Severity scores in COVID-19 pneumonia: a multicenter, retrospective, cohort study

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Abstract

Background: Identification of patients on admission to hospital with Coronavirus infectious disease 2019 (COVID-19) pneumonia who can develop poor outcomes have not yet ben comprehensively assessed.

Objective: To compare severity scores used for community acquired pneumonia to identify high-risk patients with COVID-19 pneumonia.

Design: PSI, CURB-65, qSOFA and MuLBSTA, a new score for viral pneumonia, were calculated on admission to hospital to identify high-risk patients for in-hospital mortality. Area under receiver operating characteristics curve (AUROC), sensitivity and specificity for each score were determined and AUROC were compared among them.

Participants: Patients with COVID-19 pneumonia included in the SEMI-COVID-19 Network.

Key results: We examined 10,238 patients with COVID-19. Mean age of patients was 66.6 years and 57.9% were males. The most common comorbidities were: hypertension (49.2%), diabetes (18.8%) and chronic obstructive pulmonary disease (12.8%). Acute respiratory distress syndrome (34.7%) and acute kidney injury (13.9%) were the most common complications. In-hospital mortality was 20.9%. PSI and CURB-65 showed the highest AUROC (0.835 and0.825, respectively). qSOFA and MuLBSTA had a lower AUROC (0.728 and 0.715, respectively). qSOFA was the most specific score (specificity 95.7%) albeit its sensitivity was only 26.2%. PSI had the highest sensitivity (84.1%) and a specificity of 72.2%.

Conclusions: PSI and CURB-65, specific severity scores for pneumonia, were the best scores for COVID-19 pneumonia and were better than qSOFA and MuLBSTA. Additionally, qSOFA, the simplest score to perform, was the most specific albeit the least sensitive.

Text

Background

At the end of 2019, a novel coronavirus was identified as the cause of an outbreak of pneumonia cases in Wuhan, Hubei Province, China. This virus, now known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), rapidly spread around the world, causing a pandemic that has affected more than 22·5 million people as of 21th august, 2020. [1, 2, 3] The disease that it produces is called coronavirus disease 2019 (COVID-19) and is characterized by a wide spectrum of infectious symptoms that range from mild to severe, with acute respiratory distress syndrome (ARDS) as its primary complication.[4, 5, 6] Hospitalization is required in 6% to 20% of patients. [7, 8] Mortality among hospitalized patients is high, ranging from 11% to 28%.[4, 5] Therefore, early and simple identification upon admission to hospital of patients who may have poor outcomes would be of considerable value and may help lead to prompt treatment and an optimized use of resources.

Several prognostic scores have been developed to identify elevated risk of death in patients with community-acquired pneumonia (CAP). Two of them, the Pneumonia Severity Index (PSI) and the Confusion, Urea, Respiratory rate, Blood pressure, 65 years of age and older (CURB-65) score, are well-validated scores for supporting pneumonia prognoses.[9, 10] The multilobar infiltration, hypo-lymphocytosis, bacterial coinfection, smoking history, hypertension, and age (MuLBSTA) score, which is based on six parameters routinely measured in hospitals, is a new prognostic tool for patients hospitalized with viral pneumonia[11] and has been suggested as a severity score for patients with COVID-19.[5] The quick sequential organ failure assessment scale (qSOFA),

based on the sepsis-3 definition,[12] has proven to be a useful tool in the emergency department,[13, 14] non-intensive-care-unit (ICU) wards,[15, 16, 17] and even at home [18, 19] for establishing a prognosis in patients with documented or suspected infection with different foci. Recent works indicate that qSOFA is also a useful tool for identifying patients with poor prognoses in viral infections such as influenza.[20, 21, 22] In addition, qSOFA has shown good performance in predicting prognosis in pneumonia, both in the emergency department [23, 24, 25, 26, 27] and in wards.[28] The advantage of the qSOFA score is that the variables are clinical and thus laboratory tests are not required.[12]

Objective

In this study, we aim to ascertain the applicability and prognostic prediction value of the PSI, CURB-65, MuLBSTA, and qSOFA severity scores in COVID-19 patients with pneumonia admitted to hospital.

Design

Study design and participants

This work is a multicenter retrospective cohort study of patients with SARS-CoV2 infection, aged ≥18 years, and with CAP who were hospitalized between March 1st and May 28th 2020 in Spain and included in the aforementioned SEMI-COVID-19 Registry.[29] The registry is an initiative of the Spanish Society of Internal Medicine (SEMI, for its initials in Spanish), its characteristics have been described elsewhere.[29] Data are collected retrospectively and include

epidemiological and clinical characteristics, such as comorbidities, symptoms, physical examination findings, laboratory and diagnostic imaging test results, and clinical outcomes.

Definition of variables

COVID-19 pneumonia was defined as compatible symptoms (cough, dyspnea, need for respiratory support, fever, or crackling or rales on auscultation), pulmonary infiltrates or consolidation detected by a chest X-ray or computerized tomography (CT) scan, and a positive result on either a polymerase chain reaction test of a nasopharyngeal sample or a serology test for COVID-19 antibodies.

We defined PSI, CURB-65, MuLBSTA, and qSOFA as originally described.[9, 10, 11, 12] The PSI is a scale with 19 variables with different point values.[9] A cut-off of 91 points (Risk Class IV-V) was considered positive for a poor prognosis.[24, 25, 26, 27, 28] We considered CURB-65 to be predictive of poor prognosis when three of the five variables (confusion, BUN >7 mmol/L, respiratory rate ≥30 bpm, systolic blood pressure <90 mmHg or diastolic blood pressure ≤60 mmHg, and age ≥65 years) were positive.[21, 22, 23, 24] The MuLBSTA score is a newly designed score for viral pneumonia[11] that considers the following variables: multilobar infiltrates (5 points), lymphocytes ≤0·8 x10e9/ml (4 points), bacterial infection (4 points), active smoker (3 points), prior smoker (2 points), hypertension (2 points), and age ≥60 years (2 points), with a cut-off point of 12 points or more is related with poor prognosis, as defined in the original study.[11] qSOFA was considered positive when two of the three variables (altered mental

status, respiratory rate ≥22 brpm, and/or systolic blood pressure <100 mmHg) were met, according to the Sepsis-3 definition.[12]

Outcome measures

The primary outcome measure was all-cause in-hospital mortality.

Statistical analysis

After a preliminary descriptive analysis of the data (SD, means, and percentages), we compared the differences between categorical variables using the chi-square test and continuous variables using Student's t-test or analysis of variance. Statistical data from ROC curves (area under the curve (AUROC), sensitivity, and specificity) of the scores were calculated. The SPSS statistical package version 22·0 (SPSS, Chicago, IL) was used for the statistical study and the Epidat version 3·1 program was used for comparing the AUROCs of the different scales. P values <0·05 were considered statistically significant.

Ethical aspects

Scientific and ethical permission to conduct this study was obtained from the Provincial Research Ethics Committee of Málaga (Spain). Informed consent was obtained from patients for the purpose of publication. Personal data were processed in strict compliance with Spanish Law 14/2007, of July 3, on Biomedical Research; Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data (General Data Protection Regulation); and Spanish Organic Law 3/2018, of December 5, on Personal Data Protection and the Guarantee of Digital Rights.

Key results

A total of 10238 patients were included in this study. The patient inclusion flowchart can be seen in figure 1. Epidemiological and clinical data are found in table 1. The mean age was 66·6 ± 16·2 years and 57·9% of patients were male. A total of 5830 (56·9%) patients had an age-adjusted Charlson Comorbidity Index of 3 or more points. The most frequent comorbidities were hypertension (49·2%), diabetes (18·8%), and COPD (12·2%). ARDS and acute kidney injury were the most common complications (34·7% and 13·9%, respectively).

In-hospital mortality was 20·9% (2135 cases). A total of 907 (8·9%) patients were admitted to ICU. The mean length of hospital stay was 11·2 ± 9·2 days. As expected, the patients who died were older and had more comorbidities and complications. Prognostic scores were more frequently positive in deceased patients, as can be seen in table 1. Patients who died also had a longer mean hospital stay (9·7 vs 11·6 days, p <0·001) and were more frequently admitted to the ICU (17·6% vs 6·6%, p <0·001).

The PSI and CURB-65 scores showed no statistical differences upon comparison (AUROC 0·835 vs 0·825, p=0·112) and were higher than the qSOFA and MuLBSTA scores (AUROC 0·728 and 0·715, respectively, p<0·001 for both compared to PSI and CURB-65). These findings can be seen in table 2 and figure 2. The qSOFA score showed no differences compared to the MuLBSTA score (AUROC 0·728 vs 0·715, p=0·102) and was the most specific score (95·72%), as can be seen in table 3, but it had a lower sensitivity. The PSI risk class IV-V had the highest sensitivity (84·12%) but a lower specificity

than the qSOFA and MuLBSTA scores (72·25% vs 95·72% and 91·23%, p <0·001 for both scores).

Discussion

To our knowledge, this is the largest study evaluating prognostic scores in patients with COVID-19 pneumonia. The in-hospital mortality observed in this multicenter study in Spain was high (20·9%), which could be due to the fact that the mean age of patients was 66·6 years and there was a high frequency of comorbidities. The information obtained at admission allowed us to compare severity scores for identifying patients at high risk of in-hospital death. The PSI and CURB-65 had the best prognostic accuracy, with an AUROC of 0·835 and 0·825, respectively.

The PSI was initially designed to help practitioners identify which low-risk patients with CAP could be safely treated in an outpatient setting,[9] although it has subsequently been used to assess post-discharge mortality for those treated as inpatients. The capability of PSI to predict hospital mortality in our study was similar or even slightly better than that of other previous studies in CAP, in which PSI presented an AUROC of 0·778 to predict 30-day mortality or transfer to UCI [28] and 0·812 to predict 30-day mortality.[30] Our findings provide evidence that the PSI is quite a good score for assessing the risk of in-hospital mortality for patients admitted with COVID-19 pneumonia.

CURB-65 was developed to stratify hospitalized patients with CAP into mortality risk groups, with a primary outcome measure of 30-day mortality.[10] It has shown a diagnostic performance for mortality similar to the PSI in CAP.[24] The

diagnostic performance for mortality found in our study was comparable to that found in another study on COVID-19 patients (AUROC 0·85) whose primary outcome measure was intensive respiratory or vasopressor support.[31] In addition, our results were slightly better in terms of predicting mortality than those observed in another study on patients with influenza pneumonia (AUROC 0·788).[32]

MuLBSTA is a recently described severity score for 90-day mortality in patients with viral pneumonia.[11] It has been shown to perform better than CURB-65 in viral pneumonia, mainly caused by influenza virus; human rhinovirus; and respiratory syncytial virus.[11] Chen et al. suggested using MuLBSTA as a severity score for COVID-19 in their description of 99 patients in Wuhan, China [5] because the patients who died had a high percentage of variables included in this score. In our results, the AUROC of MuLBSTA for mortality (0·715) showed lower sensitivity compared to the other scores as well as when compared to the original work (0·715 vs 0·773, p <0·001). Further studies are needed in order to prove the suitability of the MuLBSTA score.

In our study, qSOFA showed a lower sensitivity than the PSI and CURB-65 scores (AUROC 0·728 vs 0·835 and 0·825, p <0·001 for both scores). These results were in line with the results found by Su et al. [31]in their study on 116 patients with COVID-19 in China, which showed the superiority of CRB-65 vs qSOFA for prediction of intensive respiratory or vasopressor support (AUROC 0·81 vs 0·70, p 0·02). Other studies have also shown that the accuracy of qSOFA in patients with COVID-19 was limited,[33, 34] although these studies included a small number of patients. However, qSOFA has been related to

mortality in COVID-19 in another study with 191 patients (OR 12 (CI 95% 5·06-28·43).[4]

In our work, the PSI and CURB-65 showed sensitivity and specificity values similar to those found in other studies on CAP.[23, 28, 30] However, qSOFA sensitivity was lower than the other scores and lower for CAP (53% to 70·1%).[23, 26] qSOFA had a higher specificity than the other scores in our study (95·72% vs 72·25%, 90·68%, and 91·23% for PSI, CURB-65, and MuLBSTA, respectively). These results for qSOFA are consistent with the findings of Su et al.,[31] who observed a similar specificity for qSOFA and CURB-65 (98·9% and 96·7%, respectively). Despite its lower sensitivity, qSOFA has the benefit of not requiring laboratory test results.

In the study by Su et al.,[31] the CRB score was also analyzed, which also has the benefit of not requiring laboratory results. In that study, no difference was found between CRB and qSOFA.[31] These two scores had a lower accuracy than CRB-65 and CURB-65, suggesting that age is an important risk factor for mortality. Indeed, age has been shown to be an independent risk factor for mortality in patients with COVID-19.[35, 36]

This study has several limitations. First, due to its retrospective design, some possible confounding variables were not recorded and thus we could not calculate prognostic scores in 3·4% to 9·5% of cases. Second, we focused only on hospitalized patients and as such, we cannot be certain that our findings can be extrapolated to outpatients. Third, by excluding patients still hospitalized as of May 29, 2020, the case fatality rate in our study does reflect the true mortality rate of COVID-19. Fourth, this study was conducted in multiple centers in Spain

and its results may not be applicable to other settings with different populations or healthcare systems.

Lastly, it is important to note that although these scores could help physicians identify patients with COVID-19 pneumonia at admission to hospital who have different risk levels for death, there are other risk factors specific to COVID-19 that should be considered, such as lymphopenia or D-dimer,[4] which are not analyzed in these scores.

Conclusions

The PSI and CURB-65, two severity scores specific to pneumonia, were the best scores for predicting all-cause in-hospital death for patients with COVID-19 pneumonia. They performed better than the qSOFA and MuLBSTA severity scores. qSOFA, the simplest score to calculate, was the most specific, albeit the least sensitive.

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Figure 1. Flowchart of patients included from the SEMI-COVID-19 Network with COVID-19* pneumonia

*COVID-19: coronavirus infectious disease 2019

Figure 2. Receiver operating characteristic curves for PSI*, CURB65†, MuLBSTA‡, and qSOFA§ scores for in-hospital mortality in COVID19‖ pneumonia patients

* PSI: Pneumonia Severity Index; † CURB-65: Confusion, Urea, Respiratory rate, Blood pressure, and age ≥65 years; ‡ MuLBSTA: Multilobar infiltration, hypo-Lymphocytosis, Bacterial coinfection, Smoking history, hyper-Tension and Age; § qSOFA: quick Sequential Organ Failure Assessment; ‖ COVID-19: coronavirus infectious disease 2019

Table 1 Epidemiological and clinical characteristics, complications, prognostic scores and outcomes of patients with COVID-19* pneumonia

	All patients n 10238	Non-survivors n 2135	Survivors n 8103	p
Demographics				
Male sex, n (%)	5924 (57.9)	1336 (62.6)	4588 (56.6)	<0.001
Age, mean ± SD, years	66.6 ± 16.2	79.5 ± 10.6	63.2 ± 15.6	<0.001
≥ 70 years, n (%)	4765 (46.5)	1810 (38)	2955 (62)	<0.001
Comorbidities, n (%)				
Moderate or severe dependency	1504 (14.7)	787 (36.9)	717 (8.8)	<0.001
Age adjusted Charlson comorbidity index ≥3	5830 (56.9)	1934 (90.6)	3896 (48.1)	<0.001
Hypertension	5040 (49.2)	1496 (70.1)	3544 (43.7)	<0.001
Coronary artery disease	703 (6.9)	333 (15.6)	370 (4.6)	<0.001
COPD†	1250 (12.2)	502 (23.5)	748 (9.2)	<0.001
Cerebrovascular disease	250 (2.4)	116 (5.4)	134 (1.7)	<0.001
Smoking history	2424 (23.7)	646 (30.3)	1778 (21.9)	<0.001
Active smoking	492 (4.8)	98 (4.6)	394 (4.9)	<0.001
Diabetes	1926 (18.8)	618 (28.9)	1308 (16.1)	<0.001
Moderate-severe CKD‡	577 (5.6)	261 (12.2)	316 (3.9)	<0.001
Malignant tumor	595 (5.8)	199 (9.3)	396 (4.9)	<0.001
Complications, n (%)				
Shock	482 (4.7)	370 (17.3)	112 (1.4)	<0.001
Acute Kidney injury	1423 (13.9)	781 (36.6)	642 (7.9)	<0.001
Acute Pulmonary Embolism	158 (1.5)	28 (1.3)	130 (1.6)	0.790
Multi-organic failure	667 (6.5)	375 (17.6)	532 (6.6)	<0.001
ARDS§	3550 (34.7)	1730 (81)	1820 (22.5)	<0.001

Prognostic scores, n (%)				
qSOFAǁ	9887	2049 (20.7)	7838 (79.3)	··
0	5788 (58.6)	552 (26.9)	5236 (66.8)	<0.001
1	3219 (32.6)	952 (46.5)	2267 (28.9)	<0.001
2	779 (7.8)	464 (22.7)	315 (4)	<0.001
3	101 (1)	81 (3.9)	20 (0.3)	<0.001
CURB-65¶	9887	2049 (20.7)	7838 (79.3)	··
0-1	5899 (59.7)	366 (17.9)	5533 (70.6)	<0.001
2	2232 (22.6)	657 (32.1)	1575 (20.1)	<0.001
3	1282 (12.9)	679 (33.1)	603 (7.7)	<0.001
4	438 (4.4)	317 (15.5)	121 (1.5)	<0.001
5	36 (0.4)	30 (1.4)	6 (0.1)	<0.001
PSI#	9261	1906 (20.6)	7355 (79.4)	··
I-II	3376 (36.5)	55 (2.9)	3321 (45.2)	<0.001
III	2168 (23.4)	247 (12.9)	1921 (26.1)	<0.001
IV	2566 (27.7)	860 (45.1)	1706 (23.2)	<0.001
V	1151 (12.4)	744 (39.1)	407 (5.5)	<0.001
MuLBSTA**	9505	1956 (20.6)	7549 (79.4)	··
MuLBSTA ≥12	1298 (13.7)	588 (30.1)	710 (9.4)	<0.001
Outcomes, n (%)				
NIV††	528 (5.2)	269 (12.6)	259 (3.2)	<0.001
Mechanical ventilation	722 (7.1)	340 (15.9)	382 (4.7)	<0.001
Admission to ICU‡‡	907 (8.9)	375 (17.6)	532 (6.6)	<0.001
Mortality	2135 (20.9)	--	--	--
Length of hospital stay, mean ± SD, days	11.2 ± 9.2	9.7 ± 10.3	11.6 ± 8.8	<0.001

* COVID-19: coronavirus infectious disease 2019; † COPD: chronic obstructive pulmonary disease; ‡ CKD: chronic kidney disease; § ARDS: acute respiratory distress syndrome; ǁ qSOFA: quick Sequential Organ Failure Assessment; ¶ CURB-

65: Confusion, Urea, Respiratory rate, Blood pressure, and age ≥65 years; # PSI: Pneumonia Severity Index; ** MuLBSTA: Multilobar infiltration, hypo-Lymphocytosis, Bacterial coinfection, Smoking history, hyper-Tension and Age; †† NIV: non-invasive ventilation; ‡‡. ICU: intensive care unit.

Table 2. Statistical data of ROC* curve comparisons between PSI†, CURB-65‡, MuLBSTA§ and qSOFA‖ scores for in-hospital mortality in patients with COVID-19¶ pneumonia

	AUROC# (95% CI)	vs. PSI†	vs. CURB-65‡	vs. MuLBSTA§
PSI†	0.835 (0.826-0.845)	--	--	--
CURB-65‡	0.825 (0.815-0.835)	0.112	--	--
MuLBSTA§	0.715 (0.703-0.727)	<0.001	<0.001	--
qSOFA‖	0.728 (0.715-0.741)	<0.001	<0.001	0.102

* ROC: receiver operating characteristic curve; † PSI: Pneumonia Severity Index; ‡ CURB-65: Confusion, Urea, Respiratory rate, Blood pressure, and age ≥65 years; § MuLBSTA: Multilobar infiltration, hypo-Lymphocytosis, Bacterial coinfection, Smoking history, hyper-Tension and Age; ‖ qSOFA: quick Sequential Organ Failure Assessment; ¶ COVID-19: coronavirus infectious disease 2019; # AUROC: area under the receiver operating characteristic curve.

Table 3 Comparison of predictive assessments between PSI*, CURB-65†, MuLBSTA‡ and qSOFA§ scores for in-hospital mortality in patients with COVID-19‖ pneumonia

	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV¶, % (95% CI)	NPV#, % (95% CI)
PSI ≥IV	84.12 (82.45-85.79)	72.25 (71.21-73.29)	44.28 (42.65-45.91)	94.55 (93.94-95.15)
CURB-65 ≥3	82.13 (80.45-83.82)	70.59 (69.57-71.60)	42.20 (40.65-43.74)	93.79 (93.17-94.41)
MuLBSTA ≥12	27.54 (25.62-29.45)	91.23 (90.61-91.85)	45.30 (42.55-48.04)	82.69 (81.90-83.48)
qSOFA≥2	26.59 (24.66-28.53)	95.72 (95.27-96.18)	61.93 (58.66-65.19)	83.30 (82.52-84.07)

* PSI: Pneumonia Severity Index; † CURB-65: Confusion, Urea, Respiratory rate, Blood pressure, and age ≥65 years; ‡ MuLBSTA: Multilobar infiltration, hypo-Lymphocytosis, Bacterial coinfection, Smoking history, hyper-Tension and Age; § qSOFA: quick Sequential Organ Failure Assessment; ‖ COVID-19: coronavirus infectious disease 2019; ¶ PPV: positive predictive value; # NPV: negative predictive value.

Figure 1

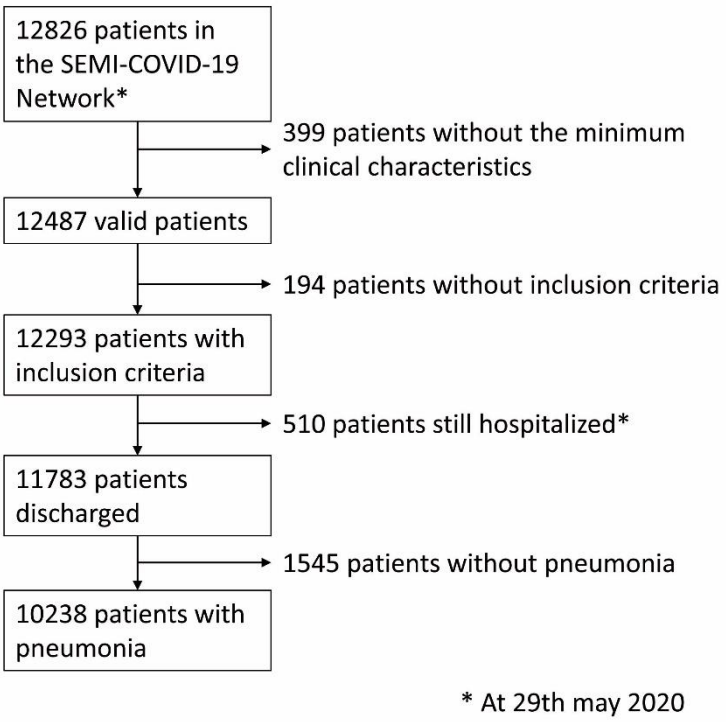
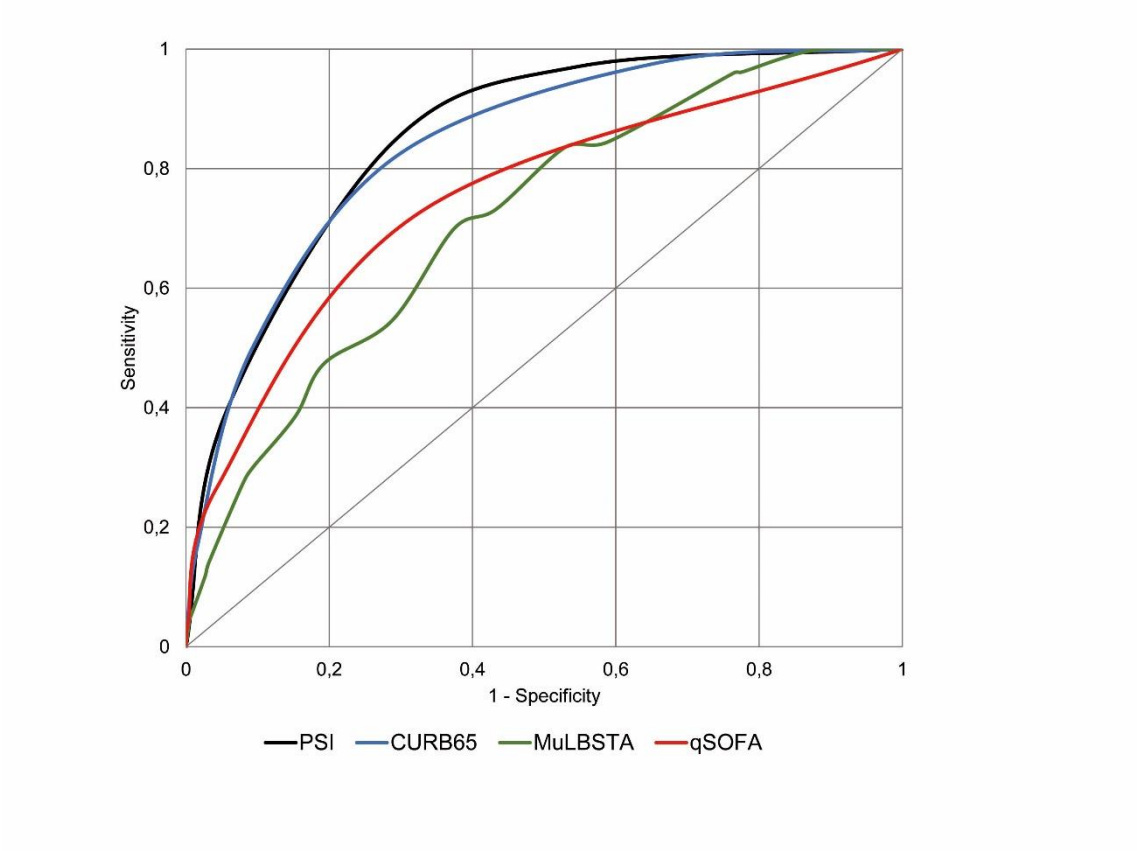

12826 patients in the SEMI-COVID-19 Network*
399 patients without the minimum clinical characteristics
12487 valid patients
194 patients without inclusion criteria
12293 patients with inclusion criteria
510 patients still hospitalized*
11783 patients discharged
1545 patients without pneumonia
10238 patients with pneumonia
* At 29th may 2020

Figure 2


1
0,8
0,6
0,4
0,2
0
Sensitivity
0
0,2
0,4
0,6
0,8
1
1 - Specificity
PSI
CURB65
MuLBSTA
qSOFA

Figures

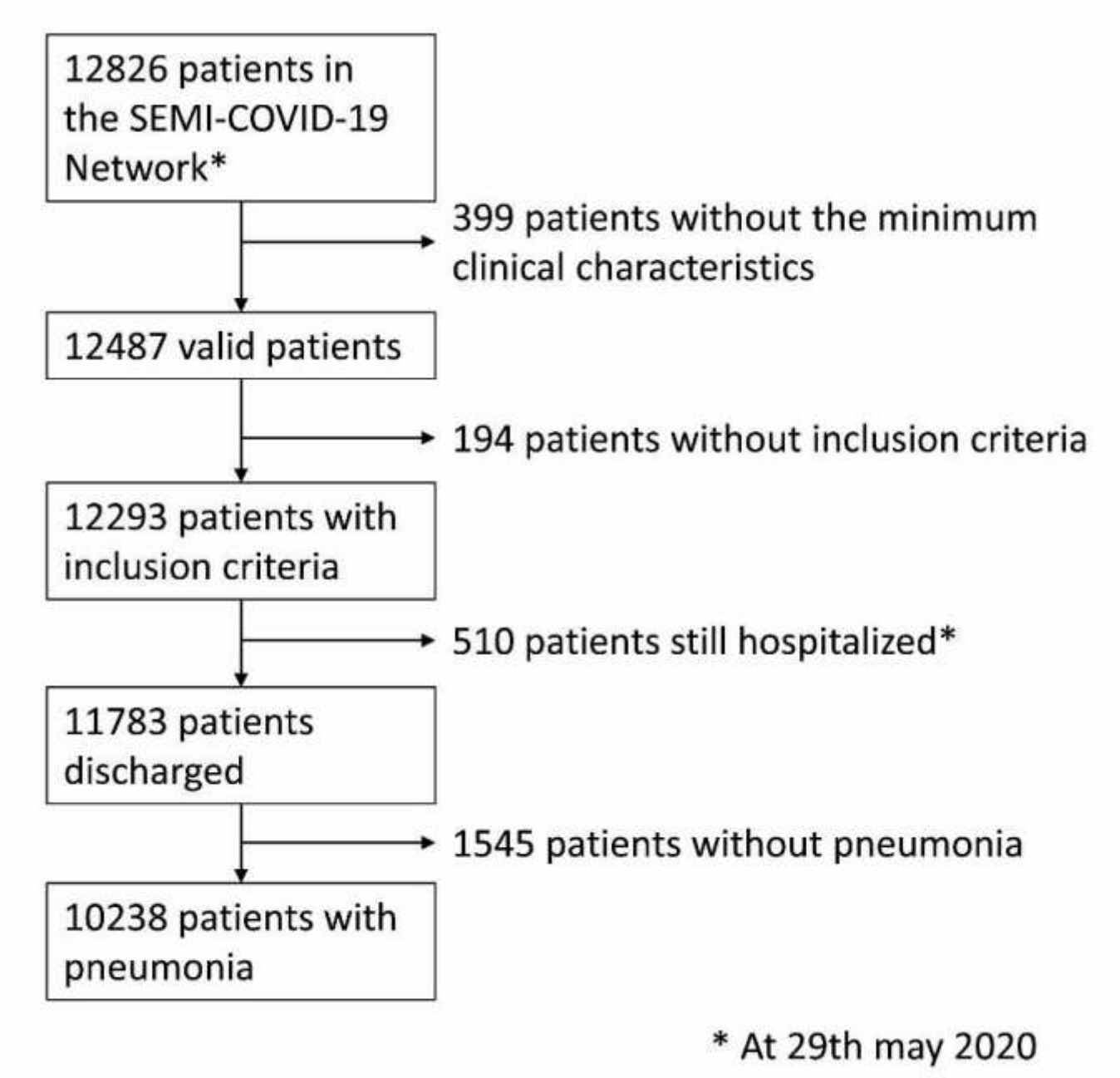


Figure 1

Flowchart of patients included from the SEMI-COVID-19 Network with COVID-19* pneumonia *COVID-19: coronavirus infectious disease 2019

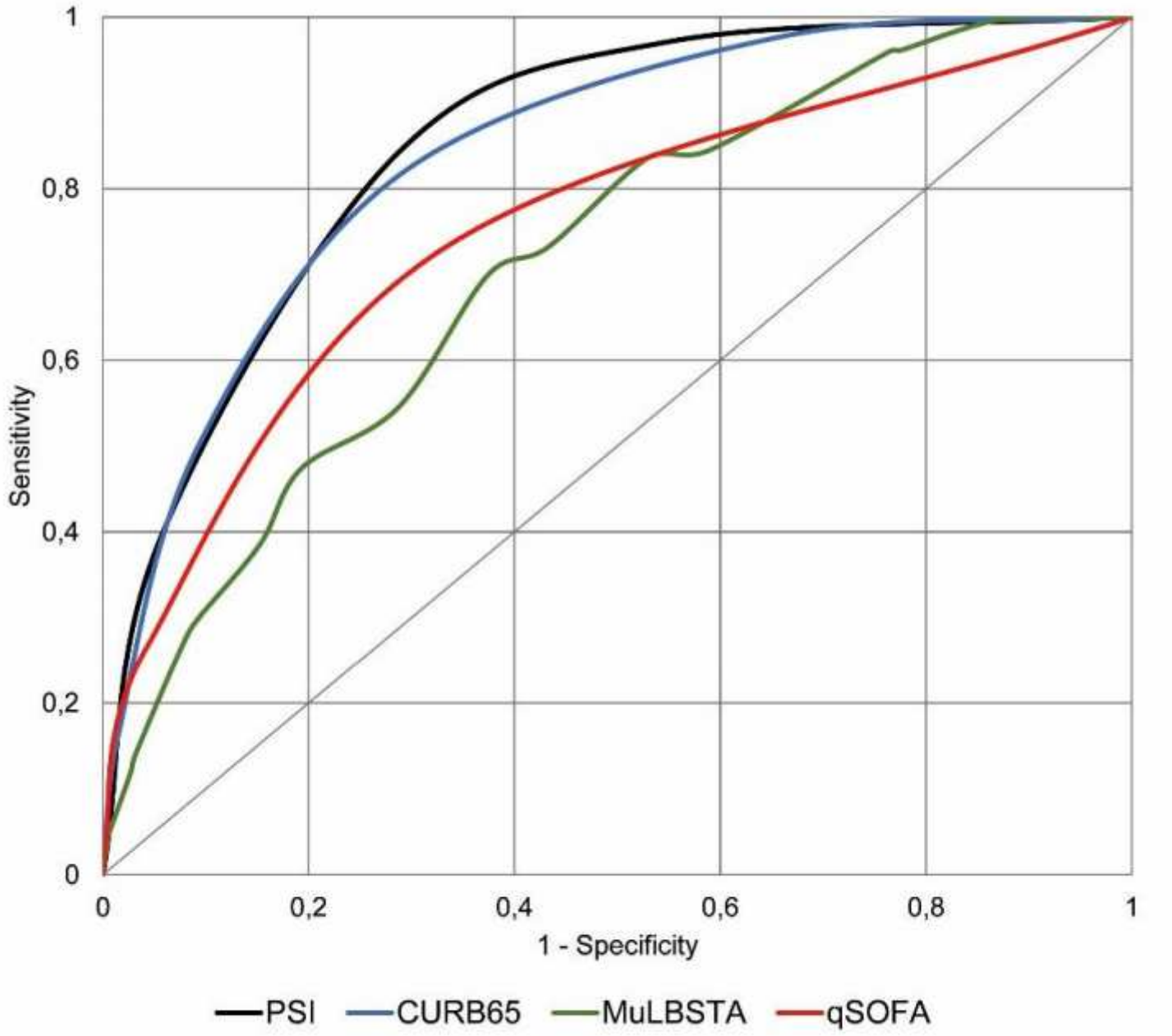


Figure 2

Receiver operating characteristic curves for PSI*, CURB65†, MuLBSTA‡, and qSOFA§ scores for in-hospital mortality in COVID19 pneumonia patients * PSI: Pneumonia Severity Index; † CURB-65: Confusion, Urea, Respiratory rate, Blood pressure, and age ≥65 years; ‡ MuLBSTA: Multilobar infiltration, hypo-Lymphocytosis, Bacterial coinfection, Smoking history, hyper-Tension and Age; § qSOFA: quick Sequential Organ Failure Assessment; COVID-19: coronavirus infectious disease 2019