Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Journal of Infection 81 (2020) e96–e98

Contents lists available at ScienceDirect

Journal of Infection

journal homepage: www.elsevier.com/locate/jinf

Applicability of the CURB-65 pneumonia severity score for outpatient treatment of COVID-19

Dear editor,

Tomlins and colleagues recently reported in this journal the clinical features of 95 sequential hospitalised patients with novel coronavirus 2019 disease (COVID-19) in the first UK cohort.[1] Interestingly, consistent with the evidence supporting the use of CURB-65 as a predictor of mortality secondary to community acquired pneumonia (CAP), non-survivors had a significantly higher CURB-65 score versus survivors (2.5 versus 1 respectively).

The CURB-65 is a severity score for CAP, comprising 5 variables, attributing 1 point for each item: new onset confusion; urea >7 mmol/L; respiratory rate ≥30/minute, systolic blood pressure <90 mmHg and/or diastolic blood pressure ≤60 mmHg; and age ≥65 years.[2] It has been extensively validated to predict 30-day mortality in CAP,[3] and divides patients into 3 groups: score 0–1: low risk of 30–day mortality (0.7–3.2%); score 2: intermediate risk (13%) and score 3–5: high risk of 30–day mortality (17–57%). The Infectious Diseases Society of America / American Thoracic Society and the British Thoracic Society guidelines suggest that patients with CURB-65 scores of 0–1 are at low risk of death and thus may be managed as outpatients.[4,5] However, whether CURB-65 can be applicable to COVID-19 patients for the decision of outpatient treatment is still unknown.

Here, we describe a retrospective single-centre study assessing the performance of the CURB-65 to predict the risk of unfavourable outcome. Hospitalized patients aged 18 or over diagnosed with COVID-19, based on positive SARS-CoV-2 real-time reverse transcriptase-polymerase chain reaction on nasal swabs, and/or typical abnormalities on chest computed tomography (CT) were included in the study. Patients were excluded if they were directly admitted to the intensive care unit (ICU). Their baseline demographics, co-morbidities, clinical symptoms, vital signs, and laboratory results on admission were retrospectively collected. CURB-65 scores were calculated retrospectively. A poor outcome was defined as the need of mechanical ventilation (non-invasive ventilation (NIV) and/or high flow nasal cannula (HFNC) and/or invasive mechanical ventilation) and/or death, whichever occurred first, within the 14 days following admission. The association between the CURB-65 and the outcome was assessed by a univariable Cox proportional hazard regression model to calculate hazard ratios (HR) and their 95% confidence intervals (95%CI). The study was approved by the local institutional review board (IRB 00006477).

A total of 279 patients hospitalized between March 15th and April 14th, 2020 were included in this study. Their baseline characteristics at admission are described in Table 1. According to the CURB-65, 171 (61.3%) patients were considered at low risk (CURB-65 0–1), 66 (23.7%) at intermediate risk (CURB-65=2), and 42 (15.1%) had high risk of 30-day mortality (CURB-65 3–5). During the study period, 88 (31.5%) patients had poor outcome: 48 (17.2%) were admitted to ICU (28 had NIV and/or HFNC, 27 had mechanical ventilation, following NIV and/or HFNC for 7, and 11 patients died within the 14 days) and 40 (14.3%) patients died without being admitted to ICU, leading to 51 (18.3%) deaths within the 14 days following admission.

In the Cox proportional hazard model, the CURB-65 was strongly associated with a poor outcome (HR 1.84, 95%CI 1.10–3.09, P=0.020 for a CURB-65 of 2 compared to 0–1; and HR 4.18, 95% CI 2.54–6.86, p<0.001 for a CURB-65 of 3–5 compared to 0–1; $P_{\text{for linear trend}}$ <0.001). However, among patients with a CURB-65 of 0–1, thus considered at low risk, 36/171 (21.1%) had a poor outcome: 27 (15.8%) were transferred for ICU for HFNC and/or NIV (N=13), and/or invasive mechanical ventilation (N=19), and 15 (8.8%) patients died within the 14 days following admission (Fig. 1).

Our results showed that the CURB-65 is associated with an unfavourable outcome, and thus its application as a severity score for COVID-19 might be promising. However, while the majority of our patients would have been considered at low risk of 30-day mortality according to this severity score, more than 20% of them had a poor outcome. Our study suggests that the applicability of CURB-65 to guide the decision of inpatient or outpatient care is scarce, as it does not safely identify patients who could be managed as outpatients.

In studies of CURB-65 in the clinical practice of CAP, many patients with low CURB-65 scores are not suitable for outpatient treatment because many factors are not incorporated in the score, including hypoxemia requiring oxygen therapy, unmet social needs[6]. In addition, this score also appears to underestimate severity in young patients with CAP. Those limitations might also apply to COVID-19, whose epidemiology and severity also differ from CAP. COVID-19 is a systemic disease, and its severity might be due to virus-activated “cytokine storm syndrome”, exacerbated inflammatory responses.[7] Many known risk factors, such as cardiovascular history, D-dimers, Interleukin-6, but also the myocardial involvement of COVID-19 might not be captured by the CURB-65 [8–10].

Thus, we express our concerns regarding the use of the CURB-65 to guide the decision of inpatient or outpatient care for COVID-19. There is an unmet need to have easy-to-use scores to detect COVID-19 patients at risk, and to guide this decision.

Declaration of Competing Interest

None of the authors declared any competing interest in link with the present study.

Acknowledgements

The authors are indebted to all persons (physicians, surgeons, radiologists, biologists, medical students, and paramedical staff) who were involved in the Beaujon COVID-19 Unit.

https://doi.org/10.1016/j.jinf.2020.05.049

Table 1
Baseline characteristics and outcomes of the study population according to the CURB 65 (N=279)

	Overall (N=279)	CURB-65			*P*
		0–1 N=171	2 N=66	3–5 (N=42)	
Age, mean (SD)	64.8 (16.1)	57.3 (14.4)	75.6 (11.6)	78.2 (9.5)	<0.001
Male sex	183 (65.6)	107 (62.6)	45 (68.2)	31 (73.8)	0.342
Diabetes	77 (27.6)	39 (22.8)	22 (33.3)	16 (38.1)	0.068
Hypertension	131 (47.0)	61 (35.7)	39 (59.1)	31 (73.8)	<0.001
CURB-65 features					
Confusion	23 (8.2)	0 (0)	8 (12.1)	15 (35.7)	<0.001
Urea >7 mmol/L	103 (36.9)	10 (5.8)	52 (78.8)	41 (97.6)	<0.001
Respiratory rate>30/min	59 (21.1)	25 (14.6)	9 (13.6)	25 (59.5)	<0.001
Hypotension	22 (7.9)	3 (1.8)	6 (9.1)	13 (31.0)	<0.001
Age >65 years	145 (52.0)	47 (27.5)	57 (86.4)	41 (97.6)	<0.001
Other clinical features					
Time from symptom onset to admission, (days)	6.76 (4.80)	7.3 (5.0)	6.9 (4.5)	3.4 (3.4)	0.001
Respiratory rate (/minute)	26.2 (6.7)	25.2 (6.1)	25.1 (6.0)	31.5 (7.8)	<0.001
Body temperature >38°C	110 (39.4)	71 (41.5)	23 (34.8)	16 (38.1)	0.630
Cough	190 (68.1)	129 (73.7)	39 (59.1)	22 (52.4)	0.003
Dyspnoea	198 (71.0)	126 (37.7)	39 (59.1)	33 (78.6)	0.043
Myalgia	58 (20.8)	43 (25.1)	8 (12.1)	7 (16.7)	0.067
Diarrhoea	55 (19.7)	41 (24.0)	9 (13.6)	5 (11.9)	0.077
Biological features					
Lymphocytes count (G/L)	1.2 (1.0)	0.7 (2.5)	1.0 (0.6)	1.0 (0.7)	0.038
C-reactive protein (mg/L)	126.3 (91.11)	117.0 (86.1)	126.1 (94.2)	164.2 (98.1)	0.013
Creatinine level (µmol/L)	108.2 (75.7)	84.1 (41.6)	134.7 (105.2)	164.1 (95.1)	<0.001
SGOT (U/L)	71.2 (101.9)	65.6 (49.4)	58.7 (38.6)	108.4 (224.5)	0.033
SPOT (U/L)	45.8 (59.1)	47.0 (43.5)	32.79 (24.6)	59.73 (114.1)	0.078
D-dimers (mg/L)	3421.5 (7303.8)	3229.8 (7209.2)	3662.21 (7544.5)	3737.0 (7639.4)	0.945
Us Troponin I (ng/L)	72.7 (421.9)	21.5 (43.8)	46.3 (63.1)	301.3 (1016.1)	0.009
Ferritin (mg/L)	1465.3 (1584.2)	1485.8 (1836.6)	1309.3 (1115.2)	1585.3 (1303.5)	0.824
Outcome					
Favourable	191 (68.5)	135 (78.9)	42 (63.6)	14 (33.3)	<0.001
Unfavourable	88 (31.5)	36 (21.1)	24 (36.4)	28 (66.7)	<0.001
HFNC or NVI	28 (10.0)	13 (11.4)	10 (29.4)	5 (26.3)	0.024
Mechanical ventilation	27 (39.1)	19 (16.2)	5 (14.7)	3 (15.8)	0.977
Deceased	51 (18.3)	15 (8.9)	15 (24.2)	21 (53.8)	<0.001

Results are expressed as count (%) for categorical variables and as mean (standard deviation) for quantitative variables. *SGOT and SPOT were available for 244 (87.5%), us troponin I levels for 157 (56.3%) patients, and ferritin for 112 (29.6%) patients. Abbreviations: AST: aspartate aminotransferase; ALT: alanine aminotransferase; HFNC: high flow nasal cannula; NVI: non-invasive ventilation.

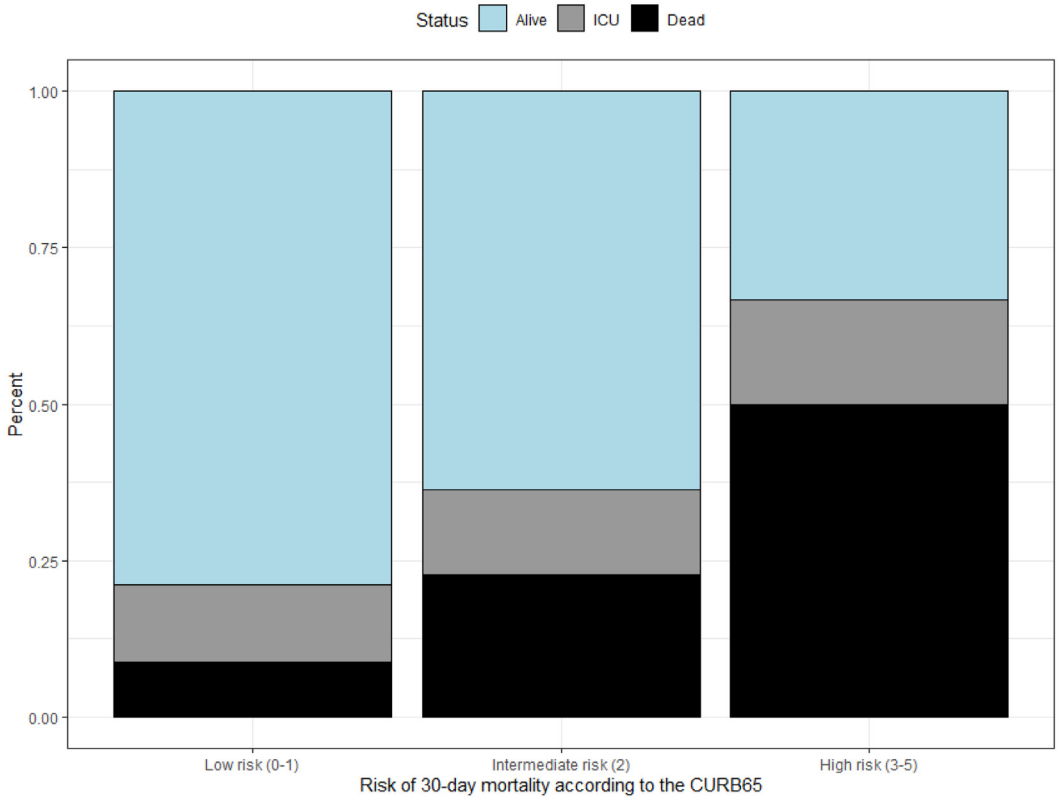

Fig. 1. Description of the outcome according to the CURB-65 (N=279).

The authors would like to thank Louise Arnaud, Victoria Bruce, Michel-Gabriel Cazenave, Lou Chantriaux, Marianne Fontaine, and Emma Solignac for their help on data collection.

Author contributions

All authors have made substantial contributions to this work and have approved the final version of the manuscript. Concept and design: YN, FC, VH, BF, AG. Acquisition of data: FC, AG. Statistical analysis: YN. Interpretation of data: YN, FC, VH, BF, AG. Writing original draft: YN, BF, AG. Writing review and editing: all authors.

Financial support

None.

References

1. Jennifer Tomlins, Fergus Hamilton, Samuel Gunning, Caitlin Sheehy, Ed Moran, Alastair MacGowan. Clinical features of 95 sequential hospitalised patients with novel coronavirus 2019 disease (COVID-19), the first UK cohort. *J Infect* 2020 S0163445320302322. doi:10.1016/j.jinf.2020.04.020.
2. Lim WS, Eerden MMvan der, Laing R, Boersma WG, Karalus N, Town GI, et al. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. *Thorax* 2003;**58**(5):377–82. doi:10.1136/thorax.58.5.377.
3. Chalmers James D, Aran Singanayagam, Akram Ahsan R, Pallavi Mandal, Short Philip M, Gourab Choudhury, et al. Severity assessment tools for predicting mortality in hospitalised patients with community-acquired pneumonia. Systematic review and meta-analysis. *Thorax* 2010;**65**(10):878–83. doi:10.1136/thx.2009.133280.
4. Lim W S, Baudouin S V, George R C, Hill A T, Jamieson C, Le Jeune I, et al. BTS guidelines for the management of community acquired pneumonia in adults: update 2009. *Thorax* 2009;**64**(Suppl 3):iii1–ii55. doi:10.1136/thx.2009.121434.
5. Metlay Joshua P, Waterer Grant W, Long Ann C, Antonio Anzueto, Jan Brozek, Kristina Crothers, et al. Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America. *Am J Respir Crit Care Med* 2019;**200**(7):e45–67. doi:10.1164/rccm.201908-1581ST.
6. Chalmers James D, Julia Rutherford. Can we use severity assessment tools to increase outpatient management of community-acquired pneumonia? *Eur J Intern Med* 2012;**23**(5):398–406. doi:10.1016/j.ejim.2011.10.002.
7. Qing Ye, Bili Wang, Jianhua Mao. The pathogenesis and treatment of the 'Cytokine Storm' in COVID-19. *J Infect* 2020;**80**(6):607–13. doi:10.1016/j.jinf.2020.03.037.
8. Chaomin Wu, Xiaoyan Chen, Yanping Cai, Jia'an Xia, Xing Zhou, Sha Xu, et al. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. *JAMA Intern Med* 2020. doi:10.1001/jamainternmed.2020.0994.
9. Fei Zhou, Ting Yu, Ronghui Du, Guohui Fan, Ying Liu, Zhibo Liu, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The Lancet* 2020;**395**(10229):1054–62. doi:10.1016/S0140-6736(20)30566-3.
10. Zhaohai Zheng, Fang Peng, Buyun Xu, Jingjing Zhao, Huahua Liu, Jiahao Peng, et al. Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis. *J Infect* 2020;**0**(0). doi:10.1016/j.jinf.2020.04.021.

Yann Nguyen*
Departement of Internal Medicine, AP-HP.Nord, Beaujon Hospital, University of Paris, Clichy, France
Center for Epidemiology and Population Health, INSERM U1018, Villejuif, France

Félix Corre, Vasco Honsel
Departement of Internal Medicine, AP-HP.Nord, Beaujon Hospital, University of Paris, Clichy, France

Sonja Curac
Department of Emergency, AP-HP.Nord, Beaujon Hospital, Clichy, France

Virginie Zarrouk, Bruno Fantin, Adrien Galy
Departement of Internal Medicine, AP-HP.Nord, Beaujon Hospital, University of Paris, Clichy, France

*Corresponding author.
E-mail address: yann.nguyen2@aphp.fr (Y. Nguyen)