Diagnostic Value of SaO_2/FiO_2 and PaO_2/FiO_2 Ratios Measured at Hospital Admission for Predicting Mortality in COVID-19 Patients

Abstract

Background:Approximately 20% of COVID-19 patients have an arterial blood oxygen partial pressure to fractional inspired oxygen concentration ratio (PaO2/FiO_2) of less than 300.
Objective: To analyze the diagnostic value ofoxygen saturation of arterial blood (SaO_2)/FiO_2 and of PaO_2/FiO_2 ratios measured on hospital admission for predicting mortality in COVID-19 patients.
Methods:Retrospective cohort study conducted at two hospitals in the Central Region of Brazil.Data were collected from the medical records.Respiratory markers were obtained from blood gasometry and pulse oximetry measurements taken on admission. Receiver Operating Characteristic curves were constructed to assess the accuracy of the studied ratios for predicting the mortality among the analysed patients.
Results:Both PaO_2/FiO_2 and SaO_2/FiO_2rates measured on hospital admission were accurate parameters for predicting mortality in COVID-19 patients. The cutoff point of 280 for $PaO_2/FiO_2$and of 290 for SaO_2/FiO_2showed satisfactory sensitivity for predicting death among the analyzed patients.
Conclusion:SaO_2/FiO_2 and PaO_2/FiO_2 ratios measured on hospital admission exhibited good sensitivity and accuracy in predicting mortality in hospitalized COVID-19 patients.

Kew-words:SaO_2/FiO_2 ratio,SaO_2/FiO_2 ratio, Mortality, COVID-19.

Introduction

Approximately 20% of COVID-19 patients are classified as severe cases, characterized by the presence of dyspnea, a respiratory rate exceeding 30 breaths per minute, and an arterial blood oxygen partial pressure to fractional inspired oxygen concentration ratio (PaO_2/FiO_2) of less than 300. The most severe forms of the disease typically manifest in the second week, with dyspnea progressing to severe respiratory failure. Older individuals and those with comorbidities such as diabetes, cardiovascular, and renal

diseases are more susceptible to developing acute respiratory distress syndrome (ARDS).[1]

ARDS is characterized by acute lung injury with increased vascular permeability and lung density, which can lead to non-cardiogenic acute pulmonary edema. Its pathophysiology involves acute hypoxemia with a PaO_2/FiO_2 ratio < 300 and is associated with acute pulmonary inflammation. This inflammation results in bilateral lung opacities and increases vascular permeability, leading to a progressive reduction in ventilated lung tissue.[2] The diagnosis of ARDS is based on clinical manifestations, imaging studies, as well as changes in pH values, partial pressure of oxygen (PaO_2), partial pressure of carbon dioxide (PCO_2), and arterial oxygen saturation (SaO_2). Derived parameters from these measures, such as PaO_2/FiO_2 and SaO_2/FiO_2 ratios, can also be altered and used as criteria for diagnosing acute lung injury and ARDS.[3]

Investigating predictive factors for clinical deterioration of patients is useful in guiding decision-making in healthcare practice and contributes to oxygen management, ranging from non-invasive to invasive ventilation. The objective of this study was to analyze the diagnostic value of SaO_2/FiO_2 and PaO_2/FiO_2 ratios measured upon hospital admission for predicting mortality in COVID-19 patients.

Materials and Methods

This is a retrospective cohort study aimed at evaluating respiratory functional parameters upon hospital admission in COVID-19 patients and their association with subsequent mortality. The study was conducted from March to August 2020 at two COVID-19 reference hospitals in the Central Region of Brazil, one privately administered and the other publicly administered. Patient selection was based on the positive COVID-19 cases recorded in each hospital unit, confirmed by real-time reverse transcription-polymerase chain reaction (qRT-PCR), rapid antigen testing on nasopharyngeal swabs, IgM/IgG antibody testing against SARS-CoV-2, or a combination of clinical data and chest computed tomography findings consistent with respiratory changes caused by the novel coronavirus.

Demographic and clinical data were obtained from the medical records of the evaluated hospitals. Information about comorbidities was considered if recorded during the patient's first medical interview upon admission. Respiratory function markers were

analyzed through arterial blood gasometry and pulse oximetry measurements taken on the patient's admission date, serving as baseline information. The results of PaO_2, SaO_2, and FiO_2 from the patient's admission blood gas analysis were used to calculate the PaO2/FiO2 and SaO_2/FiO_2 ratios. The definition of ARDS followed the Berlin criteria of 2012[4] and its severity was classified according to Falavigna et al., 2020 as mild (PaO_2/FiO_2 between 300 and 200), moderate (PaO_2/FiO_2 between 200 and 100), or severe (PaO_2/FiO_2 less than or equal to 100).[5]

Receiver Operating Characteristic (ROC) curves were constructed to assess the sensitivity and specificity of SaO_2/FiO_2 and PaO_2/FiO_2 ratios determined upon hospital admission for predicting the occurrence of mortality in COVID-19 hospitalized patients. The areas under the curve (AUC) were calculated to demonstrate the accuracies of these markers. The Youden's J Index was calculated to define empirical cutoff points corresponding to sensitivity and specificity values least likely to have occurred by chance. A significance level of alpha error at 0.05 was considered statistically significant for the analyzed variables. Statistical analyses were performed using Stata 12.0 software (Stata Corporation, College Station, TX, USA). This study was approved by the Ethics and Research Committee of Hospital Universitário Júlio Muller (HUJM) on September 1, 2020, under approval number 4252218.

Results

A total of 199 COVID-19 patients hospitalized from March to August 2020 were included in the study. Of these, 133 (66.8%) were admitted to a private hospital, and 66 (33.2%) to a public hospital. Most patients were over 50 years old, male, residents of the metropolitan area of Cuiabá (MT), with a medium to high level of education, and of white or mixed race. Among the included patients, 122 comorbidities were recorded, with the most common being arterial hypertension (40.2%), diabetes mellitus (22.6%), and obesity (18.6%).

A diagnosis of ARDS was registered in 40 patients, with 21 (52.5%) classified as mild ARDS, 10 (25.0%) as moderate ARDS, and 9 (22.5%) as severe ARDS. Of the total COVID-19 hospitalized patients, 33 (16.6%) progressed to death, of which 22 (20.6%) were part of a group of 107 and 101 patients with available information on PaO_2/FiO_2 and SaO_2/FiO_2 measured upon hospital admission, respectively. In this latter group of patients, there was a progressive increase (p=0.001) in the proportion of deaths according to the severity of ARDS (Table 1).

Upon hospital admission of the patients, the median (quartile 1; quartile 3) for PaO_2/FiO_2 was 353 (237; 465), and for SaO_2/FiO_2 was 352 (279; 471). Lower PaO_2/FiO_2 and SaO_2/FiO_2 ratios were observed among patients who died compared to those who survived (Table 2).

The ROC curves constructed from the studied ventilatory parameters showed high AUC values for both PaO_2/FiO_2 (72.7%) and SaO_2/FiO_2 (73.1%) measured upon hospital admission, for predicting mortality in this group of patients. The cutoff point of 280 for PaO_2/FiO_2 had satisfactory sensitivity (77.2%), specificity (68.2%), and accuracy (75.3%) for predicting death, and similarly, the cutoff point of 290 for SaO_2/FiO_2 showed high sensitivity (82.4%), specificity (59.1%), and accuracy (77.6%) for predicting death among the analyzed patients (Figure 1).

Discussion

The results of this study demonstrate that hospitalized COVID-19 patients are more likely to die if they are in more severe stages of ARDS or have low PaO2/FiO2 and/or SaO_2/FiO_2 ratios upon hospital admission. Furthermore, the determination of PaO_2/FiO_2 and SaO_2/FiO_2 ratios at admission showed satisfactory accuracy for predicting mortality in hospitalized COVID-19 patients.

The association between COVID-19 mortality and ARDS severity has been reported in previous studies and is directly related to the greater extent of respiratory compromise.[6,7] It is also well-established that a low PaO_2/FiO_2 ratio is significantly associated with hospital mortality in COVID-19 patients.[8] PaO_2/FiO_2 levels below 200 have been identified as predictors of higher mortality risk and shorter survival time in patients with severe ARDS.[9] In another study, a low PaO_2/FiO_2 ratio at admission in COVID-19 patients in intensive care units was found to be a predictor of mortality in a study conducted in Colombia.[10]

The main limitation of the presented results was the loss of information for a significant portion of COVID-19 patients hospitalized, primarily due to inadequate record-keeping in medical records.

Conclusion

SaO_2/FiO_2 and PaO_2/FiO_2 ratios measured upon hospital admission are reduced, with more pronounced reductions observed in COVID-19 patients with a greater chance of

progressing to moderate or severe ARDS. These two ratios exhibit good accuracy in predicting mortality in hospitalized COVID-19 patients.

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Table 1 - Distribution of deaths of patients hospitalized with COVID-19 according to the clinical stage of ARDS and according to the PaO2/FiO2 and SaO2/FiO2 ratios measured at patient admission.

Clinical feature	Death		Total	p
	YES n (%)	NO n (%)	Median (Q1; Q3)	
ARDS stage				
Without ARDS (n=61)	7 (11.5%)	54 (88.5%)	61	0.001*
Mild (n=21)	5 (23.8%)	16 (76.2%)	21	
Moderate (n=10)	4 (40.0%)	6 (60.0%)	10	
Severe (n=9)	6 (66.7%)	3 (33.3%)	9	
Respiratory biomarker	**Median (Q1; Q3)**	**Median (Q1; Q3)**		
$PaO_2/FiO2$ (n=101)	225 (98; 429)	364 (280; 483)	353 (237; 465)	0.001**
SaO_2/FiO_2 (n=107)	241 (102; 340)	392 (321; 475)	352 (279; 471)	<0.001**

Q1: First quartile
Q3: Third quartile
*: Qui-quadrado for linear trend.
**: Mann-Whitney U test

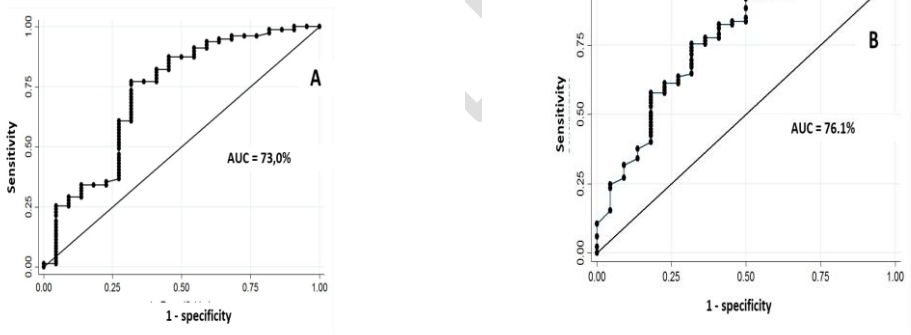

Figure 1 -ROC curve of the accuracy of the PaO2 /FiO2 [**A**] and SaO2 /FiO2 [**B**] ratio with potential diagnostic value for the outcome of death in patients hospitalized with COVID-19 from March to August 2020.