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### ► To cite this version:

Pierre Catoire, Eric Tellier, Caroline de La Rivière, Marie-Christine Beauvieux, Guillaume Valdenaire, et al.. Assessment of the SpO<sub>2</sub>/FiO<sub>2</sub> ratio as a tool for hypoxemia screening in the emergency department. American Journal of Emergency Medicine, 2021, 44, pp.116-120. 10.1016/j.ajem.2021.01.092 . hal-03366071

**HAL Id: hal-03366071**

**<https://cnrs.hal.science/hal-03366071>**

Submitted on 13 Feb 2023

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Assessment of the SpO<sub>2</sub>/FiO<sub>2</sub> ratio as a tool for hypoxemia screening in the emergency department

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The authors have no conflict of interest to declare.

Word count for article (abstract excluded) : 1937

Short title : SpO<sub>2</sub>/FiO<sub>2</sub> ratio for hypoxemia screening in the ED

Keywords : respiratory Insufficiency, oximetry, COVID-19, triage, ROC curve.

Authors contribution statement :

CP, GJC and TE conceived the study and designed the trial. GJC, TE, GM and CX provided statistical advice on study design. CP and GJC supervised the data collection, analyzed the data, drafted the manuscript, and all authors contributed substantially to its revision. CP and GJC take responsibility for the paper as a whole.

1 **Abstract:**

2 Objective: We assessed the performance of the ratio of peripheral arterial oxygen saturation to  
3 the inspired fraction of oxygen ( $SpO_2/FiO_2$ ) to predict the ratio of partial pressure arterial  
4 oxygen to the fraction of inspired oxygen ( $PaO_2/FiO_2$ ) among patients admitted to our  
5 emergency department (ED) during the SARS-CoV-2 outbreak.

6 Methods: We retrospectively studied patients admitted to an academic-level ED in France who  
7 were undergoing a joint measurement of  $SpO_2$  and arterial blood gas. We compared  $SpO_2$  with  
8  $SaO_2$  and evaluated performance of the  $SpO_2/FiO_2$  ratio for the prediction of 300 and 400  
9 mmHg  $PaO_2/FiO_2$  cut-off values in COVID-19 positive and negative subgroups using receiver-  
10 operating characteristic (ROC) curves.

11 Results: During the study period from February to April 2020, a total of 430 arterial samples  
12 were analyzed and collected from 395 patients. The area under the ROC curves of the  
13  $SpO_2/FiO_2$  ratio was 0.918 (CI 95% 0.885–0.950) and 0.901 (CI 95% 0.872–0.930) for  
14  $PaO_2/FiO_2$  thresholds of 300 and 400 mmHg, respectively. The positive predictive value (PPV)  
15 of an  $SpO_2/FiO_2$  threshold of 350 for  $PaO_2/FiO_2$  inferior to 300 mmHg was 0.88 (CI95% 0.84–  
16 0.91), whereas the negative predictive value (NPV) of the  $SpO_2/FiO_2$  threshold of 470 for  
17  $PaO_2/FiO_2$  inferior to 400 mmHg was 0.89 (CI95% 0.75–0.96). No significant differences were  
18 found between the subgroups.

19 Conclusions: The  $SpO_2/FiO_2$  ratio may be a reliable tool for hypoxemia screening among  
20 patients admitted to the ED, particularly during the SARS-CoV-2 outbreak.

## 21 **1. Introduction**

### 22 *1. 1. Background*

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

28 The development of tools for the initial assessment of the degree of hypoxemia among patients  
29 with respiratory symptoms is essential. Such a tool should reduce both under-triage, allowing  
30 critical patients to quickly receive the appropriate level of care, and over-triage, maintaining  
31 critical care capacity despite an influx of patients. An appropriate triage tool should also be  
32 applicable for all causes of respiratory distress, whether related to COVID-19 or not. Limited  
33 reliable data are available for the triage of hypoxemic patients in the ED, yet it could be  
34 particularly useful during the COVID-19 pandemic.

### 35 *1. 2. Importance*

36 Early diagnosis of critical hypoxemia is important for both COVID-19 infection and Acute  
37 Respiratory Distress Syndrome (ARDS) based on the ratio of partial pressure arterial oxygen  
38 to the fraction of inspired oxygen ( $\text{PaO}_2/\text{FiO}_2$ ) (1,2). This indicator has been validated in many  
39 pathological situations (3,4) but requires an arterial blood sample and therefore is often not  
40 immediately accessible upon the patient's admission. Arterial puncture is also a source of pain  
41 and complications (5-8).

42 Validation of a noninvasive tool could allow us to improve triage time and patient orientation  
43 upon admission. In particular, the ratio of peripheral arterial oxygen saturation to the inspired  
44 fraction of oxygen ( $\text{SpO}_2/\text{FiO}_2$ ) has been proposed by several authors (9-12). However,  
45 diagnostic performance of this index has not yet been evaluated.

46 *1. 3. Goals of this investigation*

47 This study evaluated the performance of the  $\text{SpO}_2/\text{FiO}_2$  ratio for predicting mild ( $\text{PaO}_2/\text{FiO}_2$   
48 superior to 400 mmHg) or moderate ( $\text{PaO}_2/\text{FiO}_2$  inferior to 300 mmHg) hypoxemia, and  
49 evaluated the performance of this index among patients admitted during the COVID-19  
50 outbreak, with subgroup analyses distinguishing SARS-CoV-2 positive and negative patients.

51 **2. Methods**

52 *2. 1. Study design and setting*

53 We performed a retrospective observational cohort study to assess the predictive value of  
54 SpO<sub>2</sub>/FiO<sub>2</sub> for the PaO<sub>2</sub>/FiO<sub>2</sub> ratio among adult patients admitted to our ED from February to  
55 April 2020. The study center is an academic-level hospital in France and was the regional  
56 referral center for COVID-19 patient management during the pandemic.

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

60 *2. 2. Data collection*

61 We extracted the following from our computer data system (*DxCare*® software, France): data  
62 on demographics, medical history, vital signs at admission and time of arterial blood sampling,  
63 presence of oxygen therapy, oxygen flow rate (QO<sub>2</sub>) at arterial puncture, SARS-CoV-2  
64 virological status, final diagnosis, and blood gas results for each arterial sample during ED  
65 admission including PaO<sub>2</sub>, arterial hemoglobin saturation (SaO<sub>2</sub>), and arterial carbon dioxide  
66 partial pressure (PaCO<sub>2</sub>). Data collection was planned subsequent to admission of the study  
67 population for the study period. **All patients admitted during the study period and from whom**  
68 **an arterial blood sampling was performed were reviewed.** The diagnosis of COVID-19  
69 infection was retained in our analyses in cases of a positive PCR and/or typical lesions in chest  
70 CT scans (when performed).

71 FiO<sub>2</sub> was estimated from the interface used for oxygen delivery (nasal cannulas, single mask,  
72 high-concentration mask, non-invasive ventilation) and oxygen flow rate. For nasal-cannula or  
73 single-mask oxygen therapy, FiO<sub>2</sub> was estimated from the data presented by Wettstein *et al*  
74 (14) using the formula  $FiO_2 = 4.QO_2 + 21\%$ . For the high-concentration mask, FiO<sub>2</sub> was

75 estimated at 80%. For non-invasive ventilation, the FiO<sub>2</sub> value selected was the one set on the  
76 ventilator.

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

### 82 2. 3. *Choice of PaO<sub>2</sub>/FiO<sub>2</sub> thresholds*

83 The PaO<sub>2</sub>/FiO<sub>2</sub> thresholds chosen to plot ROC curves were 300 and 400 mmHg, respectively.  
84 The 300 mmHg threshold corresponds to the definition of both severe COVID-19 (15), and  
85 ARDS (16). The 400 mmHg threshold corresponds to changes in hematosi relative to observed  
86 normal (17) and is used for early detection of hypoxemia, such as in the SOFA score (18).

### 87 2. 4. *Inclusion and exclusion criteria*

88 This study included patients over 18 years of age who were admitted to our ED and underwent  
89 vital sign recording and arterial blood gas sampling less than 1 h apart. Exclusion criteria were  
90 the absence of recording of one of the parameters studied, a suspicion of blood gas analyses  
91 using venous samples (defined as SaO<sub>2</sub> inferior to 75% with SpO<sub>2</sub> superior to 95%), and the  
92 presence of hyperoxygenation (defined as the presence of oxygen therapy despite SaO<sub>2</sub>  
93 superior to 99%). We did not exclude samples collected for extra-respiratory indications.

### 94 2. 5. *Statistical analyses*

95 Calculation of the SpO<sub>2</sub>/FiO<sub>2</sub> values and determination of the mean areas under the receiver-  
96 operating characteristic (ROC) curves of SpO<sub>2</sub>/FiO<sub>2</sub> for PaO<sub>2</sub>/FiO<sub>2</sub> threshold values of 300 and  
97 400 mmHg, as well as their confidence intervals, were performed using R software version  
98 3.6.3 (pROC package) (19). Agreement between SpO<sub>2</sub>/FiO<sub>2</sub> and PaO<sub>2</sub>/FiO<sub>2</sub> ratios was assessed  
99 using Spearman's rank correlation coefficient. Subgroup analysis of COVID-19 positive and



100 negative patients was conducted using Delong's test of equivalence on ROC curves of both  
101 subgroups for PaO<sub>2</sub>/FiO<sub>2</sub> threshold values of 300 and 400 mmHg. SpO<sub>2</sub>/FiO<sub>2</sub> thresholds were  
102 determined using the weighted closest topleft method (pROC package).

103 **3. Results**

104 *3. 1. Characteristics of the study subjects*

105 During the study period, 564 patients underwent one or more blood gas analyses for a total of  
106 765 blood samples. After application of the exclusion criteria, 430 blood samples from 395  
107 patients were included in statistical analyses. Figure 1 shows the flow chart of the study. The  
108 characteristics of the patients and blood samples are presented in Table 1.

109 *3. 2. Main results*

110 Spearman's rank correlation between SpO<sub>2</sub>/FiO<sub>2</sub> and PaO<sub>2</sub>/FiO<sub>2</sub> ratios was 0.799 (CI 95%  
111 0.747-0.842). The ROC curves of the SpO<sub>2</sub>/FiO<sub>2</sub> ratio among overall (N=430), COVID-19  
112 positive (N = 94) and negative (N = 336) subgroups for PaO<sub>2</sub>/FiO<sub>2</sub> threshold values of 300 and  
113 400 mmHg are shown in Figure 2. Delong's test for comparison of ROC curves showed no  
114 significant difference between the subgroups for PaO<sub>2</sub>/FiO<sub>2</sub> threshold values of 300 mmHg  
115 (D = 1.46, p = 0.15) and 400 mmHg (D = 0.68, p = 0.50).

116 The AUCs of ROC curves of overall patients were 0.918 (CI 95% 0.885–0.950) for a  
117 PaO<sub>2</sub>/FiO<sub>2</sub> threshold of 300 mmHg and 0.901 (CI 95% 0.872–0.930) for a PaO<sub>2</sub>/FiO<sub>2</sub>  
118 threshold of 400 mmHg. **Analysis of SpO<sub>2</sub>/FiO<sub>2</sub> performance shows** a specificity of  
119 SpO<sub>2</sub>/FiO<sub>2</sub> superior to 470 of 0.98 (CI95% 0.96–0.99) with a positive predictive value (PPV)  
120 of 0.89 (CI95% 0.75–0.96) for PaO<sub>2</sub>/FiO<sub>2</sub> superior to 400 mmHg. Specificity of SpO<sub>2</sub>/FiO<sub>2</sub>  
121 inferior to 350 was 0.95 (CI95% 0.91–0.97) with PPV of 0.88 (CI95% 0.84–0.91) for  
122 PaO<sub>2</sub>/FiO<sub>2</sub> inferior to 300 mmHg.

## 123 4. Discussion

### 124 4. 1. Synthesis of relevant results

125 The SpO<sub>2</sub>/FiO<sub>2</sub> ratio in our cohort showed a good association with the PaO<sub>2</sub>/FiO<sub>2</sub> ratio. In this  
126 series, the use of thresholds of 370 and 450 showed satisfactory diagnostic performances for  
127 the positive diagnosis of PaO<sub>2</sub>/FiO<sub>2</sub> < 300 mmHg and exclusion of a PaO<sub>2</sub>/FiO<sub>2</sub> < 400 mmHg.  
128 Performance was not significantly different between COVID-19 positive and negative patients.  
129 **Our results suggest that SpO<sub>2</sub>/FiO<sub>2</sub> can be used for the estimation of the degree of hypoxemia**  
130 **on admission to the emergency room, allowing the patient's severity to be assessed prior to**  
131 **confirmation of viral status. Without other signs of respiratory distress (including increased**  
132 **work of breathing and/or altered mental status), SpO<sub>2</sub>/FiO<sub>2</sub> superior to 450 could be used as a**  
133 **decision threshold for outpatient management, whereas SpO<sub>2</sub>/FiO<sub>2</sub> inferior to 370 could require**  
134 **referral to intensive care units. An SpO<sub>2</sub>/FiO<sub>2</sub> between 370 and 450 would require further**  
135 **clinical evaluation and possibly arterial blood gas.**

### 136 4. 2. Relationship to previous results

137 Our results support data published by Lu *et al.* (20), who found that a significant association  
138 between SpO<sub>2</sub>/FiO<sub>2</sub> decreases and increases mortality risk. Similarly, results recently published  
139 by Hamlovich *et al.* (21) showed the prognostic value of SpO<sub>2</sub> and FiO<sub>2</sub> in the initial assessment  
140 of the severity of COVID-19 patients. In this context, our results support the possibility of  
141 using SpO<sub>2</sub>/FiO<sub>2</sub> by admission nurses as a tool for triage and early referral of patients admitted  
142 for respiratory symptoms.

### 143 4. 3. Limitations

144 This study had several limitations. First, its retrospective design is subject to several biases. In  
145 particular, the SARS-CoV-2 virological status is based on the presence of a positive PCR  
146 and/or CT scan with typical lesions. The number of false positives is likely to be small; thus,  
147 we can assume the existence of many false negatives, particularly in patients who have not had

148 a CT scan or if the CT scan was performed too early, which may be negative during the first  
149 few days of symptom progression (22).

150 The population sample collected over this period cannot be considered representative of a  
151 standard sample of patients consulted in an ED. Significantly more patients were admitted for  
152 respiratory symptoms during the period. In addition, relatively fewer patients were admitted  
153 for other indications as they may have avoided consultations to reduce their exposure to viral  
154 contamination.

155 Blood gas measurements performed for acute respiratory distress were included, as well as for  
156 non-respiratory reasons, considering that validation of  $SpO_2/FiO_2$  in non-hypoxemic patients  
157 was necessary to exclude significant hypoxemia at triage. Hyperoxygenated patients were  
158 excluded from the analyses, in whom the  $SpO_2/FiO_2$  ratio is artificially lowered by a nonlinear  
159 evolution of  $SpO_2$  (limited between 99% and 100%) compared to  $FiO_2$ . This choice limits the  
160 use of these results for triage, where pre-hospital treatment may have imposed significant  
161 oxygen therapy during transport to the hospital center, leading to hyperoxygenation at  
162 admission to the ED. The use of  $SpO_2/FiO_2$  then requires a prior decrease in  $FiO_2$  to obtain an  
163  $SpO_2$  of less than 99%.

164 Finally, this study evaluated the performance of  $SpO_2/FiO_2$  based on its association with a  
165 biological criterion. An evaluation based on a clinical criterion would be more relevant and  
166 would allow for a better assessment of the interest of this index in practice. In particular,  
167 previous studies (23, 24) have shown that the relationship between  $PaO_2$  and  $FiO_2$  is not linear.  
168 Thus, the  $PaO_2/FiO_2$  ratio depends on the  $FiO_2$ , and its evolution in cases of  $FiO_2$  variation  
169 depends on the fraction of shunt and the ventilation/perfusion mismatch. As such, a perfect  
170 correlation between  $SaO_2/FiO_2$  and  $PaO_2/FiO_2$  would mean that  $SaO_2/FiO_2$  has the same  
171 drawbacks.

172 **5. Conclusion**

173 In summary, our results suggest that  $\text{SpO}_2/\text{FiO}_2$  could be a useful index for triage upon  
174 admission of patients consulting for acute respiratory symptoms, particularly with suspicion of  
175 COVID-19, and would identify patients who could be managed on an outpatient basis and  
176 patients requiring admission to the intensive care unit. The use of this index nevertheless  
177 requires oxygen titration to ensure the absence of hyperoxygenation, **and does not take into**  
178 **account the other dimensions of the respiratory assessment (including work of breathing and**  
179 **mental status).**

180 Future studies are required for a prospective evaluation of the diagnostic performance of  
181  $\text{SpO}_2/\text{FiO}_2$  among COVID-19 patients, as well as in the acute respiratory tract. In particular,  
182 the use of a clinical criterion such as mortality, length of hospitalization, the need for admission  
183 to intensive or conventional care could allow us to more accurately assess the contribution of  
184  $\text{SpO}_2/\text{FiO}_2$  in emergency medicine triage, providing options in addition to  $\text{PaO}_2/\text{FiO}_2$ .

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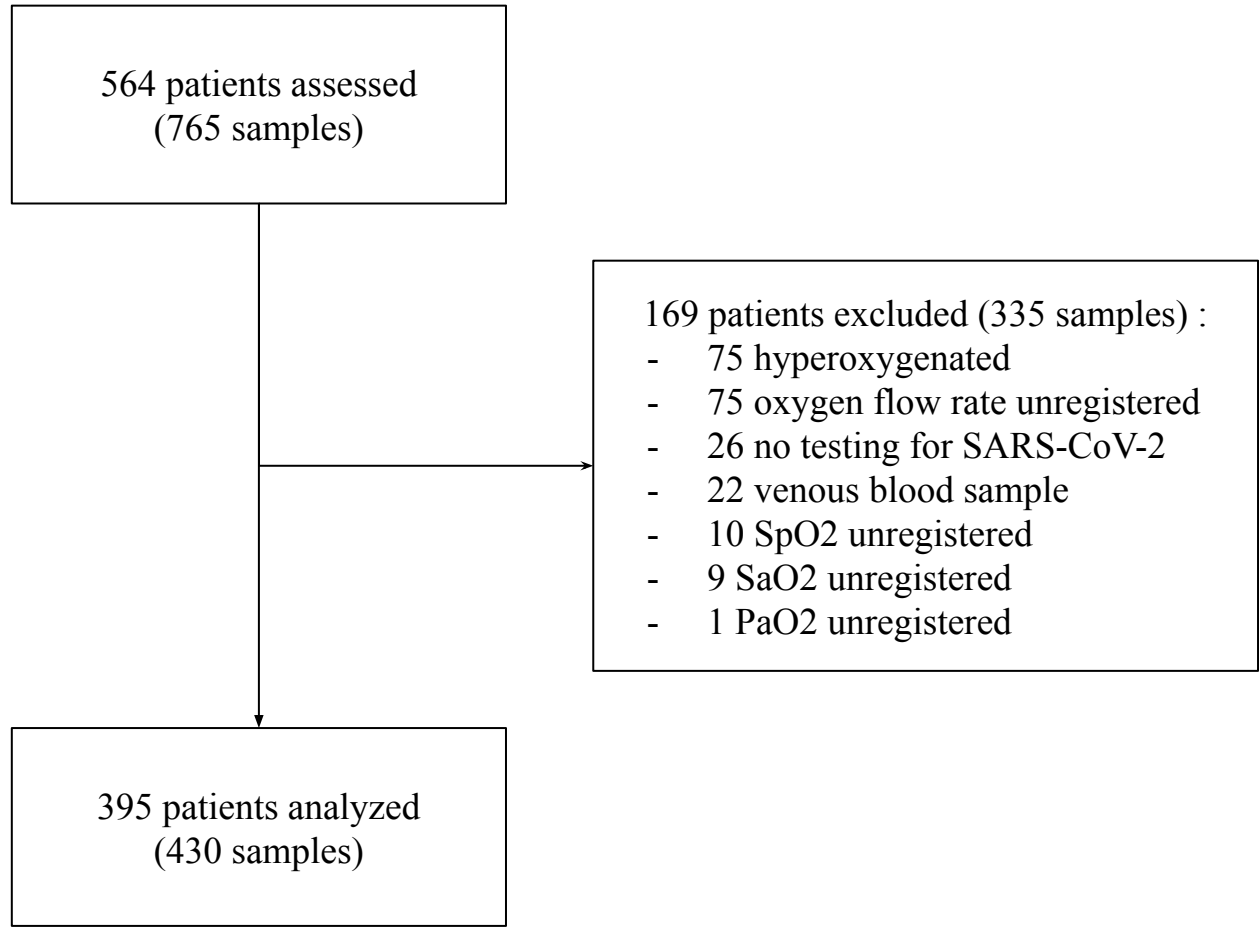
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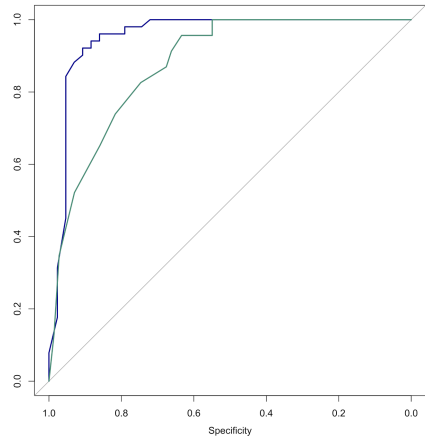
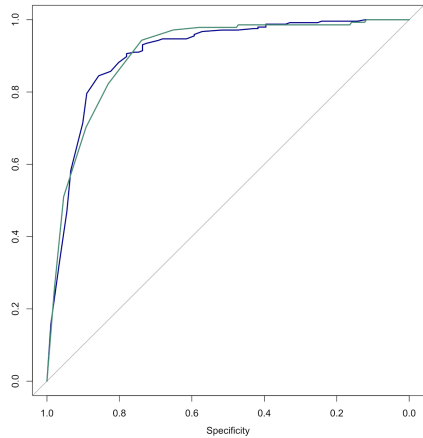
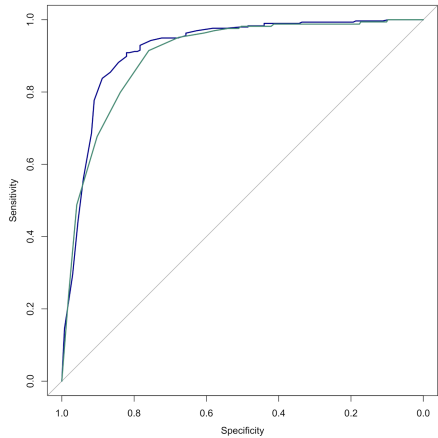


564 patients assessed  
(765 samples)

- 169 patients excluded (335 samples) :
- 75 hyperoxygenated
  - 75 oxygen flow rate unregistered
  - 26 no testing for SARS-CoV-2
  - 22 venous blood sample
  - 10 SpO2 unregistered
  - 9 SaO2 unregistered
  - 1 PaO2 unregistered

395 patients analyzed  
(430 samples)





## **Figure legends**

Figure 1. Flowchart of the study

Figure 2. ROC curves of the SpO<sub>2</sub>/FiO<sub>2</sub> ratio for PaO<sub>2</sub>/FiO<sub>2</sub> threshold values of 300 mmHg (blue) and 400 mmHg (green), for overall (left), COVID-19 negative (center) and positive (right) patients.

## **Supplemental tables legends**

Table 1. Characteristics of study subjects

**Table 1.**

<b>Patients characteristics</b>	<b>N = 395</b>
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)
SpO2, median (IQR)	97 (95-99)
Ventilatory rate, median (IQR)	22 (18-28)
Temperature (°C), median (IQR)	37 (36.6-37.5)
<b>Blood gas analysis</b>	<b>N = 430</b>
<b>Sample from COVID-19 patient, N (%)</b>	<b>94 (21.9%)</b>

FiO2 (%), median (IQR)	21 (21-29)
PaO2 (mmHg), median (IQR)	83.3 (71.3-97.5)
SaO2 (%), median (IQR)	97.9 (96.4-98.9)
PaCO2 (mmHg), median (IQR)	36.0 (32.3-40.5)
pH, median (IQR)	7.44 (7.41-7.47)
PaO2/FiO2 (mmHg), median (IQR)	364.3 (269.5-450)
- PaO2/FiO2 > 400, N (%)	164 (38.1%)
- PaO2/FiO2 300-400, N (%)	132 (30.7%)
- PaO2/FiO2 < 300, N (%)	134 (31.2%)
SaO2/FiO2, median (IQR)	461.2 (339.0-470.5)
SpO2/FiO2, median (IQR)	452.4 (337.9-466.7)