Edward E. Mays proposed the concept of "standard" PaO_2 ($_{st}PaO_2$) [7]. This metric adjusts PaO_2 based on the level of $PaCO_2$, providing an estimate of the oxygen tension that would be expected at a normal alveolar ventilation (i.e., $PaCO_2$ of 40 mmHg). For the computation, the "theoretical" alveolar air equation can be used [7]:

$$_{st}PaO_2 = 1.25 \times PaCO_2 + PaO_2 - 50.0,$$

or alternatively the equation proposed by Edward E. Mays:

$$_{st}PaO_2 = 1.66 \times PaCO_2 + PaO_2 - 66.4.$$

The standardized PaO_2/FIO_2 ratio ($_{st}PaO_2/FIO_2$) has recently demonstrated greater accuracy than the traditional PaO_2/FIO_2 ratio in predicting in-hospital mortality among patients with COVID-19-related ARF [8]. As suggested by the authors, incorporating the effects of alveolar ventilation via the $_{st}PaO_2/FIO_2$ ratio may improve the clinical interpretation of ABG [8]. Notably, Gattinoni et al. also recognized its value in identifying hyperventilation and hypocapnia as early markers of severity, potentially contributing to patient self-inflicted lung injury (P-SILI) in ARF [9]. Based on these premises, our aim was to assess clinicians' ability to distinguish between impaired ventilation and gas exchange using arterial blood gas analysis (ABG) data, and to evaluate whether adding $_{st}PaO_2$ values could improve the interpretation accuracy.

Methods

Using a spontaneous, invitation-based online survey, we explored Italian physicians' ability to interpret the physiological relationship between PaO_2 and $PaCO_2$ in ARF. Participants were presented with a clinical vignette describing three hypothetical patients with identical PaO_2 values at ABG, but varying $PaCO_2$ levels, each reflecting different underlying ARF scenarios (Table 1). Respondents were asked to identify the patient with the "most" and the "least" severe impairment in gas exchange function, specifically in terms of oxygenation. After completing the first round, they were introduced to the concept of standard $_{st}PaO_2$ and provided with its calculated values for each case, then invited to repeat the same set of questions (Table S1 and Figure S1). This design allowed us to evaluate whether the addition of $_{st}PaO_2$ could enhance ABG interpretation and support clinical reasoning. To statistically assess changes in response accuracy between the two rounds, we applied McNemar's test to the subset of participants who completed both phases of the survey. A p-value <0.05 was considered statistically significant. All analyses were performed using [SPSS®, IBM, versione 29].

Results

In 2024, a total of 25,223 emails were sent, resulting in 4,065 accesses to the online survey platform, of which 2,241 physicians completed the first part of the questionnaire (median age 53 [IQR 43–63] years, 54.1% male) with a response rate of 8.9%. The survey included a heterogeneous panel of physicians, with representation from Emergency Medicine (18-20%), Intensive Care (17-20%), Pulmonology (14-16%), Internal Medicine (11-12%), Cardiology (9-12%), and other specialties (31%). 59% of respondents (n=1,324; median age 53 [IQR 38-63] years, 54.5% male) agreed to repeat the questionnaire. The overall improvement in understanding the correlation between PaO_2 and $PaCO_2$ after the introduction of $_{st}PaO_2$ values was statistically significant. Specifically, of the 1,324 physicians who repeated the questionnaire after the explanation, the number of correct identifications increased from 122 to 213 and McNemar's test confirmed a significant within-subject change (9.2% vs 16.1%, $p <0.01$). The highest rate of correct answers was observed among physicians with less than 10 years of experience, suggesting an inverse correlation between years of service and appropriateness of responses. Regardless of medical specialty, fewer than 15% of respondents answered correctly in the first round, while critical care and emergency medicine physicians showed the greatest improvement after the $_{st}PaO_2$ explanation.

Discussion

The improvement in ABG interpretation observed after introducing the explanation of $_{st}PaO_2$ in our survey supports its potential role as both a didactic and clinical decision-support tool. Although the physiological relationship between PaO_2 and $PaCO_2$ has been described since the mid-20th century, it remains under-recognized in everyday practice, as confirmed by our findings. The concept of standard PaO_2, as well as the present survey itself, has several limitations. The calculation of $_{st}PaO_2$—whether based on the alveolar gas equation or on the empirical formula proposed by Edward E. Mays—relies on theoretical assumptions and may be influenced by physiological variables such as intrapulmonary shunt, dead space ventilation, and variations in the respiratory quotient (RQ) [7–9]. Nevertheless, our findings highlight a broader issue: a general lack of awareness among clinicians regarding both the limitations of the PaO_2/FIO_2 ratio and the interpretive role of $PaCO_2$ in ABG. Even after explanation, the persistently low proportion of correct responses, even after the $_{st}PaO_2$ explanation, suggests that clinical attention tends to focus more on hypercapnia, while the implications of hypocapnia are often overlooked. As previously highlighted by Gattinoni et al., hypocapnia driven by high respiratory drive can lead to falsely reassuring PaO_2 values, resulting in underestimation of disease severity in hyperventilating patients [9]. Although $_{st}PaO_2$ is a simplified theoretical construct, it provides a practical and accessible tool to reveal "true" hypoxemia that may be masked by hyperventilation—especially in the early phases of ARF. In this context, integrating $_{st}PaO_2$ into ABG interpretation may help correct this bias, reduce misclassification, and support more accurate and timely clinical decisions. Importantly, recognizing hypoxemic hypocapnic patients—often those with increased respiratory effort—could help identify individuals at greater risk of developing P-SILI. Early identification may guide more appropriate ventilatory strategies and escalation of care [9,10].

We acknowledge some limitations. The study was based on a voluntary online survey among an unselected cohort of Italian physicians, and the self-selected nature of participation may have introduced a degree of response bias. The response rate observed in our study is consistent with previously reported data for voluntary, non-incentivized web-based surveys targeting healthcare professionals. In their meta-analysis, Cho et al. reported an average response rate of 13% for online surveys, which generally yield the lowest participation rates among different modalities [11]. However, the number of respondents, their diverse clinical backgrounds, and the consistency of results across subgroups strengthen the external validity of the message. Ultimately, the survey results reaffirm the need for broader awareness and education around fundamental physiological concepts in ABG interpretation.

Conclusion

Including standardized PaO_2 ($_{st}PaO_2$) in arterial blood gas analysis (ABG) reports could help identify hyperventilation-induced hypocapnia that artifactually elevates PaO_2, masking underlying gas exchange abnormalities. As a simple yet informative parameter, $_{st}PaO_2$ has the potential to improve the assessment and management of acute respiratory failure (ARF)—particularly in patients with high respiratory drive—by supporting more accurate and timely clinical decision-making.

Table 1. Clinical scenarios summary. Case vignette of the survey referring to three model patients. Participants were provided with the description of the three cases, including PaO_2 and $PaCO_2$ values (blue boxes). The calculated $_{st}PaO_2$ values was shown after completing the first round (orange boxes). It should be noted that standardized $_{st}PaO_2$ becomes less reliable in hypercapnic patients, as the assumptions of a constant respiratory quotient and equivalence between arterial and alveolar CO_2 may no longer hold [9].

	#1	#2	#3
PaO_2, mmHg	65	65	65
$PaCO_2$, mmHg	20	40	60
$_{st}PaO_2$, mmHg	40	65	90
Interpretation	Severe pulmonary gas-exchange impairment "masked" by hyperventilation	Mild/moderate pulmonary gas-exchange impairment and normoventilation	"Mere" hypoventilation with preserved pulmonary gas-exchange capacity
What is sick?	The lung, severely	The lung, mildly or moderately	The muscles or neurological control
Possibile clinical scenario	Severe pneumonia	Non-severe pneumonia	Neuromuscular disease with intercurrent viral infection
What to do?	Invasive or non-invasive ventilation support, close monitoring	Medical therapy (probably oxygen not needed)	Ventilatory support, monitoring according to the acute/chronic manifestation
Prognosis quoad vitam	Poor	Good/Intermediate	Depending on underlying disease
Need of admission?	Definitely (ICU/Subintensive Care Unit)	If not other negative prognostic factors, probably not	Yes. Depending on pH (chronic?) take into consideration alternative settings (e.g. rehab)

List of abbreviations

ABG: Arterial Blood Gas analysis
ARF: Acute Respiratory Failure
FIO_2: Fraction of Inspired Oxyge
PaO_2: Arterial Partial Pressure of Oxygen
$PaCO_2$: Arterial Partial Pressure of Carbon Dioxid
$_{st}PaO_2$: Standardized Arterial Partial Pressure of Oxygen
$_{st}PaO_2/FIO_2$: Standardized PaO_2 to FIO_2 Ratio
RQ: Respiratory Quotient
P-SILI: Patient Self-Inflicted Lung Injury
ICU: Intensive Care Unit

References

1. Kufel TJ, Grant BJB. Arterial blood-gas monitoring: respiratory assessment. In: Tobin MJ, ed. Principles and practice of intensive care monitoring. New York: McGraw-Hill; 1998. p.197–215.
2. West JB, Luks A. West's respiratory physiology: the essentials. Philadelphia: Wolters Kluwer; 2020.
3. Aboab J, Louis B, Jonson B, Brochard L. Relation between PaO2/FIO2 ratio and FIO2: a mathematical description. Intensive Care Med 2006;32(10):1494–7. doi:10.1007/s00134-006-0337-9.
4. Raimondi F, Novelli L, Marchesi G, Fabretti F, Grazioli L, Riva I, et al. Worsening of gas exchange parameters at high FIO2 in COVID-19: misleading or informative? Multidiscip Respir Med 2021;16(1):759. doi:10.4081/mrm.2021.759.
5. Tobin MJ, Jubran A, Laghi F. PaO2/FIO2 ratio: the mismeasure of oxygenation in COVID-19. Eur Respir J 2021;57(3):2100274. doi:10.1183/13993003.00274-2021.
6. Riley RL, Lilienthal JL Jr. On the determination of the physiologically effective pressures of oxygen and carbon dioxide in alveolar air. Am J Physiol 1946;147:191–8. doi:10.1152/ajplegacy.1946.147.1.191.
7. Mays EE. An arterial blood gas diagram for clinical use. Chest 1973;63(5):793–800. doi:10.1378/chest.63.5.793.
8. Prediletto I, D'Antoni L, Carbonara P, Daniele F, Dongilli R, Flore R, et al. Standardizing PaO2 for PaCO2 in P/F ratio predicts in-hospital mortality in acute respiratory failure due to COVID-19: a pilot prospective study. Eur J Intern Med 2021;92:48–54. doi:10.1016/j.ejim.2021.06.002.

9. Gattinoni L, Busana M, Camporota L. Standardised PaO2/FiO2 ratio in COVID-19: added value or risky assumptions? Eur J Intern Med 2021;92:31–3. doi:10.1016/j.ejim.2021.09.004.
10. Brochard L, Slutsky AS, Pesenti A. Mechanical ventilation to minimize progression of lung injury in acute respiratory failure. Am J Respir Crit Care Med 2017;195(4):438–42. doi:10.1164/rccm.201605-1081CP.
11. Cho YI, Johnson TP, VanGeest JB. Enhancing surveys of health care professionals: a meta-analysis of techniques to improve response. Eval Health Prof 2013;36(3):382–407. doi:10.1177/0163278713496425.

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