Are shock index, modified shock index, NLR and qSOFA useful in making COVID-19 intensive care follow-up decisions?

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Markers of COVID-19 intensive care follow-up decisions

Aim: To meet the increasing intensive care and mechanical ventilator needs during the COVID-19 pandemic process, parameters that will enable rapid assessment and decision-making at the bedside are required in emergency services. The aim is to provide rational use of intensive care units by determining appropriate parameters that can be used to evaluate the intensive care follow-up indication.

Material and Methods: Demographic data, vital signs, and hemogram results were recorded during the consultation in terms of intensive care follow-up requirements of the patients. The qSOFA, shock index, modified shock index, and the neutrophil-lymphocyte ratio were calculated.

Results: Three hundred patients were included in the study. The median age was 69.2 years, 88% of the patients had at least one comorbid disease. The neutrophil-lymphocyte ratio was significant in predicting the need for intubation, but is not an independent risk factor. Male gender, qSOFA scores and need for intubation were predictors of intensive care mortality.

Discussion: We found out that no scoring system can predict the requirement of intubation, but qSOFA is effective in showing mortality when making intensive care follow-up decisions for COVID-19 patients consulted in emergency departments.

Keywords
Coronavirus, Intensive Care Units, Modified Shock Index, Neutrophil-to-Lymphocyte Ratio, qSOFA, Shock Index

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Introduction
Having broken out in Wuhan province of China in December 2019 and being caused by acute respiratory syndrome coronavirus-2 (SARS-CoV-2), Coronavirus Disease 2019 (COVID-19) rapidly spread around the world and caused a pandemic [1]. In a report of 72,314 cases, 14% of the patients were reported to be severely ill, including dyspnoea, low blood oxygen saturation ≤93%, increased respiratory rate and increased oxygen demand [2]. Moreover, 5% were critically ill accompanied by respiratory failure, septic shock and/or multi-organ dysfunction. As the COVID-19 outbreak spread, the need for intensive care units and the increasing number of patients during the pandemic process necessitated the determination of criteria for identifying patients requiring intensive care follow-up [3]. Since the first patient was diagnosed in our country, algorithms and guidelines aimed at guidance strategies in patient follow-up have been prepared and updated by expert scientific committee members [4]. However, for patients who are treated in the emergency service, there are no definitive criteria to predict cases that will develop a need for intubation or have a critical course in the decision-making process of COVID-19-related intensive care follow-up.

Shock index (SI), modified shock index (MSI), quick sequential organ failure assessment (qSOFA) and neutrophil-lymphocyte ratio (NLR) were the parameters used to diagnose patients in shock [5-8]. In patients suffering from severe COVID-19, the clinical course is acute and aggressive, following a course similar to shock [2]. However, their role in determining critically ill patients with COVID-19 is not clear. In order to determine the Intensive Care Unit (ICU) follow-up process of COVID-19 patients and to identify patients’ invasive mechanical ventilation (IMV) requirement early, parameters are necessary for rapid evaluation. Therefore, in this study, the success rate of the scoring systems was evaluated in patients consulted for an indication of ICU follow-up. Our primary study has focused on identifying appropriate parameters for the early diagnosis of critically ill patients.

Material and Methods
Following the approval of the Institutional Ethics Committee [Protocol number: 2020/514/179/13, date: 11/06/2020], informed consent was obtained from the relatives of all COVID-19 patients who were treated in the intensive care unit between March 23 and September 30, 2020. The data were retrospectively analyzed. The study was carried out according to the ethical principles stated in the guides of “Good Medical Practices” and “Good Clinical Practices” of the Declaration of Helsinki. The primary endpoint of the study was to determine the development of intubation and the need for IMV, and the secondary as the presence of mortality in the ICU.

COVID-19 diagnosis:
Nasal and oral swab samples were taken from the patients who applied to the emergency department with complaints of fever, weakness, cough, shortness of breath, chest or headache, abdominal pain, or diarrhea. The diagnosis of COVID-19 followed a positive Real-Time Reverse-Transcriptase Polymerase Chain Reaction (RT-PCR) result.

Data collection:
The demographic data including age, gender, comorbid diseases, number of days of treatment before the ICU admission, chest tomography involvement weight (Mild = less than 50% involvement, Moderate-Severe = more than 50% involvement), tracheal intubation requirement, and ICU mortality were recorded. The examined comorbid diseases were hypertension (HT), diabetes mellitus (DM), coronary artery disease (CAD), cerebrovascular disease (CVD), chronic obstructive pulmonary disease (COPD), asthma, and malignancy (CA). During the consultation, vital parameters such as respiratory rate (RR), Glasgow Coma Score (GCS), heart rate (HR), systolic (SBP) and diastolic blood pressures (DBP), calculated mean arterial pressure (MAP) and NLR were recorded. SI, MSI, qSOFA, and NLR were calculated and the relationship between these parameters and ICU survival and the need for tracheal intubation were determined. The data of the patients were evaluated according to intubation and mortality and were interpreted under two main tables.

SI was calculated with the formula \[
\text{SI} = \left( \frac{\text{SpO}2}{\text{FiO}2} \right) / \text{RR}
\]
MSI was calculated with the formula \[
\text{MSI} = \left( \frac{\text{SpO}2}{\text{FiO}2} \right) / \text{RR}
\]
The qSOFA score included 3 clinical criteria that assign 1 point each for blood pressure (SBP ≤ 100 mmHg), respiratory rate (>22 breaths / minute) and consciousness (GCS score <15). The score ranges from 0 to 3 points. A score of 2 or more was considered positive [7]. The NLR value was calculated using a hemogram test, which is routinely performed during the admission of patients to the emergency department. The study included all adult patients whose necessary data were available and who were consulted with the diagnosis of COVID-19 because of the necessity of follow-up in the ICU.

Statistical analysis:
Statistical analyzes were performed with the SPSS 21 program. Quantitative variables, expressed as mean ± Standard deviation, were compared using the One-way Anova test. Qualitative variables were expressed as percentages and compared using either the chi-square test or Fisher’s exact test. A multivariate analysis was performed to evaluate the significant variables associated with intubation and mortality. A p < 0.05 was considered significant.

Results
The data of 300 patients who were followed up in the ICU due to COVID-19 were evaluated. The median age of the patients was 69.2 years, 63.7% of them were males. In 88% of the patients, at least one comorbid disease was present, and the most common accompanying disease was hypertension with a rate of 52.2%. While 66 patients were followed without intubation, 234 patients constituted the intubated group. There was no difference between the groups in terms of age and comorbid diseases, but the male gender ratio was higher in the intubated group. The average number of treatment days the patients received before ICU admission was 1.98 ± 3.1 days, and there was no difference between the two groups according to the tracheal intubation requirement. Computed Tomography (CT) evaluation of 232 patients revealed moderate to severe involvement, and both groups were similar. To determine the need for intubation, no difference was observed between the two groups in terms of qSOFA, SI, and MSI calculated during
admission to ICU. A higher NLR was found in the intubated group (9.4 vs 17.2; p < 0.05, Table 1) in univariate analysis, but it is not an independent risk factor for intubation. Table 2 shows the relationship between patient demographics and mortality. The two groups were similar in terms of age and presence of comorbidity. Male patients had a significantly higher mortality rate (69.7%). No significant difference was observed between the CT classification of the patients and the treatment day before ICU and the presence of mortality (Table3). Table 3 also examines the criteria that can be used to predict mortality during admission of patients to ICU. There was no difference between the two groups in terms of SI and MSI during ICU admission. While 29.9% of patients with mortality were Qsofa-positive, this rate was 17.2% in patients who did not develop, and the difference was statistically significant. While the mean NLR value of 201 patients in the mortality group was 18.1, it was 10.2 in 99 patients who did not die, but it is not an independent risk factor for mortality (p=0.100). Besides, there was a significant correlation between intubation and mortality.

**Discussion**

In this study, we investigated the possibility of using SI, MSI, NLR and qSOFA scores to be indicators of mortality. Mortality was higher in cases with a high intubation ratio and positive qSOFA. In our study, male gender and the need for mechanical ventilation were associated with a high mortality rate. Our results were similar with a study conducted in Italy [9]. The mortality rate was higher in patients requiring IMV. However, mortality was not observed in a small group of extubated patients in the intensive care unit. All these patients were discharged to the ward.

Studies have shown that clinical signs of shock are present in critical COVID-19 patients, even in the absence of hypotension [10]. This has revealed the presence of a viral sepsis mechanism in COVID-19. According to the Chinese data, the prevalence of shock reported in adult patients with COVID-19 varies greatly depending on the patient population studied and the definition of shock (1% to 35%) [2]. In another analysis, acute respiratory distress syndrome (ARDS), septic shock, and acute renal failure were identified as possible clinical manifestations associated with critically ill COVID-19 patients [11, 12]. Therefore, early diagnosis of COVID-19 patients also suffering from shock may prove effective in early ICU follow-up and intubation decisions.

There are some markers used to detect early shock, such as qSOFA, SI, MSI, and NLR values. After the new definition of sepsis [7] was published, the qSOFA score was recommended for pre-evaluation in intensive care admissions with a diagnosis of septic shock [13]. We also found that qSOFA is a practical and useful indicator of COVID-19-related ICU mortality in emergency patient evaluation. Another sepsis marker is NLR. Previous studies have shown that NLR during hospitalization was an independent predictor of in-hospital mortality in COVID-19 patients with sepsis who were admitted to the emergency service. In a retrospective analysis of 63 patients in China, NLR was found to be an independent risk factor for severe COVID-19 [14]. In a meta-analysis involving 1579 patients, NLR was found to be an acceptable predictor of disease severity and mortality in COVID 19 patients. It is stated that it can contribute to reducing the overall mortality rate of 19 by helping clinicians to detect serious cases early, triage them quickly, and start their treatment effectively [8]. In this review, NLR> 9.11 has been used as an independent predictor in critically ill patients. In our study, we found that NLR is significantly higher in the mortality group, but is not an independent risk factor. It has been reported that SI is a useful parameter for early diagnosis of sepsis, acute critical illness, unplanned ICU transfers, risk stratification for pulmonary embolism, acute

**Table 1. Factors affecting the need for intubation**

<table>
<thead>
<tr>
<th>Intubation -</th>
<th>Intubation +</th>
<th>Total n: 300</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT involvement Mild</td>
<td>20 (60.3)</td>
<td>48 (60.5)</td>
<td>68 (62.2)</td>
</tr>
<tr>
<td>Moderate to Severe</td>
<td>46 (65.7)</td>
<td>115 (62.6)</td>
<td>185 (65.7)</td>
</tr>
<tr>
<td>Pre ICU treatment day</td>
<td>2.2±2.8</td>
<td>1.9±3.2</td>
<td>1.98±3.1</td>
</tr>
<tr>
<td>q SOFA (+)</td>
<td>14 (62.1)</td>
<td>63 (26.9)</td>
<td>77 (25.7)</td>
</tr>
<tr>
<td>SI</td>
<td>0.25±0.44</td>
<td>0.32±0.46</td>
<td>0.30±0.46</td>
</tr>
<tr>
<td>MSI</td>
<td>0.69±0.55</td>
<td>0.71±0.53</td>
<td>0.70±0.53</td>
</tr>
<tr>
<td>NLR</td>
<td>9.4±9.3</td>
<td>17.2±25.5</td>
<td>15.5±23.0</td>
</tr>
<tr>
<td>ICU mortality</td>
<td>9 (33.6)</td>
<td>192 (68.4)</td>
<td>201 (67.0)</td>
</tr>
</tbody>
</table>


**Table 2. The effect of demographic characteristics of the patients on mortality**

<table>
<thead>
<tr>
<th>Mortality -</th>
<th>Mortality +</th>
<th>Total n: 300</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>69.5±13.5</td>
<td>69.23±13.8</td>
<td>0.912*</td>
</tr>
<tr>
<td>Gender: Female</td>
<td>48 (64.8)</td>
<td>61 (65.7)</td>
<td>109 (63.6)</td>
</tr>
<tr>
<td>Male</td>
<td>51 (65.5)</td>
<td>140 (60.7)</td>
<td>191 (62.3)</td>
</tr>
<tr>
<td>Additional Illness</td>
<td>88 (68.9)</td>
<td>176 (68.7)</td>
<td>264 (68.8)</td>
</tr>
<tr>
<td>HT</td>
<td>55 (65.6)</td>
<td>99 (69.9)</td>
<td>154 (65.3)</td>
</tr>
<tr>
<td>DM</td>
<td>39 (62.9)</td>
<td>52 (62.9)</td>
<td>91 (63.0)</td>
</tr>
<tr>
<td>CVD</td>
<td>1 (12.1)</td>
<td>7 (63.5)</td>
<td>8 (62.7)</td>
</tr>
<tr>
<td>COPD</td>
<td>25 (62.3)</td>
<td>45 (62.4)</td>
<td>70 (62.3)</td>
</tr>
<tr>
<td>Asthma</td>
<td>24 (62.3)</td>
<td>40 (61.9)</td>
<td>64 (62.3)</td>
</tr>
<tr>
<td>CA</td>
<td>17 (67.2)</td>
<td>51 (62.4)</td>
<td>68 (62.7)</td>
</tr>
<tr>
<td>CAD</td>
<td>27 (63.7)</td>
<td>78 (68.8)</td>
<td>115 (63.8)</td>
</tr>
</tbody>
</table>

*One-way Anova, *Pearson Chi-Square, HT: Hypertension, DM: Diabetes Mellitus, CVD: Coronary Artery Disease

**Table 3. Factors affecting the ICU mortality**

<table>
<thead>
<tr>
<th>Mortality -</th>
<th>Mortality +</th>
<th>Total n: 300</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT involvement Mild</td>
<td>26 (60.3)</td>
<td>62 (60.9)</td>
<td>68 (62.2)</td>
</tr>
<tr>
<td>Moderate to Severe</td>
<td>73 (67.3)</td>
<td>159 (67.1)</td>
<td>232 (67.3)</td>
</tr>
<tr>
<td>Pre ICU treatment day</td>
<td>2.0±2.7</td>
<td>1.9±3.5</td>
<td>1.98±3.1</td>
</tr>
<tr>
<td>q SOFA (+)</td>
<td>17 (61.2)</td>
<td>60 (62.9)</td>
<td>77 (25.7)</td>
</tr>
<tr>
<td>SI</td>
<td>0.25±0.44</td>
<td>0.32±0.47</td>
<td>0.30±0.46</td>
</tr>
<tr>
<td>MSI</td>
<td>0.68±0.54</td>
<td>0.72±0.53</td>
<td>0.70±0.53</td>
</tr>
<tr>
<td>NLR</td>
<td>10.2±9.1</td>
<td>18.1±27.0</td>
<td>15.5±23.0</td>
</tr>
<tr>
<td>Intubation</td>
<td>42 (62.4)</td>
<td>192 (68.5)</td>
<td>201 (67.0)</td>
</tr>
</tbody>
</table>

myocardial infarction, and death [5, 15, 16]. Besides, the conducted studies have indicated that high shock index values are associated with death from critical illnesses [17]. In addition to similar benefits, mean blood pressure values are taken into account in MSI, and guidelines recommend the initiation and titration of vasopressor treatments based on MAP. The Surviving Sepsis Campaign guidelines on the management of adults with COVID-19 in the ICU are based on MAP monitoring, not vital signs such as SBP, to guide both fluid and vasoactive requirements [18]. Additionally, Nathan J. et al. [6] showed that there is a significant risk of death in critically ill patients with high MSI within the first 24 hours after admission to the ICU. Considering that MSI can be easily calculated at the bedside, it is stated that its use in practice may be beneficial for clinicians to initiate interventions earlier that may increase survival. Based on the fact that COVID-19 is a newly-recognized disease and progresses in combination with shock in critically ill patients, we retrospectively evaluated SI and MSI to determine the ICU follow-up indication, and found that they could not predict ICU mortality. There are also studies in the literature using similar markers to predict the need for early diagnosis of intubation in septic shock. Most COVID-19 patients with severe respiratory failure should be followed up in the ICU due to the need for intubation and IMV. However, while making this decision, it is necessary to consider a number of factors, including timing. There are also views opposing the idea that early intubation may be beneficial [19-22]. In the study by Sangita Trivedi et al. [23], pre-intubation SI and MSI were addressed as easily accessible, non-invasive, bedside clinical tools to identify patients with high complication risk. While a pre-intubation SI value of ≥ 0.90 was defined as an important predictor of post-intubation hypotension and ICU mortality, MSI was stated to be useless in predicting any outcome. Although deciding on the necessity of tracheal intubation in COVID-19 intensive care follow-up is of significance in terms of survival, we could not find any significant contribution of qSOFA, MSI, SI or NLR values in predicting intubation. Conclusion In this study, we found out that no scoring system can predict the requirement of intubation, but qSOFA is effective in showing mortality when making ICU follow-up decisions in COVID-19 patients consulted in the emergency department. We concluded that we still need parameters and studies in larger series that will guide us in making this critical decision.

Scientific Responsibility Statement
The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement
All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest
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