ORGINAL ARTICLE

Priority in interhospital transfers of patients with severe COVID-19: development and prospective validation of a triage tool

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Objectives. To develop and validate a triage scale (Spanish acronym, TIHCOVID) to assign priority by predicting critical events in patients with severe COVID-19 who are candidates for interhospital transfer.

Methods. Prospective cohort study in 2 periods for internal (February–April 2020) and external (October–December 2020) validation. We included consecutive patients with severe COVID-19 who were transported by the emergency medical service of Catalonia. A risk model was developed to predict mortality based on variables recorded on first contact between the regional emergency coordination center and the transferring hospital. The model's performance was evaluated by means of calibration and discrimination, and the results for the first and second periods were compared.

Results. Nine hundred patients were included, 450 in each period. In-hospital mortality was 33.8%. The 7 predictors included in the final model were age, comorbidity, need for prone positioning, renal insufficiency, use of high-flow nasal oxygen prior to mechanical ventilation, and a ratio of PaO_2 to inspired oxygen fraction of less than 50. The performance of the model was good (Brier score, 0.172), and calibration and discrimination were consistent. We found no significant differences between the internal and external validation steps with respect to either the calibration slopes (0.92 [95% CI, 0.91–0.93] vs 1.12 [95% CI, 0.6–1.17], respectively; *P* = .150) or discrimination (area under the curve, 0.81 [95% CI, 0.75–0.84] vs 0.85 [95% CI, 0.81–0.89]; *P* = .121).

Conclusion. The TIHCOVID tool may be useful for triage when assigning priority for patients with severe COVID-19 who require transfer between hospitals.

Keywords: COVID-19. Critical care. Emergency health services. Disaster planning. Regional health planning.

Desarrollo y validación prospectiva de la escala TIHCOVID: una herramienta de triaje y priorización del traslado interhospitalario de pacientes COVID-19 graves

Objetivo. Desarrollar y validar una escala predictiva de eventos críticos en pacientes con infección grave por COVID-19 candidatos a traslado interhospitalario (TIH) que facilite el triaje y la priorización del transporte sanitario.

Método. Estudio de cohortes prospectivo divido en dos periodos: validación interna (febrero-abril 2020) y validación externa (octubre-diciembre 2020). Se incluyeron consecutivamente los pacientes con infección grave por COVID-19 trasladados por el Sistema de Emergencias Médicas de Cataluña. Se construyó un modelo predictivo de las variables asociadas a la mortalidad recogidas en el momento del primer contacto entre el hospital emisor y el centro de coordinación. Se calculó el rendimiento del modelo y se comparó la validación interna y externa, evaluando la calibración y la discriminación.

Resultados. Se incluyeron 900 pacientes, 450 pacientes en cada periodo de estudio. La mortalidad durante el ingreso fue del 33,8%. Las 7 variables predictoras incluidas en el modelo final fueron edad, comorbilidad, pronación, insuficiencia renal aguda, uso de oxigenoterapia de alto flujo previa a la ventilación mecánica invasiva, tabaquismo activo y un valor de $PaO_2/FiO_2 < 50$. El modelo mostró un buen rendimiento (Brier = 0,172) y consistencia en la calibración y discriminación. No se objetivaron diferencias en la pendiente de calibración [0,92 (IC 95%: 0,91-0,93) *vs* 1,12 (IC 95%: 0,6-1,17); p = 0,150] ni en la capacidad discriminativa [ABC 0,81 (IC 95%: 0,75-0,84) vs ABC de 0,85 (IC 95%: 0,81-0,89), p = 0,121] entre la validación interna y externa.

Conclusiones. La escala TIHCOVID puede ser de ayuda para el triaje de pacientes con infección COVID-19 grave que precisan traslado interhospitalario.

Palabras clave: COVID-19. Cuidados críticos. Servicios de Emergencias Médicos. Planificación de desastres. Planificación de salud regional.

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Introduction

The crisis caused by the COVID-19 pandemic has shaken the healthcare system, but the lessons learned during this time have provided an opportunity for improvement[1]. The healthcare system, and hospitals in particular, have shown great plasticity increasing their healthcare personnel and the number of intensive care

unit (ICU)-linked beds to cope with a situation comparable to a multiple casualty incident sustained over time[2]. However, the hospitals with the greatest capacity to accommodate large numbers of ICU beds were located in large urban centers. An analysis that studied the distribution of healthcare resources in the United States described that the burden on the healthcare system during the pandemic could be greater in those areas far from major urban centers and with lower ICU availability[3]. On the other hand, the overload of a single hospital has been associated with an increase in mortality due to COVID-19, a fact that highlights the need for coordinated healthcare strategies[4].

Ensuring equity of access to the health care system and maximizing the benefit to patients when resources have been scarce during the pandemic has been the subject of debate and concern in the medical community[5]. It has been suggested that the management of health crisis situations such as the one experienced during the COVID-19 pandemic can best be addressed from a centralized regional coordination center capable of facilitating rapid and coordinated responses. Similarly, improving triage strategies prior to admission to the ICU is a key element in optimizing outcomes in the face of a new crisis[6]. Multiple triage scales have been published in the literature to identify patients affected by COVID-19 at risk of clinical deterioration[7]. These triage scales have been developed to facilitate the management of these patients on admission to hospital, on admission to the emergency department and even prior to hospital admission with clinical data from home[8-12].

To our knowledge, no tool has been described in the literature to aid triage prior to admission to the ICU, applied from a regional health coordination center (CeCoS) that centralizes the demand from hospitals that do not have the necessary resources. The aim of this study was to design and validate a scale predictive of critical events for patients with severe COVID-19 infection who require transfer from other hospitals.

Methods

Design and setting

Prospective observational cohort study conducted in Catalonia over two periods. It included critical patients managed by the interhospital transfer desk of the Sistema d'Emergències Mèdiques de Catalunya (SEM). The TIH-COVID (Interhospital Transfer COVID) scale was developed in the first period of the study and external validation was performed in the second period. This study is published in accordance with the TRIPOD[13] guidelines. Its design was approved by the Ethics and Clinical Research Committee of the Institut d'Investigació Sanitària Pere Virgili (107/2020). A waiver of informed consent was obtained from the participants.

The EMS is part of the Catalan public health system, offering 100% coverage of the territory. Catalonia has an area of 32 108 km^2 with a population of 7 722 203 million inhabitants distributed asymmetrically[14]. Of this population, 42.8% is concentrated in the metropolitan area of Barcelona with an area of 636 km^2, representing 2% of the total territory[15]. In February 2020, 63.2% of Catalan ICU beds were located in the metropolitan area of Barcelona and 5 hospitals with the largest capacity accounted for 54.4% of the total number of ICU beds.

The SEM centralizes and coordinates all interhospital transfers from a single CeCoS located in Hospitalet del Llobregat (Barcelona). It has an interhospital transfer desk (TIH) composed of technicians, nurses and a physician, which receives the transfer request from the sending center and searches for the best available receiving center according to the requirements and priority of each patient. During the pandemic, this table was reinforced with more personnel to meet the growing demand and the figure of the physician specialized in critical patient care was incorporated, with the objective of coordinating the team and providing support to the clinicians of the hospitals that requested it. Interhospital transfers were carried out by EMS advanced life support (ALS) units consisting of a health technician and a nurse or a technician, a nurse and a physician. During some phases of the pandemic, up to 8 EMS ALS units, which usually combine prehospital emergency care with interhospital transfers of critically ill patients, were used exclusively for the transfer of severe COVID-19 patients.

Patients and collection of variables

We consecutively included all patients with COVID-19 infection with severity criteria managed by the HIT desk at the request of the sending hospital and who, due to their clinical situation, required transfer to another hospital via an ALS unit. Patients with a positive test for COVID-19 and who were transferred for a non-respiratory disease were excluded. Severity criteria were considered to be respiratory failure requiring high-flow oxygen therapy or ventilatory support (invasive or noninvasive), sustained shock or target organ failure. The recruitment period for internal validation of the scale was from February 27 to April 31, 2020. For external validation, the period was from October 1 to December 15, 2020.

The following variables were collected: 2 demographic (age and sex); 7 referring to personal history (hypertension, diabetes, obesity defined by a body mass index > 30, smoking, history of chronic respiratory pathology including chronic obstructive pulmonary disease - COPD - GOLD A-B, asthma or obstructive sleep apnea syndrome); presence of severe comorbidities including COPD GOLD C-D, pulmonary fibrosis, stroke with residual neurological deficit, chronic heart failure with NYHA -New York Heart Association- III-IV, neurodegenerative diseases, active cancer, liver cirrhosis Child BC; baseline status with the Clinical Frailty Scale -CFS-; duration of symptoms; history of contact with

the health system in the 7 days prior to admission; type of oxygen therapy and ventilatory support; 5 variables of the acute episode at the time of contact for transfer (PAO_2/FIO_2 ratio, need for pronation, acidosis or shock, lactate > 3 mmol/L and acute renal failure); and 2 structural (ICU in the hospital of origin and location of the patient in the sending hospital). The variables were collected at the time of telephone contact with the medical staff of the sending hospital.

The primary outcome variable was a critical event defined as death from any cause during hospital admission. To obtain it, follow-up was performed until the event or discharge of the patient by means of access to the digitalized clinical history. The same variables were collected in the two study periods. In the first, they were used as an aid to establish the priority of each patient. In the second, the predictive model was applied and made available to the staff of the HIT desk, through access to an online website[16].

Development of the predictive model (internal validation cohort)

Qualitative variables were described by number of cases and percentages. Quantitative variables were described with the mean and standard deviation (SD), if they followed a normal distribution, which was tested with the Kolmogorov-Smirnov test, or with the median and interquartile range (IQR), otherwise. The analysis of the distribution of qualitative variables was performed with the chi-square test or Fisher's exact test as appropriate, and that of quantitative variables was performed with Student's t test or the Mann-Whitney U test.

To determine the predictive model of the variables associated with mortality, the bootstrapping technique was used to quantify the optimism of the final prediction model. The treatment of missing values was performed using multiple imputation techniques. Five hundred bootstrap replicates with replacement were created. Variables that had been automatically selected in at least 70% of the bootstrap samples were included in the final model. Variables that had been selected between 40% and 70% of the samples were analyzed individually and included in the model if the bilateral *P* value was < .05.

Subsequently, to reflect the weight of each variable, a logistic regression model was performed and the odds ratio (OR) was calculated with its 95% confidence interval (CI), crude and adjusted for the significant differences between the two groups found in the univariate study. In the final model, each variable was ordered into categories to facilitate its use and weighting in the construction of the nomogram. The nomogram represents the scores obtained for the different predictor variables of the model, which allows the calculation of the predicted probability of death.

The overall performance of the model was assessed with the Brier score; the discriminative ability (ability of the model to distinguish between individuals who experience the event of interest and those who do not) by the area under the curve (AUC) and the calibration (agreement between predicted and observed risk) by the slope and calibration plot. Three risk groups (low, intermediate and high) were defined according to the optimization of the cut-off points calculated for the predicted probabilities.

External validation cohort

For the external validation of the scale, the discrimination capacity and calibration were compared between both cohorts. Sensitivity, specificity, ABC with the Delong test and the slope of the calibration curve were compared. We also compared the predicted probability, score, and incidence of mortality of the 2 cohorts, according to risk groups. In all comparisons, differences were accepted as statistically significant if the bilateral *P* value was less than .05, or if the 95% CI of the OR excluded the value 1. Statistical analysis was performed with SPSS version 24.0 for Windows (SPSS Inc, Chicago, USA) and the R Studio program.

Results

During the study period, 6908 HIT were managed. During the internal validation period, 699 patients diagnosed with COVID-19 were transferred and 690 during the external validation period. Finally, 450 patients affected by severe COVID-19 were transferred using a VAS unit in each study period (Figure 1).

Internal validation cohort

The characteristics of this cohort are shown in Table 1. The patients had a mean age of 60.1 years (SD 12.3) and 69.1% were male. The hospital of origin in 129 cases (28.7%) had an ICU and 314 patients (69.8%) came from an emergency department. The mean length of stay in the sending hospital prior to transfer was 3.5 days (SD 2.7) with no differences between living and dead patients [3.8 (SD 2.6) vs. 3.2 (SD 2.9); *P* = .284]. Of all patients, 85.3% required invasive mechanical ventilation (IMV) and orotracheal intubation at the sending hospital. The median mean patient transfer time was 1.6 hours (ICER 1.2-2.7).

The final predictive model shown in Table 2 presented the following adjusted ORs: age (per year of increase) 1.06 (95% CI: 1.04-1.09; *P* < .001), comorbidities 2.08 (95% CI: 1.12-3.87; *P* = .021), need for pronation 4.27 (95% CI: 2.59-7.02; *P* = .001), acute renal failure 2.08 (95% CI: 1.21-3.57; *P* = .008), use of high nasal flow prior to IMV 0.26 (95% CI: 0.13-0.55; *P* < .001), active smoking 3.08 (95% CI: 1.07-8.87; *P* = .038) and a PaO_2/FiO_2 value < 50 1.99 (95% CI: 0.78-5.04; *P* = .148). The model showed good overall performance (Brier = 0.172) and consistency in discrimination and calibration presenting an AUC of 0.81 (95% CI: .75-.84) and a slope of the calibration curve of 0.92 (95% CI: 0.91-0.93).

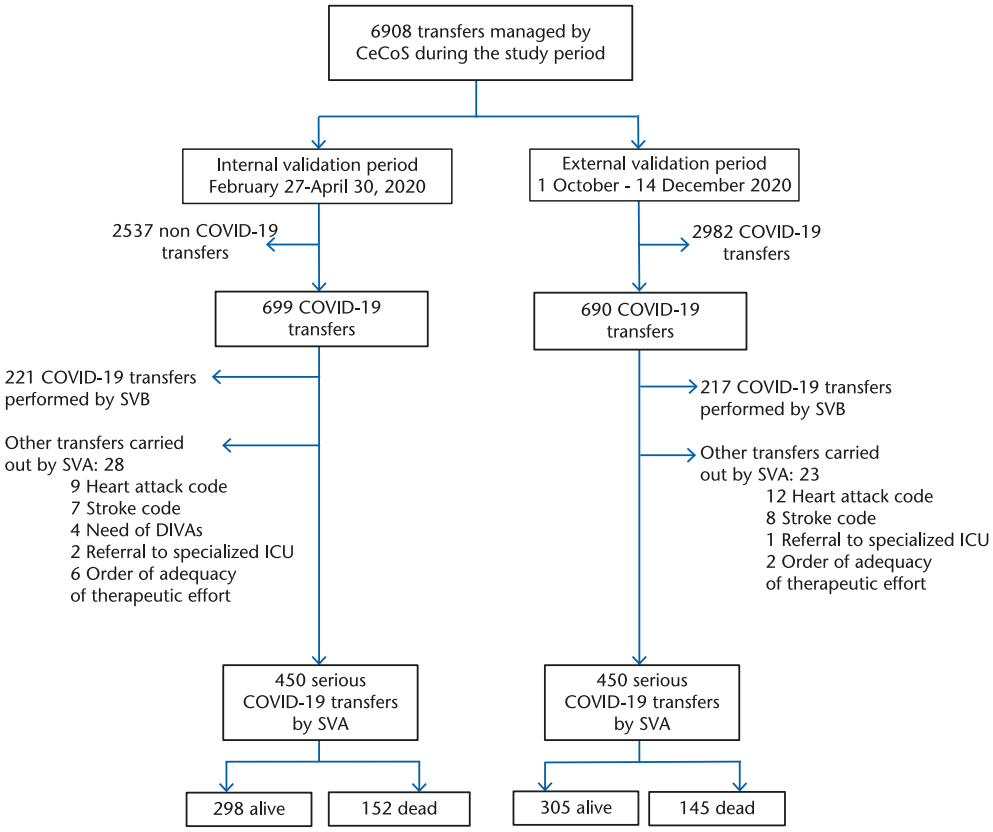


Figure 1. Flow diagram of the patients included during the study period.
*CeCos: health coordination center. **BLS: basic life support. ***ALS advanced life support (includes medical advanced life support and nursing advanced life support).
BLS: basic life support; ALS: advanced life support; DIVA: digital intravenous subtraction angiography; ICU: intensive care unit.

Figure 2 shows the details of the score for each variable, the analog normogram constructed and the relationship between its score and the probability of death. Three risk groups were created: low risk (< 100 points), intermediate (between 100 and 130 points) and high risk (> 130 points). The number of patients included in each group was 118 (27.5%) for low risk, 151 (35.0%) for intermediate risk and 161 (37.5%) for high risk, and the observed mortality for each group was 8.0%, 39.6% and 69.6%, respectively. To perform the predictive calculation of mortality an online calculator is available on the web[16].

External validation cohort

Table 1 shows the characteristics of the external validation cohort and its comparison with the internal validation cohort. In the external validation cohort, a higher percentage of patients with active smoking, respiratory history and with higher CFS scores were observed. There was a lower proportion of patients requiring IMV, but a higher percentage of patients with acidosis or shock and acute renal failure were found.

Despite these observed differences, mortality during hospital admission was similar in both groups [152 (33.8%) vs 145 (32.2%); *P* = .67]. The median number of days prior to the critical event was 9 (IQC 5-19). Figure 3 shows the comparative application of the predictive model in both cohorts. In the internal validation cohort the sensitivity was 0.79 (95% CI: 0.77-0.81) and the specificity was 0.69 (95% CI: 0.68-0.71) with an AUC of 0.81 (95% CI: 0.75-0.84). In the external validation cohort, a sensitivity of 0.82 (95% CI: 0.81-0.83) a specificity of 0.70 (95% CI: 0.69-0.71) with an ABC of 0.85 (95% CI: 0.81-0.89) was found. No significant differences were found in discriminatory ability (DeLong Test *P* = 0.121) or in the slope of the calibration curve between the two validation cohorts [0.92 (95% CI: 0.89-0.95) vs. 1.12 (95% CI: 0.6-1.17); *P* = .15].

Discussion

This prospective study has developed, and then validated, a simple risk scale composed of 7 variables with good predictive ability of critical events for patients with severe COVID-19 requiring HIT.

We cannot compare the TIHCOVID scale with other similar scales, given its specificity for assessing the TIH of a severe COVID-19 patient. It is true that other scales

Table 1. Clinical-epidemiological characteristics and severity variables of the patients included in the internal validation and external validation cohort of the TIHCOVID scale

	Internal validation cohort (n = 450)						External validation cohort (n = 450) T						
	Total n (%)	Lost value n (%)	Alive N = 298 n (%)	Dead N = 152 n (%)	Odds Ratio (CI 95%)	*p*-Value	Total n (%)	Lost value n (%)	Alive N = 305 n (%)	Dead N = 145 n (%)	Odds Ratio (CI 95%)	*p*-Value	*p*-Value*
Epidemiological variables													
Age (years) [mean (SD)]	60.1 (12.3)	0 (0.0)	57.5 (12.5)	65.3 (10.2)	NA	< .001	59.8 (13.1)	0 (0.0)	56.3 (14.3)	67.1 (9.5)	NA	< 0.001	0.993
Men	311 (69.1)	0 (0.0)	203 (68.1)	108 (71.1)	1.04 (0.92-1.19)	.597	329 (73.1)	0 (0.0)	213 (69.8)	116 (80.0)	1.14 (1.03-1.29)	.023	.211
Personal background													
Arterial hypertension	229 (51.2)	3 (0.7)	132 (44.7)	97 (63.8)	1.43 (1.20-1.70)	< .001	237 (52.9)	2 (0.4)	152 (50.2)	85 (58.6)	1.43 (0.97-2.13)	.072	.271
Diabetes	113 (25.2)	3 (0.7)	71 (24.1)	42 (27.6)	1.13 (0.85-1.50)	.480	124 (27.7)	3 (0.7)	79 (26.1)	45 (31.3)	1.29 (0.83-1.98)	.255	.870
Obesity (BMI ≥ 30 kg/m^2)	116 (26.0)	4 (0.8)	69 (23.3)	47 (31.3)	1.50 (0.97-2.32)	.069	104 (23.3)	4 (0.8)	70 (23.2)	34 (23.6)	1.03 (0.64-1.65)	.907	.292
History of smoking		4 (0.8)						3 (0.7)					.011
Never	296 (66.4)		210 (71.2)	86 (57.0)	Reference	.011	295 (66.0)		216 (71.4)	79 (54.9)	Reference	.003	
Active smoker	22 (4.9)		12 (4.1)	10 (6.6)	2.03 (1.20-4.88)	.006	43 (9.6)		25 (8.2)	18 (12.5)	1.96 (1.02-3.79)	.045	
Former smoker	128 (28.7)		73 (24.7)	55 (36.4)	1.84 (0.85-2.83)	.112	109 (24.6)		62 (20.4)	47 (32.6)	2.07 (1.30-3.26)	.002	
Respiratory history***	90 (20.1)	2 (0.4)	52 (17.6)	38 (25.0)	1.43 (0.98-2.06)	.083	123 (27.5)	3 (0.7)	76 (25.1)	47 (32.6)	1.30 (0.96-1.76)	.095	.013
Severe comorbidities****	81 (18.0)	0 (0.0)	36 (12.1)	45 (29.6)	2.45 (1.66-3.63)	< .001	100 (22.6)	7 (1.5)	43 (14.3)	57 (39.9)	2.78 (1.98-3.92)	< .001	.134
Clinical Frailty Scale (CFS)								0 (0.0)					.043
1	75 (16.7)	0 (0.0)	65 (21.8)	10 (6.6)	Reference	< .001	61 (13.6)		48 (15.7)	13 (9.0)	Reference	< .001	
2	209 (46.4)	0 (0.0)	150 (50.3)	59 (38.7)	2.56 (1.23-5.32)	.012	197 (43.7)		149 (48.9)	48 (33.1)	2.79 (1.04-5.48)	.008	
3	147 (32.7)	0 (0.0)	77 (25.8)	70 (46.1)	5.92 (2.81-12.34)	< .001	169 (37.6)		99 (32.5)	70 (48.2)	4.80 (2.35-11.77)	< .001	
≥ 4	19 (4.2)	0 (0.0)	7 (2.0)	13 (8.6)	14.08 (4.32-45.45)	< .001	23 (5.1)		9 (2.9)	14 (9.7)	13.02 (4.46-39.81)	< .001	
Duration of symptoms (days) mean (SD)	7.9 (6.6)	0 (0.0)	7.3 (5.8)	9.1 (5.4)	NA	.192	6.6 (6.1)	23 (5.1)	7.2 (5.7)	5.3 (7.3)	NA	.096	.243
Contact with the system within the previous 7 days	135 (30.1)	1 (0.2)	87 (29.3)	48 (31.6)	1.08 (0.80-1.44)	.696	112 (26.6)	29 (6.4)	74 (25.8)	38 (28.1)	1.12 (0.68-1.41)	.624	.138
Type of oxygen therapy and ventilatory support													
No need for IMV	66 (14.7)	0 (0.0)	55 (18.5)	11 (7.8)		.552	157 (34.9)	0 (0.0)	135 (44.3)	22 (15.2)		.065	< .001
Oxygen mask only	21 (4.7)		17 (5.7)	4 (2.6)	Reference		22 (4.9)		17 (5.6)	5 (3.4)	Reference		
AFN therapy	23 (5.1)		21 (7.0)	2 (1.3)	0.41 (0.07 a 2.48)	.328	56 (12.4)		54 (17.7)	2 (1.4)	0.13 (0.02-0.71)	.019	
NIV	15 (3.3)		11 (3.7)	4 (2.6)	1.55 (0.32 a 7.50)	.589	24 (5.3)		18 (5.9)	6 (4.1)	1.13 (0.29-4.41)	.857	
Both AFN and NIV	7 (1.6)		6 (2.0)	1 (0.7)	0.71 (0.07 a 7.76)	.776	55 (12.3)		46 (15.1)	9 (6.2)	0.67 (0.19-2.27)	.515	
Need for VMI	384 (85.3)	0 (0.0)	243 (81.5)	141 (92.8)		< .001	293 (65.1)	0 (0.0)	170	123		.107	< .001
Pre-oxygen mask	233 (51.8)		138 (46.3)	95 (62.5)	Reference		113 (25.1)		74 (24.3)	39 26.9)	Reference		
Previous AFN therapy	74 (16.4)		63 (21.1)	11 (7.2)	0.25 (0.13 a 0.51)	< .001	69 (15.3)		41 (13.4)	28 (19.3)	1.29 (0.70-2.40)	.411	
Previous therapy with NIV	67 (14.9)		35 (11.7)	32 (21.1)	1.33 (0.77 a 2.29)	.308	68 (15.1)		35 (11.5)	33 (22.8)	1.79 (0.97-3.31)	.063	
Both AFN and previous NIV	10 (2.2)		7 (2.3)	3 (2.0)	0.62 (0.16 a 2.47)	.500	43 (9.6)		20 (6.6)	23 (15.9)	2.18 (1.07-4.46)	.001	
Acute episode variables at the time of EMS contact													
PAO_2/FIO_2 ratio [mean (SD)]	113.2 (55.1)	4 (0.8)	116.9 (58.3)	105.8 (47.5)	NA	.097	124.2 (59.5)	8 (1.6)	132.5 (61.5)	106.9 (51.1)	NA	< .001	.190
PAO_2/FIO_2 < 50	22 (4.9)	4 (0.8)	10 (3.4)	12 (7.9)	2.09 (1.36-5.04)	.034	3 (0.7)	8 (1.6)	3 (2.1)	0 (0.0)	NA	.009	.004
Need to pronate	230 (51.9)	7 (1.5)	123 (42.0)	107 (71.3)	1.70 (1.44-2.01)	< .001	189 (42.3)	3 (0.7)	83 (27.4)	106 (73.1)	2.68 (2.17-3.30)	< .001	.194
Acidosis or shock	67 (14.9)	0 (0.0)	33 (11.1)	34 (22.4)	2.02 (1.30-3.13)	.002	140 (31.3)	3 (0.7)	69 (22.8)	71 (48.9)	2.47 (2.11-3.36)	< .001	< .001
Lactate > 3 mmol/L	55 (12.2)	0 (0.0)	27 (9.1)	28 (18.4)	1.93 (1.12-3.49)	.016	113 (26.3)	21 (4.7)	61 (21.0)	52 (37.4)	2.24 (1.44-3.50)	< .001	< .001
Acute renal failure	108 (24.0)	0 (0.0)	46 (15.4)	62 (40.8)	2.64 (1.90-3.67)	< .001	143 (31.8)	0 (0.0)	59 (19.3)	84 (57.9)	2.99 (2.29-3.92)	< .001	.045
Secondary variables													
Sending hospital with ICU	129 (28.7)	0 (0.0)	91 (30.5)	38 (25.0)	0.82 (0.59-1.13)	.263	133 (29.6)	0 (0.0)	79 (25.9)	54 (37.2)	1.44 (1.08-1.91)	.014	.826
Patient location		0 (0.0)				.434		0 (0.0)					.303
ICU	57 (12.7)		40 (13.4)	17 (11.2)	Referencia		33 (7.3)		20 (6.6)	13 (9.0)	Reference		
Emergency department	314 (69.8)		202 (67.8)	112 (73.7)	1.04 (0.49 a 2.18)	.395	353 (78.4)		245 (80.9)	108 (74.5)	0.68 (0.33-1.41)		.300
Semi-critical care unit	79 (17.6		56 (18.8)	23 (15.1)	0.77 (0.42 a 1.41)	.980	62 (13.8)		38 (12.5)	24 (16.6)	0.97 (0.41-2.31)		.227

*P-value for comparison of the internal validation cohort with the external validation cohort. **Respiratory history is defined by GOLD A-B COPD: asthma and obstructive sleep apnea syndrome. ***Presence of severe comorbidities is defined by: COPD GOLD C-D, pulmonary fibrosis, stroke with residual neurological deficit, New York Association Class III-IV heart failure, neu-rodegenerative diseases, active cancer, Child B-C liver cirrhosis.

BMI: body mass index; ICU, intensive care unit; BMI, body mass index; NIV, noninvasive ventilation; NHA, nasal high-flow ventilation; NA: not applicable; SD: standard deviation; IMV: invasive mechanical ventilation; HFV: nasal high-flow; NAU: intensive care unit.

Table 2. Final predictive model of the variables associated with the critical event

Variables	OR	95% CI	*p*-Value
Age (per year of increase)	1.06	1.04-1.09	< .001
Comorbidity	2.08	1.12-3.87	.021
Need to pronate	4.27	2.59-7.02	.001
Acute renal insufficiency	2.08	1.21-3.57	.008
Use of AFN prior to IMV	0.26	0.13-0.55	< .001
Active smoking	3.08	1.07-8.87	.038
PaO_2/FiO_2	1.99	0.78-5.04	.148

OR: odds ratio; CI: confidence interval; HFN: high nasal flow; IMV: invasive mechanical ventilation.

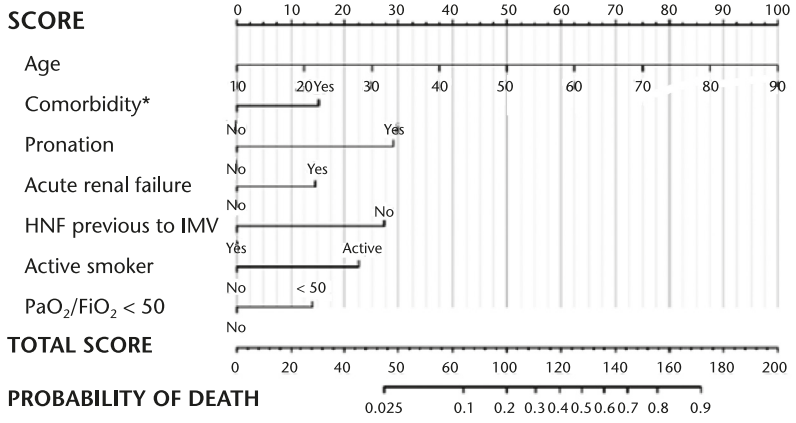
have been developed specifically for COVID-19 patients based on predictive models of clinical deterioration and mortality. The 4C Deterioration Model, available online on the web[17], was performed on the basis of a prospective cohort of COVID-19 patients from Great Britain at hospital admission, included 11 variables and obtained similar discrimination and calibration to the present model[9].

In a comparison of several scales used for the assessment of the critically ill patient, the NEWS scale applied on admission to the ED was the best predictor of admission to the ICU at 7 days and the REMS scale was the best predictor of death at 7 days[11]. Data have been reported in favor of the better performance of the COVID-19 patient-specific scales compared to other commonly used scales such as NEWS[2], MEWS, REMS and CURB-65[9,18]. The TIHCOVID scale has been developed based on a cohort of critically ill patients, and its predictor variables have also been included in predictive models of mortality in patients admitted to the ICU[19,20]. However, the smaller number of variables and

2a

Age	Score
10	0
20	12
30	25
40	38
50	50
60	62
70	75
80	88
90	100
Comorbidities*	**Score**
No	0
Yes	15
PAO_2/FIO_2 < 50%	**Score**
No	0
Yes	14
Cigarette addiction	**Score**
No/former smoker	0
Active smoker	29
ARF	**Score**
No	0
Yes	23
HNF	**Score**
No	27
Yes	0

2b



2c

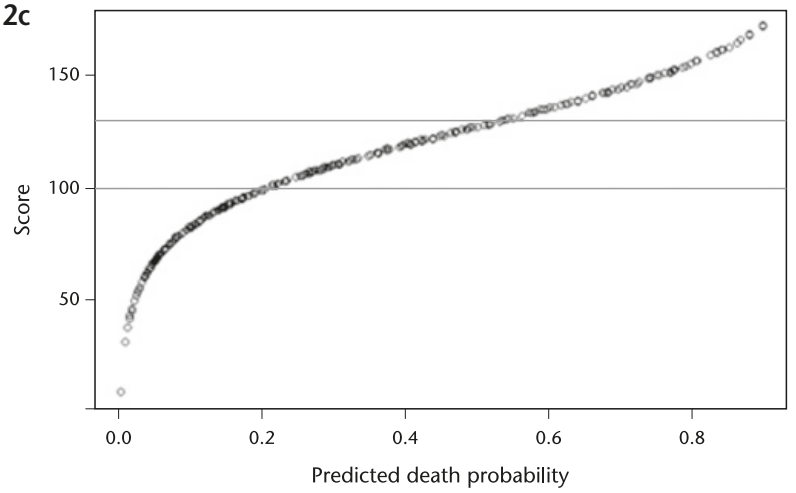


Figure 2. Scoring of the variables, normogram and probability of death. Fig. 2a. Detail of the score of each variable of the TIHCOVID-19 scale of the predictive model. Fig. 2b. Analog normogram for the calculation of the predicted probability of death. Fig. 2c Relationship of the predicted probability of death according to the risk score obtained: low risk (< 100 points), intermediate risk (between 100 and 130 points) and high risk (> 130 points).
*The presence of comorbidities is defined by: COPD GOLD III-IV, stroke with residual clinic, heart failure New York Association Class > II, neurodegenerative diseases, active neoplasia, Child B-C liver cirrhosis. ARF: presence of acute renal failure; HNF: use of high nasal flow.

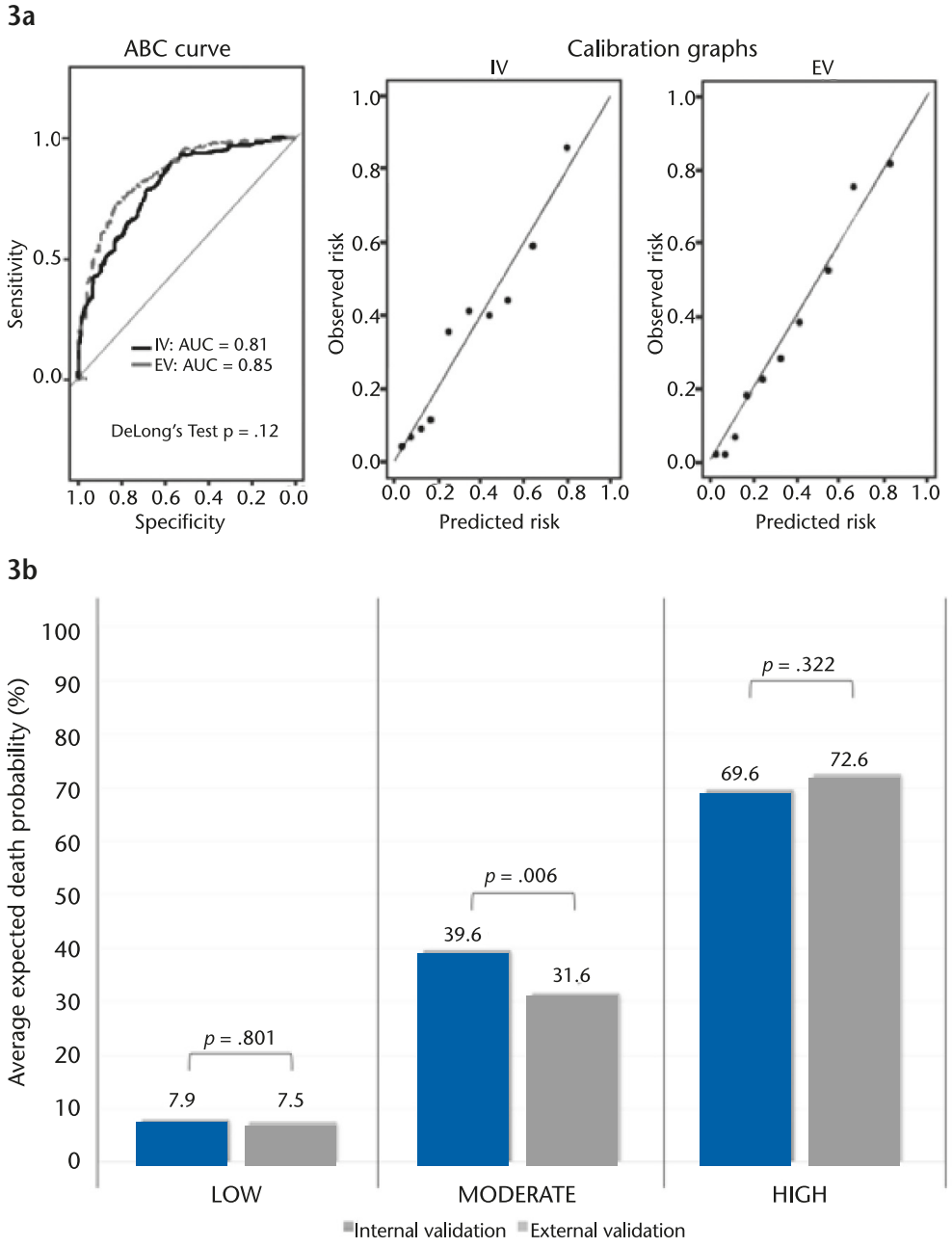


Figure 3. Comparison of the application of the TIHCOVID-19 scale in the internal validation (VI) and external validation (VE) cohorts. Fig. 3a. Comparative graph of the area under the curve (AUC) and calibration. Fig. 3b. Comparative graph of the mean expected probability of death according to risk group.

the lower weight of the analytical risk markers increase the agility and applicability of this scale from the first contact between the issuing center and the CeCoS. Age is the item with the greatest weight in the final score, and is one of the variables with the greatest evidence of poor evolution[21,22].

The same occurs with the presence of active smoking, also introduced in the calculation tool, which is widely related to worse prognostic data[23]. The need for pronation and PAFI < 50 have been two variables related to worse prognosis and reflect a high need for oxygen therapy[19,21]. One of the utilities of the TIHCOVID scale is its ability to identify the highest and lowest risk groups, which has implications for the decision on the most appropriate resource for transport. A CeCoS that centralizes emergency calls is useful for monitoring calls from the population and is helpful for decision making by health authorities during a pandemic[24,25]. Likewise, the centralization of the demand for TIH in a regional coordination center could give real-time signals of the overload of the health system. Regarding future lines of research, the TIHCOVID scale could also be applicable

to all those epidemic peaks of respiratory disease in which the health system is overloaded. The transfer times described in this study are relatively long considering the size of the region studied. Analysis of the influence of the TIHCOVID scale on total transfer times and analysis of the flow and distribution of critical patients coordinated from a centralized regional center as if it were a "single ICU" would merit future studies. It has already been described that HIT of the critical patient is not associated with an increase in adverse events when performed by trained and specialized teams[26,27]. The mortality of this series is comparable to that of large series of patients admitted to the ICU, both nationally and internationally[19,28].

With respect to limitations, this study was only performed in a single CeCos. The validation system could be considered external, since the model development cohort and the prospectively collected validation cohort are temporally separated[13]. However, a geographic and broad external validation with other coordinating centers would be desirable, so collaboration with emergency systems in other regions has been initiated. Bias in data collection cannot be ruled out, since the data were obtained by telephone at the time of the first contact between the sending center and the CeCos.

In conclusion, the TIHCOVID scale successfully predicts a critical event in patients affected by severe COVID-19 requiring transfer to another hospital and can be of help in decision making for triage and prioritization of transfer in situations of disproportion between demand and available resources in the health system.

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