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Citation for published version:
DataLoch COVID-19 Collaboration, Mutch, CP, Ross, DA, Bularga, A, Nicola Rose Cave, R, Chase-Topping, ME, Anand, A, Mills, NL, Koch, O, Mackintosh, CL & Perry, MR 2022, 'Performance status: A key factor in predicting mortality in the first wave of COVID-19 in South-East Scotland', *Journal of the Royal College of Physicians of Edinburgh*. https://doi.org/10.1177/14782715221120137

Digital Object Identifier (DOI):
10.1177/14782715221120137

Link:
Link to publication record in Edinburgh Research Explorer

Document Version:
Publisher's PDF, also known as Version of record

Published In:
Journal of the Royal College of Physicians of Edinburgh

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Journal of the Royal College of Physicians of Edinburgh
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DOI: 10.1177/14782715221120137
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Performance status: A key factor in predicting mortality in the first wave of COVID-19 in South-East Scotland

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Abstract

Background: COVID-19 mortality risk factors have been established in large cohort studies; long-term mortality outcomes are less documented.

Methods: We performed multivariable logistic regression to identify factors associated with in-patient mortality and intensive care unit (ICU) admission in symptomatic COVID-19 patients admitted to hospitals in South-East Scotland from 1st March to 30th June 2020. One-year mortality was reviewed.

Results: Of 726 patients (median age 72; interquartile range: 58–83 years, 55% male), 104 (14%) required ICU admission and 199 (27%) died in hospital. A further 64 died between discharge and 30th June 2021 (36% overall 1-year mortality). Stepwise logistic regression identified age >79 (odds ratio (OR), 4.77 (95% confidence interval (CI), 1.96–12.75)), male sex (OR, 1.83 (95% CI, 1.21–2.80)) and higher European Cooperative Oncology Group/World Health Organization performance status as associated with higher mortality risk.

Discussion: Poor functional baseline was the predominant independent risk factor for mortality in COVID-19. More than one-third of individuals had died by 1 year following admission.

Keywords

COVID-19, SARS-CoV2, mortality, clinical scores, frailty

Introduction

Our understanding of patient characteristics and clinical manifestations of COVID-19 has grown exponentially since the start of the pandemic. In this manuscript, we demonstrate the impact of the first wave in South-East Scotland showing clinical features and mortality rates on hospitalised patients with confirmed COVID-19 infection in an unvaccinated population prior to any COVID-specific therapies being widely available.

The risk factors for adverse outcomes have been well established from the UK wide ISARIC/World Health Organization (WHO) CCP/UK[1] study and OpenSAFELY study,[2] case series and retrospective cohort studies; and include advancing age, male sex, existing health conditions such as obesity, chronic respiratory, chronic cardiac and neurological disease, socio-economic status and belonging to a Black, Asian or other ethnic minority group.[1–5] The impact of hospitalisation with confirmed COVID-19 infection on long-term mortality is less well understood.

The COVID-19 pandemic first spread to Scotland in early March 2020[6] and now has led to more than 5 million deaths globally. As of the 22nd of February 2022, there have been more than 1.3 million cases in Scotland of which 210,479 laboratory confirmed cases of COVID-19 in National Health Service Lothian (NHSL) health board.[7] Of these, 6,536 patients have required admission within an NHSL acute care

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hospital, 533 have required intensive care unit (ICU) admission and 1,554 of those admitted have died.[7]

We use a comprehensive dataset of the first 726 consecutive hospitalised patients with confirmed COVID-19 within a large health board to assess the impact of risk factors and now established outcome predictors and prognostic models[8] on clinical outcomes. With increasing attention to the long-term impact of COVID-19 on mortality and other outcomes,[9–11] we include data on mortality at 1 year after the index admission episode. These detailed data will serve as a comparator for clinical features and mortality as we progress through the pandemic.

Methods

Study setting and design

In a multi-site cohort study, we evaluated clinical characteristics and outcomes in all consecutive patients with confirmed COVID-19 admitted to three acute tertiary or secondary care hospitals in the South-East of Scotland, United Kingdom. The three participating hospitals were a 900-bed tertiary referral hospital (Royal Infirmary of Edinburgh), a 570-bed tertiary referral hospital (Western General Hospital, Edinburgh) and a 550-bed secondary care hospital (St John's Hospital, Livingston), which together have a total of 51 level 2 or level 3 care beds, which were expanded for surge capacity during periods of high demand. These sites cover a surrounding catchment area of nearly 1 million people.[12]

The study was performed with approval of the local Research Ethics Committee and delegated Caldicott Guardian for the NHSL Health Board, in accordance with the Declaration of Helsinki. All data were collected from the patient record and national registries, anonymised and linked in a data repository (DataLoch™, Edinburgh, United Kingdom) within a secure Safe Haven. Consent was not sought from individual patients. Only summary data were extracted to minimise the risk of disclosure.

Participants

Consecutive hospitalised adult patients (aged ⩾18 years) with symptoms of COVID-19 who had a positive reverse transcriptase-polymerase chain reaction (RT-PCR) test for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and were admitted to one of the three acute hospitals either 2 days prior to their index positive swab or up to 28 days after this were included. In addition, those who tested positive with symptoms while hospitalised for other reasons were included. Data collection started on the 1st of March 2020 when the first confirmed Scottish case was identified and continued until the 30th of June 2020, covering the first wave of the pandemic in Scotland. Exclusion criteria were patients with laboratory confirmed SARS-CoV-2 who were asymptomatic, age <18 and negative SARS CoV-2 PCR on nasopharyngeal swab (Figure 1).

Study procedures and data sources

A data form was completed by the attending care clinician at the time of testing. Electronic healthcare records were reviewed by a team of physicians to obtain further detailed clinical characteristics including admission observations and to evaluate the Clinical Frailty Scale (CFS) Rockwood[13] and the European Cooperative Oncology Group (ECOG)/WHO performance status.[14] Clinical scores such as the National Early Warning Score 2 (NEWS2),[15] quick Sequential Organ Failure Assessment score (qSOFA),[16] confusion, uraemia, respiratory rate, blood pressure, age 65 years (CURB-65)[17] and ISARIC 4C Mortality[18] scores were calculated retrospectively using clinical variables and admission observations. Patients with missing variables were excluded, other than obesity for which patients without recorded obesity were assumed to be non-obese.

As part of the DataLoch COVID-19 Collaborative, data were automatically extracted from individual electronic patient records (TrakCare; InterSystems Corporation, Cambridge, MA, USA), laboratory information management system (iLaboratory, Advanced Expert Systems Medical, Derby, United Kingdom), the Scottish Morbidity Record and International Classification of Diseases 10th revision, the Scottish Drug Dispensing Database, the Scottish Care Information store and National Records of Scotland. Laboratory data were available for each patient for their entire hospital admission; however, for the purpose of this study, we report results of laboratory investigations performed on admission or within 24 h of a positive PCR for SARS-CoV-2 in those patients who became symptomatic during hospital admission.

National registry data were used to ensure complete follow-up for the study population. The primary outcome was all-cause mortality during the index hospital admission. Secondary outcomes were requirement for intensive care admission (ICU) during the index episode and 1-year all-cause mortality. We also evaluated duration of index hospital admission.

Statistical analysis

Baseline characteristics, admission variables and investigation results were summarised in subgroups of patients according to the primary outcome of all-cause mortality during the index hospital admission. Continuous variables are presented as median (interquartile range, IQR) or as mean (standard deviation) according to distribution and categorical variables as percentages and absolute numbers (% (*n*/*N*)). Any clinical categorical variables with a frequency of less than 5 are reported as '<5' due to data protection requirements. Group-wise comparisons were performed using Chi-square, Kruskal–Wallis or one-way analysis of variance. Statistical significance was defined as a two-sided p value <0.05. Correlations of continuous variables were assessed using the Spearman rank order correlation. Univariable and multivariable logistic regression modelling was used to assess the association between clinical variables and in-hospital mortality or admission to intensive care. Variables were excluded if they had

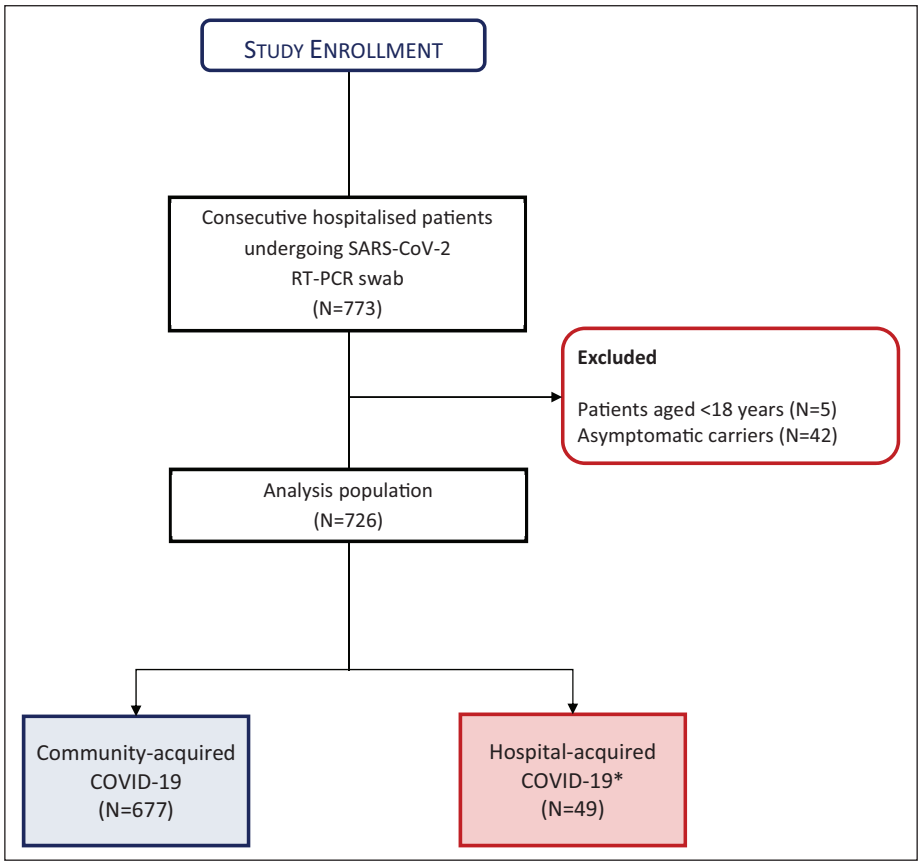

Figure 1. Consort diagram of study population.
RT-PCR: reverse transcription polymerase chain reaction.
*Hospital acquired COVID-19 defined as new symptoms and a SARS-CoV-2 RT-PCR positive ⩾8 days following admission.

>20% missing data. Missing data for continuous variables were assumed to be at random, and multiple imputation was applied using chained equations. For categorical variables, a missing category was created to allow the maximum number of patients to remain in the model for analysis. Models were refitted with categories for continuous variables such as clinical observations or biochemistry and haematology results according to accepted values for normal range to obtain odds ratios by categories of low/within range/high values as appropriate. Initially, univariable analysis was performed on all variables. Variables with $p < 0.157$ were carried forward to a multivariable logistic regression analysis based on the Akaike information criterion (AIC). Stepwise selection criteria based on improvement in AIC was used to determine the final model. Final model fit suitability was assessed using area under the curve (AUC) on a receiver operating characteristic curve. Cumulative mortality was assessed using the Kaplan–Meier curves. All analyses have been performed in R Studio (version 3.6.1) using the *pROC, MASS, Car* and *survival* packages.

Results

Study population

Between 1st March and 30th June 2020, 773 consecutive patients were hospitalised in NHS Lothian and had a positive RT-PCR test for SARS-CoV2. Of these five were excluded as they were <18 years of age and 42 were excluded as they were determined to be asymptomatic carriers (Figure 1). Our analysis population was 726 adults of which 677 were community acquired and 49 were hospital acquired (defined as new symptoms and a SARS-CoV-2 RT-PCR-positive test ⩾8 days following admission).

Baseline characteristics

The cohort had a median age of 72 (IQR: 58–83) and 398 (55%) of patients were men (Table 1). The median length of hospital admission was 8 days (IQR: 3–19). Mortality was higher in patients who were male and those in the higher age brackets (Table 1). Ethnicity data were available for 588 (81%) patients and a very low proportion of patients ($n = 28$, 4%) were from minority ethnic groups. All deprivation quintiles were represented in the hospital cohort with the smallest proportion from the least deprived quintile ($n = 104$, 14%) and the highest proportion were from the most deprived quintile ($n = 200$, 28%) (Table 1). Only 44 (6%) patients of the cohort were healthcare workers. The most common co-morbidities recorded were hypertension ($n = 298$, 41%), diabetes ($n = 169$, 23%) and a history of cancer ($n = 138$, 19%). Obesity (body mass index (BMI) > 30) was the fourth most common co-morbidity in 18% ($n = 129$) of patients but was poorly documented in electronic healthcare records and 37% of patients were not weighed during their admission.

Table 1. Baseline clinical characteristics of SARS-CoV-2-positive in-patients included in analysis.

Variable	Overall, *N* = 726	Died, *N* = 199	Discharged alive, *N* = 527	*p* Value[a]
Age at admission (years)	72 (58, 83)	81 (71, 86)	67 (53, 79)	<0.001
Age category (years)				<0.001
<40	40 (5.5%)	0 (0%)	40 (7.6%)	
40–49	64 (8.8%)	2 (1.0%)	62 (12%)	
50–59	106 (15%)	8 (4.0%)	98 (19%)	
60–69	107 (15%)	28 (14%)	79 (15%)	
70–79	170 (23%)	52 (26%)	118 (22%)	
80–90	192 (26%)	84 (42%)	108 (20%)	
>90	47 (6.5%)	25 (13%)	22 (4.2%)	
Sex				0.016
Female	328 (45%)	75 (38%)	253 (48%)	
Male	398 (55%)	124 (62%)	274 (52%)	
Ethnicity				0.200
White	560 (77%)	163 (82%)	397 (75%)	
Minority ethnic groups	28 (3.9%)	5 (2.5%)	23 (4.4%)	
Deprivation – SIMD quintile				0.600
1 (least deprived)	104 (14%)	33 (17%)	71 (13%)	
2	174 (24%)	44 (22%)	130 (25%)	
3	106 (15%)	35 (18%)	71 (13%)	
4	138 (19%)	35 (18%)	103 (20%)	
5 (Most deprived)	200 (28%)	51 (26%)	149 (28%)	
Smoking status				0.035
Non-smoker	326 (45%)	73 (37%)	253 (48%)	
Smoker	32 (4.4%)	8 (4.0%)	24 (4.6%)	
Ex-smoker	217 (30%)	67 (34%)	150 (28%)	
Previous co-morbidities				
Hypertension	298 (41%)	97 (49%)	201 (38%)	0.012
Diabetes	169 (23%)	51 (26%)	118 (22%)	0.400
Obesity (BMI ⩾ 30)[b]	129 (18%)	23 (12%)	106 (20%)	0.025
Ischaemic heart disease[b]	75 (10%)	31 (16%)	44 (8.3%)	0.007
Heart failure[b]	54 (7.4%)	25 (13%)	29 (5.5%)	0.002
Asthma	102 (14%)	19 (9.5%)	83 (16%)	0.043
COPD	102 (14%)	36 (18%)	66 (13%)	0.071
Pulmonary embolism[b]	25 (3.4%)	7 (3.5%)	18 (3.4%)	>0.900
Cancer	138 (19%)	53 (27%)	85 (33%)	0.010
Liver disease[b]	13 (1.8%)	6 (3.0%)	7 (1.3%)	0.200
Dementia[b]	83 (11%)	36 (18%)	47 (8.9%)	<0.001
Stroke[b]	54 (7.4%)	19 (9.5%)	35 (6.6%)	0.200
Parkinson's disease[b]	25 (3.4%)	8 (4.0%)	17 (3.2%)	0.800
Baseline functional status				
ECOG performance status				<0.001
Fully active (0)	215 (30%)	14 (7.0%)	201 (38%)	
Restricted in strenuous activity (1)	131 (18%)	32 (16%)	99 (19%)	
Able to self-care (2)	131 (18%)	49 (25%)	82 (16%)	
Limited self-care (3)	200 (28%)	81 (41%)	119 (23%)	
Bedbound (4)	46 (6.3%)	23 (12%)	23 (4.4%)	
Clinical frailty scale				<0.001
No frailty (1–4)	430 (59%)	68 (34%)	362 (69%)	
Moderate frailty (5–6)	224 (31%)	98 (49%)	126 (24%)	
Severe frailty (7–8)	65 (9.0%)	32 (16%)	33 (6.3%)	
Terminal illness (9)	<5	<5	<5	
Residence on admission				0.001
Home	606 (83%)	150 (75%)	456 (87%)	
Care home	91 (13%)	36 (18%)	55 (10%)	
Other supported accommodation	28 (3.9%)	12 (6.0%)	16 (3.0%)	
Package of care	139 (19%)	54 (27%)	85 (16%)	<0.001
Requires aid to walk	139 (19%)	54 (27%)	85 (16%)	<0.001

BMI: body mass index; COPD: chronic obstructive pulmonary disease; ECOG: Eastern Cooperative Oncology Group; IQR: inter-quartile range; SIMD: Scottish Index of Multiple Deprivation.

Data are presented as no. (%) or median (IQR).

[a]Comparison between patients who died and those who were discharged alive.

[b]Defined as per Scottish Morbidity Record (SMR01).

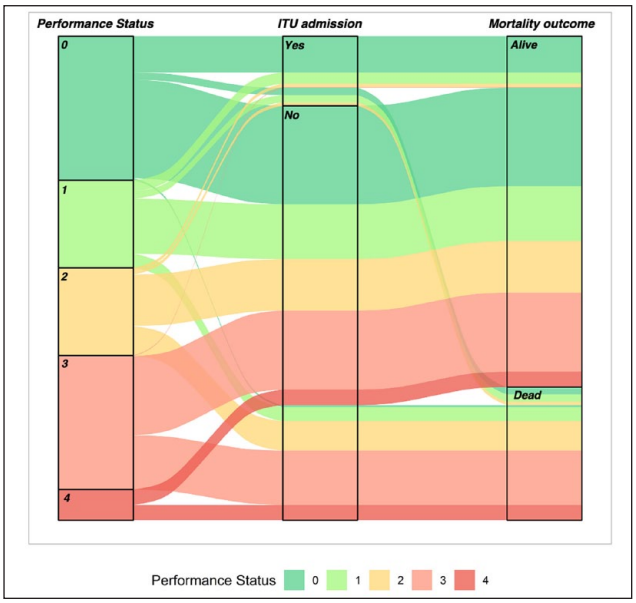

Figure 2. Alluvial plot illustrating patients' ECOG performance status stratified by ICU admission and all-cause mortality. Colours represent patient's ECOG performance status ranging from 0 – fully active, 1 – restricted in strenuous activity, 2 – able to self-care, 3 – limited self-care and 4 – bedbound. All patients for whom complete data were available for their performance status, ICU admission and mortality outcome were included in this plot (99.5% (723/726)).
ECOG: Eastern Cooperative Oncology Group; ICU: intensive care unit.

Clinical presentation

Patients presented to hospital within a median of 7 days from symptom onset (IQR: 3–8). The commonest reported symptoms were cough ($n=492$, 68%), breathlessness ($n=423$, 58%) and fever ($n=439$, 60%) (Supplemental Table S1). Fatigue ($n=279$, 38%), confusion ($n=171$, 24%) and diarrhoea ($n=157$, 22%) were less frequently reported. On presentation, patients had a median NEWS2 of 4 (IQR: 2–6) with elevated respiratory rate, pulse rate, hypoxia and fever frequently reported (Supplemental Table S1). An altered mental state was documented in 198 patients (27%). The median lymphocyte count was 0.91 (IQR: 0.62–1.3) and median C-reactive protein (CRP: 74; IQR: 29–134). Abnormal chest X-ray findings were present in 426 (59%) of patients with bilateral patchy opacification most frequently observed (Supplemental Table S1). During admission, 75 patients underwent lung computed tomography with the most frequent indication being suspected pulmonary embolism.

Baseline functional status

Within this study, premorbid functional status was evaluated in several ways. Performance status was individually derived from the social history, 246 patients (34%) had a performance status of 3–4 indicating they were capable of no or limited level of self-care and confined to a bed or chair >50% of the time. In all, 289 (40%) patients (Table 1) were defined as being moderately to severely frail on the CFS,[13] with scores of 6–8. Prior to admission, 139 (19%) patients required an aid to walk, 139 (19%) had a package of care and 91 (13%) were resident in a care home.

In-hospital management

Patients remained in hospital for a median duration of 8 days (IQR: 3–19). Supplemental O_2 was administered to 530 (73%) of patients on admission. In all, 419 (58%) of patients received empirical antimicrobials on admission, in 77 (18%) of these cases antimicrobials were stopped within 48 h and 80 (20%) of cases had escalation of antimicrobial within 48 h. In all, 76 (10%) patients were diagnosed as having a radiologically confirmed hospital-acquired pneumonia during admission. In all, 108 (15%) patients were treated with corticosteroids (Figure 2)..

In-patient outcomes

Increasing age, male sex and the pre-morbid measure of performance status increased the odds of death (univariable logistic regression, Supplemental Table S2). In total, 199 of 726 patients died (27%) during their hospital admission. In addition, the multi-morbidities of hypertension, chronic obstructive pulmonary disease (COPD), ischaemic heart disease, heart failure, dementia and cancer were independently associated with increased mortality. The admission parameter of fever was associated with reduced mortality but haemoglobin <100, neutrophilia, lymphopenia <0.5, platelets <130, creatinine >125 and CRP >99 were associated with increased risk of mortality. Deprivation measured by Scottish Index of Multiple Deprivation quintile did not affect mortality. In the multivariable analysis, age, sex, performance status, admission pulse and the laboratory parameters of haemoglobin, neutrophil count, lymphocyte count and creatinine were associated with mortality (Figure 3). No multi-morbidities were significant; however, performance status was significantly associated with multi-morbidities where patients with higher performance status had a higher number of multi-morbidities (X^2 (25, $N=726$)=317.79, p value <0.005) (Supplemental Figure S1).

The secondary outcome of ICU admission occurred in 104 patients (14%) with 76% of those admitted to ICU being discharged alive (Table 2). The median duration of ICU admission was 10 days (IQR: 4–19). Of those admitted to ICU, 69 (66%) were intubated and ventilated. Using ICU admission to represent COVID-19 disease severity, logistic regression analysis was run using patients <70 years of age as only a small proportion of the patients ⩾ 70 were admitted to ICU ($n=17$, 4.1%) (Supplemental Figure S2). The multivariable model for this <70 years age group showed that the co-morbidity of COPD was negatively associated with likelihood of admission, although this likely relates to decreased suitability for ICU rather than decreased severity of disease. Hypertension and admission clinical parameters of elevated respiratory rate, low oxygen saturations and elevated creatinine and CRP all increased risk of severe disease requiring critical care support (Figure 3).

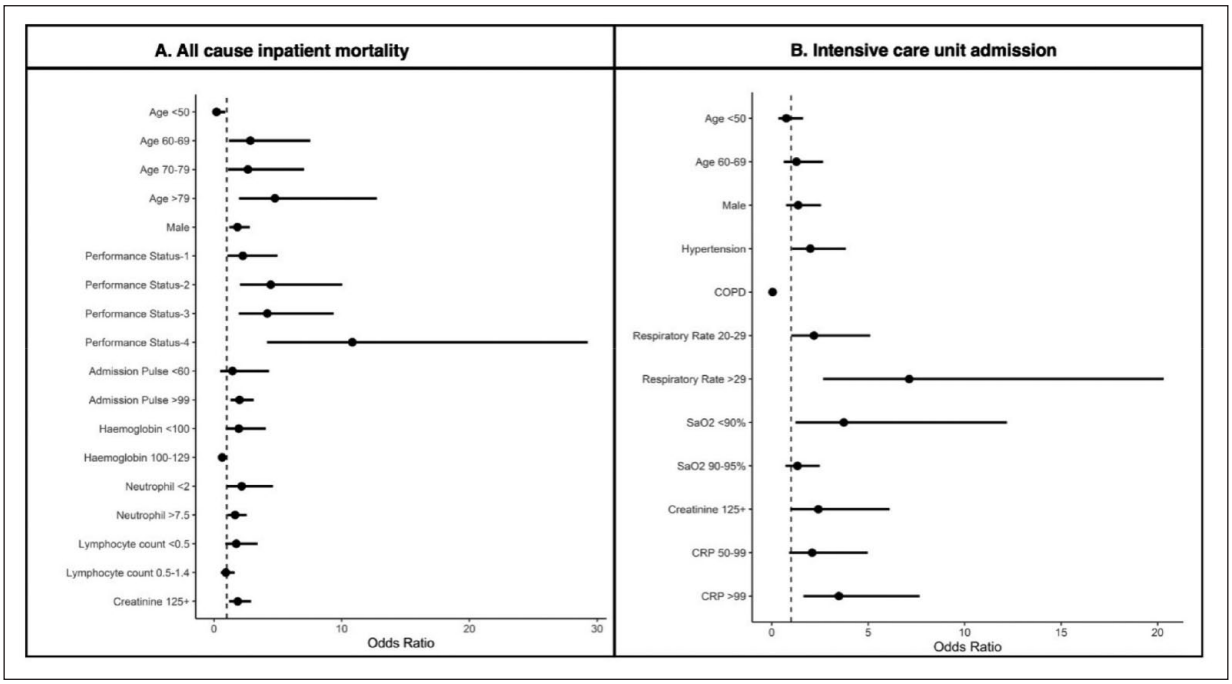

Figure 3. Forest plot demonstrating predictors of all cause inpatient mortality and ICU admission in patients with COVID-19. Multivariate stepwise regression modelling examined the association of clinical characteristics with all cause inpatient mortality and ICU admission as the response variables.
COPD: chronic obstructive pulmonary disease; ECOG: Eastern Cooperative Oncology Group; ICU: intensive care unit; CRP: C-reactive protein; SaO_2: oxygen saturations.
Unit of measurement: age years, respiratory rate breaths per minute, oxygen saturations percentage, creatinine μmol/L, CRP mg/L, admission pulse beats per minute, haemoglobin g/L, neutrophil count 10^9/L, lymphocyte count 10^9/L. Definition: ECOG performance status; 0 – fully active, 1 – restricted in strenuous activity, 2 – able to self-care, 3 – limited self-care and 4 – bedbound.

We found that pre-existing scores for severe infection such as CURB-65 and qSOFA were not useful as tools for predicting mortality (Supplemental Table S3). We applied the ISARIC 4C mortality score,[1] which was developed from a multi-centre prospective study of COVID-19 admissions to 260 UK hospitals including Lothian hospitals, to our dataset. We found this to be the most accurate predictor of mortality (AUC: 0.760), although it is worth noting that our patient cohort made a fractional contribution to the >35,000 validation cohort for this score. Performance status at 1 week prior to hospital admission is associated with increased in-hospital mortality in critically ill patients.[19] The ECOG/WHO performance status does not contain any measures of COVID-19 severity, despite this in our cohort it predicted in-hospital mortality (AUC 0.726). Higher performance status scores were highly correlated with an increased multi-morbidity count (Supplemental Figure S1).

Post-discharge outcomes

In those patients who survived to discharge, 53 (7.3%) were discharged with a new or increased package of care. All-cause inpatient mortality was 27% and all-cause mortality at a year post-admission date was 36%, with a further 64 patients dying post-discharge giving a 12% mortality rate in those who survived admission. This increased mortality at 1 year reflects the epidemiology of our patient cohort; in these 64 additional deaths, the median age was 84.5 years (IQR: 75–88) with 47 (73%) patients having a performance status of 3 or 4. Less than 5 of this group had been admitted to ICU, which may reflect the appropriateness of ICU admission.

Discussion

Using this granular dataset, we demonstrate the profound impact of measures of pre-morbid performance on mortality rate and indicate they can be almost as predictive of mortality as developed COVID-specific scores such as ISARIC 4C. Our paper describes the original cohort of 726 consecutive patients admitted with symptomatic COVID-19 infection from three acute hospitals within Lothian. Overall, the symptoms, signs and clinical features in our cohort reflect the reported characteristics of other published cohorts from a similar time period.[1,2,4]

Our in-hospital mortality rate of 27% and rate of critical care admission of 14% are also comparable to a similar cohort in the first wave of the COVID-19 pandemic phase within the UK.[4] This contrasts with 4.4% in-hospital mortality with the recent Omicron wave[20,21] in the context of multiple proven COVID-19-specific therapies and vaccination. Male sex and increasing age were associated with increased mortality but, in contrast to other studies,[4] deprivation and ethnicity did not have a statistically significant impact on mortality. It should be noted that the ethnic diversity in our cohort was low with only 3.9% of patients from a minority ethnic group. The minimal effect of deprivation on outcomes in Lothian has been explored in depth in other work.[22]

Table 2. Inpatient management and outcomes of SARS-CoV-2-positive in-patients during admission included in analysis.

Variable	Overall, *N* = 726	Died, *N* = 199	Discharged alive, *N* = 527	*p* Value[a]
Duration hospital stay (days)	8 (3, 19)	9 (4, 20)	7 (2, 19)	0.023
Clinical risk scores				
NEWS2 score	4.00 (2.00, 6.00)	5.00 (2.00, 7.00)	4.00 (2.00, 6.00)	0.005
Missing	244	74	170	
CURB-65 category				<0.001
Low risk (0–1)	231 (32%)	19 (9.5%)	212 (40%)	
Medium risk (2)	128 (18%)	47 (24%)	81 (15%)	
High risk (3–5)	124 (17%)	58 (29%)	66 (13%)	
Missing	243 (33%)	75 (38%)	168 (32%)	
qSOFA category				<0.001
Low risk (0–1)	406 (56%)	84 (42%)	322 (61%)	
High risk (2–3)	86 (12%)	45 (23%)	41 (7.8%)	
Missing	234 (32%)	70 (35%)	164 (31%)	
ISARIC 4C mortality score				<0.001
Low risk (0–3)	16 (2%)	0 (0%)	16 (3%)	
Intermediate risk (4–8)	70 (10%)	8 (4%)	62 (12%)	
High risk (9–14)	197 (27%)	58 (29%)	139 (26%)	
Very high risk (15–21)	69 (10%)	41 (20%)	28 (5%)	
Missing	374 (51%)	92 (46%)	282 (54%)	
Hospital treatment				
Oxygen supplementation	530 (73%)	180 (90%)	350 (66%)	<0.001
Empirical antimicrobials	419 (58%)	124 (62%)	295 (56%)	0.2
Empirical oral antimicrobials	214 (29%)	44 (22%)	170 (32%)	0.010
Empirical intravenous antimicrobials	227 (31%)	87 (44%)	140 (27%)	<0.001
Antibiotics escalated within 48 h	82 (11%)			
Antibiotics stopped within 48 h	77 (11%)			
Oral prednisolone (⩽40 mg/day)	66 (9.1%)	19 (9.5%)	47 (8.9%)	>0.9
High-dose steroids (>40 mg oral prednisolone or equivalent/day)	42 (5.8%)	14 (7.0%)	28 (5.3%)	0.5
Complications				
Hospital-acquired pneumonia	76 (10%)	43 (22%)	33 (6.3%)	<0.001
VTE (including DVT and PE)	22 (3.0%)	5 (2.5%)	17 (3.2%)	0.8
Clinical outcome				
ICU admission	104 (14%)	27 (14%)	77 (15%)	0.8
ICU admission duration(days)	10 (4, 19)	12 (8, 18)	8 (4, 19)	0.4
Discharge destination				
Died in hospital	199 (27%)			
Home	432 (60%)			
Discharged with no POC	413 (57%)			
Discharged with POC	111 (15%)			
Care in the community[b]	94 (13%)			

CURB-65: severity score for community-acquired pneumonia (confusion, uraemia, respiratory rate, blood pressure, age 65 years); DVT: deep vein thrombosis; ISARIC 4C: risk stratification score predicting inpatient mortality for hospitalised COVID-19; IQR: interquartile range; NEWS2: National Early Warning Score 2; PE: pulmonary embolism; POC: package of care; qSOFA: quick sepsis related organ failure assessment; VTE: venous thrombo-embolism.

Data are presented as no. (%) or median (IQR).

[a]Comparison between patients who died and those who were discharged alive.

[b]Care in the community defined as including nursing home, care home, community rehabilitation and supported accommodation.

One of the key strengths of our cohort is the thorough review undertaken of individual inpatient notes providing admission parameters, laboratory markers, symptomatology and comorbidity as well as significant granularity for assessment of pre-hospital functional baseline allowing review of this with patient outcome. Our study brings to the literature an exploration of the CFS (Rockwood) and ECOG/WHO performance status where previous data published on frailty and COVID-19 mortality have mainly been on larger but less granular datasets including multicentre cohort studies and meta-analyses.[11,23–26] Our cohort confirms the association between poor performance status and higher mortality controlling for a very broad base of confounding factors and shows that performance status, in addition to the CFS, is also an effective score to measure this vulnerability. Previous studies on performance status in

patients with cancer have found it to be an independent risk factor for increased mortality.[27,28] In our cohort, only 19% of patients had a cancer diagnosis and performance status remained an independent predictor of mortality. It was noted that performance status was strongly associated with co-morbidity count and acts as a reflection of impact of these co-morbidities on functional status.

The long-term health implications of COVID-19 disease are not yet fully known. There is limited mortality data available on patients who survive an inpatient admission. Our study presents mortality data at 1 year following the end of data collection (27% in hospital vs 36% 1-year mortality) demonstrating a significant degree of post-discharge mortality. This may represent the co-morbid and elderly population who required hospitalisation initially and whether their admission with COVID-19 increased their mortality risk at 1 year is an area we aim to explore in more depth in future research. In other centres, COVID-19 has been found to be independently associated with increased 1-year mortality in elderly patients, in keeping with our findings.[11] Comparing these outcome data to a non-COVID-19 Scottish cohort in 2015, there was a 5.8% admission mortality rate and 22.4% all cause 1-year mortality.[29] Although direct comparison is not possible due to lack of a matched cohort, our cohort had a higher rate of patients >80 years and >60 years compared to the 2015 cohort, both of which were associated with increased mortality in the 2015 cohort. Despite this in our cohort, there was a lower mortality increase between discharge and 1 year, potentially reflective of a higher in-hospital mortality rate.

We recognise our limitations with regard to sample size and specific demographics such as ethnic minorities because of limited cohort numbers. Data collection was commenced at the start of the pandemic and our knowledge around this disease evolved rapidly over the next 18 months; hence, patient factors now known to be associated with increased mortality were not initially collected and were subsequently retrieved retrospectively from electronic databases where possible. Due to our data collection methods, using clinicians and medical students, there will be variability given different adjudicators assessed patients; any inter-observer disagreement was referred for senior adjudication to a senior Clinician (either Specialty Registrar or Consultant in Infectious Diseases). We also recognise that we are only able to report outcomes for hospitalised COVID-19 patients; therefore, those who are at high risk of poor outcome accepting that some of the frailest patients were not admitted to hospital care. We also have limited outcome data on those who were discharged to community hospitals for ongoing rehabilitation as often paper notes have been used within these setting which have not been able to be accessed by our manual data extraction team.

Our data serve as a historical record of the initial patients admitted to NHSL hospitals with COVID-19 disease. Our data informed clinical practice and local healthcare service provision at a time of immense pressure on healthcare systems and emphasises the importance of pre-morbid performance status on mortality in this disease.

The future challenges from this disease remain unknown. Now in 2022 with newer variants, in-hospital mortality is significantly lower.[20,21] This detailed descriptive cohort and dataset from the first wave demonstrates how far we have come. This dataset is available upon application and will serve as a useful benchmark for granular comparison as the clinical course of COVID-19 diseases changes in response to mutations, immunity from past infections, vaccines and available therapies.

Acknowledgements

We would like to acknowledge the University of Edinburgh Undergraduate Medical Students (Arun Parajuli, Ed Whittaker, Emma K Watson, Ha Bao Trung Le, Jason Yang, Julia Guerrero Enriquez, Louisa R Carey, Oscar CN Maltby, Sarah H Goodwin, Thomas H Clouston, XinYi Ng and Zaina Sharif) alongside NHS Lothian Junior Doctors (Dr Anna K Jamieson, Dr Arjuna A Sivakumaran, Dr Hannah MM Preston, Dr John P Kelly, Dr Jonathan Wubetu, Dr Kathryn AW Knight, Dr Rosie Callender and Dr Thomas J McCormick) for their assistance in data collection. We also acknowledge Dr Clark Russell and Professor Nick Mills' Research Team for their input.

Declaration of conflicting interests

The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Funding

The authors disclosed receipt of the following financial support for the research, authorship and/or publication of this article: AB is supported by a Clinical Research Training Fellowships (MR/V007254/1) from the Medical Research Council. NLM is supported by a Chair Award (CH/F/21/90010), a Programme Grant (RG/20/10/34966) and a Research Excellence Award (RE/18/5/34216) from the British Heart Foundation.

Role of funding source

The funders played no role in the study design, in the collection, analysis and interpretation of the data, in the writing of the report, or in the decision to submit the paper for publication. The authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

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NHS Lothian eHealth and Lothian Analytical Services: Alistair Stewart, Alastair Thomson, Chris Duncan, Daniella Ene, Hazel Neilson, Juergen Caris, Maria McMenemy, Nazir Lone, Nicola Rigglesford, Paul Schofield, Sophie McCall, Stephen Young, Tracey McKinley and Tracey Rapson

Supplemental material

Supplemental material for this article is available online.

References

1. 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.
2. Williamson E, Walker AJ, Bhaskaran K et al. OpenSAFELY: factors associated with COVID-19-related hospital death in the linked electronic health records of 17 million adult NHS patients. *medRxiv* 2020.
3. Richardson S, Hirsch JS, Narasimhan M et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. *JAMA* 2020; 323: 2052–9.
4. Perez-Guzman PN, Daunt A, Mukherjee S et al. Clinical characteristics and predictors of outcomes of hospitalized patients with coronavirus disease 2019 in a multiethnic london national health service trust: a retrospective cohort study. *Clin Infect Dis* 2021; 73: e4047–57.
5. Zhou F, Yu T, Du R 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: 1054–62.
6. Hill KJ, Russell CD, Clifford S et al. The index case of SARS-CoV-2 in Scotland. *J Infect* 2020; 81: 147–78.
7. Workbook: COVID19 Overview [Internet], https://wav-tableau.luht.scot.nhs.uk/t/nhsl/views/COVID19LabResults_15851742634900/Demographics?iframeSizedToWindow=true:embed=y:showAppBanner=false:display_count=no:showVizHome=no (2022, accessed 22 February 2022)
8. Wynants L, Van Calster B, Collins GS et al. Prediction models for diagnosis and prognosis of covid-19: systematic review and critical appraisal. *BMJ* 2020; 369: m1328.
9. Günster C, Busse R, Spoden M et al. 6-Month mortality and readmissions of hospitalized COVID-19 patients: a nationwide cohort study of 8,679 patients in Germany. *PLoS One* 2021; 16: e0255427.
10. Xie Y, Xu E, Bowe B et al. Long-term cardiovascular outcomes of COVID-19. *Nat Med* 2022; 28: 583–590.
11. Di Bari M, Tonarelli F, Balzi D et al. COVID-19, vulnerability, and long-term mortality in hospitalized and nonhospitalized older persons. *J Am Med Dir Assoc* 2022; 23: 414.
12. National Records of Scotland. Mid-2019 population estimates Scotland [Internet], https://webarchive.nrscotland.gov.uk/web/20210313152406/https://www.nrscotland.gov.uk/statistics-and-data/statistics/statistics-by-theme/population/population-estimates/mid-year-population-estimates/mid-2019 (2021, accessed 16 December 2021).
13. Rockwood K, Song X, MacKnight C et al. A global clinical measure of fitness and frailty in elderly people. *CMAJ* 2005; 173: 489–95.
14. Oken MM, Creech RH, Tormey DC et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. *Am J Clin Oncol* 1982; 5: 649–55.
15. RCP London. National early warning score (NEWS) 2 [Internet], https://www.rcplondon.ac.uk/projects/outputs/national-early-warning-score-news-2 (2017, accessed 16 December 2021).
16. Singer M, Deutschman CS, Seymour C et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA* 2016; 315: 801–10.
17. Lim WS, Van Der Eerden MM, Laing R et al. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. *Thorax* 2003; 58: 377–82.
18. Knight SR, Ho A, Pius R et al. Risk stratification of patients admitted to hospital with covid-19 using the ISARIC WHO clinical characterisation protocol: development and validation of the 4C mortality score. *BMJ* 2020; 370: m3339
19. Zampieri FG, Bozza FA, Moralez GM et al. The effects of performance status one week before hospital admission on the outcomes of critically ill patients. *Intensive Care Med* 2017; 43: 39–47.
20. FFerguson N, Ghani A, Hinsley W et al. Imperial College London COVID-19 Response Team Report 50: Hospitalisation risk for Omicron cases in England[Internet], https://www.imperial.ac.uk/mrc-global-infectious-disease-analysis/covid-19/report-50-severity-omicron/ (2021, accessed 22 February 2022)
21. Maslo C, Friedland R, Toubkin M et al. Characteristics and outcomes of hospitalized patients in South Africa during the COVID-19 omicron wave compared with previous waves. *JAMA* 2022; 327: 583–4.
22. Scopazzini MS, Nicola R, Cave R et al. Scottish Index of Multiple Deprivation (SIMD) indicators as predictors of mortality among patients hospitalised with COVID-19 disease in the Lothian Region, Scotland during the first wave: a cohort study 2021. *BMC International Journal for Equity in Health*. Epub ahead of print 30 November 2021. DOI: 10.21203/rs.3.rs-1102651/v1.
23. 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 Heal* 2020; 5: e444–51.
24. Sablerolles RSG, Lafeber M, van Kempen JAL et al. Association between clinical frailty scale score and hospital mortality in adult patients with COVID-19 (COMET): an international, multicentre, retrospective, observational cohort study. *Lancet Heal Longev* 2021; 2: e163–70.
25. Koduri G, Gokaraju S, Darda M et al. Clinical frailty score as an independent predictor of outcome in COVID-19 hospitalised patients. *Eur Geriatr Med* 2021; 12: 1065–73.
26. Kastora S, Kounidas G, Perrott S et al. Clinical frailty scale as a point of care prognostic indicator of mortality in COVID-19: a systematic review and meta-analysis. *EClinicalMedicine* 2021; 36: 100896.
27. Elkrief A, Desilets A, Papneja N et al. High mortality among hospital-acquired COVID-19 infection in patients with cancer: a multicentre observational cohort study. *Eur J Cancer* 2020; 139: 181.
28. Elkrief A, Hennessy C, Kuderer NM et al. Geriatric risk factors for serious COVID-19 outcomes among older adults with cancer: a cohort study from the COVID-19 and cancer consortium. *Lancet Heal Longev* 2022; 3: e143–52.
29. Moore E, Munoz-Arroyo R, Schofield L et al. Death within 1 year among emergency medical admissions to Scottish hospitals: incident cohort study. *BMJ Open* 2018; 8: e021432.