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Brief Report

Rapid Assessment at Hospital Admission of Mortality Risk From COVID-19: The Role of Functional Status

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ABSTRACT

Objective: To evaluate the role of functional status along with other used clinical factors on the occurrence of death in patients hospitalized with COVID-19.
Design: Prospective cohort study.
Setting: Public university hospital (Madrid).
Participants and Methods: A total of 375 consecutive patients with COVID-19 infection, admitted to a Public University Hospital (Madrid) between March 1 and March 31, 2020, were included in the Prospective Cohort study. Death was the main outcome. The main variable was disability in activities of daily living (ADL) assessed with the Barthel Index. Covariates included sex, age, severity index (Quick Sequential Organ Failure Assessment, qSOFA), polypharmacy ($\geq$5 drugs in the month before admission), and comorbidity ($\geq$3 diseases). Multivariable logistic regression was used to identify risk factors for adverse outcomes. Estimated model coefficients served to calculate the expected probability of death for a selected combination of 5 variables: Barthel Index, sex, age, comorbidities, and severity index (qSOFA).
Results: Mean age was 66 years (standard deviation 15.33), and there were 207 (55%) men. Seventy-four patients died (19.8%). Mortality was associated with low Barthel Index (odds ratio per 5-point decrease 1.11, 95% confidence interval 1.03-1.20), male sex (0.23, 0.11-0.47), age (1.07, 1.03-1.10), and comorbidity (2.15, 1.08-4.30) but not with qSOFA (1.29, 0.87-1.93) or polypharmacy (1.54, 0.77-3.08). Calculated mortality risk ranged from 0 to 0.78.
Conclusions and Implications: Functional status predicts death in hospitalized patients with COVID-19. Combination of 5 variables allows to predict individual probability of death. These findings provide useful information for the decision-making process and management of patients.

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In December 2019, the first case of SARS-CoV-2 infection was reported in Wuhan, China,[1] resulting in an outbreak that was declared a pandemic on March 11, 2020, by the World Health Organization (WHO).[2] COVID-19 pandemic has had a major impact in the Madrid region, where 27,509 cases and 3603 deaths were registered on the same date (March 31, 2020, the last date of inclusion in our study).[3] Regarding age distribution, 86% of deaths have occurred in patients older than 70 years and 95% if we extend to those older than 60 years. Mortality reaches greater than 60% for patients aged $\geq$80 years.[4] Taking this fact into account, it should be expected that relevant

factors associated to mortality in older people, like functional status,[5−8] had been included in predictive models of coronavirus mortality. However, this has not been the case, with its potential impact on the decision-making process.[9]

Deterioration of functional status, as a sign of an augmented vulnerability state and a declining of biological reserves, is generally considered a strong predictor of poor outcome mainly, but not exclusively, in older people.[7,10,11] Often frailty and disability, rather than illness, have significant prognostic value.[5] In fact, frailty predicts mortality in older people independently from other clinical variables.[12−15]

The role of functional status in determining poor outcomes in old patients with COVID-19 has not yet been firmly established. Evidence is even smaller regarding the joint assessment of functioning and other classical factors used in clinical decision making, such as age, sex, comorbidity, and disease severity.[16]

Therefore, the aim of this study was to evaluate, in patients hospitalized with COVID-19, the role of limitations in activities of daily living along with other habitual clinical factors on death during hospitalization, building a predictive model.

Patients and Methods

Study Design and Participants

We analyzed the data of a cohort comprising all the patients with COVID-19 admitted to a Public University Hospital (Madrid, Spain). We have included patients hospitalized from March 1 to 31, 2020, a time period covering the peak of the pandemics in the Madrid region. All cases were selected consecutively according to the date of admission to hospital, due to COVID-19 infection confirmed by positive PCR.

Sources of Information and Data Collection

Information on COVID-19 and the current disease course was collected from hospital electronic clinical records, whereas information on drug treatment and comorbidities before admission were obtained from electronic primary health care records.

Definition of the Outcome

Main outcome included mortality during hospitalization. We followed patients until discharge, death, or June 18, 2020, whichever was first. On June 18, 2020, 2 patients were still in hospital and were excluded from the analyses.

Main Variable of Interest

Disability was the main independent (predictive) variable of interest, assessed by the Barthel Index of Activities of Daily Living (ADL).[17] In those patients with no data on the Barthel Index in their clinical records on admission, the data were recorded from the available information about their basal functioning using their primary health care clinical records. This was not possible in 5 patients, who were excluded from the analyses. Barthel Index score has been split into the following categories: 0 to 60 (severe disability), 65 to 85 (moderate disability), 90% to 95% (mild disability), and 100 (no disability).

Potential Confounders

We collected data about age, sex, and comorbidities (hypertension, diabetes mellitus, obesity, hyperlipidemia, ischemic heart disease, heart failure, atrial fibrillation, thromboembolic disease including deep vein thrombosis and pulmonary embolism, stroke, chronic

obstructive pulmonary disease, asthma, cancer, and chronic kidney disease). To evaluate the number of diseases needed to characterize significant comorbidity, we assessed the number of diseases that were associated with increased mortality (Supplementary Table 1).

Clinical severity was assessed with the Quick Sequential (Sepsis-related) Organ Failure Assessment (qSOFA) score, which identifies high-risk patients for in-hospital mortality. It includes 3 clinical criteria, assigning 1 point for low blood pressure (SBP $\leq$ 100 mmHg), high respiratory rate ($\geq$22 breaths/min), or altered consciousness (Glasgow Coma Scale score < 15). The score ranges 0-3 points.[18]

The number of drug treatments in the month preceding the current hospitalization was also collected. Patients were classified in 2 groups: with ($\geq$5 drugs) or without (<5 drugs) polypharmacy.

Statistical Analyses

Quantitative variables were expressed as means and standard deviations and qualitative variables as percentages. Differences in the quantitative variables between those who died and those surviving were assessed using the Student t test; differences in percentages were assessed using the χ^2 test.

The association between Barthel score and death were assessed using 4 nested logistic regression models: (1) raw model, adjusted for age and sex; (2) additionally adjusted for qSOFA (increases in 1 point); (3) further adjusted for polypharmacy; and (4) further adjusted for the presence of comorbidities ($\geq$3 comorbidities). In addition, using the estimated model coefficients, we computed the expected probability of death for a preselected combination of 4 variable values based on the variables remaining in the regression models for mortality (age, sex, Barthel Index, and comorbidity).

We performed 2 sensitivity analysis. We repeated the analysis excluding patients younger than 40 years, among whom deaths were not observed. The second one regarded the calculated expected probability of death, including the severity (ie, qSOFA) of the clinical status of the patient.

The level of significance was set at P <.05. The analyses were performed using the statistical package R for windows (version 3.6.1).

Ethics

Data used in this project are part of another study approved by the Ethics Research Committee of a Spanish University Hospital (Protocol ID SRAA-COVID19; version 2, March 17, 2020).[19]

Results

The study included 375 patients with a mean age of 66 years (standard deviation 15.33) and 207 men (55.2%) (Table 1). The median number of comorbidities was 2 (interquartile range 1-4). Seventy-four patients died (19.7%), and 299 (79.7%) recovered and were discharged before the end of the follow-up. Differences between the 2 groups were statistically significant for all the morbidities analyzed except for obesity, thromboembolic disease, and asthma.

The median number of morbidities in those who died was 4 (interquartile range 2-5), whereas in those who survived was 2 (interquartile range 0-3). Differences in the Barthel Index between groups were statistically significant (P < .001).

When we looked at qSOFA, 21.67% of patients who died presented at least 2 criteria of severity (median 1) vs 10.45% in the group of patients who recovered (median 0) (P = .043).

In logistic regression analysis, a 5-point lower in the Barthel score was associated with a 13% increased risk of death (OR 1.13, 95% CI 1.05-1.22; P = .002). This association remained significant after further adjustment for the other clinical variables (Table 2). Using the fully adjusted model, mortality was associated with the Barthel score (OR

Table 1
Baseline Characteristics of the Patients

	Total (n = 375)	Death (n = 74)*	Recovered (n = 299)*	P Value
Age (SD)	66.06 (15.3)	76.76 (9.7)	63.38 (15.4)	<.001
Sex, male	207 (55.2)	59 (79.77)	146 (48.8)	<.001
Morbidities				
Hypertension	179 (47.7)	55 (74.3)	123 (41.1)	<.001
Diabetes mellitus	80 (21.3)	38 (51.4)	50 (16.7)	<.001
Obesity	135 (36.0)	31 (41.9)	104 (34.9)	.57
Dyslipidemia	132 (35.2)	33 (44.6)	97 (32.4)	.023
Ischemic heart disease	34 (9.1)	17 (23)	16 (5.4)	<.001
Heart failure	55 (14.7)	28 (37.8)	26 (8.7)	<.001
Atrial fibrillation	35 (9.3)	13 (17.6)	22 (7.4)	.023
Thromboembolic disease	24 (6.4)	5 (6.8)	19 (6.4)	.93
Stroke	39 (10.4)	15 (20.3)	24 (8.0)	.008
COPD	28 (7.5)	12 (16.2)	15 (5.0)	<.001
Asthma	34 (9.1)	6 (8.1)	28 (9.4)	.86
Cancer	51 (13.6)	20 (27.0)	30 (10.0)	<.001
Chronic kidney disease	33 (8.8)	19 (25.7)	14 (4.7)	<.001
Severity index (qSOFA), no. of criteria				
0	183 (48.8)	25 (33.8)	156 (52.2)	.043
1	145 (38.7)	33 (44.6)	112 (37.5)	
2	44 (11.7)	15 (20.3)	29 (9.7)	
3	3 (0.8)	1 (1.4)	2 (0.7)	
Current treatment, no. of drugs				
<5	298 (79.5)	44 (59.5)	253 (84.6)	<.001
≥5	77 (20.5)	30 (40.5)	46 (15.4)	
Barthel Index†				
0-60	18 (4.9)	10 (13.9)	8 (2.7)	<.001
65-85	19 (5.1)	8 (11.1)	11 (3.7)	
90-95	27 (7.3)	11 (15.3)	16 (5.4)	
100	306 (82.7)	43 (59.7)	261 (88.2)	

COPD, chronic obstructive pulmonary disease; SD, standard deviation.
Unless otherwise noted, values are n (%).
*Two patients were still in hospital at the time of closing the database, so they have been excluded for the analyses by groups.
†Five patients do not have data about Barthel Index.

1.11, 95% CI 1.03-1.20; P = .008), sex male (OR 0.23, 95% CI 0.11-0.47, P < .001), age (OR 1.07, 95% CI 1.03-1.10; P < .001), and comorbidity (OR 2.15, 95% CI 1.08-4.30; P = .03) but not to an increase in qSOFA (OR 1.29, 95% CI 0.87-1.93; P = .21) or polypharmacy (OR 1.54, 95% CI 0.77-3.08; P = .23). When we analyzed the effect of each morbidity, only heart failure (OR 2.85, 95% CI 1.36-5.98; P = .006) and chronic kidney disease (OR 2.93, 95% CI 1.21-7.12; P = .018) showed relation to mortality (Supplementary Table 2).

We developed a model to predict the risk of death in male (Supplementary Table 3) and female patients (Supplementary Table 4) including the variables showing to be associated to the risk of death. However, when we made the sensitivity analysis, the inclusion of qSOFA produced moderate increases, higher than 10%, in the individual risk of patients with qSOFA score 2 or 3, mainly in older people (Tables 3 and 4), so we show this "expanded" model. Risk of mortality ranged 0% to 78%. The association between disability and risk of death

showed a dose-dependent relationship. Although mild disability (Barthel Index 90-95) increases the risk moderately, it does in a very significant way when it was moderate or severe, especially in older people.

The main results held in the sensitivity analysis excluding patients younger than 40 years (Supplementary Table 5).

Discussion

In this study, we show that in addition to other variables usually considered, functional status is an independent risk factor for death. Barthel Index remained associated with the risk of death in all the models developed in our study, with a mean increase of 10% to 15% in the risk of death by each decrease of 5 points. This finding expands those recently reported in a multicenter study about the effect of frailty on mortality.[13]

The presence of comorbidity, defined as having ≥3 comorbidities, was associated to an increased risk of mortality, like in many other publications.[20–22] Regarding the individual diseases, only heart failure and chronic kidney disease showed to increase the risk of death, whereas female gender was protective, as previously established by other authors.[23–30] Regarding qSOFA, although it did not show to be associated in the adjusted models to the risk of death, its addition to the predictive model mildly increased the risk of death. Taken as a whole, these findings suggest a modest contribution of clinical severity to the risk of death, a usual finding when functional status is taken into account.[5,7,8]

Age was one of the most important death predictors, which agrees with all previous work about prognostic factors for death in patients with COVID-19. In a large observational study where only clinical factors were studied,[29] age was by much the strongest predictor of death, with a very well-defined dose-dependent relationship. But in our study, functional status seems to modulate the effect of age on mortality. As an example, in people without comorbidity, having a low score in Barthel Index (60) mimics the effect of being 15 years older, with a higher absolute effect as the age of the patients increases. This effect remains in the presence of comorbidity or a poor clinical condition, although slightly moderated, highlighting the prognostic value of function in older people, even higher than the one provided by the diseases.[5–7]

This study has several strengths. We included all the patients admitted along 1 month in our hospital, thus avoiding any kind of selection bias. It must be highlighted that this month (March) was the one where the peak of the pandemic was reached, both in terms of contagion and admissions to hospitals in Spain and in Madrid region.[3] Moreover, the possibility of accessing to the clinical records of the patients in primary care allowed us to check the prehospitalization conditions and diseases, the drugs taken by the patients and their functional status. In fact, this was not possible in only 5 patients out of 375. In our patients, the youngest patient who died had 40 years. To assess this potential source of bias, we repeated the analyses after excluding those patients younger than 40 years, without observing

Table 2
Logistic Regression Model for Mortality

	Model 1		Model 2		Model 3		Model 4	
	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value
Gender: female	0.23 (0.12-0.47)	<.001	0.23 (0.11-0.46)	<.001	0.23 (0.12-0.47)	<.001	0.23 (0.11-0.47)	<.001
Age: 1 y	1.08 (1.05-1.11)	<.001	1.08 (1.05-1.11)	<.001	1.07 (1.04-1.10)	<.001	1.07 (1.03-1.10)	<.001
Barthel Index, 5 points	1.13 (1.05-1.22)	.002	1.12 (1.04-1.21)	.004	1.12 (1.04-1.21)	.005	1.11 (1.03-1.20)	.008
qSOFA: 1 point			1.28 (0.87-1.90)	.21	1.34 (0.90-2.00)	.14	1.29 (0.87-1.93)	.21
Polypharmacy: ≥5 drugs					2.05 (1.07-3.92)	.030	1.54 (0.77-3.08)	.23
Comorbidity: ≥3 diseases							2.15 (1.08-4.30)	.030

Model 1: adjusted by gender, age, and Barthel; model 2: adds qSOFA to model 1; model 3: adds polypharmacy (≥5 drugs) to model 2; model 4: adds ≥3 morbidities to model 3.

Table 3
Risk of Mortality in Men

Age	Comorbidities	qSOFA	Barthel Index			
			100	90	75	60
35 y	<3	0	0.02	0.02	0.03	0.04
		1	0.02	0.03	0.03	0.05
		2	0.03	0.03	0.04	0.06
		3	0.03	0.04	0.05	0.07
	≥3	0	0.04	0.05	0.07	0.09
		1	0.05	0.06	0.08	0.11
		2	0.06	0.07	0.10	0.13
		3	0.08	0.09	0.12	0.16
50 y	<3	0	0.04	0.05	0.07	0.09
		1	0.05	0.06	0.09	0.11
		2	0.06	0.08	0.11	0.14
		3	0.08	0.10	0.13	0.17
	≥3	0	0.10	0.12	0.16	0.21
		1	0.12	0.15	0.19	0.24
		2	0.15	0.18	0.23	0.29
		3	0.18	0.21	0.27	0.33
65 y	<3	0	0.10	0.13	0.17	0.21
		1	0.13	0.15	0.20	0.25
		2	0.15	0.18	0.24	0.30
		3	0.19	0.22	0.28	0.35
	≥3	0	0.23	0.27	0.33	0.40
		1	0.27	0.31	0.38	0.46
		2	0.31	0.36	0.44	0.51
		3	0.36	0.41	0.49	0.57
80 y	<3	0	0.24	0.28	0.34	0.42
		1	0.28	0.32	0.39	0.47
		2	0.32	0.37	0.45	0.53
		3	0.37	0.42	0.50	0.58
	≥3	0	0.43	0.49	0.57	0.64
		1	0.49	0.54	0.62	0.69
		2	0.54	0.60	0.67	0.74
		3	0.60	0.65	0.72	0.78

Table 4
Risk of Mortality in Women

Age	Comorbidities	qSOFA	Barthel Index			
			100	90	75	60
35 y	<3	0	0.00	0.00	0.01	0.01
		1	0.00	0.01	0.01	0.01
		2	0.01	0.01	0.01	0.01
		3	0.01	0.01	0.01	0.02
	≥3	0	0.01	0.01	0.02	0.02
		1	0.01	0.01	0.02	0.03
		2	0.01	0.02	0.03	0.03
		3	0.02	0.02	0.03	0.04
50 y	<3	0	0.01	0.01	0.02	0.02
		1	0.01	0.02	0.02	0.03
		2	0.02	0.02	0.03	0.04
		3	0.02	0.02	0.03	0.04
	≥3	0	0.03	0.03	0.04	0.06
		1	0.03	0.04	0.05	0.07
		2	0.04	0.05	0.06	0.08
		3	0.05	0.06	0.08	0.10
65 y	<3	0	0.03	0.03	0.04	0.06
		1	0.03	0.04	0.05	0.07
		2	0.04	0.05	0.07	0.09
		3	0.05	0.06	0.08	0.11
	≥3	0	0.06	0.08	0.10	0.14
		1	0.08	0.09	0.12	0.16
		2	0.09	0.11	0.15	0.20
		3	0.12	0.14	0.18	0.23
80 y	<3	0	0.07	0.08	0.11	0.14
		1	0.08	0.10	0.13	0.17
		2	0.10	0.12	0.16	0.21
		3	0.12	0.15	0.19	0.24
	≥3	0	0.15	0.18	0.23	0.29
		1	0.18	0.21	0.27	0.34
		2	0.22	0.25	0.32	0.39
		3	0.26	0.30	0.37	0.45

any significant change in the results. Finally, we provide individual risk-of-death tables, for male and female patients, considering the main clinical risk factors easy to collect, providing to the clinician a useful tool for the decision-making process in daily clinical practice.

On the other hand, our study was conducted in only one center. However, this fact unlikely affected the results. In a recent publication done by our group jointly with 7 other hospitals in Madrid, the characteristics of the patients attended to in all of them were quite similar.[19] In addition, we have assessed only clinical risk factors. Although in some studies laboratory biomarkers have been shown to be more strongly associated with critical illness and its outcomes than age and clinical markers,[21,22] this is not always the case.[20,29] Our study was done during the peak of the first epidemic wave, when the lethality was the highest. If this lethality is lower in future waves, the relationship between function and mortality could change. Only 7 patients lived in a nursing home, making these results not applicable to patients of nursing homes. However, this fact is unlikely to modify the meaning of our findings; patients from nursing homes are characterized by a poor functional status plus a high mortality, supporting the relationship observed in our study.

Conclusions and Implications

Functional status is a strong predictor of the risk of death in people admitted to hospitals by COVID-19. Functional status seems to account, at least partially, for the association between age and mortality, although other factors explaining this association cannot be excluded. These findings are of high clinical significance. They refine the prognosis of the patients and provide a tool to improve the decision-making process.

References

1. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 2020;382:727−733.
2. Cucinotta D, Vanelli M. WHO declares COVID-19 a pandemic. Acta Bio-Medica 2020;91:157−160.
3. Department of Homeland Security. Spain.. Available at: https://www.dsn.gob.es/es/actuality/press-room/coronavirus-covid-19-31-march-2020. Accessed June 21, 2020.
4. Borobia AM, Carcas AJ, Arnalich F, et al. A cohort of patients with COVID-19 in a major teaching hospital in Europe. J Clin Med 2020;9:1733.
5. Castro-Rodríguez M, Carnicero JA, Garcia-Garcia FJ, et al. Frailty as a major factor in the increased risk of death and disability in older people with diabetes. J Am Med Dir Assoc 2016;17:949−955.
6. Abizanda P, Romero L, Sánchez-Jurado PM, et al. Age, frailty, disability, institutionalization, multimorbidity or comorbidity. Which are the main targets in older adults? J Nutr Health Aging 2014;18:622−627.
7. Hoogendijk EO, Romero L, Sánchez-Jurado PM, et al. A new functional classification based on frailty and disability stratifies the risk for mortality among older adults: The FRADEA Study. J Am Med Dir Assoc 2019;20:1105−1110.
8. Landi F, Calvani R, Tosato M, et al. Impact of physical function impairment and multimorbidity on mortality among community-living older persons with sarcopaenia: Results from the ilSIRENTE prospective cohort study. BMJ Open 2016;6:e008281.
9. Level C, Tellier E, Dezou P, et al. Outcome of older persons admitted to intensive care unit, mortality, prognosis factors, dependency scores and ability trajectory within 1 year: A prospective cohort study. Aging Clin Exp Res 2018;30:1041−1051.
10. Rozzini R, Sabatini T, Cassinadri A, et al. Relationship between functional loss before hospital admission and mortality in elderly persons with medical illness. J Gerontol A Biol Sci Med Sci 2005;60:1180−1183.
11. Shah R, Borrebach JD, Hodges JC, et al. Validation of the Risk Analysis Index for evaluating frailty in ambulatory patients. J Am Geriatr Soc 2020;68:1818−1824.
12. Guidet B, de Lange DW, Boumendil A, et al. The contribution of frailty, cognition, activity of daily life and comorbidities on outcome in acutely admitted patients over 80 years in European ICUs: The VIP2 study. Intensive Care Med 2020;46:57−69.
13. Hewitt J, Carter B, Vilches-Moraga A, et al. The effect of frailty on survival in patients with COVID-19 (COPE): A multicentre, European, observational cohort study. Lancet Public Health 2020;5:e444−e451.

14. Belelli G, Rebora P, Valsecchi MG, et al. Frailty Index predicts poor outcome in COVID-19 patients. Intensive Care Med 2020;46:1634–1636.
15. Chong E, Chan M, Tan HN, Lim WS. COVID-19: Use of the Clinical Frailty Scale for critical care decisions. J Am Geriatr Soc 2020;68:E30–E32.
16. Mannelli C. Whose life to save? Scarce resources allocation in the COVID-19 outbreak. J Med Ethics 2020;46:364–366.
17. Mahoney FI, Barthel DW. Functional evaluation: The Barthel Index. Md State Med J 1965;14:61–65.
18. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016;315: 801–810.
19. de Abajo FJ, Rodríguez-Martín S, Lerma V, et al. Use of renin-angiotensin-aldosterone system inhibitors and risk of COVID-19 requiring admission to hospital: A case-population study. Lancet 2020;395:1705–1714.
20. Giacomelli A, Ridolfo AL, Milazzo L, et al. 30-day mortality in patients hospitalized with COVID-19 during the first wave of the Italian epidemic: A prospective cohort study. Pharmacol Res 2020;158:104931.
21. Petrilli CM, Jones SA, Yang J, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: Prospective cohort study. BMJ 2020;369:m1966.
22. Du RH, Liang LR, Yang CQ, et al. Predictors of mortality for patients with COVID-19 pneumonia caused by SARS-CoV-2: A prospective cohort study. Eur Respir J 2020;55:2000524.
23. Esai Selvan M. Risk factors for death from COVID-19. Nat Rev Immunol 2020; 20:407.
24. Parohan M, Yaghoubi S, Seraji A, et al. Risk factors for mortality in patients with Coronavirus disease 2019 (COVID-19) infection: A systematic review and meta-analysis of observational studies. Aging Male Off J Int Soc Study Aging Male 2020 Jun 8. [Epub ahead of print].
25. Shenoy A, Ismaily M, Bajaj M. Diabetes and COVID-19: A global health challenge. BMJ Open Diabetes Res Care 2020;8:e001450.
26. Zhang J, Wu J, Sun X, et al. Association of hypertension with the severity and fatality of SARS-CoV-2 infection: A meta-analysis. Epidemiol Infect 2020;148: e106.
27. Yang K, Sheng Y, Huang C, et al. Clinical characteristics, outcomes, and risk factors in patients with cancer and COVID-19 in Hubei, China: A multicentre, retrospective, cohort study. Lancet Oncol 2020;21: 904–913.
28. Cheng Y, Luo R, Wang K, et al. Kidney disease is associated with in-hospital death of patients with COVID-19. Kidney Int 2020;97:829–838.
29. Docherty AB, Harrison EM, Green CA, et al. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: Prospective observational cohort study. BMJ 2020;369:m1985.
30. Cummings MJ, Baldwin MR, Abrams D, et al. Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: A prospective cohort study. Lancet 2020;395:1763–1770.

Supplementary Table 1
Multivariate Logistic Regression on Mortality According to Number of Comorbidities

	≥1 Comorbidity		≥2 Comorbidities		≥3 Comorbidities		≥4 Comorbidities		≥5 Comorbidities	
	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value
Gender: female	0.23 (0.11-0.47)	<.001	0.23 (0.11-0.47)	<.001	0.23 (0.11-0.47)	<.001	0.26 (0.13-0.53)	<.001	0.26 (0.13-0.53)	<.001
Age: 1 y	1.07 (1.04-1.10)	<.001	1.07 (1.04-1.10)	<.001	1.07 (1.03-1.10)	<.001	1.07 (1.04-1.10)	<.001	1.07 (1.04-1.10)	<.001
qSOFA: 1 point	1.31 (0.89-1.95)	.17	1.34 (0.90-1.99)	.15	1.27 (0.86-1.89)	.23	1.31 (0.87-1.95)	.19	1.34 (0.90-2.01)	.16
Barthel Index: 5 points	1.13 (1.04-1.22)	.002	1.12 (1.04-1.21)	.004	1.11 (1.03-1.21)	.007	1.11 (1.02-1.20)	.014	1.11 (1.03-1.21)	.008
Comorbidity	2.63 (0.61-1.39)	.20	1.82 (0.74-4.47)	.20	2.15 (1.07-4.31)	.032	2.60 (1.31-5.17)	.006	2.91 (1.37-6.15)	.005
Polypharmacy: ≥5 drugs	1.85 (0.98-3.48)	.06	1.74 (0.91-3.35)	.10	1.49 (0.76-2.94)	.25	1.31 (0.65-2.66)	.45	1.33 (0.65-2.70)	.44

qSOFA, Quick Sequential Organ Failure Assessment.

Supplementary Table 2
Multivariate Logistic Regression on Mortality by Individual Diseases

	OR (95% CI)	P Value	OR (95% CI)	P Value
Gender: female	0.25 (0.12-0.51)	<.001	0.27 (0.13-0.54)	<.001
Age: 1 y	1.07 (1.04-1.10)	<.001	1.07 (1.04-1.10)	<.001
Barthel: 5 points	1.12 (1.04-1.22)	.004	1.11 (1.03-1.20)	.010
qSOFA: 1 point	1.23 (0.82-1.85)	.32	1.38 (0.92-2.06)	.12
Polypharmacy: ≥5 drugs	1.51 (0.75-3.05)	.25	1.68 (0.85-3.32)	.14
Heart failure	2.85 (1.36-5.98)	.006		
Chronic kidney disease			2.93 (1.21-7.12)	.018

qSOFA, Quick Sequential Organ Failure Assessment.

Supplementary Table 3
Risk of Mortality in Men Excluding qSOFA

Age	Morbidities	Barthel Index			
		100	90	75	60
35	<3	0.02	0.02	0.03	0.04
	≥3	0.04	0.05	0.07	0.10
50	<3	0.05	0.06	0.08	0.11
	≥3	0.11	0.13	0.18	0.23
65	<3	0.12	0.14	0.19	0.24
	≥3	0.25	0.29	0.37	0.45
80	<3	0.27	0.31	0.39	0.47
	≥3	0.48	0.53	0.61	0.69

Supplementary Table 4
Risk of Mortality in Women Excluding qSOFA

Age	Morbidities	Barthel Index			
		100	90	75	60
35	<3	0.00	0.01	0.01	0.01
	≥3	0.01	0.01	0.02	0.03
50	<3	0.01	0.01	0.02	0.03
	≥3	0.03	0.03	0.05	0.07
65	<3	0.03	0.04	0.05	0.07
	≥3	0.07	0.09	0.12	0.16
80	<3	0.08	0.10	0.13	0.17
	≥3	0.18	0.21	0.27	0.34

Supplementary Table 5
Sensitivity Analysis: Multivariate Logistic Regression on Mortality (≥41 Years)

	Model 1		Model 2		Model 3		Model 4	
	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value
Gender: female	0.23 (0.12-0.47)	<.001	0.23 (0.11-0.46)	<.001	0.23 (0.11-0.47)	<.001	0.23 (0.11-0.47)	<.001
Age: 1 y	1.08 (1.05-1.11)	<.001	1.08 (1.05-1.11)	<.001	1.07 (1.04-1.10)	<.001	1.06 (1.03-1.10)	<.001
Barthel: 5 points	1.13 (1.05-1.22)	.002	1.12 (1.04-1.21)	.004	1.12 (1.04-1.21)	.005	1.11 (1.03-1.20)	.008
qSOFA: 1 point			1.29 (0.87-1.91)	.202	1.35 (0.91-2.01)	.137	1.30 (0.87-1.94)	.197
Polypharmacy: ≥5 drugs					2.05 (1.07-3.91)	.030	1.54 (0.77-3.08)	.223
Comorbidity: ≥3 morbidities							2.14 (1.07-4.27)	.031

qSOFA, Quick Sequential Organ Failure Assesssment.
Model 1: adjusted by gender, age, and Barthel; model 2: adds qSOFA to model 1; model 3: adds polypharmacy (≥5 drugs) to model 2; model 4: adds ≥3 morbidities to model 3.