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Letter to the Editor

Clinical characteristics and 28-day mortality of medical patients admitted with COVID-19 to a central London teaching hospital

Dear Editor,

Clinical Characteristics and 28-day mortality of COVID-19 in London

We read with interest the article by Galloway et al. describing a clinical risk score to identify patients with COVID-19 at high risk of critical care admission or death.[1] We undertook a prospective cohort study of adult patients ($\geq$ 18 years old) with laboratory-confirmed COVID-19 admitted to the Chelsea & Westminster Hospital during a one-month period between 7th March and 7th April 2020 to identify predictors of survival at 28-days.

Methods

We excluded patients who were diagnosed with nosocomial-acquired COVID-19 and those who had received novel agents as part of concurrently running research trials to minimise confounding and avoid duplication of findings. We collected clinical characteristics: age, sex, gender, ethnicity, smoking status, duration of symptoms, comorbidities, observations, laboratory results, radiology, pharmacological treatments administered, use of continuous positive airways pressure (CPAP), non-invasive ventilation (NIV), requirement for intubation, and outcome (survival to discharge or death). Discharged patients, or if unreachable, their primary care physicians were contacted by telephone to confirm vital status at 28-days. Copies of death certificates were acquired. Predictors were computed from baseline characteristics using multivariable analyses. The final date of follow-up was the 8th May 2020. COVID-19 infection was confirmed using nucleic acid real-time reverse transcriptase polymerase chain reaction (RT-PCR) on combined nasal and oropharyngeal swabs. The study was approved by the research governance committee.

Results

We identified 255 consecutive medical patients admitted with laboratory-confirmed COVID-19 between 7th March to 7th April 2020. We excluded 35 (12 who were diagnosed with nosocomial-acquired COVID-19 infection, 23 who received novel agents as part of a concurrently running research trial).

The mean age of the patients was 66.9 years (95% CI: 64.7–69.2). 59.1% were male and 45.5% were non-white. 43.1% had a history of smoking. A median of 2 (1–3) comorbidities was reported, mainly hypertension (45%), diabetes (27.7%) and hyperlipidaemia (22.7%). The principal symptoms were dyspnoea (61.4%), fever (58.6%), malaise (50%), and dry cough (45.9%). The median duration of symptoms was 6 (3–10) days. On admission, 33% were pyrexial ($\geq$ 37.8 °C), with 81% developing a fever during their inpatient stay. 62% were tachypnoeic (>20 respirations per minute) and 34% were tachycardic (>100 beats per minute). The median P/F ratio was 240.1 mmHg (144.5 – 306.7). Lymphopenia (56%), hypoalbuminaemia (67%), elevated D-dimer (84%), and CRP (99%) were frequent findings. Chest x-rays demonstrated bilateral consolidation in 56.7%, localised consolidation in 18.9%, atelectasis, pleural effusion and/or cardiomegaly in 11.1%, and no abnormality in 11.1%. 91.8% of patients received an antimicrobial agent: 60.0% penicillin, 56.4% a cephalosporin, 56.4% a tetracycline, and 44.1% a macrolide. 79.1% were administered prophylactic anticoagulation and 12.3% therapeutic dosing. (13.2% were receiving oral anticoagulation prior to admission). 80 of 220 patients required respiratory support: 19.1% CPAP, 1.8% NIV, and 15.5% invasive ventilation. (Table 1).

The primary composite endpoint, defined as a perceived indication for invasive mechanical ventilation or in-hospital death, was reached by 35.9%. These individuals were distinguished by greater age ($p = 0.018$), male gender ($p = 0.008$), greater comorbidity ($p = 0.001$), pyrexia ($p = 0.036$) and higher respiratory rate ($p < 0.001$). They demonstrated higher levels of CRP ($p < 0.001$), D-dimer ($p = 0.001$), troponin ($p < 0.001$), urea ($p < 0.001$), creatinine ($p < 0.001$), lower lymphocyte count ($p = 0.014$), albumin ($p < 0.001$) and P/F ratio ($p < 0.001$).

162 of 220 inpatients (73.6%) survived to discharge – their median length-of-stay was 9 (5–15) days. 158 of 217 traceable patients survived to 28-days (72.8%). 58 of the 59 deaths (98.3%) were attributed to COVID-19. Those individuals who died within 28-days were of advanced age ($p < 0.001$), male gender ($p = 0.031$), experienced a greater burden of comorbidities ($p < 0.001$; notably hypertension), shorter symptom duration ($p = 0.009$), and higher respiratory rate on admission ($p = 0.035$). They had higher levels of CRP ($p = 0.010$), D-dimer ($p = 0.013$), troponin ($p < 0.001$), urea ($p < 0.001$) and creatinine ($p < 0.001$), lower levels of lymphocytes ($p = 0.013$), platelets ($p = 0.030$) and albumin ($p < 0.001$). (table 1).

Using a cut-off of $p \leq 0.1$ from univariate analyses, an 11-component model multivariate analysis (excluding composite scores) confirmed the following predictors of mortality at 28-days: greater age (HR 1.04, 95% CI 1.01–1.07; $p = 0.014$), male gender (HR 2.30, 95% CI 1.23–4.29; $p = 0.009$), more comorbidities (2–3: HR 3.24, 95% CI 1.31–7.97; $p = 0.011$ and 4+: HR 6.78, 95% CI 2.58–17.84; $p < 0.001$), higher respiratory rate (>20: HR 2.51, 95% CI 1.27–4.95; $p = 0.008$), and CRP (>90: HR 2.36, 95% CI 1.25–4.45; $p = 0.008$). Higher blood pressure approached statistical significance (>140: HR 2.12, 95% CI 1.00–4.50; $p = 0.050$). (Fig. 1).

Applying the risk index developed by Galloway et al.,[1] a score of $\geq$4-points corresponded to a 28-day cumulative incidence of critical care admission or death of 83% versus 61% for scores <4-points (log rank $p < 0.001$).

Table 1
Clinical characteristics of patients surviving to discharge and to 28-days.

Clinical characteristic	(n)	All patients	Survival to discharge			Survival to 28 days		
			Yes $n = 162$	No $n = 58$	p value	Yes $n = 158$	No $n = 59$	p value
Demographics								
Age, years	(220)	66.9 (95% CI: 64.7–69.2)	63.8 (95% CI: 61.1–66.4)	75.8 (95% CI: 72.5–79.2)	<0.001*	64.0 (95% CI: 61.3–66.6)	76.1 (95% CI: 72.7–79.4)	<0.001*
Age groups (years), no. (%)								
18 – 34		8 (3.6)	7 (4.3)	1 (1.7)	<0.001†	6 (3.8)	1 (1.7)	<0.001†
35 – 49		22 (10.0)	22 (13.6)	0 (0)		21 (13.3)	0 (0)	
50 – 64		73 (33.2)	64 (39.5)	9 (15.5)		63 (39.9)	9 (15.3)	
≥65		117 (53.2)	69 (42.6)	48 (82.8)		68 (43.0)	49 (83.1)	
Gender, male no. (%)	(220)	130 (59.1)	89 (54.9)	41 (70.7)	0.036†	87 (55.1)	42 (71.2)	0.031†
Ethnicity, no. (%)	(220)							
White		120 (54.5)	86 (53.0)	34 (58.6)	0.585†	85 (53.8)	35 (59.3)	0.599†
Black		31 (14.1)	24 (14.8)	7 (12.1)		21 (13.3)	7 (11.9)	
Asian		28 (12.7)	19 (11.7)	9 (15.5)		19 (12.0)	9 (15.3)	
Other		41 (18.6)	33 (20.4)	8 (13.7)		33 (20.9)	8 (13.6)	
Smoking history, no. (%)	(204)	88 (43.1)	60 (39.7)	28 (52.8)	0.098†	58 (39.5)	28 (51.9)	0.115†
Duration of symptoms, days	(210)	6 (3.0–10.0)	7.0 (3.0– 10.0)	5.0 (1.5– 9.0)	0.015	7.0 (3.0–10.0)	4.5 (1.0–8.5)	0.009
Symptoms (at presentation), no. (%)	(220)							
Fever		129 (58.6)	101 (62.3)	28 (48.3)	0.062†	98 (62.0)	29 (49.2)	0.087†
Chills/rigors		18 (8.2)	15 (9.3)	3 (5.2)	0.330†	15 (9.5)	3 (5.1)	0.295†
Malaise		110 (50.0)	87 (53.7)	23 (39.7)	0.066†	85 (53.8)	23 (39.0)	0.052†
Myalgia		47 (21.4)	39 (24.1)	8 (13.8)	0.101†	38 (24.1)	8 (13.6)	0.092†
Headache		16 (7.3)	13 (8.0)	3 (5.2)	0.473†	13 (8.2)	3 (5.1)	0.431†
Change in taste/smell		20 (9.3)	19 (11.7)	1 (1.7)	0.023†	19 (12.0)	1 (1.7)	0.019†
Nasal congestion		6 (2.7)	6 (3.7)	0 (0)	0.137†	5 (3.2)	0 (0.0)	0.167†
Sore throat		19 (8.6)	16 (9.9)	3 (5.2)	0.274†	15 (9.5)	3 (5.1)	0.295†
Dry cough		101 (45.9)	75 (46.3)	26 (44.8)	0.847†	73 (46.2)	26 (44.1)	0.779†
Productive cough		59 (26.8)	46 (28.4)	13 (22.4)	0.378†	45 (28.5)	13 (22.0)	0.340†
Haemoptysis		13 (5.9)	8 (4.9)	5 (8.6)	0.307†	7 (4.4)	5 (8.5)	0.246†
Dyspnoea		135 (61.4)	97 (59.9)	38 (65.5)	0.449†	96 (60.8)	38 (64.4)	0.623†
Chest pain		33 (15.0)	27 (16.7)	6 (10.3)	0.247†	25 (15.8)	6 (10.2)	0.290†
Anorexia		51 (23.2)	44 (27.2)	7 (12.1)	0.019†	44 (27.7)	7 (12.1)	0.016†
Nausea & vomiting		38 (17.3)	33 (20.4)	5 (8.6)	0.042†	32 (20.3)	5 (8.5)	0.040†
Diarrhoea		51 (23.2)	48 (29.6)	3 (5.2)	< 0.001†	47 (29.7)	3 (5.1)	<0.001†
Total Comorbidities	(220)	2 (1–3)	2 (0–3)	3 (2–4)	< 0.001	2 (1–3)	3 (2–4)	<0.001
Comorbidities, no. (%)								
Asthma		23 (10.5)	20 (12.3)	3 (5.2)	0.125†	20 (12.7)	3 (5.1)	0.107†
COPD		20 (9.1)	14 (8.6)	6 (10.3)	0.699†	14 (8.9)	6 (10.2)	0.767†
Cardiovascular Disease[a]		24 (10.9)	14 (8.6)	10 (17.2)	0.071†	13 (8.2)	11 (18.6)	0.029†
Hypertension		99 (45)	63 (38.9)	36 (62.1)	0.002†	62 (39.2)	37 (62.7)	0.002†
Hyperlipidaemia		50 (22.7)	34 (21.0)	16 (27.6)	0.303†	34 (21.5)	16 (27.1)	0.383†
Diabetes		61 (27.7)	40 (24.7)	21 (36.2)	0.093†	40 (25.3)	21 (35.6)	0.134†
CKD		16 (7.3)	5 (3.1)	11 (19.0)	<0.001†	4 (2.5)	12 (20.3)	<0.001†
CVA		21 (9.5)	10 (6.2)	11 (19.0)	0.004†	10 (6.3)	11 (18.6)	0.006†
Dementia		24 (10.9)	15 (9.3)	9 (15.5)	0.190†	15 (9.5)	9 (15.3)	0.229†
Malignancy[b]		28 (12.7)	17 (10.5)	11 (19.0)	0.097†	16 (10.1)	11 (18.6)	0.091†
Liver Disease		6 (2.7)	1 (0.6)	5 (8.6)	0.001†	1 (0.6)	5 (8.5)	0.002†
Other comorbidities[c]		95 (43.2)	55 (34.0)	40 (69.0)	<0.001†	54 (34.2)	41 (69.5)	<0.001†
Observations								
Temperature, °C	(219)	37.2 (36.5–37.9)	37.3 (36.6– 37.9)	37.2 (36.1–38.2)	0.600	37.2 (36.6–37.8)	37.2 (36.1–38.1)	0.779
Fever (≥37.8 °C) on presentation, no. (%)		73 (33.2)	51 (31.5)	22 (38.6)	0.327†	48 (30.4)	23 (39.7)	0.198†
Fever (≥37.8 °C) during admission, no. (%)		178 (81.3)	133 (82.6)	45 (77.6)	0.400†	129 (82.2)	46 (78.0)	0.483†
Respiratory rate, rpm	(218)	22.0 (20.0–28.0)	22.0 (19.0–26.5)	25.0 (20.5– 29.0)	0.025	22.0 (19.0–27.5)	25.4 (20.0– 28.5)	0.035
Heart rate, bpm	(220)	90 (78.0–105.0)	89.5 (77.0–104.3)	92.0 (80–105.5)	0.554	89.0 (77.0– 104.3)	91.0 (80.0–105.0)	0.523
Systolic BP, mmHg	(220)	131 (113.3–145.0)	129.0 (112.8–143.0)	140.5 (116.8–150.0)	0.068	129.5 (113.8–143.0)	140.0 (113.0–150.0)	0.109

(*continued on next page*)

Table 1 (*continued*)

Clinical characteristic	(n)	All patients	Survival to discharge			Survival to 28 days		
			Yes $n = 162$	No $n = 58$	p value	Yes $n = 158$	No $n = 59$	p value
Laboratory								
PaO$_2$/FiO$_2$ ratio, mmHg	(154)	240.1 (144.5–306.7)	247.8 (173.4–315.4)	207.9 (92.8–296.2)	0.053	245.1 (172.3–318.1)	207.9 (92.8–296.2)	0.060
Haemoglobin, g/L	(219)	136 (124–147)	137.0 (127.0–146.5)	133.5 (107.8– 149.3)	0.197	138.0 (127.0–158.0)	149.0 (133.0– 158.0)	0.145
Neutrophil count, 10^9/L	(220)	4.8 (3.7–7.3)	4.7 (3.6–7.0)	5.3 (3.8–8.6)	0.230	4.7 (3.6–6.9)	5.5 (3.8–8.7)	0.152
Lymphocyte count, 10^9/L	(220)	0.9 (0.6–1.3)	0.9 (0.6–1.3)	0.7 (0.5–1.2)	0.019	0.9 (0.6–1.3)	0.7 (0.5–1.1)	0.013
Platelets, 10^9/L	(220)	207.5 (156.0–258.5)	214.0 (160.0–262.0)	183.5 (140.0–241.5)	0.046	214.0 (161.0–262.0)	179.0 (140.0–241.0)	0.030
D-dimer, ng/ml	(79)	1215.0 (704.0–2214.0)	1019.0 (682.0–1868.0)	2062.0 (1217.5–3122.3)	0.010	1088.0 (668.5–1887.0)	2062.0 (1217.5–3122.3)	0.013
C-reactive protein, mg/L	(220)	90.5 (50.9–153.0)	84.7 (47.1–138.1)	120.0 (72.0–178.9)	0.005	85.5 (47.1–138.1)	118.0 (69.9–176.0)	0.010
Ferritin, μg/L	(101)	762.0 (420.0–1294.0)	691.0 (380.0–1187.0)	896.0 (473.3–1399.5)	0.391	710.5 (415.3–1210.5)	839.0 (464.5–1392.0)	0.615
LDH, unit/L	(75)	476.0 (346.0–668.0)	465 (327.5–680)	499.5 (403.3–602.0)	0.756	461.0 (325.0–684.0)	499.5 (403.3–602.0)	0.682
Troponin, μg/L	(148)	13.5 (6.0–36.5)	10.0 (5.0–26.0)	34.5 (14.0–90.0)	<0.001	10.0 (5.0–26.0)	35.0 (14.0–89.0)	<0.001
BNP, ng/L	(69)	37 (13–97)	31.0 (10.5–69.5)	137.0 (34.0–359.5)	0.003	32.5 (11.5–69.8)	137.0 (34.0–359.5)	0.003
Urea, mmol/L	(214)	6.2 (4.3–10.4)	5.6 (4.0–8.5)	10.4 (6.6–16.1)	<0.001	5.6 (4.0–8.6)	10.4 (6.8–15.6)	<0.001
Creatinine, μmol/L	(216)	90.0 (73.0–118.0)	86 (72.0–105.0)	118.0 (79.0–178.0)	<0.001	86.0 (72.0–105.0)	118.0 (79.5–181.5)	<0.001
Albumin, g/L	(213)	33.0 (30.0–35.0)	34.0 (31.0–36.0)	31.0 (27.3–33.8)	<0.001	34.0 (31.0–36.0)	31.0 (27.5–34.0)	<0.001
Bilirubin, μmol/L	(212)	9.0 (7.0–13.0)	9.0 (7.0–13.0)	10.0 (8.0–16.0)	0.054	9.0 (7.0–13.0)	10.0 (8.0–16.0)	0.033
ALT, unit/L	(213)	30.0 (17.0–50.0)	30.0 (18.0–50.0)	27.5 (14.3–47.0)	0.335	31.0 (18.0–50.5)	26.0 (14.0–47.0)	0.222
ALP, unit/L	(214)	80.5 (61.0–104.0)	78.0 (60.5–97.0)	90.0 (66.0–119.5)	0.070	79.0 (59.5–97.0)	88.5 (66.0–118.8)	0.085
Imaging								
Chest Radiograph, no. (%)	(217)		160 (98.8)	57 (98.3)		156 (98.7)	58 (98.3)	
Normal		24 (11.1)	18 (11.3)	6 (10.5)	0.881†	18 (11.5)	6 (10.3)	0.806†
Localised consolidation		41 (18.9)	33 (20.6)	8 (14.0)	0.275†	33 (21.2)	8 (13.8)	0.224†
Bilateral consolidation		123 (56.7)	87 (54.4)	36 (63.2)	0.251†	83 (53.2)	37 (63.8)	0.165†
Other[d]		24 (11.1)	22 (14.0)	7 (12.3)	0.104†	22 (14.1)	7 (12.1)	0.699†
Pharmacological treatment	(220)							
Penicillin, no. (%)		132 (60.0)	104 (64.2)	28 (48.3)	0.034†	100 (63.3)	29 (49.2)	0.059†
Cephalosporin, no. (%)		124 (56.4)	83 (51.2)	41 (70.7)	0.010†	82 (51.9)	41 (69.5)	0.020†
Carbapenem, no. (%)		19 (8.6)	13 (8.0)	6 (10.3)	0.589†	10 (6.3)	6 (10.2)	0.335†
Macrolide, no. (%)		97 (44.1)	70 (43.2)	27 (46.6)	0.660†	70 (44.3)	27 (45.8)	0.847†
Tetracyclines, no. (%)		124 (56.4)	97 (59.9)	27 (46.6)	0.079†	93 (58.9)	28 (47.5)	0.132†
Quinolones, no. (%)		31 (14.2)	23 (14.3)	8 (13.8)	0.926†	23 (14.6)	8 (13.6)	0.839†
Therapeutic Anticoagulation, no. (%)		27 (12.3)	22 (13.6)	5 (8.6)	0.323†	22 (13.9)	5 (8.5)	0.279†
Respiratory support	(220)							
CPAP, no. (%)		42 (19.1)	15 (25.9)	27 (16.7)	0.126†	26 (16.5)	15 (25.4)	0.133†
NIV, no. (%)		4 (1.8)	2 (1.2)	2 (3.4)	0.279†	2 (1.3)	2 (3.4)	0.301†
Invasive ventilation, no. (%)		34 (15.5)	21 (13.0)	13 (22.4)	0.088†	21 (13.3)	13 (22.0)	0.115†
Severity scores								
CURB-65	(220)	1.0 (1.0–2.0)	1.0 (0–2.0)	2.0 (1.0–3.0)	<0.001	1.0 (0–2.0)	2 (1.0–3.0)	<0.001
NEWS2	(220)	5.0 (3.0–7.0)	5.0 (2.0–6.0)	7.0 (4.0–8.3)	<0.001	5.0 (4.0– 8.0)	7.0 (4.0–8.0)	<0.001
SOFA	(212)	2.0 (1.0–3.0)	2.0 (1–2.0)	3.0 (2.0–4.0)	<0.001	2.0 (1.0–2.0)	3.0 (2.0–4.0)	<0.001
qSOFA	(220)	1.0 (0–1.0)	1.0 (0–1.0)	1.0 (1.0–1.0)	0.007	1.0 (0–1.0)	1.0 (1.0–1.0)	0.014

Categorical data are presented as n (%) and compared using the Chi-square test†. Non-parametric continuous data are presented as median (interquartile range; IQR) and compared using the Mann-Whitney test unless otherwise stated. Parametric continuous data are presented as mean (95% confidence intervals, CI) and compared using an unpaired *t*-test*. Statistical significance was set at $p < 0.05$. ALP, alkaline phosphatase; ALT, alanine aminotransferase; bpm, beats per minute; BP blood pressure; CPAP, continuous positive airways pressure, CT, computed tomography; FiO$_2$, fraction of inspired oxygen; PaO$_2$/FiO$_2$, Horowitz ratio; LDH, lactate dehydrogenase; NEWS2, national early warning score 2; NIV, non-invasive ventilation; PaO$_2$, partial pressure of oxygen; rpm, respiratory rate per minute; SOFA, sequential organ failure assessment score.

[a] Cardiovascular disease includes ischaemic heart disease and congestive cardiac failure.

[b] All types of cancer were included.

[c] Other comorbidities include interstitial lung disease, bronchiectasis, tuberculosis, obstructive sleep apnoea, pulmonary hypertension, pulmonary embolism, congenital heart disease, arrhythmias, valvular heart disease, cardiomyopathy, peripheral vascular disease, thyroid disorders, pituitary disorders, epilepsy, parkinson's disease, subdural haematoma, connective tissue disease, inflammatory bowel disease, HIV, organ transplant, sarcoidosis.

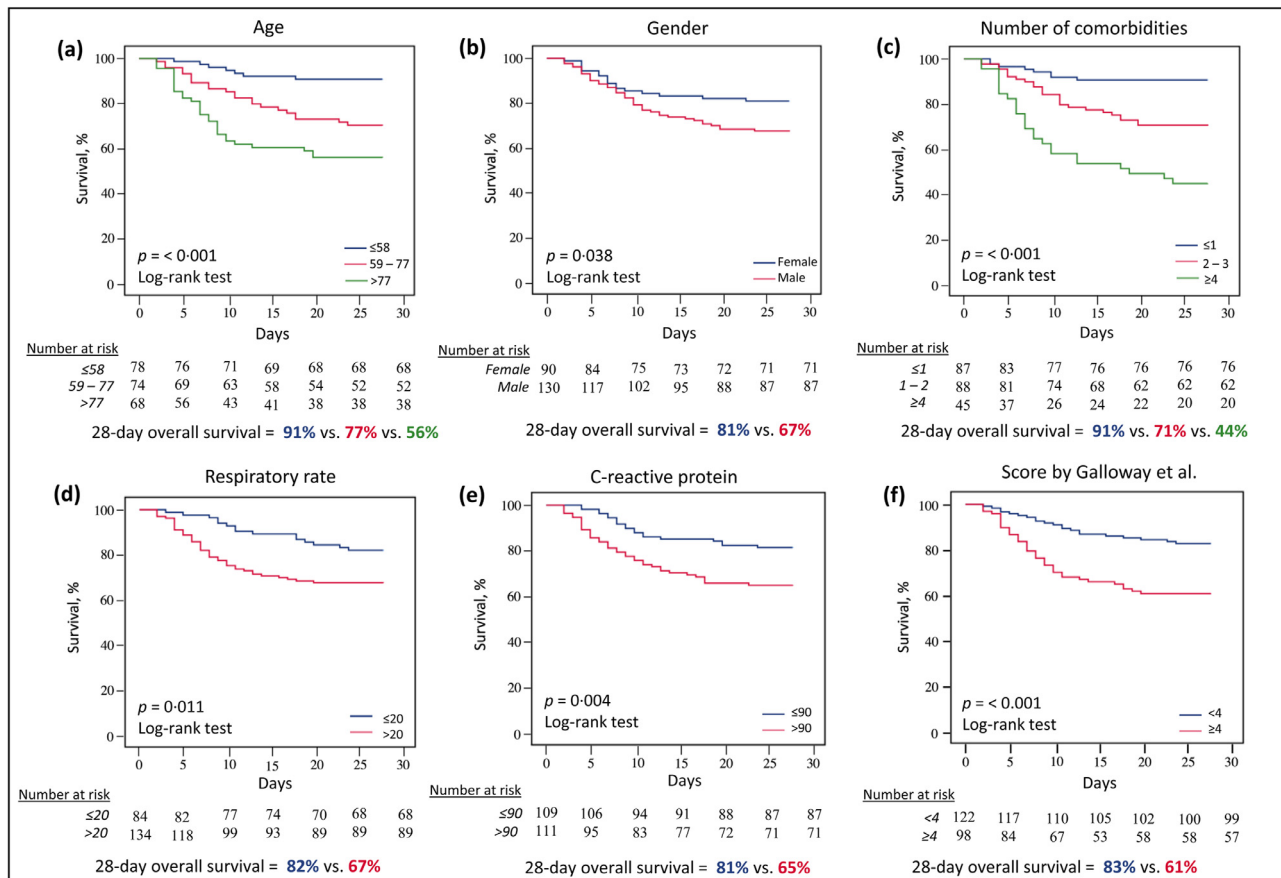[d] Other imaging findings included atelectasis, pleural effusion, cardiomegaly.

Fig. 1. Kaplan-Meier curves showing 28-day survival by (a) age, (b) gender, (c) comorbidities, (d) respiratory rate, (e) C-creative protein and (f) risk score by Galloway at al.

Conclusions

Individuals with poorer outcomes i.e. requirement for invasive ventilation or in-hospital death were characterised by advanced age, male gender and a greater burden of comorbid conditions, particularly hypertension. Blood profiling demonstrated higher levels of CRP, D-dimer, troponin, urea and creatinine, lower lymphocyte, platelet and albumin counts. 28-day mortality was independently predicted by advanced age, male gender, higher number of pre-existing comorbidities, respiratory rate, and CRP on admission. Application of a UK-specific risk score[1] demonstrated significant dichotomy in survival. Our findings reflect those in the growing international literature[2–5] and add support to their use in prognostication.[6]

Interestingly, ethnicity was not an independent predictor of mortality in our cohort – the reasons for this are unclear and whilst it may reflect the local population's diversity, the finding warrants comparison to regional disaggregated data.[7]

The majority of patients received antimicrobial therapy and this is supported by Zhu et al. who found bacterial co-infections were common and featured in 236 of 243 laboratory-confirmed COVID-19 patients (91.8%).[8] A small proportion of individuals were administered respiratory support - their role and timing are yet to be determined.[9] Our study has its limitations - it is a small single-centre experience.

In summary, we have identified advanced age, male gender, more comorbidities, higher respiratory rate, and CRP as independent predictors of 28-day mortality in a cohort of laboratory-confirmed COVID-19 patients admitted to a London teaching hospital. Furthermore, application of a UK-developed risk score[1] assists early prognostication, vital for triaging the large patient numbers attending healthcare systems globally.

Contributors

K. Khalil and J.L. Garner designed the analysis. K.Khalil, K. Agbontaen, D. McNally, A. Love collected the data and together with J.L. Garner wrote the first draft of the manuscript and made revisions after feedback from co-authors. S Mandalia and W. Banya evaluated the data. All the authors meet the definition of an author as stated by the International Committee of Medical Journal Editors, and all have seen and approved the final manuscript.

Declaration of Competing Interest

No competing interests declared.

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