ORIGINAL RESEARCH

Role of integrated pulmonary index in respiratory monitoring of spontaneously breathing COVID-19 patients with moderate to severe respiratory symptoms

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ABSTRACT

Background & objective: Most of the COVID-19 patients suffered from moderate to severe respiratory symptoms. Many of them needed oxygen supplementation or even mechanical ventilation. There is little data available about the use of either end-tidal CO₂ (EtCO₂) or integrated pulmonary index (IPI) in these patients. The aim of this study to investigate the difference in IPI values for subjects requiring mechanical ventilation compared to those managed without ventilation and the correlation between EtCO₂ and SpO₂.

Methods: This prospective observational study involved adult COVID-19 patients admitted to the ICU with moderate to severe respiratory symptoms. All patients were connected to a portable respiratory monitor with the IPI algorithm (Medtronic Capnostream 35) and treated according to a standardized protocol. Oxygen flow was adjusted to maintain oxygen saturation (92–96%). If respiratory rate did not fall below 30 breaths per minute and/or the SpO₂ did not reach the target, non-invasive ventilation (NIV) was initiated. Patients with NIV failure was eligible for invasivemechanical ventilation.

Results: SpO₂ was significantly lower, while RR was significantly higher in intubated group compared to non-intubated group (P < 0.001 and 0.018, respectively). However, IPI, EtCO₂, and HR did not differ among both groups. There was a significant positive correlation between EtCO₂ and SpO₂ at baseline before oxygen therapy (r = 0.419; P = 0.007). There was a significant negative correlation between CT score and SpO₂ (r = -0.408; P = 0.01); however, there was no correlation between CT score and both IPI and end tidal CO₂ at baseline (r = 0.017; P = 0.9).

Conclusion: The integrated pulmonary index cannot be used as a single parameter for assessing respiratory severity in COVID-19 patients.

Abbreviations: EtCO₂ - end-tidal CO₂; IPI - integrated pulmonary index; NIV - non-invasive ventilation;
Keywords: Integrated Pulmonary Index, COVID-19, EtCO₂, CT severity score.


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1. INTRODUCTION

The most common complication of advanced COVID-19 is acute hypoxemic respiratory insufficiency or failure requiring oxygen and ventilation therapies.¹ The hypoxemic respiratory failure is the marked discrepancy between relatively well-preserved lung compliance and a severely compromised pulmonary gas exchange, leading to grave hypoxemia yet without proportional signs of respiratory distress.² Three The compensatory ventilatory response to hypoxemia, increased minute ventilation, which may lead to extreme hypocapnia and respiratory alkalosis. The physiological hallmarks of respiratory alkalosis are shift of the oxyhemoglobin dissociation curve to the left, thereby increasing hemoglobin’s oxygen affinity, evident from a decrease in the PS0 value and an increase in arterial oxygen saturation (SaO₂).³

The current guideline recommends starting with conventional oxygen therapy to maintain oxygen saturation (SpO₂) at 92% to 96%.⁴ However, without knowledge of the accompanying PaCO₂ value, it is impossible to infer from SpO₂, the degree of hypoxemia and consequently the severity of the respiratory failure.⁵

The FDA-cleared integrated pulmonary index (IPI) algorithm utilizes the real-time measurement and interactions of four parameters (EtCO₂, breathing frequency, heart rate, and SpO₂) to provide a rapid assessment of a patient’s respiratory status.⁶ The algorithm is designed to calculate IPI from various combinations of these measured parameters using a fuzzy logic model that mimics human thinking and associated clinical decision-making based on a group of clinical experts.⁷ IPI is displayed as a single indexed value from 1 to 10. In a clinical validation study by Ronen et al., an IPI < 4 was thought to require immediate clinical intervention due to deterioration in the patient’s respiratory status.

We investigated the difference in IPI values for COVID-19 patients with moderate to severe respiratory symptoms requiring mechanical ventilation compared to non-ventilated ones as well as the correlation between EtCO₂ and SpO₂.

2. METHODOLOGY

This prospective observational study was carried out on 50 patients, aged more than 18 y, from both sexes, with clinical criteria of severe respiratory symptoms defined as fever or suspected respiratory infection plus one of the following: respiratory rate (RR) > 30 breaths/min; severe respiratory distress; or SpO₂ ≤ 93% on room air. The study was done after approval from the ethical committee of Faculty of Medicine, Kasr Al-Ainy Teaching Hospital, Cairo, Egypt. Exclusion criteria included patients requiring intubation and mechanical ventilation before ICU admission.

Expired gas sampling lines were attached to the patients upon admission to the ICU. The initial EtCO₂, RR, SpO₂, pulse rate, and IPI values were recorded. These parameters were measured until patients were transferred out of the ICU by Capnostream™ 35 (Medtronic, USA.) The device measures the EtCO₂ and RR by sampling exhaled gas and the SpO₂ and pulse rate by pulse oximetry. Furthermore, the IPI is calculated automatically from four parameters, and all values are displayed on a screen. The calculation methods use a fuzzy logic inference model based on expert clinical opinions. After the provisional IPI is assigned according to the matrix table of RR and EtCO₂, the definite IPI is decided, finally adding the evaluation of SpO₂ and PR. This algorithm was verified by comparison to experts’ scoring of clinical scenarios.

All patients were treated according to our standardized respiratory protocol. The oxygen flow was adjusted to maintain an oxygen saturation (SpO₂) of 92%–96%. If the RR did not fall below 30 breaths per minute and/or the SpO₂ did not reach the target, non-invasive ventilation (NIV) was initiated. The following features were considered as NIV failure: worsening of dyspnea, worsening or lack of improvement of hypoxemia (defined as SpO₂ < 90%), persistence of RR > 35 breaths/min, appearance of respiratory acidosis (defined as pH < 7.3 and arterial carbon dioxide tension > 50 mmHg), circulatory shock (defined as the use of a vasopressor to maintain the mean arterial pressure at > 65 mmHg), or altered sensorium. A patient who developed any feature of NIV failure was qualified to receive invasive mechanical ventilation.

2.1. Chest CT severity score

The lungs were divided into the following five zones according to the anatomical structure of the lung: left
upper lobe, left lower lobe, right upper lobe, right middle lobe, and right lower lobe. Each lung lobe was assigned a score that was based on the following criteria: score 0 = 0% involvement; score 1 = < 5% involvement; score 2 = 5% to < 25% involvement; score 3 = 25% to < 50% involvement; score 4 = 50% to < 75% involvement; and score 5 = ≥ 75% involvement. The summation of scores provided a semi-quantitative evaluation of overall lung involvement (the maximum CT score for both lungs was 25.4).

All patients underwent CT imaging at hospital admission, and the images were scored by an experienced radiologist who was blinded to the clinical data. The primary outcome was the difference in IPI values for subjects requiring oxygen therapy compared to those in need of non-invasive ventilation. While the secondary outcomes were the correlation between EtCO₂ and SpO₂ at baseline before oxygen therapy, correlation of IPI score with CT severity score; correlation of EtCO₂ with CT severity score; need for mechanical ventilation; and ICU length of stay.

2.2. Sample size calculation

The sample size calculation was done by G*Power 3.1.9.2 (Universitat Kiel, Germany). According to a previous study,¹² the mean ± SD of IPI (the primary outcome) was 1.47 ± 0.74 in patients with respiratory compromise and 0.93 ± 0.74 in patients without respiratory compromise. The sample size was based on 1.09 effect size, 95% confidence limit, 90% power of the study, and two cases were added to each group to overcome drop out. Therefore, we recruited 40 patients.

2.3. Statistical analysis

Statistical analysis was done by SPSS v26 (IBM Inc., Chicago, IL, USA). Continuous quantitative normally distributed data were expressed as means and standard deviations (SD). Qualitative categorical data were expressed as frequency (%). The correlation was evaluated using the Spearman’s correlation coefficient. ROC curve was used to show the diagnostic accuracy.

3. RESULTS

We assessed 50 patients for eligibility; 10 patients were excluded as they needed mechanical ventilation. Forty patients were included in the study. Thirty-three patients received oxygen therapy from the start, while seven patients needed non-invasive ventilation (NIV) (Figure 1).

The patients had a median age of 57 y. Out of 40, 27 (67.5%) patients were males and 13 (32.5%) were females. The mean weight was 100.0 (85.0-107) kg and Charlson Comorbidity Index was 3.0 (1.0 - 4.0) (Table 1).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>57.0 (51.0-63.0)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>- Male</td>
<td>27 (67.5)</td>
</tr>
<tr>
<td>- Female</td>
<td>13 (32.5)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>100.0 (85.0-107)</td>
</tr>
<tr>
<td>CCI</td>
<td>3.0 (1.0-4.0)</td>
</tr>
</tbody>
</table>

CCI: Charlson Comorbidity Index; Data presented as median (IQR), or n (%)
There was a significant positive correlation between \( EtCO_2 \) and \( SpO_2 \) (\( r = 0.419; P < .007 \)).

Patients who received oxygen therapy had significantly higher \( SpO_2 \) and \( EtCO_2 \) and significantly lower RR and HR compared to patients who received NIV. However, IPI did not differ among both groups (Table 2).

Twenty-one patients who received oxygen therapy and six patients who received an NIV required intubation. In an effort to predict which factor could predict the need for invasive mechanical ventilation, IPI and all its components were compared at baseline on room air. \( SpO_2 \) was significantly lower, while RR was significantly higher in intubated groups compared to non-intubated groups (\( P < 0.001 \) and 0.018), respectively. However, IPI, \( EtCO_2 \), and HR did not differ among both groups (Table 3).

The cut-off value of the \( SpO_2 \) to predict the need for intubation was

<table>
<thead>
<tr>
<th>Table 2: The Integrated Pulmonary Index (IPI) and its components among study cohort data presented as median</th>
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<tbody>
<tr>
<td>Variable</td>
</tr>
<tr>
<td>----------</td>
</tr>
<tr>
<td>IPI-r</td>
</tr>
<tr>
<td>( SpO_2 )-r</td>
</tr>
<tr>
<td>( EtCO_2 )-r</td>
</tr>
<tr>
<td>Rr-r</td>
</tr>
<tr>
<td>Hr-r</td>
</tr>
</tbody>
</table>

\( IPI-r \): integrated pulmonary index on room air, \( SpO_2 \): oxygen saturation, Rr: respiratory rate, Hr: heart rate; \( P < 0.05 \) considered as significant

<table>
<thead>
<tr>
<th>Table 3: The integrated pulmonary index and its components among patients: data presented as median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
</tr>
<tr>
<td>----------</td>
</tr>
<tr>
<td>IPI-r</td>
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<tr>
<td>( SpO_2 )-r</td>
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<tr>
<td>( EtCO_2 )-r</td>
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<tr>
<td>Rr-r</td>
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<tr>
<td>Hr-r</td>
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</tbody>
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\( IPI \): integrated pulmonary index, \( SpO_2 \): oxygen saturation, \( EtCO_2 \): end tidal CO\(_2\), Rr: respiratory rate, Hr: heart rate; \( P < 0.05 \) considered as significant

Figure 2: Receiver-operating characteristic curves comparing the abilities of \( SpO_2 \), RR, \( EtCO_2 \) and IPI for the need for intubation (\( SpO_2 \): peripheral oxygen saturation) RR: respiratory rate, \( EtCO_2 \): end tidal CO\(_2\); IPI: integrated pulmonary index)
It showed 0.719 AUC (95% CI: 0.555 to 0.850, P = 0.018). There was a significant negative correlation between CT score and SpO₂ (p = 0.01). However, there was no correlation between CT score and both IPI and EtCO₂ at baseline (Table 4). Among the patients who needed mechanical ventilatory support, 18 patients died, which represent 45% of all patients in the study.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Correlation coefficient</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SpO₂ → r</td>
<td>-0.408</td>
<td>0.01*</td>
</tr>
<tr>
<td>IPI → r</td>
<td>-0.303</td>
<td>0.07</td>
</tr>
<tr>
<td>EtCO₂ → r</td>
<td>0.017</td>
<td>0.923</td>
</tr>
</tbody>
</table>

Table 4: Correlation between CT score and different parameters

**SpO₂**: oxygen saturation, **IPI**: integrated pulmonary index, **EtCO₂**: end tidal CO₂ (p value significant < 0.05).

4. DISCUSSION

The IPI was not significantly different between patients requiring oxygen therapy and those requiring non-invasive ventilation (NIV), but all components of IPI were significant. This was due to the fact that the IPI algorithm uses real-time measurements and interactions of four parameters (EtCO₂, RR, HR, and SpO₂) to provide a quick assessment of a patient’s respiratory status, and IPI is displayed as a single indexed value ranging from 1 to 10. As the main predictor for IPI was SpO₂, and the median range of SpO₂ in our study was below 85%, the IPI was low (around 1), so the IPI was not significant, according to the calculation methods, which used fuzzy logic inference models.

In our study there was a positive correlation between the end tidal CO₂ and SpO₂. EtCO₂ levels were lower in patients with the COVID-19 virus who developed tachypnea and hypoxia. This was in line with a study by Hu et al., which examined the relationship between EtCO₂ levels and oxygen saturation in COVID-19 patients. They discovered a correlation between the low level of EtCO₂ concentration and low oxygen saturation. This is due to breathlessness, poor pulmonary perfusion, and increased alveolar dead space.

In our study, the cut-off value of the SpO₂ to predict the need for intubation was ≤ 69%, with a sensitivity of 84%, specificity of 85.7%, and an AUC of 0.8 (95% CI 0.7–0.9, P < 0.0001).

It was in line with Mokhtar et al., who described SpO₂ as a predictor for mechanical ventilation. The cut-off value was ≤ 78%, with a sensitivity of 70% and a specificity of 100%, and the AUC was 0.9 (95% CI 0.8–0.96, P < 0.0001). The difference between the cut-off values because in our study we didn’t conduct the study on intubated patients, but in Mokhtar et al., they conducted the study between intubated patients and non-invasive ventilation therapy.

In our study, there was no correlation between the IPI and the CT, who described the correlation between the SpO₂ and CT score and revealed that there was a negative correlation between them (r = −0.6 and P < 0.0001). This is in line with Marco Francone et al., who described the relation between CT score and clinical findings of COVID-19 patients and revealed that CT score is positively correlated with severity of clinical categories and disease phases.

There was no correlation between CT score and EtCO₂ in our study. But a study conducted by Hu, D et al., described the correlation between decreased EtCO₂ levels and disease severity, and revealed that decreased EtCO₂ levels were positively correlated with the severity of the disease. So, we claimed that there was a correlation between CT score and EtCO₂ as both values detected the severity of the disease, but this is contrary to our study results.

5. LIMITATIONS

The study did not provide power in the investigation between IPI and the mortality rate. The CT score used in our study was based on a scoring system specific to COVID-19 patients and did not use the CT score of ARDS to assess the correlation between the CT score and IPI.

6. CONCLUSION

The integrated pulmonary index cannot be used as a single parameter for assessing the severity of the respiratory status of the COVID-19 patients.

7. Data availability

The numerical data generated during this research is available with the authors.

8. Conflict of interest

The authors declare no conflict of interests, and no external or industry funding was involved.

9. Authors’ contribution

SMK: Concept; conduct of the study work
MKA, AMM: Drafting the manuscript; editing.
ASE: Writing study protocol
MAM, SF: Editing of manuscript.
SF: Editing the manuscript.
10. REFERENCES


