

RESEARCH ARTICLE

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Prognostic Value of Integrated Pulmonary Index (IPI) Value in Determining Pneumonia Severity in Patients Diagnosed with COVID-19 Pneumonia in the Emergency Department

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Abstract

Objective: This study aimed to examine the predictive power regarding prognosis of the Integrated Pulmonary Index (IPI) values measured at admission for patients diagnosed with COVID-19 pneumonia in the emergency department. In addition, the correlation between CURB-65 and PSI scores and IPI values in COVID-19 pneumonia was also examined.

Methods: The study was conducted between April 2020 and December 2020 as a prospective study. We evaluated respiratory function using IPI monitoring system that includes oxygen saturation, end-tidal CO₂, respiratory rate, and pulse rate. For patients diagnosed with COVID-19 pneumonia in the emergency department, the IPI value was measured at the time of admission and PSI and CURB-65 scores were calculated. The predictive power of the IPI value in patients with clinical severity and the correlations between clinical severity and PSI, CURB-65 and IPI scores were examined. All of the data that was obtained during the study was recorded in the study form and evaluated using the IBM SPSS 22.0 statistical program in which P <0.05 was considered to be statistically significant.

Results: A total of 81 patients were included in the study. When the severity of pneumonia was compared with the CURB-65, PSI and IPI values, a statistically significant difference was found between the clinical severity groups for all scores (p<0.001 for each score). Although the correlation between clinical severity, CURB-65 and PSI scores was positive and moderate (r:0.556 and r:0.613, respectively), the correlation between clinical severity and IPI value was found to be inverse and strong (r:0.824). While the IPI value was green, the sensitivity to predict mild pneumonia was 94.92%, and the specificity was 54.55%.

Conclusion: Although all of the scores showed a significant correlation with clinical severity in patients with COVID-19 pneumonia, this correlation was moderate in PSI and CURB-65 scores, while there was a strong inverse correlation between IPI value and clinical severity. Considering the ease of use of the IPI value and its correlation with the clinic, we believe that it is more successful than CURB-65 and PSI scores in predicting clinical severity in patients with COVID-19 pneumonia.

Key words: COVID-19 pneumonia, integrated pulmonary index, pneumonia severity index, CURB-65

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INTRODUCTION

Scales such as the pneumonia severity index (PSI) and CURB-65 are used to determine the severity and necessary management of the disease in patients that were admitted with pneumonia to the emergency services. However, the predictive value of these scales for COVID-19 pneumonia is unknown.

The Integrated Pulmonary Index (IPI) is a newly-adapted monitor of measurement which can be used to evaluate ventilation and oxygenation in patients, and allows for quick evaluation of the respiratory status of the patient. Arterial oxygen saturation (SpO₂), end-tidal carbon dioxide (PetCO₂), respiratory rate (RR) and heart rate (HR) parameters are frequently used to evaluate respiratory functions in patients. IPI is created by combining SpO₂, PetCO₂, SS and HR values in a mathematical model and can provide the clinician with the opportunity to evaluate all these parameters through a single data form. This index value can be followed continuously on the monitor as digital data or as a waveform (1). Through a noninvasive, dynamic and real-time measurement, IPI monitoring provides guidance in assessing the patient's respiratory status swiftly and determining whether there is a need for intervention (1).

Health systems across the world have become overburdened as an increasing number of patients have been checking as a result of the COVID-19 pandemic (2). When it comes to

clinical management, a measurement tool suitable for use in triage can be very valuable for emergency physicians in identifying patients with mild clinical severity COVID-19 pneumonia who can be treated as outpatients.

The aim of this study is to examine the predictive power regarding prognosis of the IPI values measured at admission for patients diagnosed with COVID-19 pneumonia in the emergency department. In addition, the correlation between the aforementioned pneumonia scores and IPI values in COVID-19 pneumonia was also investigated.

METHODS

This study is a prospective study. It was conducted following the approval of the local ethics committee between April 2020 and December 2020 in the emergency department of a training and research hospital.

Study population

Study population was defined with consecutive sampling. Patients over the age of 18 who came to the emergency department with complaints such as fever, cough, and shortness of breath and were subsequently diagnosed with COVID-19 pneumonia were included in the study. Patients whose information could not be accessed in the hospital registry system for any reason, who were under the age of 18, had a history of recent hospitalization (within the last 2 weeks), were pregnant, and/or refused to participate in the study were excluded.

Pneumonia diagnosis criteria were defined according to the current guidelines: the patient had at least one additional symptom of lower respiratory tract disease in addition to coughing (such as phlegm, dyspnea, pleuritic chest pain, tachypnea), new focal chest findings in physical examination (rale or bronchial breath sounds), at least one systemic finding (such as sweating, aching, chills, fever, body temperature above 38°) and these complaints could not be explained in any other way (3). The diagnosis of COVID-19 pneumonia was given by the presence of positive PCR (polymerase chain reaction) results and characteristic thoracic tomography findings in addition to the existing pneumonia definition criteria.

Patients were classified as mild, moderate, or severe according to local COVID-19 pneumonia management and treatment guidelines (4). Patients with symptoms such as fever, muscle/joint pain, cough and sore throat, whose respiratory rate is <30 /minute, $SpO_2 > 90$ in room air with mild-moderate pneumonia findings on chest X-ray or tomography are considered to have mild-moderate pneumonia. According to the guideline, those with a respiratory rate of <24 /minute and $SpO_2 \geq 94\%$ in room air was in the mild pneumonia group, and it was suggested that they could be followed up on as outpatients provided that the involvement was below 50% in thorax tomography. Pneumonia patients with respiratory rate between 24-29/minute and

SpO_2 level between 91-93% in room air are categorized in the moderate group, and it is recommended that these patients be admitted and followed up in the service. Severe pneumonia patients have symptoms such as fever, muscle/joint pain, cough and sore throat, their respiratory rates are ≥ 30 /minute, SpO_2 level $\leq 90\%$ in room air, and have bilateral pneumonia findings of more than 50% on chest X-ray or tomography. It is recommended that these patients be monitored in the intensive care unit (ICU).

Data collection

Demographic data, physical examination findings, comorbid diseases, vital signs, consciousness at the time of admission, laboratory and radiological imaging results, pneumonia severity and clinical outcomes of the patients included in the study were recorded in a form that was prepared in advance. PSI and CURB-65 scores were calculated for all patients.

IPI measurement was carried out simultaneously as the examination and treatment began, after detailed anamnesis and physical examination was done for patients who were thought to be pre-diagnosed with COVID-19 pneumonia. This measurement was conducted with a Microstream Bedside Capnography Monitoring® device with a probe attached to the index finger of the left hand and a nasal cannula (Oridion Filter Line®) to be used for $etCO_2$ measurement. The probe was

attached for two minutes, and the value at the end of the second minute was taken as the measurement value. The IPI value is a scoring category which uses red, yellow, and green to classify the severity of the patients' respiratory status. If the IPI value is 1-4 it is classified as red, 5-7 as yellow, and 8-10 as green (1). As the IPI value decreases, the clinical severity of the patient increases and indicates the need for urgent intervention. Score definition was given in appendix.

Appendix 1: Numeric score definition of IPI

Ipi Score	Patient's Condition
10	Normal
8-9	Close to normal
7	Close to normal but should be monitored
5-6	Should be monitored, intervention may be required
3-4	Intervention is required
1-2	Immediate intervention is required

Outcomes

Primary outcome of this study was to examine predictive power of IPI value to severity of COVID-19 pneumonia. Secondary outcome was defined as correlation of IPI value with existing pneumonia severity scores in patients with COVID-19 pneumonia.

Statistical Analysis

Data analysis was performed using SPSS for Windows 22 package program (Chicago, Illinois, USA). After determining whether the data was normally distributed with the Kolmogorov-Smirnov test, all data was presented as mean±standard deviation or the

median and the interquartile range (IQR 25%-75%). Categorical variables were evaluated with the Chi-square test and continuous variables were evaluated with the Kruskal Wallis test or Mann Whitney U test. The relationship between the PSI, CURB-65 scores and IPI values of the patients was examined with the Pearson or Spearman correlation test. IPI scores and congruence with clinical severity were evaluated with the diagnostic 2x2 table. The statistical significance level was accepted as $p < 0.05$ for all calculations.

Power analysis

First this study was planned as a prospective study on patients with community acquired pneumonia and sample size had been calculated according to it. Later, because of the impact of COVID-19 pandemic, most of the patients were diagnosed as COVID-19 pneumonia and analyses done at this subgroup.

This studies post hoc power analyses were done by G* Power 3 1 9 7 program (5). With the data of the study with total sample size of 81, correlation for primary outcome of the study was calculated as 0.824. For correlation analyses with %5 type I error ($\alpha:0.05$), power of the study was calculated as 0.99.

RESULTS

A total of 81 patients diagnosed with COVID-19 pneumonia were included in the study, and the mean age of the patients was 62 ± 15 years. A total of 45 of the patients were women. According to the severity of COVID-

19 pneumonia, 22 of the patients were in the mild, 14 in the moderate and 45 in the severe pneumonia group. Demographic data, vital signs and radiological imaging findings of the patients are shown in Table 1.

Table 1. Demographic Characteristics of the Patients, Distribution of Pneumonia Severity, Vital findings and Radiological imaging findings (n=81)

Age (Years)	62 ± 15
Sex	
Female	45
Male	36
Pneumonia Severity category	
Mild	22
Moderate	14
Severe	45
Vital findings	
Systolic blood pressure (mmHg)	130 (IQR 115 – 140)
Diastolic blood pressure (mmHg)	80 (IQR 66 – 83)
Pulse (/min)	95 ± 14,5
Temperature (°C)	38 (IQR 37,25 – 38,35)
Respiratory Rate (/min)	31 ± 9,4
SpO2 (%)	89 (IQR 84 – 94)
End Tidal CO2	29 (IQR 23,5 – 32)
Radiological imaging findings	
Lobar or Segmental Consolidation	58
Ground-Glass Infiltration	80
Pleural Effusion	10
Air Bronchogram	7
	5

*Data are given as n, mean ± standard deviation or median (interquartile range %25 – %75).

When the severity of pneumonia was compared with the CURB-65, PSI and IPI values, a statistically significant difference was found between the clinical severity groups for all scores ($p < 0.001$ for each score). When pairwise comparisons were made in terms of all scores, it was found that the statistical difference for CURB-65 was due to the difference between mild and severe pneumonia groups. There appeared to be no significant difference between mild-moderate and

moderate-severe pneumonia groups in terms of CURB-65 score (p value < 0.001 , 0.06, 0.06, respectively). Although there was a noteworthy difference in all subgroup analyzes (mild-moderate, moderate-severe, mild-severe) in terms of PSI and IPI values, it was shown that this difference was more significant for the IPI value (p values of mild-moderate, moderate-severe and mild-severe groups for PSI were 0.045, 0.024, < 0.001 , respectively; and were 0.001, < 0.001 , < 0.001 for IPI, respectively) (Table 2).

When the correlation between the scores was analyzed, a statistically significant correlation was found between all paired groups (CURB-65 and PSI, CURB-65 and IPI, PSI and IPI) ($p < 0.001$, $r: 0.828$, $r: -0.720$ and -0.748 , respectively). While the strongest correlation was found between CURB-65 and PSI as a positive correlation, a strong-level inverse correlation was found between IPI and the other two scores. The correlation of CURB-65, PSI and IPI values with the clinical severity group was also examined in the patients, and a statistically significant correlation was found for all scores ($p < 0.001$). While the correlation between clinical severity and CURB-65 and PSI scores was positive and moderate ($r: 0.556$ and $r: 0.613$, respectively); the correlation between clinical severity and IPI value was found to be inverse and strong ($r: 0.824$) (Table 3).

The IPI value is categorized as red, yellow, green. It is classified as red if the IPI value is 1-4, yellow if 5-7, and green if 8-10. The prognostic value of the color categories in terms of clinical severity was also calculated. While the IPI value was green, the sensitivity to predict mild pneumonia was 94.92%, and the

specificity was 54.55%. The positive likelihood ratio (PLR) and negative likelihood ratio (NLR) were 2.09 and 0.09, respectively. When the IPI value was red, its sensitivity was 97.78% and its specificity was 83.33% in predicting severe pneumonia. PLR and NLR were 5.87 and 0.03, respectively (Table 4).

Table 2: Relationship between CURB-65, PSI and IPI scores with disease severity of patients

Scores	All of the patients n(81)	Mild pneumonia n(22)	Moderate pneumonia n(14)	Severe pneumonia n(45)	P value
CURB-65	1 (1 – 3)	1 (0 – 1)	1 (0,75 – 2,25)	2 (1 – 3)	<0,001
<i>Mild to moderate</i>					0.06
<i>Moderate to severe</i>					0.06
<i>Mild to severe</i>					<0,001
PSI	77 (56,5-108,5)	53 (38,75-62,25)	65,5 (48,75-118,5)	97 (78,5-123)	<0,001
<i>Mild to moderate</i>					0.045
<i>Moderate to severe</i>					0.024
<i>Mild to severe</i>					<0,001
IPI	3 (1 – 6)	8 (6 – 9)	5 (3,75 – 6,5)	1 (1 – 3)	<0,001
<i>Mild to moderate</i>					0.001
<i>Moderate to severe</i>					<0,001
<i>Mild to severe</i>					<0,001

*Data are given as median (interquartile range %25 – %75). Abbreviation: CURB-65: confusion, uremia, respiratory

rate, blood pressure, age older than 6, PSI: Pneumonia severity index, IPI: integrated pulmonary index

Table 3: Evaluation of the correlations of the used scores with each other and with the severity of the disease

	P value	R value
Correlation between score pairs		
• CURB-65 and PSI	<0,001	0.828
• CURB-65 and IPI	<0,001	-0.720
• PSI and IPI	<0,001	-0.748
Correlation between the scores and disease severity		
• Disease severity and CURB-65	<0,001	0.556
• Disease severity and PSI	<0,001	0.613
• Disease severity and IPI	<0,001	-0.824

Table 4: Prognostic value of IPI color

	Predictive value for mild pneumonia when IPI is green	Predictive value for severe pneumonia when IPI is red
Sensitivity (%)	%94,92	%97,78
%95CI*	(%85,85- %98,94)	(%88,23- %99,94)
Specificity (%)	%54,55	%83,33
%95CI	(%32,21- %75,61)	(%67,19- %93,63)
PLR	2.09	5.87
%95CI	(1,32- 3,32)	(2,82- 12,2)
NLR	0.09	0.03
%95CI	(0,03- 0,29)	(0- 0,21)
Accuracy	%83,95	%91,36
%95CI	(%74,12- %91,17)	(%83- %96,45)

DISCUSSION

There are two main results of the study in which the effectiveness of the IPI value measured at the time of admission in patients diagnosed with COVID-19 pneumonia in the emergency department in predicting the severity of pneumonia in the patient and the correlations of the IPI value with the PSI and CURB-65 scores were studied. First and foremost, it was found out that the IPI score had gradually decreasing values in patients with mild, moderate and severe pneumonia, and a statistically significant difference was found between these groups. This result means that by using the IPI score, it is possible to have an idea about the clinical severity of the patient in the early period. Thus, with the early detection of patients with mild pneumonia, unnecessary examinations and long stays in the emergency department can be avoided. Early detection of severe pneumonia patients, on the other hand, may improve patient management by giving the physician a chance to intervene earlier on behalf of these patients.

The second result is that a highly significant, inverse correlation was found between the IPI value and the PSI and CURB-65 scores. The reason why the correlation was found to be inverse is because in the IPI score worst prognosis is given to the lowest score, not the highest score, as it is in the other two types of scores. When the correlation of the clinical severity of the cases included in the study with the IPI value, CURB-65 and PSI scores was

examined, a moderately significant positive correlation was found between CURB-65 and IPI scores and pneumonia severity, although a highly significant inverse correlation was found between IPI score and pneumonia severity. Due to this fact, it is thought that in COVID-19 pneumonia, the IPI value is a better indicator in determining mild, moderate and severe pneumonia in patients compared to other scores.

COVID-19 is a disease in which viral pneumonia is the most common organ involvement, and its clinical course is often mild to moderate (81%). However, it may be severe (14%) in some patients, and might even be so severe that intensive care follow-up is required (5%) (6). Mortality rate is very high in hospitalized patients, ranging from 11-28% (7). Therefore, a marker that can be used at the time of admission to predict patients prone quickly and easily to more severe cases provide physicians with an opportunity for early intervention and appropriate resource use.

In case of pneumonias, it is strongly recommended to routinely use structured clinical decision algorithms such as the pneumonia severity index (PSI) and CURB65 in determining the severity and management of the disease in patients that were admitted (8). These algorithms allow early identification of the severe patient group and prompt commencement of absolute treatment, as well as preventing unnecessary hospitalizations of low-risk patient groups and encouraging safe discharge. There are

publications suggesting that CURB-65 and PSI scores can be used to assess clinical severity and determine the risk of 14-day mortality in COVID-19 patients (9, 10). However, the accuracy of these scores in COVID-19 pneumonia has not yet been clearly demonstrated (11). Moreover, in the present study, the correlation between clinical severity and IPI were found to be much higher than the correlation between clinical severity and CURB-65 and PSI.

Another aspect that makes the use of the IPI value advantageous is that it provides an easy interpretation by reducing many vital parameters to a single value, which makes it possible to quickly evaluate the respiratory status of the patient in triage through a noninvasive and real-time measurement (1). The PSI score includes many parameters such as patient demographics, medical history, emergency department admission vitals, laboratory parameters and radiological findings; however, it takes time to make that calculation (12). Therefore, considering the patient load created by the pandemic, the nature of it limits its use by emergency physicians. The CURB-65 score is a more convenient score that assesses patients' age, level of consciousness, respiratory rate, systolic blood pressure, and blood urea levels (13). However, these scores do not seem to take hypoxemia into account, despite the fact that it is a parameter directly related to clinical severity. Aliberti S. et al. reported that 127 out of 218

patients with a CURB-65 score of 0-1 were hospitalized, and hypoxemia was shown as the biggest reason for hospitalization (14).

When the prognostic value of IPI color was examined, it was seen that while IPI was green, its sensitivity to predict mild pneumonia was 94.92%, its specificity was 54.55%, and the PLR (positive likelihood ratio) and NLR (negative likelihood ratio) values were 2.09 and 0.09, respectively. This result suggests that the IPI value may be a good triage score for early detection and rapid discharge from the emergency department of COVID-19 patients with mild pneumonia. When IPI was red, it had a sensitivity of 97.78%, a specificity of 83.33%, and a PLR value of 5.87 and an NLR value of 0.03 in detecting severe pneumonia. IPI is an algorithm calculated based on momentary vital signs, and baseline vital values may change after initial treatment in the emergency department. Therefore, the PLR value was low, as we predicted the outcome with a single IPI value measured at the beginning. The IPI value re-measured after emergency treatment may be more effective in predicting the outcome.

LIMITATIONS

Due to the study protocol, the IPI value was only measured at the time of admission to the emergency department. Since IPI is a value that is affected by momentary vital parameters, changes in vital signs after primary care in the emergency department may increase the IPI value. Therefore, in order to better demonstrate

the power of IPI in predicting the final outcome, conducting another measurement after the first line treatment in the emergency department would be appropriate. Second important limitation of this study was determining COVID-19 pneumonia severity according to local guidelines. Since that was a new emerged disease, there was not any global recommendation and management of the patients were done with local guidelines at every country.

CONCLUSION

It was shown that the IPI score in patients with COVID-19 pneumonia is significantly reduced in patient groups with mild, moderate and severe pneumonia. Although all of the scores showed a significant correlation with clinical severity, this correlation was moderate in PSI and CURB-65 scores, while there was a strong inverse correlation between IPI value and clinical severity. In addition, it was shown that the IPI value predicts mild pneumonia with high sensitivity and NLR in the green category, while it predicts severe pneumonia with high sensitivity and specificity in the red category. Considering the ease of use of the IPI value and its correlation with the clinic, we believe that it is more successful than CURB-65 and PSI scores in predicting clinical severity in patients with COVID-19 pneumonia.

Ethics Committee Approval: Ethics committee approval was received for this study from local ethics

committee at Keçiören Training and Research Hospital in 2019, file number 2012-KAEK-15/2010.

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