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Impact of Right Ventricular Dysfunction on Mortality in Patients Hospitalized with COVID-19 according to Race

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Impact of Right Ventricular Dysfunction on Mortality in Patients Hospitalized with COVID-19 according to Race

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Short title: Moody *et al.*; Right Ventricular Dysfunction in COVID-19

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Brief summary:

This is the first study to assess the influence of race on echocardiographic findings in patients hospitalized with COVID-19 disease. In high-risk patients hospitalized with advanced COVID-19 disease, right ventricular (RV) dilatation and dysfunction are common; RV dysfunction (measured using the simple standard measures FAC and TAPSE) is independently associated with early mortality, and is associated with elevated D-dimer and high-sensitivity cardiac Troponin. There are, however, no racial differences in echocardiographic findings, biomarkers, or mortality.

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Abstract

Background: Epidemiological studies suggest that black, Asian and minority ethnic (BAME) patients may be at risk of worse outcomes from Coronavirus-19 (COVID-19) but the pathophysiological drivers for this association are unknown. This study sought to investigate the relationship between findings on echocardiography, mortality and race in COVID-19 pneumonia.

Methods: This was a multicenter, retrospective, observational study including 164 adults (61±13years; 78% male; 36% BAME) hospitalized with COVID-19 undergoing echocardiography between March 16 and May 9, 2020 at 3 days (IQR 2 – 5) from admission. The primary outcome was all-cause mortality.

Results: After a median follow up of 31 days (IQR 14 – 42 days), 58 (35%) patients had died. The right ventricle (RV) was dilated in 62 (38%) patients, and 58 (35%) patients had RV systolic dysfunction. Only 2 (1%) patients had left ventricular (LV) dilatation and 133 (81%) had normal or hyperdynamic LV systolic function. Reduced tricuspid annulus planar systolic excursion was associated with elevated D-dimer ($\rho = -0.18$, $p = 0.025$) and high-sensitivity cardiac Troponin ($\rho = -0.30$, $p < 0.0001$). Reduced RV systolic function (HR, 1.80; 95% CI, 1.05 – 3.09; $p = 0.032$) was an independent predictor of all-cause mortality after adjustment for demographic and clinical risk factors. Comparing white and BAME individuals, there were no differences in echocardiography findings, biomarkers or mortality.

Conclusions: In patients hospitalized with COVID-19 pneumonia, reduced RV systolic function is prevalent and associated with all-cause mortality. There is however, no racial variation in the early findings on echocardiography, biomarkers or mortality.

Keywords: Doppler Echocardiography; COVID-19; Right Ventricle; Cardiac Biomarkers; Ethnicity.

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Introduction

As the number of coronavirus disease 2019 (COVID-19) cases rises across the globe, there is evidence from epidemiological studies that individuals of black and minority ethnic (BAME) ancestry may be at higher risk of adverse outcomes [1-3]. In the US, a report from the Centers for Disease Control and Prevention (CDC) compiled using data from 14 states, described a disproportionate increase in the number of African Americans hospitalized for COVID-19 [4]. It has been suggested that a clustering of co-morbidities (including hypertension, diabetes mellitus, cardiovascular disease, obesity, and chronic lung disease), as well as lower socio-economic status and greater social deprivation may be responsible for a higher overall rate of infection. In turn, this might explain the greater number of BAME patients requiring admission to critical care for COVID-19 compared to pre-COVID historic data (2017 – 2019) [5]. UK data from 17.4 million suggest however, that increased risk in BAME may be only partly attributable to confounders (including age and socio-demographic characteristics) and that there may be an ethnic variation in response to COVID-19 infection [3]. In contrast, in a large US cohort from Louisiana, BAME ancestry was not associated with higher mortality than white race in those already hospitalized with COVID-19 [6]. These discrepant epidemiological findings support the need for investigation into differences in the pathophysiological response to COVID-19 among BAME individuals infected with COVID-19.

Elevated circulating levels of D-dimer and high-sensitivity cardiac troponin (HScTn) are both established powerful predictors of in-hospital mortality in patients with COVID-19 [7, 8]. Patients of black race are more likely to have a positive D-dimer than whites in conventional thromboembolic disease [9]. Given the post-mortem data highlighting the role of diffuse pulmonary small vessel endothelialitis and thrombus

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formation [10], together with evidence that injury to the RV (dilatation and dysfunction) is the primary cardiac manifestation of COVID-19 on transthoracic echocardiography (TTE) [11-14], further investigation into the influence of ethnicity on the relationship between these biomarkers, echocardiographic findings and outcomes is warranted.

In the UK, the Midlands urban catchment area has had a high prevalence of BAME minorities presenting late with COVID-19 disease, many of whom have required admission to the intensive care unit (ICU). The *a priori* hypothesis of this study is that BAME patients hospitalized with COVID-19 pneumonia develop greater right ventricular injury compared with white individuals, related to differences in fibrin formation and degradation (D-dimer), which is associated with increased early mortality.

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Materials and methods

Study Design. This multicenter, retrospective, observational, cohort study included adults aged 18 years or older hospitalized with COVID-19 pneumonia that underwent transthoracic echocardiography (TTE) between March 16 and May 9, 2020. A study CONSORT diagram is available in **Figure 1**. The conduct and reporting of this study was in line with the principles of the Declaration of Helsinki and guided by the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement [15]. Clinical data were manually extracted from electronic health records. For patients with COVID-19 disease, the need for individual consent was waived by national UK guidance covering research during the COVID-19 pandemic as the data were collected by members of usual clinical care teams for the primary purposes of clinical need and/or locally approved service evaluation. This study was reviewed and approved by the University Hospitals Birmingham NHS Foundation Trust COVID-19 Related Research and Audit Board.

Study Population. Patients were identified after admission to one of three UK centers: the Queen Elizabeth Hospital, Birmingham; the New Cross Hospital, Wolverhampton; and Russell's Hall Hospital, Dudley. Before inclusion, all cases were confirmed as having COVID-19 pneumonia through reverse-transcriptase–polymerase-chain-reaction assays performed on nasopharyngeal swabs and confirmation of pulmonary infiltrates on chest radiograph. Patients were referred for TTE at the discretion of the clinician responsible for the patient's care, with one or more of the following indications: hemodynamic instability, chest pain, arrhythmia and electrocardiographic abnormality. In order to minimize the risk of unnecessary exposure to COVID-19 on echocardiographers, a cardiovascular imaging consultant confirmed that each referral for

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inpatient TTE was appropriate. Suspected or proven COVID-19 patients proceeded to TTE only if there was documentation of an elevated high-sensitivity cardiac Troponin above reference range for the institution or, if unavailable at the time of triage, where urgent assessment was needed to guide escalation or withdrawal of care. During the period of study, departmental echocardiographers were available 24/7 and to our knowledge, performed all scanning in COVID-19 patients to the exclusion of other point of care ultrasound. Patients with previously abnormal echocardiography and those with images of insufficient quality to make objective RV measurements were excluded.

Clinical data. Demographic and anthropometric data were routinely collected as part of standard clinical care into the patient's electronic record. Standard hematology and biochemistry indices were recorded from the time of admission. Biomarkers including D-dimer, HScTn and C-reactive protein were recorded on admission and at peak levels.

Echocardiography. Echocardiography was performed (Sparq 795090CC or Affinity ultrasound systems, Philips Healthcare, Netherlands, Philips Healthcare, Netherlands) using a phased array S5 probe by experienced, accredited echocardiographers (level 2 proficiency accreditation British Society of Echocardiography (BSE)) following a modified level 1 focused protocol with assessment of chamber size and function, valvular disease and likelihood of pulmonary hypertension [16].

Measurements were performed retrospectively, off-line using the archived images by BSE level 2 accredited observers blinded to the clinical data, in accordance with the 2015 joint guidelines from the American Society of Echocardiography and the European Association of Cardiovascular Imaging (EACVI) [17]. The right ventricle (RV) was

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assessed in the right ventricular-focused view. The RV was defined as dilated if the RV basal diameter measured >41 mm; RV systolic dysfunction was defined as a fractional area change (FAC) <35% *or* a tricuspid annular plane systolic excursion (TAPSE) <17mm [17]. The echocardiographic probability of pulmonary hypertension was assessed in accordance with EACVI guidelines [18]. Left ventricular size was assessed using the absolute LV end-diastolic dimension according to sex measured in a parasternal long axis view [17]. LV systolic function was assessed visually, as per the BSE level 1 guidance [16].

Radiology. All patients underwent routine chest radiography. CT pulmonary angiography was performed in selected cases at the discretion of the clinical team.

Statistics. The primary outcome measure was all-cause death. Length of hospital stay was examined as a secondary outcome. Statistical analyses were performed with SPSS version 25 (IBM, Armonk, New York, US). Data are expressed as mean ± SD, median (interquartile range), or frequency (%), unless otherwise stated. The normality of distribution for continuous variables was determined using normality plots and the Kolmogorov-Smirnov test. Baseline characteristics of the population were examined according to ethnicity. The Mann-Whitney U test was used to compare continuous non-parametric data. Contingency table analysis was performed using chi-square or Fisher's exact tests where appropriate. Kaplan-Meier analysis of outcomes was based on discrete categories of RV function according to accepted thresholds as defined by TAPSE and FAC measurements. The date of hospital admission was used as time zero. Two-sided log rank tests were used to determine significance. Multivariate Cox proportional hazards models were used to identify the association between time to all-cause death and

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baseline demographic, clinical risk factors, biomarkers and echocardiogram results. A P-value < 0.05 was considered statistically significant for all analyses.

Results

Of 2,217 patients admitted with suspected or proven COVID-19 pneumonia across the 3 centers, 180 patients were identified having undergone TTE. Of those, a total of 16 were excluded (6, negative nasopharyngeal reverse-transcriptase–polymerase-chain-reaction assay; 7, previous abnormal echocardiogram; 3, poor image quality) leaving 164 subjects for inclusion in the present analysis (**Figure 1**). The baseline demographics and clinical characteristics of the study cohort are summarized in **Table 1**. Mean age was 61±13years, 78% were male, and 36% were BAME. Compared with white patients, BAME subjects were younger, more often female, more frequently had diabetes and were less likely to be current smokers. Admission hemoglobin levels were lower and platelet count was higher in BAME compared with white patients, although there were no significant differences between groups in neutrophil-to-lymphocyte ratio, D-dimer, HScTn or CRP.

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After a median follow up of 31 days (IQR 14 – 42 days), 58 (35%) patients had died, and of those 30 (52%) had reduced RV function. **Table 2** summarizes the echocardiographic findings for all patients. The median time between admission and TTE imaging was 3 days (IQR, 2 – 5). RV systolic dysfunction was present in 58 (35%) patients, and was associated with increased mortality on Kaplan-Meier analysis (**Figure 2**). There was a higher proportion of subjects (28% vs. 21%) with globally reduced RV function (as defined by FAC < 35%) than reduced longitudinal RV function (as defined by TAPSE < 17mm). Across all groups, impaired longitudinal RV systolic function

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assessed by TAPSE was associated with the highest mortality (**Figure 3**). The RV was dilated in 62 (38%) patients. Although a higher number of deaths occurred in patients with RV dilatation, there was no significance difference in time to all-cause death by Kaplan-Meier analysis (log rank test, $p = 0.246$). In contrast, there was a low prevalence of abnormalities in left ventricular size and function; only 2 (1%) patients had LV dilatation and in 133 (81%) patients, LV systolic function was either normal or hyper-dynamic.

Comparing white and BAME individuals, there were no differences in the requirements for mechanical ventilation or vasopressor support. There were also no significant differences between groups in echocardiography measures. The median RV basal dimension was smaller in BAME than in white patients although a greater proportion of BAME subjects were female. There was no difference in mortality or hospital length of stay between white and BAME groups.

The peak HScTn correlated with reduced TAPSE ($\rho = -0.30$, $p < 0.0001$) and increased RV basal diameter ($\rho = 0.22$, $p = 0.007$), although there was no significant association with LV function. Higher D-dimer levels were also associated with lower TAPSE ($\rho = -0.18$, $p = 0.025$) and lower FAC ($\rho = -0.17$, $p = 0.045$), and there was an inverse association between neutrophil-to-lymphocyte ratio and TAPSE ($\rho = -0.24$, $p = 0.004$, respectively). Levels of CRP did not correlate with any RV parameters. There was no significant association between the Horowitz ratio (PaO2 / FiO2 ratio), a marker of ARDS severity, and measures of RV size and function (TAPSE, FAC or RV basal diameter).

In multivariable cox regression analysis, age (HR, 1.05; 95% CI, 1.03 – 1.08; p < 0.001) and reduced RV systolic function (HR, 1.80; 95% CI, 1.05 – 3.09; p = 0.032) were the only factors independently associated with all cause mortality after adjustment for sex, peak HScTn, diabetes mellitus, hypertension, chronic lung disease and malignancy (**Table 3**). To date, only 51 patients (31%) have been discharged from hospital.

Baseline demographics, risk factors, laboratory, and clinical characteristics according to the presence of right ventricular systolic dysfunction are presented in **Table 4**. Patients characterized with reduced RV function demonstrated significantly higher levels of D-dimer and elevated neutrophil:lymphocyte ratio on admission as well as higher peak HScTn levels. There was no association between the requirement for mechanical ventilation and RV dysfunction. In patients that required ventilation, however, those subjects with reduced RV function had a numerically lower PaO2 / FiO2 ratio coupled to higher FiO2 and positive end-expiratory pressure (PEEP) requirements, although these results did not meet statistical significance. CT pulmonary angiography was performed in 48 out of the 164 patients (29%) and pulmonary embolism was detected more frequently among patients with abnormal RV function (P = 0.04).

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Discussion

This study has demonstrated the chief echocardiographic abnormalities in patients with severe COVID-19 pneumonia and elevated HScTn, include RV dilatation and impaired RV systolic function, while LV function is usually preserved or hyperdynamic. Reduced RV systolic function is an independent predictor of all-cause mortality outperforming conventional risk factors including sex, hypertension, and diabetes mellitus, with a nearly two-fold increase in mortality hazard. This is the first series to explore the influence of race on the cardiac response to acute COVID-19 as defined by echocardiography. There were no significant differences between white and BAME individuals in outcomes, RV dysfunction, or biomarker evidence of myocardial necrosis or fibrin turnover.

No increase in mortality in hospitalized BAME patients was demonstrated in our study. This result is in keeping with a recent US report from Louisiana, which showed that although black race was associated with higher odds of hospital admission than white race, after adjustment for differences in socio-demographic and baseline co-morbidity, it was not associated with increased in-hospital mortality [6]. This finding is also consistent with a more contemporaneous report from the Office for National Statistics that after accounting for confounders including age, measures of self-reported health and socio-demographic characteristics, suggests South Asian females are at no more risk of dying from COVID-19 than white individuals and, although elevated risk may persist in South Asian males, the residual attributable mortality is small [19]. Our data are consistent and suggest that once patients reach the intensive care unit (or even hospital) with COVID-19, factors other than ethnicity have a greater influence on outcome. Certainly, the risk profile of our patients was worse than in the larger epidemiological

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studies, with a high demand for mechanical ventilation (73%) and an in-patient mortality rate of 35%. Rather than in-hospital differences in acute medical care, the disparities in risk and outcomes of COVID-19 in BAME groups may be attributed to social deprivation and a greater likelihood of living in densely populated areas and dwellings increasing their risk of initial exposure. The lack of impact of ethnicity on mortality in our study could also reflect selection bias; our BAME group was significantly younger, more often female and less likely to smoke than the white group. In the current study, the RV measured smaller among BAME patients compared with white patients likely reflecting the higher proportion of females but no other significant differences in RV response were found. There are both UK and international data indicating smaller ventricular volumes in South Asian populations but the larger studies have focused on the LV dimensions at rest and there are no data that investigate differences in myocardial response under stress [20, 21].

Our finding of RV injury with relative LV sparing in severe COVID-19 pneumonia is consistent with a previous smaller echocardiographic study of 120 consecutive patients treated in Wuhan [12]. On Receiver Operator Curve analysis, Li *et al.* demonstrated RV free wall strain (RVFWS) was a more accurate marker of mortality than conventional indices such as FAC and TAPSE, corroborating earlier data on the sensitivity of this marker [22]. Although RVFWS may be more sensitive, we made a pragmatic decision before the arrival of COVID-19 in the UK to perform a limited level 1 study and minimize the time spent by echocardiographers with infected patients, an approach that has subsequently been adopted by major imaging societies [23, 24]. Furthermore, RVFWS could not be obtained in 24 out of 120 subjects in the Wuhan study, which also identified cut-offs for FAC and TAPSE well within the normal range (TAPSE < 23mm;

FAC < 43.5%) to discriminate those at higher risk. In contrast, we adopted consensus agreed thresholds of normality for RV parameters of systolic function (FAC <35% and TAPSE <17mm) and these provided robust prognostication in the current study acquired as part of a rapid, focused study. In a recent Italian study of non-ICU patients (n=200) hospitalized with COVID-19, the presence of pulmonary hypertension but not RV dysfunction was associated with a higher rate of mortality or ICU admission [25]. The absence of an association between RV dysfunction and adverse outcome contrasts with the present study, however, this discrepancy may relate to their cohort being less sick with a lower requirement for mechanical ventilation (4%), lower event rates (19 deaths), and a shorter median follow up (9 days).

Levels of D-dimer and HScTn were both elevated across the cohort and associated with reduction in RV longitudinal function. D-dimer is the fibrin degradation product released upon cleavage of cross-linked fibrin by plasma and is routinely used for diagnosis of disseminated intravascular coagulation and venous thromboembolism. Given the increasing evidence for thromboembolism and the adverse outcomes associated in COVID-19 [26], the implication is that RV injury in our cohort may have been secondary to pulmonary thrombosis. CT pulmonary angiography was only performed in a small proportion of this cohort at the discretion of the clinician and it is, therefore, impossible to confirm or refute this. Recent post-mortem data however, confirm widespread small pulmonary arteriolar fibrin thrombi and widespread alveolar capillary thrombi specific to COVID-19 compared to influenza cases, supporting the concept that RV dilatation is partly due to pressure overload [10]. Moreover, while previous data have found patients of black race are more likely to have a positive D-dimer than whites [9], no ethnic differences were found in our study. Elevated HScTn

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was also associated with RV injury in our cohort, without evidence of either LV dysfunction or regional wall motion abnormalities to suggest type 1 or type 2 myocardial infarction. HScTn is a vital prognostic marker in COVID-19, with multiple potential causes, including myocarditis, stress cardiomyopathy, coronary microvascular ischemia and tachycardiomyopathy [27]. Our findings are supported by a systematic echocardiographic study from Tel Aviv, which suggested that for the majority of patients admitted with COVID-19, RV rather than LV injury is the more likely explanation for a raised HScTn [28]. An echocardiographic study including 82 critical care patients has suggested pulmonary hypertension rather than RV dysfunction has a more robust association with increased in-hospital mortality, although the authors concede the presence of elevated pulmonary pressures are likely multifactorial and could relate to hypoxemia-related pulmonary vasoconstriction and increased PEEP [29]. In our cohort, while there was echocardiographic evidence of an intermediate or high likelihood of pulmonary hypertension in about a quarter of subjects, the association does not appear strong enough to suggest that RV injury was solely due to increased afterload.

Limitations:

Selection bias is an inherent limitation of this study's retrospective observational design. These findings can, therefore, only be generalized to those patients presenting with severe COVID-19 pneumonia and elevated HScTn. The decision to only include those patients with positive reverse-transcriptase–polymerase-chain-reaction assays for COVID-19 means those subjects with false negative nasopharyngeal PCR swab results have been excluded. Acknowledging the difficulties in estimating pulmonary pressures using echocardiography in critically ill patients requiring mechanical ventilation, we

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have not calculated estimated pulmonary artery systolic pressures but in accordance with ESC guidelines, offer an echocardiographic estimation of pulmonary hypertension . Finally, it is possible that some patients with RV dysfunction suffered undiagnosed thromboembolic disease because the decision to perform CT pulmonary angiography was based on the physician's discretion.

Conclusion

The major effect of COVID-19 pneumonia on cardiac structure and function is RV injury associated with elevated HScTn; in contrast, the LV is much less often affected. Reduced RV systolic dysfunction is independently associated with all-cause mortality and is also associated with increased HScTn and elevated D-dimer, reflecting increased fibrin formation and degradation. There are no differences in echocardiographic findings, biomarker evidence of myocardial necrosis or fibrin turnover, or mortality between BAME and white patients hospitalized with severe COVID-19 disease.

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Table 1. Baseline demographics, risk factors, laboratory, and clinical characteristics according to ethnicity (N = 164).

Variable	All patients (N = 164)	White (N = 108)	Black, Asian and Minority Ethnic (N = 56)	P Value
Baseline demographics and risk factors				
Age (mean ± SD) – yr	61 ± 13	62 ± 14	58 ± 12	0.036
Male – no. (%)	127 (78)	87 (81)	40 (71)	0.19
Ethnicity White – no. (%) South Asian – no. (%) Afro-Caribbean – no. (%)	 108 (66) 47 (29) 9 (5)	 108 (100) 0 (0) 0 (0)	 0 (0) 47 (84) 9 (16)	 -
Body mass index (mean ± SD) – kg / m^2	30.6 ± 6.4	30.4 ± 6.2	30.7 ± 6.7	0.83
Hypertension – no. (%)	68 (41)	39 (36)	29 (52)	0.13
Diabetes mellitus – no. (%)	53 (32)	24 (22)	29 (52)	< 0.001
Current smoker – no. (%)	22 (14)	19 (18)	3 (5)	0.03
Chronic kidney disease – no. (%)	19 (12)	10 (9)	9 (16)	0.34
Previous stroke – no. (%)	12 (7)	7 (7)	5 (9)	0.57
Chronic lung disease – no. (%)	20 (12)	10 (9)	10 (18)	0.11
History of coronary artery disease – no. (%)	21 (13)	11 (10)	10 (18)	0.16
History of malignancy – no. (%)	12 (7)	9 (8)	3 (5)	0.75
Laboratory findings				
Full blood count Hemoglobin (mean ± SD) g/L Platelet count (median (IQR)) – /mm³ White cell count (median (IQR)) – /mm³ Neutrophils (median (IQR)) – /mm³ Lymphocytes (median (IQR))– /mm³ Neutrophil-to-Lymphocyte ratio (median (IQR))	 130 ± 25 220 (169 – 299) 15.9 (11.8 – 21.3) 10.3 (6.3 – 14.6) 0.98 (0.61 – 1.60) 10.6 (5.5 – 18.4)	 135 ± 24 201 (162 – 284) 15.8 (11.5 – 20.9) 10.2 (6.4 – 14.6) 0.87 (0.54 – 1.50) 10.8 (5.8 – 19.0)	 122 ± 23 244 (185 – 337) 16.0 (11.9 – 21.6) 10.5 (6.1 – 14.9) 1.10 (0.72 – 1.76) 9.5 (5.3 – 16.7)	 0.003 0.031 0.88 0.74 0.026 0.26
HScTn, peak (median (IQR)) – ng/L	38 (12 – 185)	43 (14 – 196)	33 (10 – 142)	0.19

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D-dimer, admission (median (IQR)) – ng/L	884 (482 - 3782)	934 (518 – 4464)	878 (438 - 3184)	0.66
D-dimer, peak (median (IQR)) – ng/L	4165 (1502 – 11938)	4701 (1210 – 11938)	3714 (1794 – 12305)	0.94
C-reactive protein, admission (median (IQR)) – mg/dL	156 (79 – 257)	147 (77 – 244)	186 (81 – 281)	0.29
C-reactive protein, peak (median (IQR)) – mg/dL	312 (227 – 393)	305 (216 – 402)	321 (247 -388)	0.48
Chest radiograph findings				
Bilateral pulmonary infiltrates – no. (%)	164 (100)	108 (100)	56 (100)	1.0
During hospital stay				
Vasopressor support – no. (%)	91 (58)	57 (52)	34 (61)	0.56
Invasive mechanical ventilation – no. (%)	120 (73)	77 (74)	43 (77)	0.74
Pulmonary embolism* – no. (%)	7 (4)	5 (5)	2 (4)	1.0
Ventilatory parameters†				
Fraction of inspired oxygen (mean ± SD)	0.60 ± 0.35	0.60 ± 0.41	0.59 ± 0.22	0.92
PaO2/FiO2 (mean ± SD) – mmHg	144 ± 56	148 ± 57	138 ± 54	0.41
Positive end-expiratory pressure (mean ± SD) – cmH_2O	9.0 ± 2.8	9.1 ± 2.6	9.0 ± 3.0	0.93
Outcomes				
Death – no. (%)	66 (40)	49 (45)	17 (30)	0.06
Discharged from hospital – no. (%)	51 (31)	30 (28)	21 (38)	0.20
Length of hospital stay (median (IQR) – days	28 (12 – 35)	26 (12 – 37)	29 (13 – 35)	0.98

* Diagnosis made on CT pulmonary angiography.

† Available data in 94 patients

Abbreviations: HScTn, high sensitivity cardiac troponin; CRP, C reactive protein; PO2/FiO2 (also known as the Horowitz or P/F ratio), the ratio of arterial oxygen concentration in mmHg to the fraction of inspired oxygen.

The normality of distribution for continuous variables was determined using the Kolmogorov–Smirnov test. Continuous data were analyzed using an independent samples Student *t* test if normally distributed or a Mann-Whitney U test for if not normally distributed. Categorical data were analyzed using Chi-square or where appropriate, Fisher's exact tests.

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Table 2. Echocardiographic characteristics (N = 164).

Echocardiographic parameters	All patients (N = 164)	White (N = 108)	Black, Asian and Minority Ethnic (N = 56)	P Value
LV size				
Normal – no. (%)	138 (84)	92 (85)	46 (82)	
Dilated – no. (%)	4 (2)	4 (4)	0 (0)	0.06
Small – no. (%)	21 (13)	12 (11)	9 (16)	
LV end-diastolic dimension (median (IQR)) – mm	40 (29 – 45)	40 (20 – 45)	49 (29 – 43)	0.53
LV systolic function				
Hyper-dynamic – no. (%)	46 (28)	23 (22)	23 (41)	
Normal – no. (%)	87 (53)	61 (57)	26 (46)	
Mildly impaired – no. (%)	24 (15)	18 (17)	6 (11)	0.35
Moderately impaired – no. (%)	2 (1)	1 (1)	1 (2)	
Severely impaired – no. (%)	4 (3)	4 (4)	0 (0)	
LV ejection fraction (median (IQR)) – %	60 (55 – 67)	58 (55 – 66)	62 (59 – 70)	0.10
RV size				
Normal – no. (%)	102 (62)	64 (59)	38 (68)	
Dilated – no. (%)	62 (38)	44 (41)	18 (32)	0.06
RV basal diameter (median (IQR)) – mm	40 (37 – 45)	42 (38 – 46)	39 (35 – 43)	0.003
RV systolic function				
Fractional area change (mean ± SD) – %	40 ± 11	40 ± 8	39 ± 12	0.19
TAPSE (mean ± SD) mm	20 ± 5	21 ± 5	20 ± 5	0.55
Fractional area change < 35% – no. (%)	46 (28)	34 (31)	12 (21)	0.18
TAPSE < 17mm – no. (%)	34 (21)	26 (24)	8 (14)	0.14
Fractional area change < 35% *and* TAPSE < 17mm – no. (%)	23 (14)	16 (15)	7 (13)	0.65
Pulmonary hypertension				

Low probability – no. (%)	24 (15)	21 (20)	3 (5)	
Intermediate probability – no. (%)	27 (16)	18 (11)	9 (16)	0.16
High probability – no. (%)	27 (16)	18 (11)	9 (16)	
Unable to estimate* – no. (%)	85 (52)	50 (47)	35 (63)	0.25
Peak tricuspid regurgitation velocity (mean ± SD)**	2.9 ± 0.5	3.0 ± 0.6	2.9 ± 0.4	0.76
Pericardial effusion – no. (%)	13 (8)	6 (11)	7 (7)	0.50

* Due to an incomplete tricuspid regurgitation continuous wave Doppler signal.
** In the 79 patients with measurable tricuspid regurgitation continuous wave Doppler signal.
Abbreviations: LV, left ventricular; RV, right ventricular; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation.
The normality of distribution for continuous variables was determined using the Kolmogorov–Smirnov test. Continuous data were analyzed using an independent samples Student *t* test if normally distributed or a Mann-Whitney U test for if not normally distributed. Categorical data were analyzed using Chi-square or where appropriate, Fisher's exact tests.

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Table 3. Multivariate Predictors of In-Patient All-Cause Mortality.

Variable	All-cause death	
	Hazard Ratio (95% CI)	**P Value**
Age (yr)	1.05 (1.03 – 1.08)	< 0.001
Gender (female)	0.52 (0.88 – 3.25)	0.12
Diabetes	0.84 (0.63 – 1.12)	0.23
Hypertension	2.51 (0.64 – 9.91)	0.19
Chronic lung disease	1.36 (0.83 – 2.23)	0.22
History of malignancy	1.75 (0.93 – 3.23)	0.08
Right ventricular dysfunction	1.80 (1.05 – 3.09)	0.032
HScTn (ng/L)	1.00 (1.00 – 1.00)	0.75

Abbreviation: HScTn, high-sensitivity cardiac Troponin.
Variables were simultaneously entered into a multivariate Cox regression model.
Age and high-sensitivity cardiac Troponin were entered as continuous variables.
All other variables were entered as categorical variables.

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Table 4. Baseline demographics, risk factors, laboratory, and clinical characteristics according to right ventricular systolic function (N = 164).

Variable	All patients (N = 164)	Normal right ventricular systolic function (N = 106)	Impaired right ventricular systolic function (N = 58)	P Value
Baseline demographics and risk factors				
Age (mean ± SD) – yr	61 ± 13	62 ± 13	61 ± 14	0.62
Gender				
Male – no. (%)	127 (78)	78 (74)	49 (84)	0.12
Ethnicity				
White – no. (%)	108 (66)	64 (60)	44 (76)	0.06
Black, asian and minority ethnic – no. (%)	56 (34)	42 (40)	14 (24)	
Body mass index (mean ± SD) – kg / m^2	30.6 ± 6.4	30.6 ± 6.6	30.4 ± 6.2	0.87
Hypertension – no. (%)	68 (41)	50 (47)	18 (31)	0.09
Diabetes mellitus – no. (%)	53 (32)	37 (35)	16 (28)	0.34
Chronic kidney disease – no. (%)	19 (12)	12 (11)	7 (12)	0.75
Previous stroke – no. (%)	12 (7)	10 (9)	2 (3)	0.22
Current smoker – no. (%)	22 (13)	15 (14)	7 (12)	0.69
Chronic lung disease – no. (%)	20 (12)	16 (15)	4 (7)	0.13
History of coronary artery disease – no. (%)	21 (13)	16 (15)	5 (9)	0.24
History of malignancy – no. (%)	12 (7)	8 (8)	4 (7)	1.00
Laboratory findings				
Full blood count				
Hemoglobin (mean ± SD) g/L	130 ± 25	129 ± 23	132 ± 28	0.45
Platelets (median (IQR)) – /mm³	220 (169 – 299)	224 (170 – 296)	206 (169 – 315)	0.73
White cell count (median (IQR)) – /mm³	15.9 (11.8 – 21.3)	15.0 (11.1 – 19.6)	17.7 (13.7 – 24.4)	0.025
Neutrophils (median (IQR)) – /mm³	10.3 (6.3 – 14.6)	9.6 (5.5 – 13.3)	13.1 (8.0 – 19.9)	0.001
Lymphocytes (mean ± SD) – /mm³	0.98 (0.61 – 1.60)	0.97 (0.16 – 1.52)	1.00 (0.61 – 1.90)	0.74

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Neutrophil-to-Lymphocyte ratio (median (IQR))	10.6 (5.5 – 18.4)	9.1 (5.2 – 16.6)	12.4 (6.8 – 20.8)	0.030
HScTn, peak (median (IQR)) – ng/L	38 (12 – 185)	32 (11 – 131)	49 (21 – 252)	0.036
D-dimer, admission (median (IQR)) – ng/L	884 (482 – 3782)	739 (368 – 3015)	2050 (609-8705)	0.014
D-dimer, peak (median (IQR)) – ng/L	4165 (1502 – 11938)	4075 (1557 – 11938)	4495 (1043 – 11938)	0.63
C-reactive protein, admission (median (IQR)) – mg/dL	156 (79 – 257)	155 (78 – 244)	157 (81 – 292)	0.70
C-reactive protein, peak (median (IQR)) – mg/dL	312 (227 – 393)	301 (226 – 378)	333 (214 – 409)	0.33
Chest radiograph findings				
Bilateral pulmonary infiltrates – no. (%)	164 (100)	106 (100)	58 (100)	1.00
During hospital stay				
Vasopressor support – no. (%)	91 (58)	59 (57)	32 (55)	0.76
Invasive mechanical ventilation – no. (%)	120 (73)	77 (73)	43 (74)	0.84
Pulmonary embolism* – no. (%)	7 (4)	2 (2)	5 (9)	0.04
Ventilatory parameters†				
Fraction of inspired oxygen (mean ± SD)	0.60 ± 0.35	0.58 ± 0.39	0.64 ± 0.21	0.47
PaO2/FiO2 (mean ± SD) – mmHg	144 ± 56	148 ± 53	135 ± 61	0.30
Positive end-expiratory pressure (mean ± SD) – cmH_2O	9.0 ± 2.8	8.8 ± 2.9	9.6 ± 2.4	0.19
Outcomes				
Death – no. (%)	66 (40)	36 (34)	30 (52)	0.027
Discharged from hospital – no. (%)	51 (31)	39 (37)	12 (17)	0.07
Length of hospital stay (median (IQR) – days	28 (12 – 35)	28 (11 – 35)	29 (15 – 41)	0.56

Abbreviations: as for Table 1.

The normality of distribution for continuous variables was determined using the Kolmogorov–Smirnov test. Continuous data were analyzed using an independent samples Student *t* test if normally distributed or a Mann-Whitney U test for if not normally distributed. Categorical data were analyzed using Chi-square or where appropriate, Fisher's exact tests.

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Figure 1. Study CONSORT Flow Diagram.
Of the original 2,217 patients admitted with probable COVID-19, 1,582 patients subsequently tested positive for COVID-19 on naso-pharyngeal throat swab PCR testing.

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Figure 2. Kaplan-Meier curves for unadjusted cumulative survival from all-cause death among **(A)** all patients, **(B)** white patients and **(C)** BAME patients dichotomized according to right ventricular systolic function. Two-sided log rank tests were used to determine significance.

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Figure 3. Kaplan-Meier curves for unadjusted cumulative survival from all-cause death among **(A)** all patients, **(B)** white patients and **(C)** BAME patients dichotomized according to TAPSE <17mm. Two-sided log rank tests were used to determine significance.

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