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Assessment of the SpO₂/FiO₂ ratio as a tool for hypoxemia screening in the emergency department

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ABSTRACT

Objective: We assessed the performance of the ratio of peripheral arterial oxygen saturation to the inspired fraction of oxygen (SpO₂/FiO₂) to predict the ratio of partial pressure arterial oxygen to the fraction of inspired oxygen (PaO₂/FiO₂) among patients admitted to our emergency department (ED) during the SARS-CoV-2 outbreak.

Methods: We retrospectively studied patients admitted to an academic-level ED in France who were undergoing a joint measurement of SpO₂ and arterial blood gas. We compared SpO₂ with SaO₂ and evaluated performance of the SpO₂/FiO₂ ratio for the prediction of 300 and 400 mmHg PaO₂/FiO₂ cut-off values in COVID-19 positive and negative subgroups using receiver-operating characteristic (ROC) curves.

Results: During the study period from February to April 2020, a total of 430 arterial samples were analyzed and collected from 395 patients. The area under the ROC curves of the SpO₂/FiO₂ ratio was 0.918 (CI 95% 0.885–0.950) and 0.901 (CI 95% 0.872–0.930) for PaO₂/FiO₂ thresholds of 300 and 400 mmHg, respectively. The positive predictive value (PPV) of an SpO₂/FiO₂ threshold of 350 for PaO₂/FiO₂ inferior to 300 mmHg was 0.88 (CI95% 0.84–0.91), whereas the negative predictive value (NPV) of the SpO₂/FiO₂ threshold of 470 for PaO₂/FiO₂ inferior to 400 mmHg was 0.89 (CI95% 0.75–0.96). No significant differences were found between the subgroups.

Conclusions: The SpO₂/FiO₂ ratio may be a reliable tool for hypoxemia screening among patients admitted to the ED, particularly during the SARS-CoV-2 outbreak.

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1. Introduction

1.1. Background

Acute respiratory distress is a common reason for emergency department (ED) admission. Since the end of 2019, healthcare workers have been facing the coronavirus disease (COVID-19) pandemic due to SARS-CoV-2, with a major risk of overcrowding in the ED. Severe COVID-19 infections are associated with hypoxemia, the severity of which can quickly become life-threatening.

The development of tools for the initial assessment of the degree of hypoxemia among patients with respiratory symptoms is essential.

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Such a tool should reduce both under-triage, allowing critical patients to quickly receive the appropriate level of care, and over-triage, maintaining critical care capacity despite an influx of patients. An appropriate triage tool should also be applicable for all causes of respiratory distress, whether related to COVID-19 or not. Limited reliable data are available for the triage of hypoxemic patients in the ED, yet it could be particularly useful during the COVID-19 pandemic.

1.2. Importance

Early diagnosis of critical hypoxemia is important for both COVID-19 infection and Acute Respiratory Distress Syndrome (ARDS) based on the ratio of partial pressure arterial oxygen to the fraction of inspired oxygen (PaO₂/FiO₂) [1,2]. This indicator has been validated in many pathological situations [3,4] but requires an arterial blood sample and therefore is often not immediately accessible upon the

patient's admission. Arterial puncture is also a source of pain and complications [5–8].

Validation of a noninvasive tool could allow us to improve triage time and patient orientation upon admission. In particular, the ratio of peripheral arterial oxygen saturation to the inspired fraction of oxygen (SpO_2/FiO_2) has been proposed by several authors [9–12]. However, diagnostic performance of this index has not yet been evaluated.

1.3. Goals of this investigation

This study evaluated the performance of the SpO_2/FiO_2 ratio for predicting mild (PaO_2/FiO_2 superior to 400 mmHg) or moderate (PaO_2/FiO_2 inferior to 300 mmHg) hypoxemia, and evaluated the performance of this index among patients admitted during the COVID-19 outbreak, with subgroup analyses distinguishing SARS-CoV-2 positive and negative patients.

2. Methods

2.1. Study design and setting

We performed a retrospective observational cohort study to assess the predictive value of SpO_2/FiO_2 for the PaO_2/FiO_2 ratio among adult patients admitted to our ED from February to April 2020. The study center is an academic-level hospital in France and was the regional referral center for COVID-19 patient management during the pandemic.

We followed the Standards for Reporting of Diagnostic Accuracy criteria for diagnostic performance studies [13]. Our study is in accordance with the current regulations in France relative to protection of personal health and privacy data.

2.2. Data collection

We extracted the following from our computer data system (DxCare® software, France): data on demographics, medical history, vital signs at admission and time of arterial blood sampling, presence of oxygen therapy, oxygen flow rate (QO2) at arterial puncture, SARS-CoV-2 virological status, final diagnosis, and blood gas results for each arterial sample during ED admission including PaO_2 , arterial hemoglobin saturation (SaO_2), and arterial carbon dioxide partial pressure ($PaCO_2$). Data collection was planned subsequent to admission of the study population for the study period. All patients admitted during the study period and from whom an arterial blood sampling was performed

were reviewed. The diagnosis of COVID-19 infection was retained in our analyses in cases of a positive PCR and/or typical lesions in chest CT scans (when performed).

FiO_2 was estimated from the interface used for oxygen delivery (nasal cannulas, single mask, high-concentration mask, non-invasive ventilation) and oxygen flow rate. For nasal-cannula or single-mask oxygen therapy, FiO_2 was estimated from the data presented by Wettstein et al [14] using the formula $FiO_2 = 4 \cdot QO_2 + 21\%$. For the high-concentration mask, FiO_2 was estimated at 80%. For non-invasive ventilation, the FiO_2 value selected was the one set on the ventilator.

Pulsed oxygen saturation was measured using pulse oximeters (Space Labs Healthcare Qube™, USA). The quality of the measurement was controlled by a nurse with simultaneous visualization of the plethysmography curve. Arterial blood gas analyses were performed immediately after sampling with a Werfen Instrumentation Laboratory GEM Premier 5000™ (Spain).

2.3. Choice of PaO_2/FiO_2 thresholds

The PaO_2/FiO_2 thresholds chosen to plot ROC curves were 300 and 400 mmHg, respectively. The 300 mmHg threshold corresponds to the definition of both severe COVID-19 [15], and ARDS [16]. The 400 mmHg threshold corresponds to changes in hematosi relative to observed normal [17] and is used for early detection of hypoxemia, such as in the SOFA score [18].

2.4. Inclusion and exclusion criteria

This study included patients over 18 years of age who were admitted to our ED and underwent vital sign recording and arterial blood gas sampling less than 1 h apart. Exclusion criteria were the absence of recording of one of the parameters studied, a suspicion of blood gas analyses using venous samples (defined as SaO_2 inferior to 75% with SpO_2 superior to 95%), and the presence of hyperoxygenation (defined as the presence of oxygen therapy despite SaO_2 superior to 99%). We did not exclude samples collected for extra-respiratory indications.

2.5. Statistical analyses

Calculation of the SpO_2/FiO_2 values and determination of the mean areas under the receiver-operating characteristic (ROC) curves of SpO_2/FiO_2 for PaO_2/FiO_2 threshold values of 300 and 400 mmHg, as

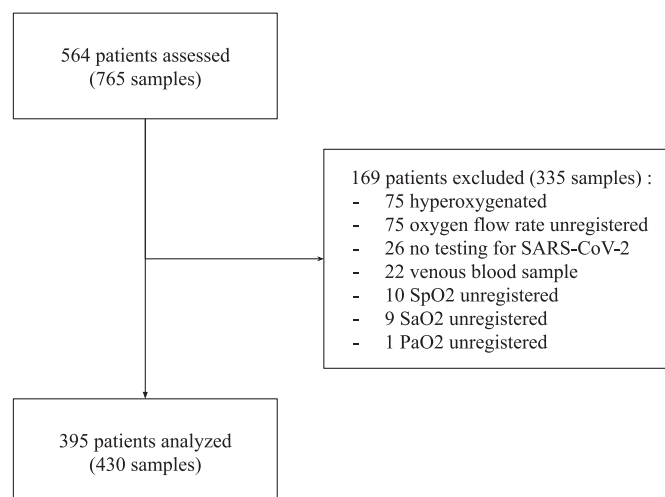


Fig. 1. Flowchart of the study.

well as their confidence intervals, were performed using R software version 3.6.3 (pROC package) [19]. Agreement between SpO₂/FiO₂ and PaO₂/FiO₂ ratios was assessed using Spearman's rank correlation coefficient. Subgroup analysis of COVID-19 positive and negative patients was conducted using Delong's test of equivalence on ROC curves of both subgroups for PaO₂/FiO₂ threshold values of 300 and 400 mmHg. SpO₂/FiO₂ thresholds were determined using the weighted closest topleft method (pROC package).

3. Results

3.1. Characteristics of the study subjects

During the study period, 564 patients underwent one or more blood gas analyses for a total of 765 blood samples. After application of the exclusion criteria, 430 blood samples from 395 patients were included in

Table 1
Characteristics of study subjects

Patients characteristics	N = 395
Age, median (IQR)	60 (44–78)
Gender, male, N (%)	193 (48.9%)
Comorbidities:	
cardiac, N (%)	91 (23.0%)
heart failure, N (%)	71 (18.0%)
atrial fibrillation, N (%)	40 (10.1%)
coronary artery disease, N (%)	30 (7.6%)
other cardiac disease, N (%)	33 (8.4%)
pulmonary, N (%)	118 (29.9%)
asthma, N (%)	48 (12.2%)
Chronic obstructive pulmonary disease(COPD), N (%)	51 (12.9%)
lung carcinosis, N (%)	10 (2.53%)
restrictive lung disease, N (%)	16 (4.05%)
other, N (%)	10 (2.53%)
Acute kidney failure, N (%)	33 (8.4%)
Chronic kidney disease, N (%)	29 (7.34%)
COVID-19 status	
positive, N (%)	90 (22.8%)
negative, N (%)	305 (77.2%)
Diagnosis at discharge	
pulmonary disease, N (%)	291 (73.7%)
SARS-CoV-2, N (%)	90 (22.8%)
COPD exacerbation, N (%)	21 (5.32%)
Acute asthma, N (%)	18 (4.56%)
Pneumonia, N (%)	49 (12.4%)
Cardiogenic pulmonary oedema, N (%)	21 (5.32%)
respiratory acute viral syndrome (undetermined), N (%)	72 (18.3%)
others, N (%)	20 (5.06%)
Extra-respiratory disease, N (%)	104 (26.3%)
Vital signs:	
Heart rate, median (IQR)	88 (77–101)
Systolic blood pressure, median (IQR)	129 (115–144)
Diastolic blood pressure, median (IQR)	77 (68–87)
SpO ₂ , median (IQR)	97 (95–99)
Ventilatory rate, median (IQR)	22 (18–28)
Temperature (°C), median (IQR)	37 (36.6–37.5)
Blood gas analysis	N = 430
Sample from COVID-19 patient, N (%)	94 (21.9%)
FiO ₂ (%), median (IQR)	21 (21–29)
PaO ₂ (mmHg), median (IQR)	83.3 (71.3–97.5)
SaO ₂ (%), median (IQR)	97.9 (96.4–98.9)
PaCO ₂ (mmHg), median (IQR)	36.0 (32.3–40.5)
pH, median (IQR)	7.44 (7.41–7.47)
PaO ₂ /FiO ₂ (mmHg), median (IQR)	364.3 (269.5–450)
PaO ₂ /FiO ₂ > 400, N (%)	164 (38.1%)
PaO ₂ /FiO ₂ 300–400, N (%)	132 (30.7%)
PaO ₂ /FiO ₂ < 300, N (%)	134 (31.2%)
SaO ₂ /FiO ₂ , median (IQR)	461.2 (339.0–470.5)
SpO ₂ /FiO ₂ , median (IQR)	452.4 (337.9–466.7)

statistical analyses. Fig. 1 shows the flow chart of the study. The characteristics of the patients and blood samples are presented in Table 1.

3.2. Main results

Spearman's rank correlation between SpO₂/FiO₂ and PaO₂/FiO₂ ratios was 0.799 (CI 95% 0.747–0.842). The ROC curves of the SpO₂/FiO₂ ratio among overall (N = 430), COVID-19 positive (N = 94) and negative (N = 336) subgroups for PaO₂/FiO₂ threshold values of 300 and 400 mmHg are shown in Fig. 2. Delong's test for comparison of ROC curves showed no significant difference between the subgroups for PaO₂/FiO₂ threshold values of 300 mmHg (D = 1.46, p = 0.15) and 400 mmHg (D = 0.68, p = 0.50).

The AUCs of ROC curves of overall patients were 0.918 (CI 95% 0.885–0.950) for a PaO₂/FiO₂ threshold of 300 mmHg and 0.901 (CI 95% 0.872–0.930) for a PaO₂/FiO₂ threshold of 400 mmHg. Analysis of SpO₂/FiO₂ performance shows a specificity of SpO₂/FiO₂ superior to 470 of 0.98 (CI95% 0.96–0.99) with a positive predictive value (PPV) of 0.89 (CI95% 0.75–0.96) for PaO₂/FiO₂ superior to 400 mmHg. Specificity of SpO₂/FiO₂ inferior to 350 was 0.95 (CI95% 0.91–0.97) with PPV of 0.88 (CI95% 0.84–0.91) for PaO₂/FiO₂ inferior to 300 mmHg.

4. Discussion

4.1. Synthesis of relevant results

The SpO₂/FiO₂ ratio in our cohort showed a good association with the PaO₂/FiO₂ ratio. In this series, the use of thresholds of 370 and 450 showed satisfactory diagnostic performances for the positive diagnosis of PaO₂/FiO₂ < 300 mmHg and exclusion of a PaO₂/FiO₂ < 400 mmHg. Performance was not significantly different between COVID-19 positive and negative patients.

Our results suggest that SpO₂/FiO₂ can be used for the estimation of the degree of hypoxemia on admission to the emergency room, allowing the patient's severity to be assessed prior to confirmation of viral status. Without other signs of respiratory distress (including increased work of breathing and/or altered mental status), SpO₂/FiO₂ superior to 450 could be used as a decision threshold for outpatient management, whereas SpO₂/FiO₂ inferior to 370 could require referral to intensive care units. An SpO₂/FiO₂ between 370 and 450 would require further clinical evaluation and possibly arterial blood gas.

4.2. Relationship to previous results

Our results support data published by Lu et al. [20], who found that a significant association between SpO₂/FiO₂ decreases and increases mortality risk. Similarly, results recently published by Hamlovich et al. [21] showed the prognostic value of SpO₂ and FiO₂ in the initial assessment of the severity of COVID-19 patients. In this context, our results support the possibility of using SpO₂/FiO₂ by admission nurses as a tool for triage and early referral of patients admitted for respiratory symptoms.

4.3. Limitations

This study had several limitations. First, its retrospective design is subject to several biases. In particular, the SARS-CoV-2 virological status is based on the presence of a positive PCR and/or CT scan with typical lesions. The number of false positives is likely to be small; thus, we can assume the existence of many false negatives, particularly in patients who have not had a CT scan or if the CT scan was performed too early, which may be negative during the first few days of symptom progression [22].

The population sample collected over this period cannot be considered representative of a standard sample of patients consulted in an ED. Significantly more patients were admitted for respiratory symptoms during the period. In addition, relatively fewer patients were admitted

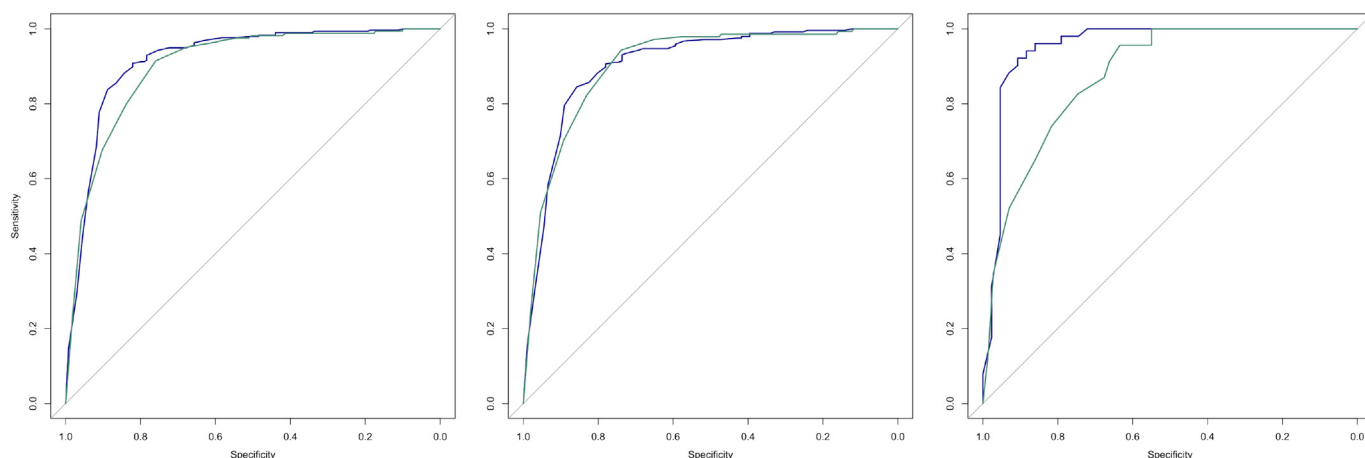


Fig. 2. ROC curves of the SpO₂/FiO₂ ratio for PaO₂/FiO₂ threshold values of 300 mmHg (blue) and 400 mmHg (green), for overall (left), COVID-19 negative (center) and positive (right) patients.

for other indications as they may have avoided consultations to reduce their exposure to viral contamination.

Blood gas measurements performed for acute respiratory distress were included, as well as for non-respiratory reasons, considering that validation of SpO₂/FiO₂ in non-hypoxemic patients was necessary to exclude significant hypoxemia at triage. Hyperoxygenated patients were excluded from the analyses, in whom the SpO₂/FiO₂ ratio is artificially lowered by a nonlinear evolution of SpO₂ (limited between 99% and 100%) compared to FiO₂. This choice limits the use of these results for triage, where pre-hospital treatment may have imposed significant oxygen therapy during transport to the hospital center, leading to hyperoxygenation at admission to the ED. The use of SpO₂/FiO₂ then requires a prior decrease in FiO₂ to obtain an SpO₂ of less than 99%.

Finally, this study evaluated the performance of SpO₂/FiO₂ based on its association with a biological criterion. An evaluation based on a clinical criterion would be more relevant and would allow for a better assessment of the interest of this index in practice. In particular, previous studies [23,24] have shown that the relationship between PaO₂ and FiO₂ is not linear. Thus, the PaO₂/FiO₂ ratio depends on the FiO₂, and its evolution in cases of FiO₂ variation depends on the fraction of shunt and the ventilation/perfusion mismatch. As such, a perfect correlation between SaO₂/FiO₂ and PaO₂/FiO₂ would mean that SaO₂/FiO₂ has the same drawbacks.

5. Conclusion

In summary, our results suggest that SpO₂/FiO₂ could be a useful index for triage upon admission of patients consulting for acute respiratory symptoms, particularly with suspicion of COVID-19, and would identify patients who could be managed on an outpatient basis and patients requiring admission to the intensive care unit. The use of this index nevertheless requires oxygen titration to ensure the absence of hyperoxygenation, and does not take into account the other dimensions of the respiratory assessment (including work of breathing and mental status).

Future studies are required for a prospective evaluation of the diagnostic performance of SpO₂/FiO₂ among COVID-19 patients, as well as in the acute respiratory tract. In particular, the use of a clinical criterion such as mortality, length of hospitalization, the need for admission to intensive or conventional care could allow us to more accurately assess the contribution of SpO₂/FiO₂ in emergency medicine triage, providing options in addition to PaO₂/FiO₂.

Declaration of Competing Interest

The authors have no conflict of interest to declare.

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