Abstract

Background: Recent reports have demonstrated high troponin levels in patients affected with COVID-19. In the present study, we aimed to determine the association between admission and peak troponin levels and COVID-19 outcomes.

Methods: This was an observational multi-ethnic multi-center study in a UK cohort of 434 patients admitted and diagnosed COVID-19 positive, across six hospitals in London, UK during the second half of March 2020.

Results: Myocardial injury, defined as positive troponin during admission was observed in 288 (66.4%) patients. Age (OR:1.68 [1.49-1.88], p<0.001), hypertension (OR:1.81 [1.10-2.99], p=0.020) and moderate chronic kidney disease (OR: 9.12 [95%CI4.24-19.64] p<0.001) independently predicted myocardial injury. After adjustment, patients with positive peak troponin were more likely to need non-invasive and mechanical ventilation (OR: 2.50 [95%CI: 1.31-4.79], p=0.006, and OR: 6.82 [95%CI: 3.40-13.68], p<0.001, respectively) and urgent renal replacement therapy (OR: 4.14 [95%CI: 1.34-12.78], p=0.013). With regards to events, and after adjustment, positive peak troponin levels were independently associated with acute kidney injury (OR: 6.50, [95%CI:3.24-13.04], p<0.001), venous thromboembolism (OR: 12.84 [95%CI: 3.42-48.24], p<0.001), development of atrial fibrillation (OR: 10.02 [95%CI: 1.50-96.36], p=0.019), and death during admission (OR: 2.48 [95%CI: 1.38-4.64], p<0.001). In addition, median length of stay in days increased alongside with troponin tertiles: 8 (5-13) first tertile, 14 (7-23), second tertile, and 16 (10-23) third tertile (p<0.001). Similar associations were observed for admission troponin.

Conclusions: Admission and peak troponin appear to be predictors for cardiovascular and non-cardiovascular events and outcomes in COVID-19 patients, and their utilization may have an impact on patient management.

Introduction

Coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 is a global pandemic[1]. So far, it has affected more than 80 million people worldwide, and is associated with multi-organ dysfunction and high mortality rates[1].

Studies suggest that some patients present to hospital and have a relatively benign course, being discharged within a few days. However, for other patients the disease course is more aggressive, requiring multiple interventions, while they experience higher mortality and longer in hospital stay[2]. It would therefore be important to have a biomarker which could help to distinguish between these two groups of patients, not only for prognosis, but also potentially, for treatment decisions.

Troponin is a marker of myocardial injury, but it is also found to be raised in several conditions. Recent reports demonstrated high troponin levels in patients affected by COVID-19. These were found to have higher mortality rates during the initial outbreak in Wuhan cohorts[3, 4]. In addition, higher mortality rates have been observed in the UK, as an older and multi-ethnic population with more comorbidities was affected by the disease[5].

It still unknown which patients are more likely to develop myocardial injury in the setting of COVID-19, and whether or not, after adjustment for confounders associated with rise in troponin, myocardial injury can be used as an independent predictor of the disease in Western multi-ethnic populations. Yet, it remains to be determined if admission troponin can be used as a predictor, and if the magnitude of troponin rise translates into different outcome rates (i.e. whether patients with a higher rise in troponin levels experience a more severe disease progression than those with negative or mildly positive troponin levels).

We aimed to assess: 1) the risk factors for myocardial injury; 2) the impact of myocardial injury on different COVID-19 associated outcomes; and 3) whether admission troponin, peak troponin and magnitude of troponin rise have a similar prognosticator capacity.

Methods

In this multi-center study, we assessed the association between high-sensitivity troponin (hsTrop) and COVID-19 intra-hospital clinical trajectory (comprising mortality, utilization of procedures, and cardiovascular and non-cardiovascular outcomes) in a UK cohort of 434 patients admitted and diagnosed positive, across six hospitals in London, UK. All patients admitted to the participant hospitals from the 16th to the 30th of March 2020 with a diagnosis of COVID-19 and having at least one troponin measurement were considered eligible for analysis. This observational study was approved by the Clinical Effectiveness Unit at Barts Health NHS Trust (*Project ID: 11103; Title: COVID-19 and cardiovascular disease (CVD) outcomes)* and by the Quality Governance Department at Royal Free London NHS Trust (*Cardiovascular Implications of Outcomes of Patients With COVID-19*; 22/04/2020).

Patient demographic characteristics, laboratory results, procedures, comorbidities, procedures and outcomes were extracted from the electronic records and paper notes. In order for patients to be included in the study, these should be diagnosed COVID-19 positive, as confirmed by polymerase chain reaction (PCR) swab. Patients with 2 positive swabs and older than 16 years were included in the study.

Routine bloods were obtained from each patient. Troponin T levels were measured with a high-sensitivity assay on and during admission as per Trusts' protocols.

Measurement of blood parameters

Routine bloods were obtained from patients on and during admission. Routine hospital laboratory methods were used for the analysis. These were available on the electronic systems and included: full blood count parameters, high-sensitivity troponin T, C-reactive protein (CRP), lactate dehydrogenase (LDH), N-terminal pro B-type natriuretic peptide (NT-proBNP), international normalised ratio (INR), creatine kinase (CK), D-Dimers, activated partial thromboplastin time (APTT), fibrinogen, thrombin time and creatinine. Glomerular filtration rate (eGFR) was estimated using the Modification of Diet in Renal Disease (MDRD) Study equation. Patients were classified as having moderate CKD when eGFR was less than 60ml/min.

Troponin measurements were performed based on clinical indication or based on local protocols for risk stratification of Covid-19 patients.

The term *"myocardial injury"* was used for patients with positive troponin levels. Troponin-T levels were measured in all patients and were considered as positive when these were equal or greater (≥) 15ng/mL on admission. Peak troponin for each patient was measured and based on these values, troponin tertiles were defined. Patients with levels ≤14 were in the lower tertile of troponin levels in our cohort, which corresponded to negative troponin levels (absence of myocardial injury). Fifteen was the positivity for our labs (above the 99th percentile in our normal population). Patients in the upper tertile of troponin had peak levels ≥47ng/mL.

Study endpoints

The study primary endpoint was defined as all-cause mortality/death. We also assessed the cohort for differences occurring across troponin groups related to: (i) pneumonia, (ii) acute kidney injury (defined as a 50% increase in creatinine compared to chronic/baseline levels), (iii) myocardial injury (defined as high sensitivity troponin above the 99th percentile of normal), (iv) acute heart failure, (v) acute atrial fibrillation episode, (vi) stroke, (vii) venous thromboembolic disease (including pulmonary embolism and/or deep vein thrombosis), and (viii) utilization of procedures (non-invasive ventilation, mechanical ventilation, extracorporeal membrane oxygenation and renal replacement therapy (RRT)).

Statistical analysis

Descriptive data are presented as rates and median and inter-quartile. Parametric or the equivalent non-parametric tests (Chi-square, Mann-Whitney or Kruskal-Wallis) were used where appropriate for comparisons among groups.

Binary logistic regression was used to assess for predictors of myocardial injury using the Forward likelihood ratio (LR) method, with probability for stepwise 0.05. We used logistic regression to obtain the probability of sustaining a given event (e.g. mortality or one of the other endpoints). The probability for every given subject depends on the presence/absence of the explanatory variables included in the model. Explanatory variables need to be independent predictors (i.e. to associate with the event of interest independently of all other tested variables; this association is measured as the odds ratio). The odds ratio represents the odds of an outcome occurring due to exposure to a variable. Depending on its value, it can suggest a higher (>1) or lower (<1) likelihood of the outcome happening. In the forward likelihood ratio method, significant predictors identified on univariate analysis are tested for inclusion in the model. The model is created through a stepwise process with the strongest independent predictor entering the model at each step as long as it significantly improves its predictive capacity.

When assessing for the association of myocardial injury or troponin tertiles with the pre-defined outcomes, adjustment for clinical baseline differences (age, hypertension, diabetes, previous myocardial infarction/ischaemic heart disease, asthma, chronic obstructive pulmonary disease (COPD) and eGFR) observed across the different categories was performed with binary logistic regression using Method Enter. Unlike the previous method (Forward LR Method), when using Method Enter all variables are included into the model on the same step and the resulting odds ratio of the tested variable (in this case presence of myocardial injury or troponin tertiles) is adjusted for all the other variables included in the model.

Results with $p<0.05$ were considered as significant. PASW Statistics (SPSS Inc, Chicago, IL) version 18.0 was used for statistical analysis.

Results

During the study period 629 patients were admitted and diagnosed with COVID-19. Among those, troponin measurements were performed during admission in 434 patients (Figure 1). Demographic characteristics of the patients enrolled in this study are presented in Table 1. The median age was 66 (56-80) years, and 62.9% of patients were men. A positive troponin was detected at least once during admission in nearly two thirds of patients. Seventeen patients (3.9%) were diagnosed with myocardial infarction during the admission. Median left ventricular ejection fraction was significantly lower for troponin positive patients as compared to troponin negative patients ($p=0.015$).

Patients with positive troponin levels were significantly older ($p<0.001$), and more frequently had risk factors such as hypertension ($p<0.001$), hyperlipidemia ($p<0.001$), asthma ($p=0.031$) or COPD ($p=0.026$) as compared to troponin negative patients. Troponin positive patients had significantly higher white blood cell

count, lower haemoglobin levels, higher creatinine levels, lower eGFR, higher D-Dimer levels, and higher NT-proBNP levels (Table 2).

Factors associated with myocardial injury

Our analysis showed that age, Asian ethnicity (as compared to Caucasian), hypertension, diabetes, asthma, COPD and moderate CKD were associated with myocardial injury on univariate analysis (Table 3). However, after adjusting for baseline differences only age, hypertension and moderate CKD independently predicted myocardial injury on multivariate analysis (i.e. after correcting for confounders, the probability of myocardial injury was found to increase by 1.68 per every 10 additional years of age, and was 1.81 and 9.12 times higher when in the presence of hypertension and/or moderate CKD, respectively).

Myocardial injury and cardiovascular & non-cardiovascular events, and procedures

Median length of in-hospital stay was 12 (6-20) days. This was longer for troponin positive patients [15 (9-23) versus 8 (5-13) in negative troponin patients, $p<0.001$].

Among patients with troponin measurements, 109 patients had two troponin measurements, 33 patients had 3 measurements and 61 patients had 4 or more troponin measurements. During these repeat measurements, an additional 24 patients who initially tested negative presented with positive troponin results.

Seven patients stayed in hospital for less than 24 hours: 4 were discharged and 3 died within the first day. All the patients who died within 24 hours had a positive troponin in the higher tertile, and those discharged on the same day had a negative troponin.

After adjustment for baseline differences (age, hypertension, diabetes, previous myocardial infarction/ischaemic heart disease, asthma, COPD and eGFR), patients with at least one positive troponin result during admission (i.e. a positive peak troponin level) were more likely to need both non-invasive and mechanical ventilation (2.50 and 6.82 significantly higher odds, respectively) and significantly more likely to require urgent RRT (4.14 higher odds of RRT) (Table 4).

With regards to events, after adjustment to the previously mentioned confounders, positive troponin during admission was significantly associated with acute kidney injury (6.50 higher odds), thromboembolic events (12.84 higher odds) and presence of atrial fibrillation (10.02 higher odds). Importantly, raised troponin levels were significantly and independently associated with death during admission (2.48 higher likelihood of dying when a positive troponin was detected) (Table 4).

Patients in whom no troponin measurement was performed during admission had comparable hospitalization length and mortality rate when compared to patients with measured troponin (14.6±11.5 vs. 15.3±12.9 days, p=0.475 and 32.3% vs. 33.0%, p=0.856, respectively).

Magnitude of troponin rise and Admission troponin vs. Outcomes

Median length of in hospital stay (in days) increased alongside with troponin tertiles: 8 (IQR 5-13) first tertile, 14 (IQR 7-23), second tertile, and 16 (IQR 10-23) third tertile (p<0.001). All outcomes which were significantly associated with presence of at least one positive troponin measurement, seemed to occur significantly more frequently in the upper tertile (translated into higher ORs), except for mortality and venous thromboembolic disease which had comparable incidence in the 2nd and 3rd tertiles (S-Table 2 and Figure 2).

All the significant associations previously reported for myocardial injury (observed anytime throughout the admission) were also observed for admission troponin levels, except for non-invasive ventilation (S-Table 1 and Figure 2).

Discussion

In the present study, we report our experience on the association between troponin levels and COVID-19 outcomes. We have found that nearly two thirds of admitted patients are troponin positive. These patients have a longer in hospital stay, which appears to be associated with magnitude of troponin rise. Troponin positive patients were more likely to need both non-invasive and mechanical ventilation as well as urgent RRT. Raised troponin levels were associated with acute kidney injury, thromboembolic events and presence of atrial fibrillation. Higher levels of troponin were associated with further increase in the risk of complications: all complications except for mortality and venous thromboembolism were more frequent in patients with higher troponin levels (i.e. in the upper tertile).

Admission troponin levels also had good predictive value, being associated with most of the assessed cardiovascular and non-cardiovascular outcomes. Importantly, positive troponin levels were significantly associated with death during admission.

Early experience from China, Italy and USA suggests that COVID-19 can be a mild condition in most individuals[6-8]. People who will more often require intensive care unit admission are the elderly and those with several other comorbidities including CVD.

In a cohort of 416 positive patients, Shi et al.[3] reported that 86 patients had evidence of myocardial damage as indicated by increased in troponin levels. Those patients with higher troponin levels had also increased in hospital mortality. Similar results were reported by Guo et al.[4], with highest mortality rates in those with elevated troponin levels and underlying CVD. Interestingly, our cohort displayed a 3-fold higher frequency of positive troponin levels in COVID-19 patients admitted to hospital (60% as compared to 20% in previous populations from the region of Wuhan.

In the aforementioned study by Guo et al.[4], troponin levels were associated with CRP and NT-proBNP levels correlating myocardial injury and ventricular dysfunction. We did not observe the same association for CRP levels, but higher white blood cell count, D-Dimers and lower haemoglobin levels suggested that positive troponin can occur as a result of an inflammatory process. Importantly, we found that NT-proBNP levels were significantly higher in the troponin positive patients, who also had higher in-hospital mortality. This is in agreement with previous studies suggesting that NT-proBNP might be an independent risk factor for in hospital death in patients with severe COVID-19[9]. The observed changes in INR and D-dimers also suggest that positive troponin can translate some of the coagulation changes observed in this group. Finally, the higher creatinine and lower eGFR levels in these patients may be signalling the presence of more frequent micro and macrovascular vascular disease. Further research underpinning the association of positive troponin with changes in these pathways is required for further understanding of the pathophysiology of COVID-19 and the associated cytokine storm.

In addition to myocardial injury, arrhythmias are also known to occur in COVID-19. In a study[10] including 138 patients with COVID-19 there was a 16.7% incidence of arrhythmias. This was much higher in patients requiring admission to intensive care compared to those who did not. We did not observe high prevalence of ventricular arrhythmias as described in previous cohorts of COVID-19 positive patients[4, 10]. In our cohort, combining atrial fibrillation and ventricular tachycardia, sustained arrhythmias occurred in only 7% of patients, half to a third of what was reported in Wuhan.

We have shown that increased troponin levels occurred in patients with CVD risk factors, as well as in those with COPD and those in angiotensin-converting enzyme inhibitors (ACE-I) and statin therapy. Of the parameters we examined, age, hypertension and moderate CKD were independent predictors of myocardial injury.

It is known that troponin levels can be increased in patients with renal failure due to the high prevalence of coronary artery disease[11]. However, changes of baseline level with a distinct rise and fall supports the presence of myocardial injury. This is illustrated in our findings with presence of moderate CKD, measured through estimated glomerular filtration rate <60mL/min, using the MDRD equation, being independently associated with a 9-fold increase in myocardial injury after adjustment (Table 3).

Our results raise several hypotheses. Bed management and hospital capacity is one of the concerns during the COVID-19 pandemic. We wonder if utilizing troponin levels (single or repeated measurements), alongside with other clinical and laboratory variables commonly used for assessing if a patient is fit for hospital discharge (time of disease progression, acceptable oxygen saturation, and improved respiratory symptoms, improvement of blood markers of infection, etc.)[12], can be used for deciding which patients can be treated in the ambulatory care. Furthermore, presence of myocardial injury can potentially be a good criterion for inclusion in a clinical decision rule (alongside other risk factors and biomarkers) in selecting patients for aggressive treatment with drugs aiming at reducing viral load or blocking the cytokine storm phase. However, these hypotheses need to be assessed in a randomised trial. Optimal number and frequency of troponin measurements during admission, or in patients receiving ambulatory care, remains to be determined.

We acknowledge that the present study has limitations. The use of cardiac magnetic resonance or echocardiography were limited due to safety and logistic issues, and hence we were not able to assess for specific features of acute myocardial injury. In addition, we cannot prove a direct effect of COVID-19 on myocardium or involvement of inflammation in the observed outcomes. However, our multi-ethnic cohort is significantly larger and more applicable to other ethnicity groups when compared to the very early Wuhan cohorts which were limited to the Chinese population.

Conclusions

Patients with CKD, hypertension and more advanced age are more likely to present with myocardial injury during COVID-19 hospitalization. Admission and peak troponin appear to be predictors for cardiovascular and non-cardiovascular events and outcomes in COVID-19 patients. Further research is needed on the potential usefulness of troponin for the management and treatment decisions in COVID-19 patients.

Disclosure statement

The authors report no conflicts of interest.

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Competing interests

None declared.

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Figures

Figure 1. Flowchart illustrating cohort selection.

Figure 2. Association (adjusted OR) of the different troponin-derived variables with Procedures and Clinical Events.

Tables

Table 1. Demographic characteristics of the study population.

Table 2. Laboratory test results on admission.

Table 3. Predictors of myocardial injury (positive troponin).

Table 4. Association of positive peak troponin with outcomes.

Supplementary material

S-Table 1. Admission troponin and outcomes.

S-Table 2. Tertiles of peak troponin and outcomes.

Table 1. Demographic characteristics of the study population.

	All (n=434)	Negative hsTrop ≤14ng/L (n=146)	hsTrop ≥15ng/L (n=288)	P
Demographics & Risk Factors				
Age	66 (56-80)	59 (51-64)	72 (58-81)	<0.001
Men	62.9% (273)	58.9% (86)	64.9% (187)	0.219
BMI	26.6 (23.7-31.1)	26.2 (22.9-30.1)	26.0 (22.7-30.7)	0.680
Ethnicity: Caucasian	42.9% (186)	34.2% (50)	47.2% (136)	0.002
Asian	37.1% (161)	48.6% (71)	31.3% (90)	
Afro-Caribbean	20.0% (87)	17.1% (25)	21.5% (62)	
Hypertension	48.6% (211)	31.5% (46)	57.3% (165)	<0.001
Type 2 DM	33.9% (147)	25.7% (37)	38.3% (110)	0.007
Dyslipidaemia	38.7% (168)	24.0% (35)	46.2% (133)	<0.001
Smokers	3.2% (14)	4.1% (6)	2.8% (8)	0.415
Ex-Smokers	20.3% (88)	17.1% (25)	21.9% (63)	
IHD	14.1% (61)	6.2% (9)	18.2% (52)	0.001
Moderate CKD	33.6% (146)	6.2% (9)	47.4% (137)	<0.001
Asthma	11.8% (51)	16.4% (24)	9.4% (27)	0.031
COPD	10.8% (47)	6.2% (9)	13.2% (38)	0.026
Chronic Medication				
ACE-I	21.4% (93)	11.0% (16)	26.7% (77)	<0.001
ARB	12.9% (56)	12.3% (18)	13.2% (38)	0.799
Statin	48.0% (208)	29.5% (43)	57.5% (165)	<0.001
Disease Presentation				
Symptom onset before admission (days)	7 (3-10)	7 (2-9)	4 (1-7)	0.003
Symptom at onset				
Cough	27.4% (119)	15.8% (23)	33.3% (96)	<0.001
Fever	17.1% (74)	19.9% (29)	15.6% (45)	
Both	36.4% (158)	52.7% (77)	28.1% (81)	
Other	19.1% (83)	11.6% (17)	22.9% (66)	

Abbreviations. hsTrop: high-sensitivity Troponin-T; BMI: body-mass index; DM: diabetes mellitus; IHD: ischemic heart disease; CKD – chronic kidney disease; COPD: chronic obstructive pulmonary disease; ACE-I: angiotensin-converting enzyme inhibitors; ARB: angiotensin receptor blockers.

Table 2. Laboratory test results on admission.

	All (n=434)	**Negative hsTrop ≤14ng/L (n=146)**	**hsTrop ≥15ng/L (n=288)**	**P**
Laboratory Data – Admission				
WBC (10^9/L)	7.4 (5.4-10.5)	6.3 (4.8-8.2)	8.4 (5.8-11.3)	<0.001
Lymphocytes (10^9/L)	0.9 (0.7-1.3)	0.9 (0.7-1.2)	0.9 (0.6-1.3)	0.404
Haemoglobin (g/l)	12.7 (11.2-13.9)	13.0 (12.2-14.4)	12.2 (10.7-13.8)	<0.001
Platelets (10^9/L)	217 (166-285)	214 (177-265)	217 (167-304)	0.785
CRP (mg/L)	97 (43-181)	102 (46-185)	111 (62-194)	0.834
Creatinine (umol/L)	91 (72-125)	77 (67-92)	102 (78-151)	<0.001
eGFR mL/min MDRD	72 (50-93)	87 (74-110)	65 (42-85)	<0.001
D-Dimers (mg/mL)	1.18 (0.55-2.49)	0.63 (0.38-1.32)	1.60 (0.85-3.62)	<0.001
NT-proBNP (pg/mL)	537 (176-2329)	153 (48-330)	1219 (346-3563)	<0.001
aPTT (seconds)	27.0 (24.0-29.0)	26.7 (24.9-28.5)	27.0 (24.0-30.7)	0.196
INR (ratio)	1.1 (1.0-1.2)	1.1 (1.0-1.1)	1.1 (1.1-1.2)	<0.001
Thrombin time (sec)	16 (15-18)	15 (14-16)	18 (15-20)	0.002

Abbreviations. WBC: white blood cell count; CRP: C-reactive protein; eGFR: estimated glomerular filtration rate; aPTT: activated partial thromboplastin time; INR: international normalised ratio.

Table 3. Predictors of Myocardial Injury (positive troponin).

	Univariate		Multivariate	
Variables	**OR 95%CI**	**P**	**OR 95%CI**	**P**
Age (per 10 years)	1.80 1.62-1.99	<0.001	1.68 1.49-1.88	<0.001
Men	1.29 0.86-1.94	0.220	-	-
BMI	1.00 0.99-1.01	0.538	-	-
Ethnicity:				
Asians vs. Caucasians	0.47 0.30-0.73	0.001	-	-
Afro-Caribbean vs. Caucasians	0.91 0.52-1.61	0.749	-	-
Hypertension	2.92 1.92-4.44	<0.001	1.81 1.10-2.99	0.020
Type2 DM	1.83 1.18-2.85	0.007	-	-
Dyslipidaemia	2.72 1.74-4.25	<0.001	-	-
Smokers	0.71 0.24-2.09	0.529	-	-
Ex-Smokers	1.34 0.80-2.24	0.271	-	-
IHD	3.38 1.62-7.08	0.001	-	-
Asthma	0.56 0.29-0.95	0.033	-	-
COPD	2.31 1.09-4.93	0.030	-	-
Moderate CKD (eGFR < 60ml/min)	13.81 6.77-28.18	<0.001	9.12 4.24-19.64	<0.001

Abbreviations. BMI: body-mass index; IHD: ischemic heart disease; DM: diabetes mellitus, COPD: chronic obstructive pulmonary disease; CKD: chronic kidney disease; eGFR: estimated glomerular filtration rate. Note: Method Forward LR, probability for stepwise 0.05.

Table 4. Association of Positive Peak Troponin with Outcomes.

	All (n=434)	Negative hsTrop ≤14ng/L (n=146)	hsTrop ≥15ng/L (n=288)	Adjusted OR 95%CI	P
Procedures					
Non-Invasive Ventilation	18.4% (80)	15.8% (23)	19.8% (57)	2.50 1.31-4.79	0.006
Mechanical Ventilation	22.8% (99)	13.0% (19)	27.8% (80)	6.82 3.40-13.68	<0.001
ECMO	0.9% (4)	0.7% (1)	1.0% (3)	1.86 0.06-62.05	0.728
Urgent RRT	8.3% (35)	3.4% (5)	10.8% (30)	4.14 1.34-12.78	0.013
Cardiac Pacing	0.5% (2)	0% (0)	0.7% (2)	N/A	N/A
PCI	0.2% (1)	0% (0)	0.3% (1)	N/A	N/A
Outcomes					
Pneumonia	80.2% (348)	82.2% (120)	79.2% (228)	1.28 0.68-2.42	0.445
Acute Kidney Injury	36.3% (154)	10.3% (15)	50.0% (139)	6.50 3.24-13.04	<0.001
Acute HF	7.6% (33)	2.1% (3)	10.4% (30)	2.39 0.62-9.23	0.205
Ischaemic Stroke	3.7% (16)	2.7% (4)	4.2% (12)	1.31 0.34-5.07	0.700
Venous Thromboembolic Disease	7.4% (32)	2.1% (3)	10.1% (29)	12.84 3.42-48.24	<0.001
AF episode	6.9% (30)	0.7% (1)	10.1% (29)	10.02 1.50-96.36	0.019
Ventricular Tachycardia	0.7% (3)	0% (0)	1.0% (3)	N/A	N/A
Death During Admission	33.1% (140)	16.4% (24)	41.9% (116)	2.48 1.38-4.64	<0.001

Abbreviations. PCI: percutaneous coronary intervention; HF: heart failure; hsTrop: high-sensitivity Troponin-T; ECMO: extracorporeal membrane oxygenation; AF: atrial fibrillation; RRT: renal replacement therapy. Note: Adjustment for clinical baseline differences: age, hypertension, diabetes, previous myocardial infarction/ischaemic heart disease, asthma, COPD and eGFR (Method: Enter).