Internal and Emergency Medicine (2022) 17:1795–1801
https://doi.org/10.1007/s11739-022-03006-9

EM - ORIGINAL

CovHos score for predicting severe respiratory failure in COVID-19 patients presenting at the emergency department

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Received: 7 March 2022 / Accepted: 14 May 2022 / Published online: 24 June 2022

Abstract

Hospitalization of COVID-19 patients in low-intensity wards may put patients at risk in case of clinical deterioration. We tested CovHos score in predicting severe respiratory failure (SFR) at emergency department (ED) admission. This is a monocentric observational prospective study enrolling adult COVID-19 patients admitted to the ED of IRCCS AOU di Bologna Policlinico S.Orsola in October 2020, both discharged and hospitalized. Patients were then dichotomized based on days from symptoms onset. Main outcome was the occurrence of SRF. Receiver operating characteristic (ROC) analysis was used to identify cut-off and corresponding accuracy. A CovHos cut-off of 22 yielded a sensitivity of 84.7% and specificity of 75.3% in predicting SRF (AUROC 0.856; CI 95% 0.813–0.898). In patients with symptoms onset up to 8 days, a CovHos cut-off of 22 was able to predict SRF with a sensitivity of 91.7% and a specificity of 78.6% (AUROC 0.901; CI 95% 0.861–0.941). Negative predictive value (NPV) was 97.1%. A CovHos score lower than 22, in patients with COVID-19 symptoms onset dated 8 or less days prior to the ED admittance, had a NPV of 97.1% for the development of SRF, meaning that almost none of those patients will evolve into SRF and could be therefore suitable for a lower intensity of care.

Keywords COVID-19 · Severe respiratory failure · CovHos score

Introduction

Prevention strategies against SARS-CoV-2 infection, such as lockdown periods, quarantine and vaccination, are able to reduce its impact on healthcare systems. However, a new wave of contagion periodically shows up, lately due to gradual decline in efficacy of vaccines, estimable in about 6% every two months [1]. During the COVID-19 pandemic, several strategies to manage surge capacity of space, supply and workforce have been applied. All countries developed plans to set up additional intensive care unit (ICU) beds within the existing facilities, often involving the private healthcare system. Private hospitals were temporarily used to hospitalize COVID-19 patients, generally in case of moderately severe infections [2].

Emergency clinicians are responsible for deciding whether to discharge or to admit patients to the hospital on a daily basis and, eventually, for picking the appropriate setting. With a rapidly deteriorating condition such as COVID-19, sending patients to low-intensity wards, especially in private facilities located far from the Emergency Department (ED), could put the patient at risk and stress the system even more in case of need of re-transfer. Many scores have been studied to identify clinical deterioration in COVID-19, such as National Early Warning Score (NEWS) and its latest iteration (NEWS2) [3] and Quick COVID-19 Severity Index [4], both able to detect the need of ICU admission within 24 h with a 70% accuracy; however, sample sizes were small and Arterial Blood Gas (ABG) parameters were not included in those scores, whereas ABG is routinely performed in ED due to its fundamental role in the evaluation of respiratory failure.

We have recently proposed CovHos score, an effective tool to assist emergency clinicians in predicting the need of hospitalization based on five variables easily obtainable in the ED: male sex, age > 65, Alveolar-to-arterial Oxygen Gradient percentage increase compared to that expected for age (A-aDO2%), Neutrophils/Lymphocytes ratio (N/L) and C-reactive protein (CRP) (5). In particular, a CovHos score cut-off of 12 points predicted hospitalization with

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85% sensitivity and 82.4% specificity (AUC 0.909; 95% CI 0.884–0.935) and a cut-off of 22 had 79% sensitivity and 77% specificity in predicting mortality (AUROC 0.824; 95% CI 0.782–0.866).

Bartoletti et al. recently demonstrated that age, obesity, body temperature, respiratory rate (RR), lymphocytes, CRP, creatinine and LDH > 350 IU/L, considered together in the so-called PREDI-CO score, had a good accuracy in predicting the occurrence of severe respiratory failure (SRF), defined according to WHO criteria as: $SpO_2 < 93\%$ with 100% FiO_2 (reservoir mask or continuous positive airway pressure ventilation or other non-invasive ventilation), respiratory rate (RR) > 30 breaths/minute or respiratory distress (AUROC 0.89; 95% CI 0.86–0.92). PREDI-CO had 80% sensitivity and 76% specificity in predicting SRF with a score over 3 points [6]. However, PREDI-CO score does not take into consideration ABG and the only parameter influenced by respiratory dynamics is RR (which is often unaltered in COVID-19 patients regardless of the severity of the disease).

The aim of the current study was to evaluate CovHos score in predicting the occurrence of SRF.

Methods

We conducted a monocentric observational prospective study enrolling all adult patients referred to the ED of IRCCS AOU di Bologna Policlinico S.Orsola with SARS-CoV-2 infection, both those directly discharged and those hospitalized or dead in ED. The infection was confirmed through a positive real-time reverse transcription polymerase chain reaction (RT-PCR) assay for nasal swab between October 1, 2020 and October 30, 2020. Demographic, case history and clinical data were collected, laboratory tests (ABG, general blood tests) and radiological exams (lung ultrasound, chest X-ray and/or high-resolution computed tomography—HRCT) were performed. NEWS2 was assessed for each patient from six physiological variables (RR, oxygen saturation, temperature, systolic blood pressure, heart rate and level of consciousness). A higher NEWS2 value correlates with a higher risk of clinical deterioration [3].

Epidemiological, demographic, clinical, laboratory, treatment and outcome data as well as the occurrence of SRF during hospital stay were extracted from electronic medical records.

The study was approved by our local Ethic Committee (number: 551/2020/Oss/AOUBo). All patients provided oral informed consent to be included in the study.

CovHos score:

CovHos score was calculated using the formula:

$$(AaDO_2\% \times 5.212) + (N/L \times 1.099) + (CRP \times 1.247),$$

adding 1.856 in case of male sex and 6.796 in case of age > 65 years as previously described [5]. All variables refer to admission to the ED and have been filled in spreadsheet previously prepared.

Statistical analysis

All data have been presented as median (min–max) for continuous variables and frequencies for categorical variables. Comparison among groups has been performed using chi-square test of Mann–Whitney where appropriated. Receiver operating characteristic (ROC) analysis was used to identify accuracy of CovHos score in predicting hospitalization, SRF occurrence or 30-day mortality and to define the optimum cut-off. ROC analysis was used also to assess accuracy of NEWS2 in predicting SRF occurrence and 30-day mortality. P values < 0.05 were considered statistically significant. Statistical analysis was conducted using SPSS (version 25).

Results

A total of 365 patients have been evaluated: among these, 70 patients have been excluded due to missing data (mainly regarding ABG data); 295 patients have been included in the final analysis (168 males and 127 females). Patients' demographics and baseline clinical features are reported in Table 1.

The median number of days from symptoms onset was 5 days (0–27). Vital signs, laboratory, ABG and radiological findings are listed in Table 2. Maximum oxygen support, setting of care, length of hospital stay and 30-day mortality are shown in Table 3. Continuous positive airway pressure (CPAP) was used in two patients in "no SRF group" even if they did not fulfill SRF criteria.

Half of the patients (50.9%) did not require oxygen during the entire hospital stay, 28% needed nasal cannulas/Venturi mask/Reservoir and 14.3% required non-invasive ventilation (NIV). Endotracheal intubation (ETI) became necessary in 10% of patients. Worthy to remind that 28 patients (9.5% of the study population) died during hospital stay. Therefore, their maximum oxygen support was uncertain. Lastly, 61 patients in the final series had pO2 values greater than 85 mmHg on ABG.

About one-third of patients (31.9%) were discharged directly from the ED. Ninety-nine patients (33.6%) were managed in an ordinary ward as a maximum intensity of care, 12 (4.1%) in a sub-intensive care setting and 41 patients (13.9%) were admitted to ICU. Twenty-eight patients (9.5%) died during hospital stay and 21 (7.12%) were transferred to another hospital. Total count of

Table 1 Demographics and baseline clinical features

	All patients ($n=295$)	SRF group ($n=72$)	No SRF group ($n=223$)	p value
Characteristics				
Age	64 (19–98)	75 (25–95)	58 (19–98)	.000
Sex				
F/M	127 /168 (43.05/56.95)	21/51 (29.33/70.67)	106/117 (47.53/52.47)	.006
Comorbidities				
Hypertension	112 (38.75%)	38 (52.78%)	74 (34.10%)	.005
Diabetes	35 (12.11%)	11 (15.28%)	24 (11.06%)	NS
COPD	15 (5.19%)	8 (11.11%)	7 (3.23%)	.014
Asthma	10 (3.46%)	2 (2.78%)	8 (3.69%)	NS
Other respiratory diseases	12 (4.15%)	6 (8.33%)	6 (2.77%)	NS
Ischemic heart disease	20 (6.92%)	7 (9.72%)	13 (5.99%)	NS
Active cancer	11 (3.82%)	3 (4.17%)	8 (3.70%)	NS
Chronic kidney disease	15 (5.19%)	5 (6.94%)	10 (4.61%)	NS
Previous stroke/TIA	6 (2.09%)	0 (0%)	6 (2.79%)	NS
Immunodeficiency	3 (1.04%)	2 (2.78%)	1 (0.46%)	NS
Number of comorbidities				
No comorbidities	137 (47.41%)	20 (27.78%)	117 (53.92%)	
1 comorbidity	88 (30.45%)	30 (41.67%)	58 (26.73%)	
2 comorbidities	47 (16.26%)	15 (20.83%)	32 (14.75%)	
3 comorbidities	17 (5.88%)	7 (9.72%)	10 (4.61%)	
Days from symptoms onset	5 (0–27)	6 (0–20)	5 (0–27)	
Symptoms at ED admission				
Fever	255 (88.54%)	61 (87.14%)	192 (88.07%)	NS
Dyspnea	112 (39.16%)	36 (51.43%)	76 (35.19%)	.017
Cough	160 (55.94%)	35 (50%)	124 (57.41%)	NS
Conjunctivitis	1 (0.35%)	0 (0%)	1 (0.46%)	NS
Sore Throat	16 (5.59%)	2 (2.86%)	14 (6.48%)	NS
Headache	28 (9.79%)	2 (2.86%)	26 (12.04%)	NS
Fatigue	67 (23.43%)	15 (21.43%)	51 (23.61%)	NS
Myalgia/Arthralgia	47 (16.43%)	6 (8.57%)	41 (18.98%)	.042
Diarrhea	45 (15.73%)	10 (14.29%)	34 (15.74%)	NS
Anosmia	30 (10.49%)	4 (5.71%)	26 (12.04%)	NS
Ageusia/Dysgeusia	39 (13.64%)	5 (7.14%)	34 (15.74%)	NS
Chest Pain	20 (6.99%)	0 (0%)	20 (9.26%)	.005

Data are median (min–max) or *n* (%). *F* female, *M* male, *COPD* Chronic obstructive pulmonary disease, *TIA* Transient ischemic attack

hospital stay ranged from a minimum of one day to a maximum of 60 days (median 8 days). Thirty-day mortality from admission to the ED was 10.9% (32 patients).

Once data were collected, population was split into 3 groups: those who were discharged directly from the ED, those who were admitted to an ordinary ward, and lastly, those who were managed in a higher setting of care (sub-intensive care or ICU) or died. Median value of CovHos Score was calculated for each group: 8.8 in the discharged group (−7 to 33), 19.3 in the ordinary ward group (−7.7 to 74.7), and 30.4 in the sub/intensive care unit or dead group (11.9–94.3). The difference among CovHos median values of the three subpopulations was statistically significant (p value < 0.001).

As seen in the original study, CovHos score was used to predict the need of hospitalization using a cut-off of 12. On our population and using the same cut-off, CovHos score was able to predict the need of hospital admission with a sensitivity of 84% and specificity of 64% (p value $= 0.001$, AUROC 0.854; CI 95% 0.809–0.898). Positive predictive value (PPV) was 83.3% and negative predictive value (NPV) was 65.2%.

However, hospitalization, being influenced by local hospital resources and physicians' judgment, could not be

Table 2 Vital signs, arterial blood gas, laboratory and radiological findings

	All patients ($n=295$)	SRF group ($n=72$)	No SRF group (223)	p value
Vital signs				
Systolic blood pressure (mmHg)	127 (90–190)	125 (90–170)	129 (90–190)	NS
Diastolic blood pressure (mmHg)	77 (50–100)	70 (50–95)	80 (50–100)	.010
Mean blood pressure (mmHg)	93.33 (63.3–130)	92.5 (63.3–116.7)	93.33 (66.7–130)	NS
Heart rate (beats/minute)	88 (56–125)	84.5 (56–121)	88 (58–125)	NS
Respiratory rate (breaths/minute)	18 (12–42)	20 (12–33)	18 (12–42)	.000
SpO_2(%)	97 (55–100)	93 (55–100)	97 (86–100)	.000
Body temperature(°C)	37 (35.4–39.6)	37.5 (36–39.6)	36.9 (35.4–39.3)	.048
SpO_2/FiO_2	4.62 (2.6–4.8)	4.43 (2.6–4.8)	4.62 (3.3–4.8)	.000
Arterial blood gas				
pH	7.45 (7.26–7.7)	7.45 (7.26–7.56)	7.44 (7.3–7.7)	NS
pO_2 (mmHg)	72 (32–106)	60.15 (32–90)	77 (54–106)	.000
pCO_2 (mmHg)	32 (13.5–61)	31.25 (14.6–43.4)	33 (13.5–61)	.030
P/F	342,5 (92–504)	280 (92–409)	365 (257–504)	.000
Lactates	1.03 (0.46–5)	1.30 (0.6–3.53)	0.99 (0.46–5)	.005
A-aDO2	36.45 (0.9–94)	52.1 (16.8–94)	31.75 (0.9–89.6)	.000
% Increase of A-aDO2 compared to the expected for age	+80% (− 92% to +364%)	136% (− 39% to +364%)	+64% (− 92% to +332%)	.000
Laboratory tests				
WBC ($\times 10^9$/L)	5.63 (1.23–22.1)	6.29 (2.32–22.1)	5.34 (1.23–16.58)	.004
Neutrophils ($\times 10^9$/L)	3.98 (0.55–21.17)	4.72 (1.7–21.17)	3.61 (0.55–14.87)	.000
Lymphocytes ($\times 10^9$/L)	1.06 (0.36–4.69)	0.94 (0.4–3.91)	1.11 (0.36–4.69)	.004
N/L ratio	3.65 (0.6–39.94)	4.76 (0.66–39.94)	3.32 (0.6–28.06)	.000
Lymphopenia	150 (50.85%)	44 (61.11%)	106 (47.53%)	NS
Eosinophils($\times 10^9$/L)	0.01 (0–1.01)	0 (0–0.27)	0.01 (0–1.01)	.000
Platelets ($\times 10^9$/L)	187 (32–462)	178 (32–365)	195 (34–462)	.024
aPTT	1.09 (0.64–3.18)	1.24 (0.8–3.18)	1.07 (0.64–2.99)	.000
INR	1.08 (0.9–4.38)	1.13 (0.97–3.26)	1.08 (0.9–4.38)	.000
Glycemia (mg/dL)	109 (58–338)	124 (81–338)	104 (58–302)	.000
Creatinine (mg/dL)	0.91 (0.43–10.52)	1.04 (0.58–8.30)	0.87 (0.43–10.52)	.000
Sodium (mmol/L)	138 (120–155)	138 (129–155)	138 (120–152)	NS
Potassium (mmol/L)	4.1(2.8–6.3)	4 (2.8–5.7)	4.1 (3.1–6.3)	NS
LDH (U/L)	258 (84–894)	341.5 (150–825)	234 (84–894)	.000
PCT (ng/mL)	0.1 (0–186.6)	0.1 (0–186.6)	0 (0–1.8)	.000
CRP (mg/dL)	3.05 (0.05–33.7)	9.28 (0.71–33.7)	2.02 (0.05–29.76)	.000
HRTC findings				
Ground glass	199 (88.84%)	59 (96.72%)	140 (88.84%)	.029
Single consolidation	10 (4.46%)	1(1.64%)	9 (4.46%)	NS
Multiple consolidations	188 (83.93%)	58 (95.08%)	130 (83.93%)	.004
Pleural effusion	17 (7.59%)	6 (9.84%)	11 (7.59%)	NS

Data are median (min–max) or *n* (%). *PaCO2, PaO2* arterial carbon dioxide and oxygen tensions, *P/F* arterial oxygen partial pressure/fractional inspired oxygen ratio, *A-aDO2* Alveolar-to-arterial Oxygen Gradient, *WBC* white blood cells, *N/L ratio* Neutrophils/Lymphocytes ratio, *LDH* lactate dehydrogenase, *PCT* Procalcitonin, *CRP* C-reactive protein

considered an objective criterion. Primary endpoint was to use CovHos score to predict SRF at first medical contact in an ED setting. CovHos score cut-off of 22 yielded a sensitivity of 84.7% and specificity of 75.3% in predicting SRF (p value < 0.001. AUROC = 0.856; CI 95% 0.813–0.898), as shown in Fig. 1. PPV was 52.6% and NPV was 93.9%. NEWS2 accuracy in predicting SRF was lower than CovHos score (AUROC 0.797; CI 95% 0.697–0-897; sensitivity of NEWS2 ≥ 5 was 46.4% and specificity was 92%.

Table 3 Maximum respiratory support and intensity of care, length of hospital stay, 30-day mortality

	All patients ($n=295$)	SRF group ($n=72$)	No SRF group (223)	p value
Max respiratory support				
No oxygen	142 (50.90%)	0 (0%)	144 (64.57%)	.000
Nasal cannula	30 (10.75%)	0 (0%)	30 (13.64%)	.000
Ventimask	44 (15.77%)	0 (0%)	44 (19.73%)	.000
Reservoir	4 (1.43%)	0 (0%)	3 (1.36%)	.000
CPAP	9 (3.23%)	7 (12.28%)	2 (0.9%)	.000
NIV	19 (6.81%)	19 (33.33%)	0 (0%)	.000
Endotracheal intubation	28 (10.04%)	28 (49.12%)	0 (0%)	.000
HFNC	3 (1.08%)	3 (5.26%)	0 (0%)	.000
Highest intensity of care during hospital stay				
Discharged	94 (31.86%)	0 (0%)	94 (42.15%)	.000
Ordinary Ward	99 (33.56%)	0 (0%)	99 (44.40%)	.000
Sub-intensive	12 (4.07%)	3 (4.17%)	9 (4.04%)	NS
Intensive Care (total)	41 (13.90%)	41 (56.94%)	0 (0%)	.000
Intensive care directly from ED	21 (7.12%)	21 (29.17%)	0 (0%)	.000
Intensive Care from Ordinary Ward	20 (6.78%)	20 (27.78%)	0 (0%)	.000
Deaths	28 (9.49%)	28 (38.89%)	0 (0%)	.000
Transferred to other facility	21 (7.12%)	0 (0%)	21 (9.42%)	.000
Days of hospital stay:	8 (1–60)	13 (2–60)	6 (1–34)	.000
30-day mortality	32 (10.85%)	28 (38.89%)	4 (1.79%)	.000

Data are median (min–max) or *n* (%). *CPAP* Continuous positive airway pressure. *NIV* Non-invasive ventilation. *HFNC* High flow nasal cannula. *ED* Emergency department

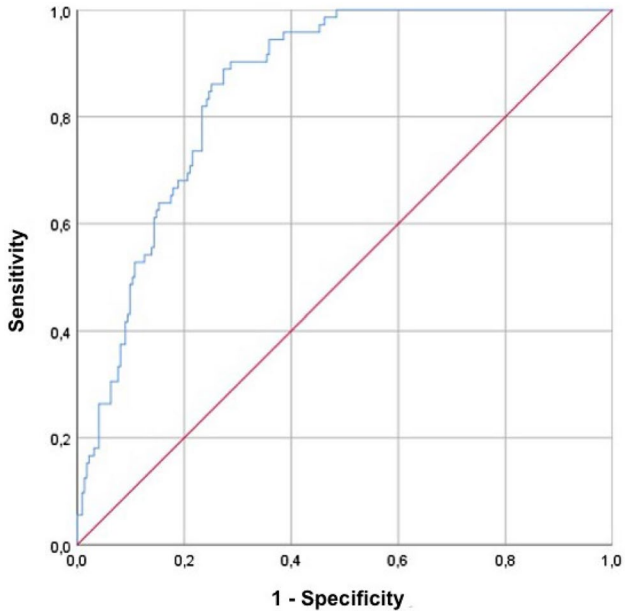

Fig. 1 Receiver operating characteristic (ROC) analysis of CovHos Score in predicting severe respiratory failure (SRF) in COVID-19 patients

Moreover, we evaluate the ability of CovHos Score in predicting SRF in patients presenting to the ED with symptoms onset up to 8 days versus 9 or more days. CovHos cut-off of 22 was able to predict SRF in patients with symptoms onset up to 8 days with a sensitivity of 91.67% and a specificity of 78.57% (AUROC = 0.901; CI 95% 0.861–0.941) as shown in Fig. 2. PPV was 55% but NPV was 97.1%.

Patients presenting to the ED with symptoms occurred 9 or more days before were also tested using CovHos Score. A cut-off of 22 had a 63.64% sensitivity and a 64.9% specificity in predicting SRF (AUROC = 0.672; 95%CI 0.585–0.798). PPV was 41.2% and NPV was 81.8%.

Furthermore, CovHos score was tested for predicting 30-day mortality. The ROC analysis allowed to define 28 points as the most accurate cut-off in predicting 30-day mortality: it showed a sensitivity of 69% and a specificity of 79% (AUROC 0.816; CI 95% 0.759–0.873, p value < 0.001). PPV and NPV were respectively 28.6% and 95.4%. NEWS2 proved to be less reliable also in predicting mortality (AUROC 0.670; sensitivity of NEWS2 ≥ 5 was 35.3% and specificity was 89.2%).

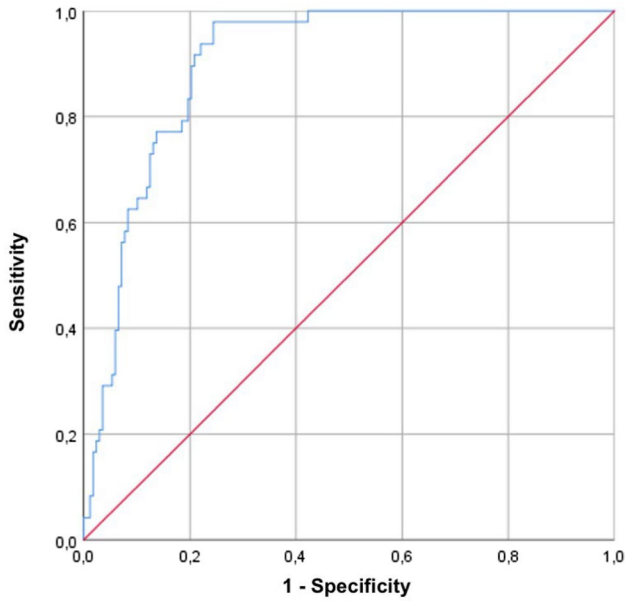

Fig. 2 Receiver operating characteristic (ROC) analysis of CovHos score in predicting severe respiratory failure (SRF) in COVID-19 patients admitted to the Emergency Department up to 8 days from symptoms onset

Limitations

Some limitations should be noted, such as the monocentric nature of the study, the small number of patients included and the different SARS-CoV-2 variants circulating at the time of data collection.

Conclusion and discussion

COVID-19 could be a suddenly deteriorating disease that needs prompt recognition and management. Considering the unexpected evolution of this condition and the burden on healthcare systems all over the world, it is crucial to early identify standard parameters able to predict the need of higher intensity of care at first medical contact such as the admission to the ED.

This study aims to validate CovHos score on a different population of COVID-19 patients admitted to the ED.

Primary endpoint of this study was to determine a CovHos Score cut-off able to detect the risk of evolving into SRF or 30-day mortality in COVID-19 patients presenting to the ED.

Population was divided into three groups based on the maximum intensity of care given: patients discharged directly from the ED, patients admitted to an ordinary ward and lastly patients who required a sub-intensive or intensive management or died during hospital stay.

In our population, a CovHos score of 12 points had 84% sensitivity and 64% specificity in predicting the need of hospital admission. Sensitivity was consistent with the previous study (85%), while specificity was considerably lower compared to that population (82.4%). The difference between these results is probably due to the diversity of the population investigated and to a lack of objective hospitalization criteria.

SRF, defined according to WHO criteria as: $SpO_2 < 93\%$ with 100% FiO_2 (reservoir mask, continuous positive airway pressure ventilation or other non-invasive ventilation), $RR > 30$ breaths/minute or respiratory distress, was then chosen as a more reliable and standardized indicator. Statistical analysis of all patients developing SRF during hospitalization allowed us to identify a new CovHos cut-off of 22 in predicting SRF at the ED admittance. A CovHos of 22 or more yielded 84.7% sensitivity and 75.3% specificity in predicting SRF at the time of admission to the ED. In particular, a CovHos score cut-off of 22 or more had 91.7% sensitivity and 78.6% specificity in detecting SRF prior to its development in patients presenting to the ED up to 8 days from symptoms onset; meanwhile, sensitivity and specificity were significantly lower in the group complaining symptoms for longer than 8 days (63.6% and 64.3% respectively). Key point of our study is that a CovHos score lower than 22, in patients with COVID-19 symptoms onset dated 8 or less days prior to the ED admittance, had a NPV of 97.06% for the development of SRF, meaning that almost none of those patients will evolve into SRF and could therefore be suitable for a lower intensity of care. On the other hand, PPV was 55% showing that patients with a CovHos score of 22 or more would not necessarily develop SRF. The need of a new score for COVID-19 patients emerged also from the comparison with NEWS2, which performed poorer than CovHos score in predicting the occurrence of SRF, probably due to its lower discriminating power between COVID-19 admissions and non-COVID-19 admissions [7].

Correlation between CovHos score and 30-day mortality was also investigated. A CovHos score lower than 28 had 69% sensitivity and 79% specificity for the prediction of 30-day mortality at the time of admission to the ED, with a NPV of 95.4% and a PPV of 28.6%, denoting that almost all patient with a CovHos score lower than 28 will not undergo death.

In conclusion, CovHos is an effective tool to guide ED physicians in predicting SRF at the time of first medical contact, especially in patients affected by an unpredictable disease such as COVID-19. We believe CovHos could be helpful in deciding the correct setting of care, as in selecting patients who might be eligible for home management or may be at risk of sudden worsening and would require a higher intensity of care, especially during a global pandemic

where resources are limited and clinical pathways are often complex.

Funding None.

Availability of data and materials The dataset analyzed during the current study is available from the corresponding author on reasonable request.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Ethics approval This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of the University of Bologna (number: 551/2020/Oss/AOUBo). Informed consent was obtained from all individual participants included in the study.

Human and animal rights statement The study was approved by our local Ethics Committee (approval number: 551/2020/Oss/AOUBo).

Informed consent All patients provided oral informed consent to be included in the study.

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