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High Thrombus Burden in Patients with COVID-19 Presenting with ST-Elevation Myocardial Infarction

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Brief title: Increased thrombus burden in COVID-19 patients with ST-elevation myocardial infarction

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Abstract

Background Coronavirus disease 2019 (COVID-19) is thought to predispose patients to thrombotic disease. To date there are few reports of ST-elevation myocardial infarction (STEMI) caused by type 1 myocardial infarction in COVID-19 patients.

Objectives The aim of this study was to describe the demographic, angiographic, and procedural characteristics alongside clinical outcomes of consecutive cases of COVID-19 positive STEMI patients compared to COVID-19 negative patients.

Methods This was a single-centre, observational study of 115 consecutive patients admitted with confirmed STEMI treated with primary percutaneous coronary intervention at Barts Heart Centre between 01/03/2020 and 20/05/2020.

Results STEMI patients presenting with concurrent COVID-19 infection had higher levels of Troponin T, lower lymphocyte count, but elevated D-dimer and C-reactive protein. There was significantly higher rates of multi-vessel thrombosis, stent thrombosis, higher modified thrombus grade post first device with consequently higher use of GP IIb/IIIa inhibitors and thrombus aspiration. Myocardial blush grade and left ventricular function were significantly lower in COVID patients with STEMI. Higher doses of heparin to achieve therapeutic ACTs were also noted. Importantly, STEMI patients presenting with COVID-19 infection had a longer in-patient admission and higher rates of intensive care admission.

Conclusions In patients presenting with STEMI and concurrent COVID-19 infection there is a strong signal towards higher thrombus burden and poorer outcomes. This supports the need for establishing COVID status in all STEMI cases. Further work is required to understand the mechanism of increased thrombosis and the benefit of aggressive anti-thrombotic therapy in selected cases.

Condensed Abstract

This was a single-centre, observational study of 115 consecutive STEMI patients with and without COVID-19 infection treated with primary percutaneous coronary intervention. STEMI patients presenting with concurrent COVID-19 infection had significantly higher rates of multi-vessel thrombosis, stent thrombosis, higher modified thrombus grade post first device, increased use of GP IIb/IIIa inhibitors and thrombus aspiration, elevated D-dimers and lower myocardial blush grade and left ventricular function. Importantly, STEMI patients presenting with COVID-19 infection had a longer in-patient admission and higher rates of intensive care admission. This supports the need for establishing COVID status in all STEMI cases.

Keywords COVID-19, ST elevation myocardial infarction, primary percutaneous coronary intervention, thrombosis.

Abbreviations

COVID-19 – Coronavirus disease 2019
SARS-CoV-2 – severe acute respiratory syndrome coronavirus-2
STEMI – ST-elevation myocardial infarction
PCI – percutaneous coronary intervention
PPE – personal protective equipment

Introduction

Coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has been shown to result in coagulation abnormalities and predisposes patients to thrombotic disease, both in the venous and arterial circulations. (1) This is believed to be secondary to inflammation, platelet activation, endothelial dysfunction, and stasis. (2) Despite this exaggerated risk, reduced presentations with ST-elevation myocardial infarction (STEMI) and other thrombotic disorders such as cerebrovascular accident have been seen during the pandemic, mainly as a result of social isolation and behavioral changes. Furthermore, emergency cardiac catheterisation reveals a variety of findings in COVID-19 patients with ST-elevation, including classic type 1 myocardial infarction (obstructive coronary artery disease), angiographically normal epicardial coronary arteries, and/or left ventricular dysfunction due to myocarditis or stress-induced cardiomyopathy. (3–5) Some institutions and opinion leaders have suggested thrombolytic therapy as the preferred initial mode of reperfusion in order to protect health care providers, (6) although clinical bodies have advocated continuation of primary percutaneous coronary intervention (PCI) as the default strategy. (7,8) There are limited reports of treating COVID-19 positive patients presenting with type I MI leading to STEMI who receive primary PCI, highlighted by recent studies finding only 10 out of 18 patients with STEMI on electrocardiogram having obstructive disease. (4)

Understanding the natural history and treatment responses of COVID-19 patients presenting with STEMI is essential to inform patient management decisions and protect healthcare workers. As the largest coronary intervention centre in the UK, Barts Heart Centre is well placed to provide contemporary analysis of STEMI cases during the COVID-19 era. We describe the demographic, angiographic, and procedural characteristics as well as clinical

outcomes in consecutive cases of COVID-19 positive STEMI patients comparing outcomes to COVID-19 negative patients.

Methods

Study design and patient population

This was a single-centre, observational study of 115 consecutive patients admitted with confirmed STEMI at Barts Heart Centre between 01/03/2020 and 20/05/2020. This study was designed to assess the incidence of COVID-19 amongst patients admitted with STEMI and to compare their baseline characteristics, angiographic, procedural and clinical outcomes to STEMI patients who were COVID-negative. Patients were included if they were admitted to Barts Heart Centre via the London Ambulance Service either directly from home or via partner district hospitals with cardiac chest pain and STEMI (ST elevation in 2 or more contiguous leads ≥0.2 mV) on their ECG or patients admitted with an out of hospital cardiac arrest (OOHCA) and ECG meeting diagnostic criteria for STEMI after return of spontaneous circulation (ROSC). Angiographic confirmation of occlusive coronary disease was performed in all cases. Patients with OOHCA who did not achieve ROSC, and those with non-STEMI were excluded from the study.

Interventional procedures

Full personal protective equipment (PPE) was worn by all healthcare professionals involved in each of the procedures; this was hospital policy for all STEMI cases during the study period. The interventional strategy was at the discretion of the operator, including the use of direct stenting, pre/post-dilatation, aspiration thrombectomy and treatment of bystander non-infarct related artery stenoses. All patients received a loading dose of aspirin 300 mg and either clopidogrel 600 mg or ticagrelor 180 mg prior to the procedure. All patients then received 75 mg

aspirin per day plus either 75 mg clopidogrel per day or 90 mg ticagrelor twice-daily maintenance therapy. During primary PCI, unfractionated heparin was administered in a loading dose of 70-100 U/kg with the activated clotting time (ACT) maintained >250 sec. ACTs were recorded at 10-15 minute intervals after the initial dose of heparin. Glycoprotein (GP) IIb/IIIa inhibitors were used at the operator's discretion and according to local guidelines.

Investigations

All patients with STEMI had baseline serological samples prior to cardiac catheterization for full blood count, renal and liver function tests, C-reactive protein, D-dimer, fibrinogen, clotting, ferritin, lactate dehydrogenase (LDH), ferritin, creatine kinase (CK) and high sensitivity (hs)-Troponin T. Post-catheterization, all patients underwent routine nasal/pharyngeal swab for the SARS-CoV-2 virus using real time-polymerase chain reaction (RT-PCR) irrespective of symptoms.

Patients with COVID-19 had a confirmed diagnosis based on the identification of SARS-CoV-2 on nasal/pharyngeal swab or, preceding COVID-19 symptoms alongside diagnostic radiological chest imaging. All of these patients were managed as COVID positive as per centre policy.

Data collection

The following data-fields were collected as part of our centre's routine practice for the British Cardiovascular Intervention Society (BCIS) audit submissions including patient age, sex, ethnicity, height, weight, cardiovascular risk factors, time of symptom onset, and time of arrival at primary PCI hospital. In addition, the following procedure related data were collected prospectively: target vessel, number of diseased vessels,; use of diagnostic devices such as intravascular ultrasound (IVUS), optical coherence tomography (OCT) or pressure wire, use of

aspiration thrombectomy, post-dilatation and use of GP IIb/IIIa inhibitor. Data regarding intra-procedural anticoagulant use and ACTs were collected from patient records with data collectors blinded to patients' COVID-19 status.

Endpoints

The primary endpoint was all-cause in-hospital mortality. Secondary endpoints included thrombus burden, Thrombolysis in Myocardial Infarction (TIMI) flow, myocardial blush grade, length of hospitalisation and the need for intensive care unit admission. A panel of three interventional cardiologists, blinded to patient COVID-19 status, retrospectively reviewed cine-angiographic images of all patients and scored pre- and post-PCI TIMI flow in the infarct-related artery, thrombus burden pre- and post-PCI (modified thrombus grade for Grade 5 thrombus post initial balloon inflation) (9) and myocardial blush grade. (10)

All patient data were anonymised prior to analysis. The local ethics committee advised that formal ethical approval was not required.

Statistical Analysis

Descriptive statistical analyses were performed using SPSS Statistics version 25.0 (IBM, New York). A 2-sided p-value <0.05 defined statistical significance. Variables are expressed as counts (percentages), mean ± standard deviation (SD), and median [lower quartile-upper quartile] as appropriate. Chi-squared analysis or Fisher's-exact test was used to compare categorical data between groups. The independent samples Student t-test or ANOVA test was used to compare normally-distributed continuous data between groups and the Mann-Whitney U test was used to compare the distribution of skewed continuous data between groups. Correlation performed using Pearson's correlation analysis and Spearman's correlation analysis in the case of skewed variables.

Results

The study population consisted of 115 consecutive patients with confirmed STEMI who were admitted during a 12 week period. The median age was 62 years, 78% were male and 48.7% were from Black, Asian or Minority ethnic groups. Of the 115 patients, 39 (33.9%) were diagnosed with concurrent COVID-19 infection while 76 (66.1%) patients showed no clinical evidence of COVID-19 infection (non-COVID group).

Patient characteristics

There were no significant differences in age, sex, ethnic background or body mass index (BMI) between the two groups. Patients presenting with concurrent COVID-19 infection were more likely than non-COVID patients to be diabetic (46% vs 26%, p=0.038), hypertensive (72% vs 42%, p=0.003), hyperlipidaemic (62% vs 37%, p=0.038) and were more likely to have a history of previous PCI (23% vs 7%, p=0.016). Time from symptoms to reperfusion, ECG presentations, rates of cardiogenic shock and requirement for pre-hospital intubation were similar in both groups. However, there was a higher incidence of cardiac arrest in patients who were COVID positive compared to the non-COVID group (28% vs 9%, p=0.0013).

Patients with concurrent COVID-19 infection had higher levels of hs-Troponin (1221ng/L vs 369 ng/L, p=0.0028), D-dimer (1.86mg/L vs 0.52mg/L, p=0.0012) and C-reactive protein (12mg/L vs 50mg/L, p=0.01) but lower lymphocyte counts (1.3 10^9/L vs 1.7 10^9/L, p=0.0002) than non-COVID patients. Similar levels of LDH, fibrinogen and ferritin were seen in the two groups, although trends to higher levels in the COVID-19 group were seen in all three measurements (p=0.14, p=0.08, p= 0.09, respectively).

Procedural characteristics

All patients underwent a primary PCI procedure in both groups (**Table 2**). Median door to balloon times were within 60 minutes and similar for both groups. There was evidence of higher thrombogenicity in the COVID group with significantly higher rates of multi-vessel thrombosis (p=0.0003) and stent thrombosis (p=0.04). Despite similar levels of baseline TIMI 0/1 flow and thrombus grade 4/5, the modified thrombus grade post first device for cases with thrombus grade 5 was significantly higher in the COVID group (modified thrombus grade 4/5 in 75% vs 31%, p=0.0006). In keeping with this, there was significantly greater use of GP IIb/IIIa inhibitors (p<0.0001) and aspiration thrombectomy (p=0.0021) in patients with COVID-19. While TIMI 3 flow was achieved at similar high levels in both groups, myocardial blush grade was significantly lower in the COVID group (myocardial blush grade of 2-3 in 54% vs 93%, p<0.0001), median peak plasma hs-Troponin concentration was greater and left ventricular ejection fraction was significantly lower in the COVID group compared with the non-COVID group (42.5% vs 45%, p=0.019).

Levels of blood D-dimer correlated with modified thrombus grade (r=0.299, p=0.068), myocardial blush grade (r=0.501, p=0.0003) (**Figure 1**) and level of heparinisation required to maintain ACT>250s during primary PCI (r=0.488, p=0.0029) (**Figure 2**).

There were no significant differences between groups in the total dose of heparin administered (COVID 11,125U vs non-COVID 10,066U, p=0.15), and similar average ACTs were achieved during the procedures (p=0.261). While first measured ACTs correlated with administered baseline heparin dose in the whole cohort (r=0.401, p=0.0002), and in the non-COVID group (r=0.461, p=0.0004), this correlation was not seen in the COVID group (r=0.279, p=0.144) suggesting that more heparin was required in the COVID group to achieve similar ACTs. A trend to higher heparin dose per Kg (p=0.15) was observed in the COVID group,

however this was not statistically significant and no difference was seen when adjusting for procedural time (p=0.14).

In-hospital outcomes

The COVID group had significantly longer in-patient stays (p=0.0004) and were more likely to require intensive care (p=0.003) reflecting a greater level of morbidity in this STEMI cohort. However, despite numerically higher rates of in-hospital mortality among the COVID STEMI patients, this did not reach significance (17.9% vs 6.5%, p=0.10) (**Figure 3**).

Discussion

This observational study represents the first comparative data to describe the impact of COVID-19 infection on patients presenting with STEMI to a primary PCI center (**Central Illustration**). This analysis demonstrates a clear signal of increased thrombus burden in STEMI patients who are infected with COVID-19 compared with STEMI patients who are not infected. This is evidenced by a higher incidence of multiple thrombotic culprit lesions as well as stent thrombosis, higher thrombus grade, lower resultant myocardial blush grade and associated increased use of GP IIb/IIIa inhibition and thrombus aspiration. Consistent with this, COVID-19 infection was associated with greater myocardial damage with lower left ventricular systolic function and increased troponin levels, despite similar median ischaemia times in the two groups. Higher rates of pre-hospital cardiac arrest, intensive care admission, longer in-patient stays and a trend towards increased in-hospital mortality were also seen in this patient group.

STEMI patients who were COVID positive more often had diabetes, hypertension and blood abnormalities reflecting a systemic inflammatory response (lymphopaenia, elevated D-dimers and C-reactive protein levels) compared with COVID negative patients. These features are those previously reported to be associated with more aggressive infection and poorer

outcomes in COVID cohorts without STEMI. (12–15) Interestingly, levels of D-dimer were found to correlate with thrombus grade, myocardial blush grade and levels of heparin requirement during the primary PCI procedure, with a suggestion of higher heparin doses required to achieve therapeutic ACTs in this cohort. Taken together, these data support the role of early assessment of COVID status in all STEMI patients as it may have major implications in patient management.

COVID-19 infection is associated with a pro-thrombotic state. The occurrence of venous thrombo-embolic complications, both clinically apparent and subclinical, appears to be an important manifestation of the disease and one which is related to disease severity and outcome. (1,16–18) Increased thrombogenicity in acute ischaemic stroke has also been described. (19) Moreover, emerging data from large COVID-19 cohorts without STEMI (20) suggests that the use of anticoagulation confers mortality benefit in this patient group. However, to date there have been no reports of increased coronary artery thrombus burden rather, the number of patients presenting with STEMI has reduced with an increased incidence of non-obstructed coronary arteries in the published small case series of STEMI patients. (3,4) Here we describe features apparent on angiographic assessment such as multi-vessel thrombosis, stent thrombosis, and high thrombus burden that should raise the suspicion of COVID-19 infection. STEMI was the first manifestation of the disease in this cohort and our data suggests that presentation of STEMI might itself be considered a thrombotic complication of COVID-19 infection. Of note, the median duration of symptoms to reperfusion was four hours in both COVID positive and COVID negative patients. Therefore, delayed presentation in COVID positive patients could not account for the observed differences between groups.

Mechanisms that trigger presentation with STEMI and its associated higher arterial thrombus burden in COVID-19 patients are as yet unknown. Relative to venous thromboembolism, arterial thrombus formation is more likely to be due to platelet activation and endothelial dysfunction. Pre-COVID data regarding the influenza virus suggest that patients with acute respiratory infections are at significantly elevated risk for developing atherosclerotic plaque rupture leading to myocardial infarction as a result of the profound inflammatory response and haemodynamic changes. (21) SARS-CoV-2 infection causes a systemic inflammatory response which leads to endothelial and haemostatic activation, including activation of platelets and the coagulation cascade. (22) Patients in the coronary risk groups of diabetes and hypertension have shown increased incidence of COVID and subsequent case fatality. (12) In keeping with this, the data presented here shows significantly higher rates of diabetes, hyperlipidaemia and hypertension in the COVID group suggesting that these conditions may also confer an increased risk of STEMI in COVID infected patients. Mechanisms for this might include increased endothelial dysfunction or their effects on the immune system. (22–26)

While our data points towards a higher morbidity and mortality in the COVID group compared to the non-COVID group, the rate of in-hospital mortality was lower than that previously published in a smaller cohort of 18 COVID positive STEMI patients (4) (18% compared with 72% in-hospital mortality). This is likely to be related to the difference in the cohorts studied. While our study focused on patients presenting through the primary PCI pathway, with STEMI as their first presentation of COVID, all receiving PCI, the previous case series is a more heterogeneous cohort, of which only 6 individuals presented through this pathway and received emergent coronary assessment with the remaining patients developing ECG changes while admitted with advanced COVID-19 infection. Therefore it is likely that the

severity of COVID-19 infection may have been less in our study cohort in which 12.8% of patients were ventilated compared to 70% in other series.

The COVID era has presented numerous challenges for emergency intervention services, which have required restructuring in order to maintain healthcare delivery. (11) COVID status is invariably not known at the time of presentation. Most primary PCI units manage STEMI patients as if they are COVID positive due to the risk of peri-procedure cardiac arrest and the potential for aerosol generation. Changes have been required in the management of access to the unit, the designation of COVID cathether laboratories, the use of personal protective equipment, deep laboratory cleaning after cases, ward reorgansiation, and patient COVID testing protocols. Despite these challenges, primary PCI was delivered within existing guidelines (median door-to-balloon times 50 minutes).

The strength of this study is that it presents real-world consecutive data from all patients with STEMI admitted to a single centre during the COVID-19 outbreak in the UK, both with and without the infection. The compared COVID and non-COVID group faced the same healthcare restrictions and were managed according to the same, modified, COVID primary PCI pathway and protocol. Moreover, our centre had an early adoption of COVID testing for all STEMI patients. All STEMI patients received a nasal/pharyngeal swab as well as chest imaging and laboratory testing for markers of severe COVID-19 infection to assist in diagnosis in the event of a negative nasal/pharyngeal swab.

Study Limitations

Despite this being the largest series to date, it is a relatively small retrospective observational study in a single centre and therefore has all the limitations of this type of analysis including bias and the potential for confounding. Furthermore, as has been universally accepted,

the sensitivity of diagnostic testing for SARS-CoV-2 is modest at approximately 60-70% with nasal/pharyngeal swab. (27)

Conclusion

We present the largest comparative dataset of COVID vs non-COVID patients presenting with STEMI. Concurrent infection with COVID-19 presents new procedural challenges and is associated with poorer outcomes. The strong signal towards significantly higher thrombus burden is a novel finding that raises the question of more aggressive anti-thrombotic therapy in selected COVID STEMI cases and provides a rationale for establishing COVID status in all STEMI cases. Further work is required to unravel the underlying mechanism of coronary thrombosis in patients with COVID-19 infection.

Clinical perspectives

Competency in Patient Care and Procedural Skills: Patients presenting with STEMI who test positive for COVID-19 have a higher thrombus burden than those without COVID-19.

Translational Outlook: Further work is necessary to understand the mechanisms responsible for increased thrombus burden in patients with concurrent STEMI and COVID-19 infection and establish optimum antithrombotic management.

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Figure legends

Figure 1. Increased arterial thrombogenicity associated with D-dimer levels. a) Correlation between D-dimer and thrombus grade in all patients (p=0.068); b) Correlation between D-dimer and myocardial blush grade for all patients (p=0.0003).

Figure 2. Requirement for heparin during primary PCI. a) Correlation between D-dimer and total heparin dose units/kg/min required to maintain ACT>250 during primary PCI procedure for all patients (p=0.0029); b) Correlation between baseline heparin dose and first ACT measured after a 10-15 minute interval in all patients (p=0.0002); c) Correlation between baseline heparin dose and first ACT measured after a 10-15 minute interval in COVID group (p=0.144); d) Correlation between baseline heparin dose and first ACT measured after a 10-15 minute interval in non-COVID group (p=0.0004).

Figure 3. In-hospital outcomes for non-COVID and COVID groups. These include intensive care admission, in-hospital mortality and admission length.

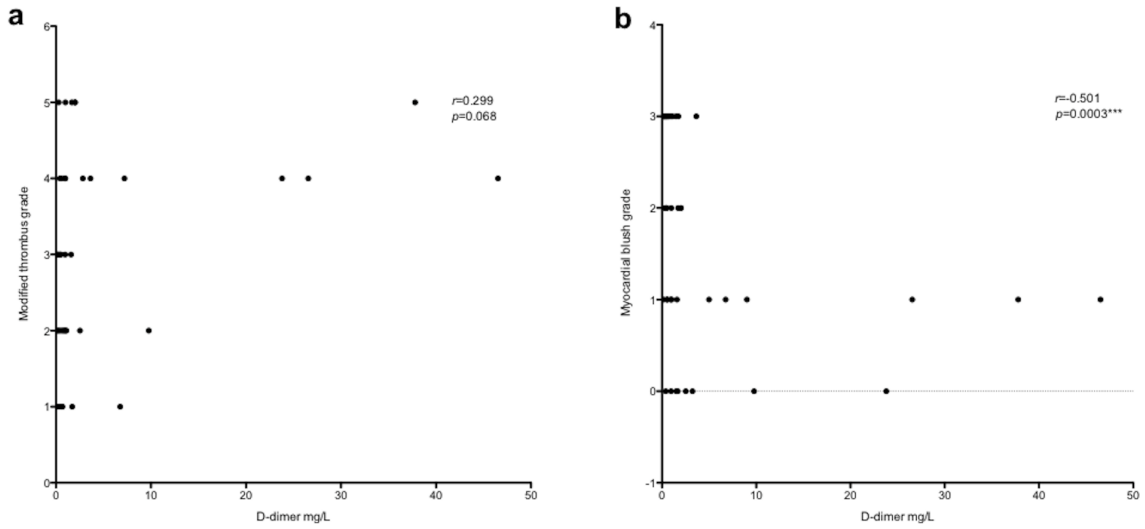
Central Illustration. Characteristics of STEMI in COVID-19 infection. STEMI in COVID-19 infection is associated with significantly higher rates of stent thrombosis (p=0.0445), multivessel thrombus (p=0.0003), modified thrombus grade 4-5 (p=0.0006), lower rates of myocardial blush grade 2-3 (p=0.0001) and raised D-dimer levels (p=0.012).

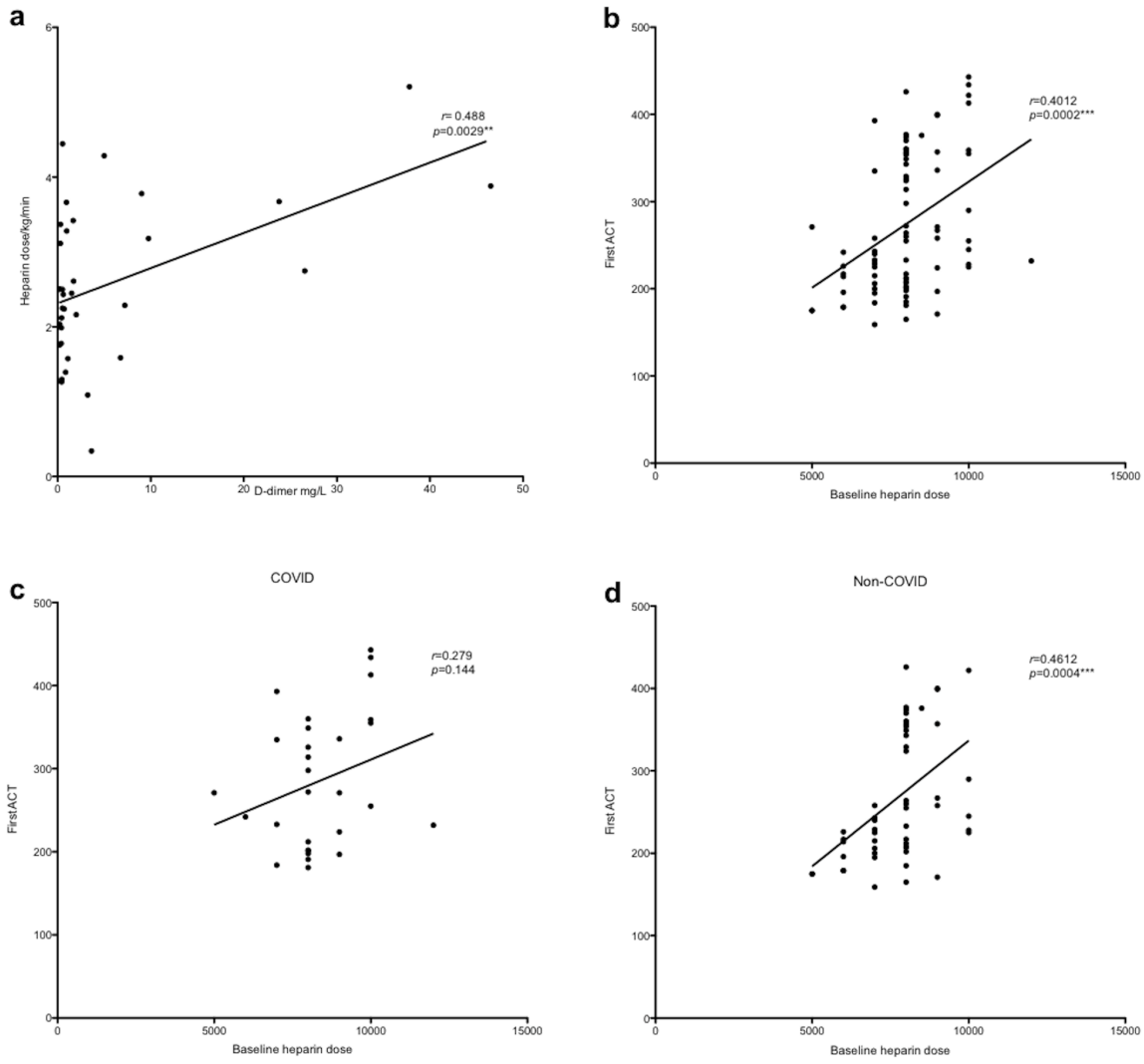
Table 1. Baseline patient characteristics

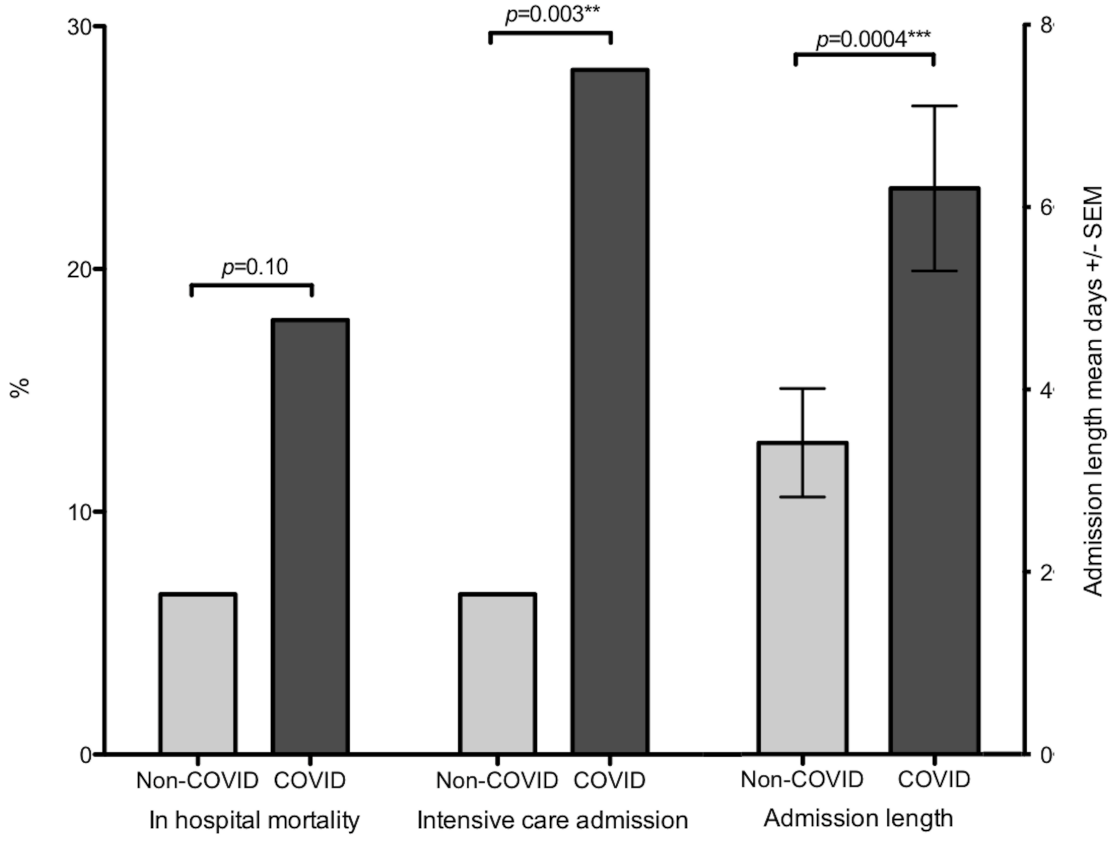
	Non-COVID n=76	COVID n=39	p-value
Age (Mean ± SD) – yr	61.7 (12.6)	61.7 (11.0)	0.633
Male sex – no. (%)	57 (75.0%)	33 (84.6%)	0.340
Black, Asian, Minority Ethnic – no. (%)	34 (44.7%)	22 (56.4%)	0.246
Median BMI (IQR)	26.87 (22.6-29.4)	26.7 (24.8-30.7)	0.363
Past Medical History – no. (%):			
Hypertension	32 (42.1%)	28 (71.8%)	0.003**
Hypercholesterolemia	28 (36.8%)	24 (61.6%)	0.017*
Diabetes mellitus	20 (26.3%)	18 (46.2%)	0.038*
Smoking history	35 (46.1%)	24 (61.6%)	0.167
Previous MI	3 (3.9%)	6 (15.4%)	0.060
Previous PCI	5 (6.6%)%	9 (23.1)%	0.016*
STEMI presentation:			
Median time chest pain to reperfusion (IQR) – Hr	4 (2-7)	4 (2-6)	0.845
ECG presentation – no. (%)			0.707
Anterior/LBBB	43 (56.7%)	24 (61.6%)	-
Inferior	27 (35.5%)	11 (28.2%)	-
Lateral	3 (3.9%)	3 (7.7%)	-
Posterior	3 (3.9%)	1 (2.6%)	
Cardiac arrest – no. (%)	7 (9.2%)	11 (28.2%)	0.0133*
Cardiogenic shock – no. (%)	8 (10.5%)	6 (15.4%)	0.549
Intubated – no. (%)	5 (6.6%)	5 (12.8%)	0.303
Median laboratory values (IQR):			
Troponin T – ng/L	369 (78.5-1109)	1221 (179-4143)	0.0028**
White-cell count – 10^9/L	12.2 (9.7-14.9)	12.9 (10.6-16.4)	0.596
Lymphocyte count– 10^9/L	1.7 (1.3-2.2)	1.3 (0.7-2.0)	0.0002***
LDH – unit/L	374.5 (268-707)	553 (340-935)	0.1489
D-Dimer – mg/L	0.52 (0.40-1.0)	1.86 (0.98-6.6)	0.0012**
Fibrinogen –g/L	3.88 (3.2-4.6)	4.26 (3.2-7.3)	0.0842
Ferritin – ug/L	194 (121-308)	323 (174-859)	0.0976
Creatinine – umol/L	81 (72-98)	80 (71-118)	0.827
Creatine kinase (CK) – u/L	641.5 (163.5-1376)	493 (165-1613)	0.822
C-reactive protein (CRP)– mg/L	12 (5-50)	50 (8-185)	0.010*

Table 2. Procedural characteristics

	Non-COVID n=76	COVID n=39	p-value
Coronary intervention – no. (%)	74 (97.3%)	38 (97.4%)	1.000
Median door-to-balloon time (IQR) - min	50 (34.8-57.5)	52 (39-70)	0.248
Median duration of case (IQR) - min	50 (39-70)	55 (44-90)	0.054
Culprit vessel – no. (%):			0.621
LMS	1 (1.4%)	2 (5.1%)	-
LAD	41 (55.4%)	22 (56.4%)	-
Cx	1 (1.4%)	4 (10.3%)	-
RCA	24 (32.4%)	10 (25.6%)	-
Multi-vessel thrombosis	0 (0%)	7 (17.9%)	0.0003***
Stent thrombosis – no. (%)	1 (1.2%)	4 (10.3%)	0.0445*
Baseline TIMI flow 0-1 – no. (%)	60 (80%)	32 (82.1%)	0.798
Baseline thrombus grade (4-5) – no. (%)	59 (77.3%)	33 (84.6%)%	0.440
Modified Thrombus grade post first device	n = 51	n = 28	0.005**
0	2 (3.9%)	0 (0%)	
1	9 (17.6%)	0 (0%)	
2	11 (21.6%)	1 (3.6%)	
3	13 (25.5%)	7 (25.0%)	
4	12 (23.5%)	12 (42.9%)	
5	4 (7.8%)	8 (28.6%)	
Modified thrombus grade (4-5) – no. (%)	16 (31.4%)	21 (75%)	0.0006***
GP IIb/IIIa inhibitor use – no. (%)	7 (9.2%)	23 (59.0%)	<0.0001***
Aspiration thrombectomy use – no. (%)	1 (1.3%)	7 (17.9%)	0.0021**
Total heparin dose (Mean ± SD) – units	10066 ± 3176	11125 ± 3875	0.151
Average ACT (Mean ± SD)	287.8 ± 66.9	270.6 ± 69.5	0.261
Total heparin dose per Wt (Mean ± SD) – units/kg	134.1 ± 35.9	146.2 ± 43.5	0.151
Total heparin dose per Kg per minute of case (Mean ± SD) – units/kg/min	2.6 ± 0.9	2.3 ± 0.8	0.144
Multi-vessel PCI	5 (6.8%)	8 (20.5%)	0.033*
Procedural success:			
Post PCI TIMI 3 flow – no. (%)	70 (93.3%)	35 (89.7)%	0.687
Myocardial blush grade (end) 2-3 – no. (%)	70 (93.3%)	21 (53.8%)	<0.0001***
Median LV ejection fraction (IQR) - %	45 (40-55)	42.5 (30-50)	0.019*




a
r= 0.488
p=0.0029**
Heparin dose/kg/min
D-dimer mg/L
b
r=0.4012
p=0.0002***
First ACT
Baseline heparin dose
c
COVID
r=0.279
p=0.144
FirstACT
Baseline heparin dose
d
Non-COVID
r=0.4612
p=0.0004***
First ACT
Baseline heparin dose


p=0.10
p=0.003**
p=0.0004***
%
Admission length mean days +/- SEM
30
20
10
0
8
6
4
2
0
Non-COVID
COVID
In hospital mortality
Non-COVID
COVID
Intensive care admission
Non-COVID
COVID
Admission length