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Review Article

Change in Coronary Thrombotic Burden in Patients with ST-Elevation Myocardial Infarction During The COVID-19 Pandemic: A Single-Center Retrospective Analysis

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Abstract

Background: Coronavirus disease 2019 (COVID-19) is thought to be prothrombotic, and this can affect atherothrombotic diseases. **Methods:** This is a single-center retrospective observational study conducted on patients with ST-segment-elevation myocardial infarctions. We enrolled 277 subjects, respectively, between 1 March and 31 December 2019 (cohort A, N° 85), 1 March and 31 December 2020 (cohort B, N° 76) and 1 March and 31 December 2021 (cohort C, N° 116). The coronary thrombotic burden was assessed using the thrombus grade score. **Results:** Patients in cohorts B and C present a higher coronary thrombosis burden than patients in cohort A. However, this does not correlate with worse clinical outcomes; in fact, there is neither an increase in hospitalization days nor a reduction in left-ventricle ejection fractions, and the in-hospital death rate is similar among the three patient cohorts. There are no significant differences in the incidence of non-coronary thrombotic events. The subgroup of vaccinated patients in cohort C present no significant differences in coronary thrombotic burden. **Conclusions:** In patients with ST-segment-elevation myocardial infarctions during the COVID-19 pandemic, an increase in coronary thrombotic burden is observed while the in-hospital death rate does not change significantly.

Keywords: STEMI; COVID-19 Pandemic; SARS-Cov-2; Thrombus Grade

Abbreviations: **COVID-19**: Coronavirus Disease 2019; **CXa**: Circumflex artery; **DAa:** Diagonal Artery; **ECG:** Electrocardiogram; **FMC-Hemo Time:** time elapsed between the First Medical Contact and the arrival in the hemodynamic room; **GP IIbIIIa-I:** Glycoprotein IIbIIIa Inhibitor; **Hs-cTnT:** High-sensitive cardiac Troponin T; **IRa:** Intermedius Ramus Artery; **LADa:** Left Anterior Descending artery; **LMSa:** Left Main-Stem artery; **OMa:** Obtuse Marginal artery; **PAI-1:** type-I Plasminogen-Activator Inhibitor; **PCI:** Percutaneous Coronary Intervention; **PTE:** Pulmonary Thromboembolism; **SARS-CoV-2:** Severe Acute Respiratory Syndrome Coronavirus 2; **RCA:** Right Coronary Artery; **RT-PCR:** Reverse Transcription Polymerase Chain Reaction; **SO-FMC Time:** time elapsed between the Symptom

Onset and the First Medical Contact; **STEMI:** acute coronary syndrome with ST-Elevation Myocardial Infarction; **TIMI:** Thrombolysis in Myocardial Infarction; **TB:** Thrombus Burden; **TF:** Tissue Factor; **TG:** Thrombus Grade; **UFH:** Unfractionated Heparin; **vWF:** von Willebrand Factor

Introduction

The coronavirus disease 2019 (COVID-19) pandemic, also known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is an infectious respiratory disease caused by the virus known as COVID-19 belonging to the coronavirus family. Although COVID-19 presents tropism for the epithelial cells of the respiratory tract that express the angiotensin-converting enzyme-2 (ACE-2) receptor, patients with COVID-19 infection may present symptoms of hyper-systemic inflammation that can sometimes cause an increase in clotting, and thus predispose them to thrombotic events in both venous and arterial circulation [1]. Moreover, thrombotic complications in SARS-CoV-2 infections are an important cause of morbidity and mortality [2,3].

This thrombogenicity is thought to be secondary to a process of systemic inflammation, platelet activation and endothelial dysfunction [4].

A wide variety of studies show the impaired haemostatic balance in SARS-CoV-2 infection, both in hypercoagulation and hypofibrinolytic states [5-8]. Unfortunately, the mechanisms underlying the haemostatic disorders associated with SARS-CoV-2 infection are not yet completely defined.

A severe inflammatory response to the virus, known as "thrombus inflammation" [2], was confirmed in other coronavirus infections, such as severe acute respiratory syndrome coronavirus 1 (Sars-Cov-1) and Middle-Eastern respiratory syndrome (MERS) [9].

The intense inflammatory response can also cause widespread endothelial damage. It is currently unknown whether the virus has a direct effect on platelet activity [10-11].

Endothelial damage causes the exposure to subendothelial collagen and tissue factor (TF), which, together with the von Willebrand factor (vWF), leads to the activation of the coagulation cascade and platelet adhesion pathways [12-13]. Furthermore, angiotensin II upregulates the expression of the type-I plasminogen-activator inhibitor (PAI-1) in endothelial cells [14], thus creating a prothrombotic condition.

SARS-CoV-2 vaccines used, at present, to prevent COVID-19 encode for the spike protein. However, thrombotic events with associated thrombocytopenia were reported in subjects receiving viral vector vaccines [15-18], probably caused by the cross-reaction of platelet-activating factor-4 antibodies [19].

Among the four SARS-CoV-2 vaccines approved in Italy at the time of enrollment of our patients, two were mRNA vaccines (Pfizer and Moderna) and two were viral vector vaccines (AstraZeneca and Johnson & Johnson).

STEMI remains an important cause of cardiovascular mortality and morbidity, and coronary thrombosis is the main pathophysiological mechanism. In addition, thrombotic burden, coronary artery type or number of vessels involved, distal embolization and no reflow affect the short- and long-term mortality rates of heart attack patients [20-22].

The literature data show that COVID-19 infection may increase the risk of ischemic cardiovascular events. Similar to other acute infections, the underlying mechanisms may include cytokine-mediated plaque destabilization and blood hypercoagulability [23-26].

However, it is difficult to establish the actual prevalence of COVID-19 infection in the general population, as often the disease may be completely asymptomatic.

This study aims to identify whether, during the COVID-19 pandemic, there was an increase in the coronary thrombotic load in patients with STEMI, and then specifically assess whether there was a change in the coronary thrombus burden (TB) in patients with STEMI in the period during 2020–2021 compared to the pre-pandemic period (2019). This evaluation is constructed by analyzing the coronarography images acquired during the revascularization procedure, performed in urgency/emergency, in patients with STEMI treated with primary angioplasty at the Hemodynamics Laboratory of the Grosseto Hospital.

The materials and drugs used during the revascularization procedure, medical records and discharge letters were consulted. For the period during 2020–2021, the presence of any previous SARS-CoV-2 infection and/or vaccination for SARS-CoV-2 that occurred prior to the STEMI event was evaluated.

Materials and Methods

This was a single-center retrospective observational study. A total of 277 subjects were included for the analysis, observed, respectively, between 1 March and 31 December 2019 (cohort A, N 85), between 1 March and 31 December 2020 (cohort B, N 76), and between 1 March and 31 December 2021 (cohort C, N 116).

The inclusion criteria were the presence of ST-elevation myocardial infarction (STEMI) with epicardial coronary thrombotic obstruction treated with primary percutaneous coronary intervention. As for the patients enrolled in 2020–2021, the presence of a negative SARS-CoV-2 test at the time of hospital

admission for STEMI was considered.

The exclusion criteria were the absence of epicardial coronary thrombotic obstruction, a history of pro-thrombotic diseases and the presence of a positive SARS-CoV-2 test at the time of hospital admission for STEMI. The age and sex of patients; height and weight; prevalence of cardiovascular risk factors, including hypertension (PA >140/80 or chronic antihypertensive therapy patients); dyslipidemia (higher than normal cholesterol/triglyceride values or patient in hypolipidemic therapy); diabetes mellitus (Hb glycate higher than 6.5%, fasting blood sugar higher than 128 mg/dl or patient in hypoglycemic therapy); obesity evaluated as body mass index (BMI) >25 Kg/h2 and previous or current exposure to smoking were recorded.

Among the data related to the procedure, we analyzed the culprit vessel, the total number of diseased vessels, the use of thrombectomy systems (such as manual thrombus aspiration) and the use of the glycoprotein IIb-IIIa inhibitor (GP IIb/IIIa-I). The interventional coronary artery strategy was an operator's choice, including the use of stents, pre- and post-dilatation and manual thrombectomy. Upon the initial medical contact, all patients were treated with a loading dose of intravenous aspirin and a UFH bolus of 80 IU/kg; only immediately before the revascularization procedure was a second antiplatelet agent, among the P2Y12 inhibitors, administered.

An ACT consistently longer than 250 seconds was achieved during primary percutaneous coronary intervention (PCI). ACT was recorded at 15-minute intervals after the initial dose of heparin. There were no significant differences between cohorts in the total dose of UFH administered. GP IIb/IIIa-I was used based on the operator's choice.

The primary endpoint of this study was to evaluate coronary thrombus burden (TB) through a retrospective analysis of the coronary imaging of patients with STEMI and an angiographic demonstration of epicardial coronary thrombotic obstruction. The angiographic aspect of the coronary obstruction, the pre- and post-PCI TIMI flow in the artery related to the heart attack and the thrombotic load through the thrombus grade (TG) score were analyzed. TG is a radiological assessment classified (G) as G0 = no thrombus, G1 = possible thrombus, G2 = small (maximum size 1/2 vessel diameter (VD)), G3 = moderate (> 1/2 but < 2VD), G4 = large (> 2VD) and G5 = impossible to evaluate thrombosis due to total vessel occlusion. Patients with G5 may be reclassified to another TG category after passing a small guide wire or balloon [27]. TG score was evaluated by three different operators and subsequently each patient was assigned a TG value corresponding to the mean of the three measurements.

Where possible, myocardial blush (MB) analysis was performed. The MB grade was defined as follows: 0, no myocardial blush or contrast density; 1, minimal myocardial blush or contrast density; 2, moderate myocardial blush or contrast density, but less than that obtained during angiography of a contralateral or ipsilateral non-infarct-related coronary artery; and 3, normal myocardial blush or contrast density [28]. However, MB was evaluated in a limited sample of patients, because it was not always feasible to obtain images that allowed this type of analysis to be performed.

The secondary endpoint was to assess whether coronary TB changed particularly in patients who underwent SARS-CoV-2 vaccinations prior to the STEMI event. In addition, the prevalence of non-coronary cardiovascular events, such as ischemic stroke or pulmonary thromboembolism, recorded concurrently with the STEMI event or in the previous period, was assessed in the three cohorts of patients. For each group, any previous COVID-19 infection and any vaccination for SARS-CoV-2 with the relative timing was then recorded.

A further analysis was performed on the timing of the presentation and assistance of patients during STEMI; in particular, in the three patient cohorts, we evaluated the time that elapsed between the onset of symptoms (SO) and the first medical contact (FMC), and the time between the FMC and access to the hemodynamics room (Hemo). Furthermore, in cohort-C patients, SO-FMC and FMC-Hemo times were compared with TG values.

Statistical analysis

A value of 2-tails $p < 0.05$ defined statistical significance. The variables were expressed as counts (percentages), average DS and average as appropriate. The calculation of the standard error on a normal distribution was used for the comparison between averages. Chi-squared analysis was used to compare the categorical data between groups. Student's t-test was used to compare the continuous data normally distributed between groups. The correlation was performed using Pearson's correlation analysis and Spearman's correlation analysis in the case of asymmetric variables.

Institutional Review Board Statement

The study was approved by the Tuscan regional ethics committee (SPACE, ID: 22673; 20/07/2022).

Results

We observed no significant differences in age, gender or body mass index between the cohorts of patients. The same prevalence of cardiovascular risk factors was also observed in the three cohorts. Blood levels of hemoglobin, platelets, creatinine and lipid values were also observed to be overlapping between the different cohorts of patients. The prevalence of dysthyroidism was the same in the three cohorts.

High-sensitive cardiac troponin T (Hs-cTnT) levels were higher in cohorts B and C compared to cohort A, but without statistical significance see in (Table 1).

Variables	**Cohort A (N° 85)**	**Cohort B (N°76)**	**Cohort C (N°116)**	**Cohorts B and C (N° 192)**	***p*-value**
Age	**68,0 ± 4,0**	67,2 ± 6,1	65,2 ± 3,1	**66,2 ± 4,3**	**ns**
Male	**57 (60,1%)**	47 (61,8%)	83 (71,6%)	**130 (67,7 %)**	**ns**
Hypertension	**44 (51,7 %)**	39 (51,3 %)	63 (54,3 %)	**102 (53,1 %)**	**ns**
Diabetes mellitus	**16 (18,8 %)**	18 (23,6 %)	22 (18,9 %)	**40 (20,8 %)**	**ns**
Dyslipidemia	**42 (49,4 %)**	40 (52,6 %)	62 (53,4 %)	**102 (53,1 %)**	**ns**
Smoking	**38 (44,7 %)**	34 (44,7 %)	56 (48,2 %)	**90 (46,8 %)**	**ns**
Dysthyroidism	**9 (10,5 %)**	8 (10,5 %)	12 (10,3 %)	**20 (10,4 %)**	**ns**
BMI	**26,0 ± 0,6**	26,3 ± 0,8	26,8 ± 0,4	**26,6 ± 0,5**	**ns**
History of ischemic stroke	**4 (4,6%)**	3 (3,9 %)	4 (3,4%)	**7 (3,6 %)**	**ns**
History of PTE	**0 (0.0%)**	1 (1,3 %)	2 (1,7%)	**3 (1,5 %)**	**p = 0,1**
Blood Tests	**Cohort A (N° 85)**	**Cohort B (N°76)**	**Cohort C (N°116)**	**Cohorts B and C (N° 192)**	**p-value**
Hemoglobin(g/dl)	**13,0 ± 0,1**	13,1 ± 0,1	12,8 ± 0,1	**12,9 ± 0,1**	**ns**
Platelet (migl/mmc)	**242,9 ± 143,9**	247,9 ± 82,6	228,2 ± 78,1	**240,9 ± 80,3**	**ns**
TOTAL cholesterol (mg/dl)	**180,4 ± 36,3**	174,7 ± 33,6	179,4 ± 28,4	**179,1 ± 31,0**	**ns**
HDL cholesterol (mg/dl)	**43,1 ± 2,8**	44,9 ± 3,5	41,7 ± 1,1	**46,8 ± 2,4**	**ns**
LDL cholesterol (mg/dl)	**116,7 ± 28,8**	117,9 ± 33,4	116,6 ± 20,3	**115,1 ± 25,8**	**ns**
Triglycerides (mg/dl)	**130,1 ± 77,4**	133,7 ± 86,7	137,4 ± 90,0	**132,5 ± 89,5**	**ns**
Creatinine (mg/dl) ± DS	**1,1 ± 0,7**	1,1 ± 0,4	1,0 ± 0,2	**1,0 ± 0,3**	**ns**

Hs-cTnT (ng/l) (interquartile range)	**3543 (2150-4023)**	3827 (1425-4192)	4168 (1282-5530)	**3999 (1307-5219**	**p = 0,4**
Culprit Vessel	**Cohort A (N° 85)**	**Cohort B (N°76)**	**Cohort C (N°116)**	**Cohorts B and C (N° 192)**	***p*-value**
LADa	**44 (51,7 %)**	35 (46,1 %)	52 (44,8%)	**87 (45,3 %)**	**ns**
CXa	**9 (10,6 %)**	11 (14,5 %)	10 (8,6 %)	**21 (10,9 %)**	**ns**
RCA	**20 (23,3 %)**	23 (30,3 %)	36 (31,0 %)	**59 (30,7 %)**	**ns**
IRa	**2 (2,3 %)**	2 (2,6 %)	4 (3,4 %)	**6 (3,1 %)**	**ns**
OMa	**3 (3,5 %)**	1 (1,3 %)	5 (4,3 %)	**6 (3,1 %)**	**ns**
D1a	**3 (3,5 %)**	2 (2,6%)	8 (6,9 %)	**10 (5,2 %)**	**ns**

Table 1: Baseline characteristics of patients.

Primary endpoint: B- and C-cohort patients had a coronary thrombotic burden, evaluated with the TG score, significantly higher than cohort-A patients see in (Figure 1). However, rates of stent thrombosis and the use of thrombectomy systems did not vary significantly between the three cohorts of patients.

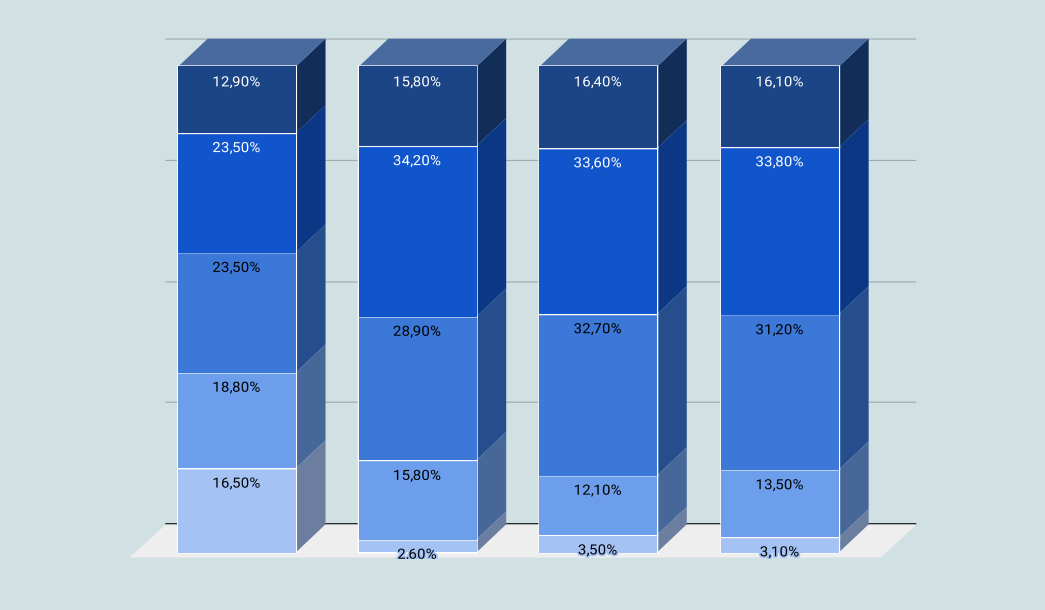

Figure 1: Modified thrombus grade in the three patient cohorts and the comparison between cohorts before and after the COVID-19 pandemic.

In addition, cohort-B and -C patients had basal values of TIMI flow-grades 0-1 and TG 4 or 5 significantly greater than the cohort-A patients. TIMI flow-grade 3 in the culprit vessel, at the end of the procedure, was obtained from almost all patients undergoing a revascularization procedure and overlapped in the three cohorts of patients.

There were significantly higher rates of multivessel involvement in B- and C-cohort patients than in cohort A. Cardiogenic shock rates were similar in the three cohorts of patients. Additionally, there were no significant differences in left ventricular systolic dysfunction and days in intensive care. The most involved vessel in STEMI was the left anterior descending (LAD) artery in all patient cohorts see in (Table 2).

Baseline and procedural characteristics of patients	**Cohort A (N° 85)**	**Cohort B (N°76)**	**Cohort C (N°116)**	**Cohorts B and C (N° 192)**	**Compared Cohort A to Cohorts B and C (*p*-value)**
Baseline TIMI flow-grade-scores 0 or 1	**53 (62,4 %)**	63 (82,9 %)	84 (72,4 %)	**147 (76,6%)**	**p = 0,01**
Baseline thrombus grade scores 4 or 5	**31 (36,4 %)**	38 (50 %)	58 (50,0 %)	**96 (50 %)**	**p <0,05**
Modified thrombus grade post first device (average)	**2,85 ± 0,31**	3,41 ± 0,24	3,45 ± 0,20	**3,43 ± 0,15**	**p = 0,001**
Stent thrombosis	**2 (2,4 %)**	6 (7,9 %)	7 (6,0 %)	**13 (6,8 %)**	**p = 0,1**
Multi-vessel lesions (> or = 2)	**20 (23,5 %)**	32 (42,1 %)	40 (34,5 %)	**72 (37,5 %)**	**p <0,05**
Aspiration thrombectomy use	**7 (8,2 %)**	10 (13,2%)	15 (12,9%)	**25 (13,0 %)**	**p = 0,1**
GPIIb-IIIa inhibitors	**5 (5,9 %)**	4 (5,3 %)	6 (5,2 %)	**10 (5,2 %)**	**ns**
Cardiogenic shock	**15 (17,6 %)**	12 (15,8 %)	18 (15,5 %)	**30 (15,6 %)**	**ns**
In-hospital deaths	**4 (4,7%)**	3 (3,9%)	6 (5,2%)	**9 (4,7%)**	**ns**
LVEF >50% LVEF <35%	**39 (46,0 %)** **11 (12,9%)**	31 (40,0 %) 10 (13,1 %)	41 (35,3%) 13 (11,2%)	**72 (37,5%)** **23 (11,9%)**	**p = 0,1** **p = 0,1**
Average N° of days of hospitalization	**8,5 ± 0,5**	8,4 ± 0,9	8,2 ± 1,3	**8,3 ± 1,1**	**ns**
Post PCI TIMI flow-grade 3	**82 (96,4 %)**	74 (97,4 %)	112 (96,6 %)	**186 (96,8 %)**	**ns**

Table 2: Procedural characteristics of patients and results.

MB analysis was performed on a limited sample of patients because adequate angiographic images for this analysis were not always available. Therefore, the final MB score 2-3 (expressed as a percentage) was significantly lower in cohorts B and C than in cohort A (p-value <0.01) (Figure 2).

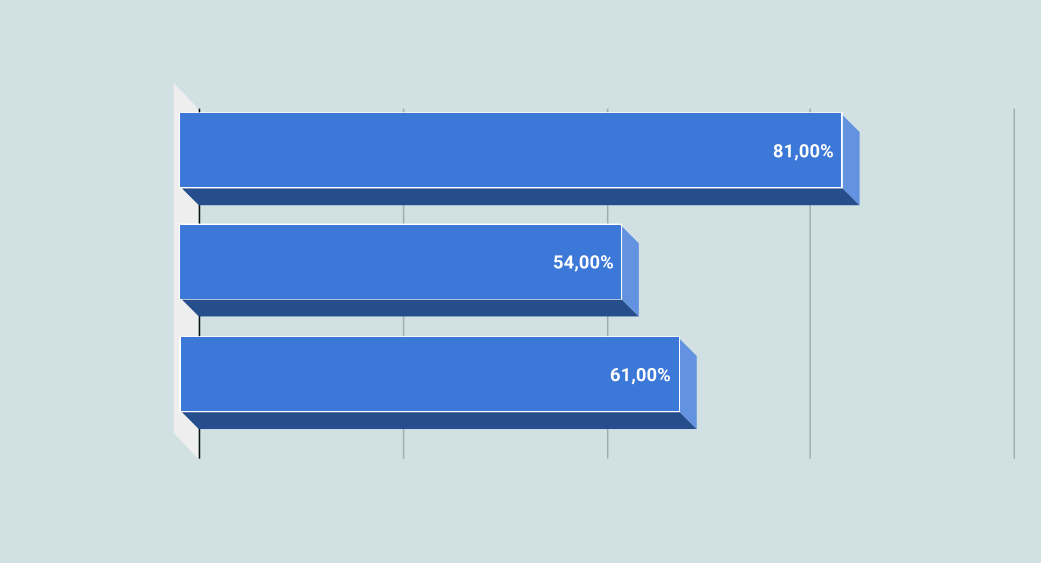

Figure 2: Analysis of myocardial blush (MB), evaluated at the end of the procedure, in samples obtained from the three patient cohorts.

Secondary endpoint: In cohort C, 90 patients were vaccinated for SARS-CoV-2 with at least 1 dose of the vaccine, of which 82 patients received a second dose and 60 patients received a third dose; 76 patients received at least 1 dose of vaccine before the STEMI event, while 22 were patients never vaccinated for SARS-CoV-2 see in (Table 3).

Cohort C (N° 116)	Pfizer	Moderna	AstraZeneca	Johnson	Vaccinated Patients
I° dose	70	7	8	5	90
II° dose	64	9	7	2	82
III° dose	38	22	0	0	60

Table 3: Prevalence of SARS-CoV-2 vaccinations in cohort C.

There were no statistically significant differences in coronary TB evaluated with the TG score between vaccinated and unvaccinated patients for SARS-CoV-2.

Furthermore, there was no significant difference in the baseline TIMI flow between vaccinated and unvaccinated patients see in (Table 4).

Cohort C (N° 116)	Unvaccinated patients (26)	Patients vaccinated with 1 dose (83)	Patients vaccinated with 2 doses (79)	Patients vaccinated with 3 doses (56)	All patients vaccinated before the acute event (N 76)	*p*-value
Thrombus grade score	**3,33 ± 0,06**	3,55 ± 0,02	3,55 ± 0,03	3,56 ±0,03	**3,46 ± 0,03**	**ns**
Average TIMI flow	**0,92 ± 0,1**				**0,96 ± 0,0**	**ns**

Table 4: Modification of TB in unvaccinated versus vaccinated patients.

In cohort C, among those vaccinated with the first dose (77.5% of patients), 86% received a viral mRNA vaccine while 14% received a viral vector vaccine. In the 2-dose vaccines (70% of patients), 90% received a viral mRNA vaccine while only 10% received a viral vector vaccine. In the 3-dose vaccines (51% of patients), no subjects received a viral vector vaccine (Table 3).

Again, in our comparison analysis of the different types of vaccines administered (mRNA versus viral vector vaccines), there were no significant differences in thrombus burden (TB), or in subjects vaccinated with one dose (p-value = 0,62), or in subjects vaccinated with two doses (p-value = 0,74).

The symptom onset and first medical contact (SO-FMC) time was longer in cohorts B and C than in cohort A (p-value = 0,01). On the other hand, the first medical contact–hemodynamic room (FMC-Hemo) time was not statistically different see in (Figure 3).

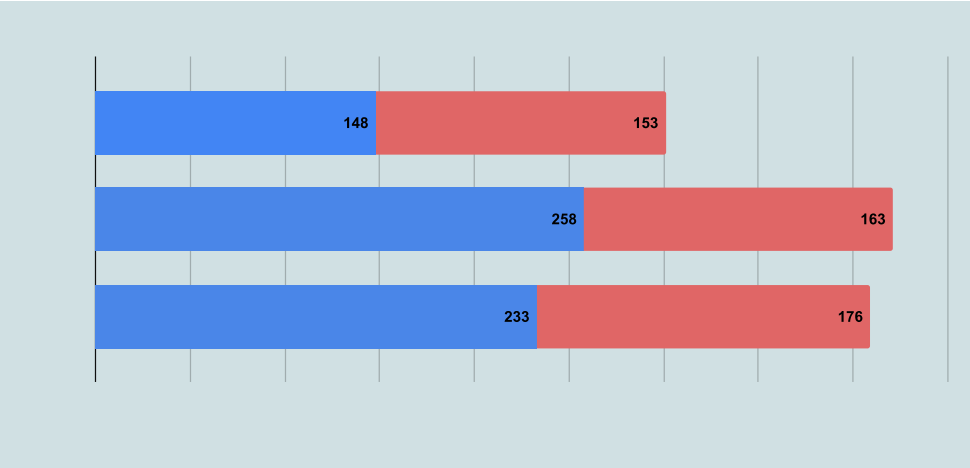

Figure 3: Analysis of the time between the symptom onset (SO) and first medical contact (FMC) and the time between the FMC and patients in the hemodynamics room (Hemo).

Again, by analyzing the SO-FMC time and comparing it with TB using a correlation analysis, we observed that there were no significant differences between patients with low TB (TG 1-3) compared to patients with higher TB (TG 4-5) (p-value> 0,1) see in (Figure 4).

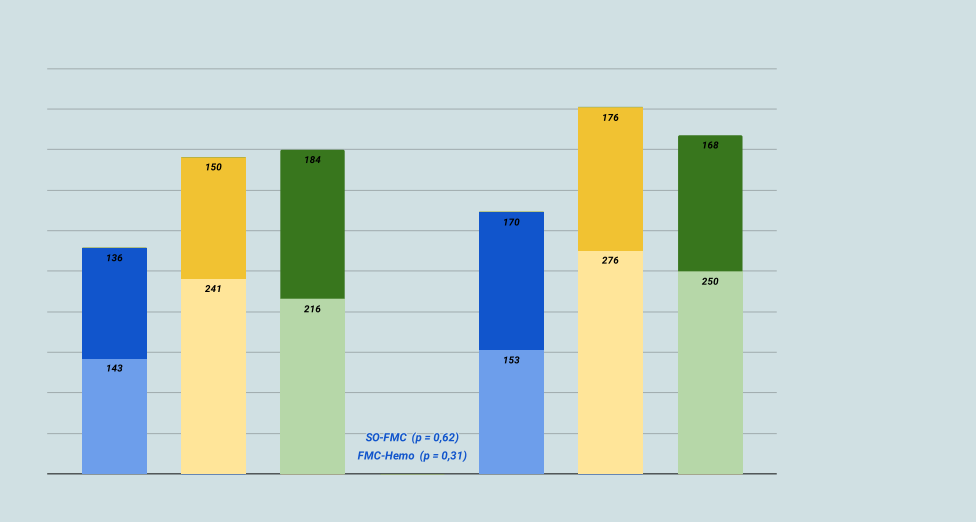

Figure 4: Modified thrombus grade related to the time (minutes) between symptom onset (SO) and first medical contact (FMC) and the time between FMC and patients in the hemodynamics room (Hemo).

Regarding the prevalence of non-coronary thrombotic events, such as cerebral ischemic stroke, there were no significant differences between the three patient cohorts. We recorded more pulmonary thromboembolism (PTE) cases in cohorts B and C in comparison to cohort A, but without statistical significance.

Discussion

This observational study described the impact that COVID-19 infection can have on patients with ST-elevation myocardial infarction (STEMI) in a primary percutaneous coronary intervention (PCI) center. This analysis demonstrated a clear signal of increased coronary thrombotic load in STEMI patients in the COVID-19 era compared to the pre-pandemic period. This was evidenced by a higher thrombus burden (TB), a higher incidence of multiple thrombotic lesions and a lower TIMI flow baseline grade. In cohorts of patients with STEMI during the COVID-19 pandemic, myocardial blush (MB) analysis demonstrated the presence of a lower MB 2-3 grade (assessed at the end of the procedure). This was also associated with an increased use of intracoronary thrombectomy systems. Previous studies demonstrated that the pre-procedural TIMI flow is associated with worse outcomes [29].

Nevertheless, STEMI in the COVID-19 era would not seem to be associated with major myocardial damage; in fact, the left ventricular systolic function in patients from cohorts B and C was not lower than that of patients in cohort A, and there was no increase in the number of days in intensive care or in the duration of hospitalization. Even the incidence of cardiogenic shock in cohorts B and C was not significantly higher than in cohort A.

Although rare episodes of prothrombotic immune thrombocytopenia were reported following SARS-CoV-2 vaccinations [30], in our comparison analysis between vaccinated and unvaccinated patients, there were no significant differences in TB and TIMI flow at baseline. However, even among vaccinated patients there were no significant differences in TB in relation to the different types of vaccines.

In the time of care for patients with STEMI, there was a significant increase in the SO-FMC time in cohorts B and C compared to cohort A; this was, however, in line with the data obtained from the literature [31] and could be explained by the longer delay of acute coronary syndrome (ACS) patients to alert emergency services or to go to hospital during the COVID-19 pandemic. This could therefore be a relevant cofactor in causing an increase in TB; however, the analysis obtained by comparing the symptoms onset–first medical contact (SO-FMC) time with the thrombus grade (TG) did not present a statistically significant correlation; therefore, the increased TB during the COVID-19 pandemic cannot be explained solely by the longer coronary occlusion time.

It is known that COVID-19 infection can be associated with a prothrombotic state that can affect both the arterial and venous districts; in fact, an increase in the thrombogenicity of COVID-19 infection has been described in the literature both in pulmonary thromboembolism (PTE) [1] and acute ischemic stroke [32]. However, in our three patient cohorts, we observed no significant differences in the incidence of PTE or ischemic stroke that preceded or was concomitant with STEMI.

The pro-thrombotic mechanisms that result in increased arterial TB associated with STEMI in patients with COVID-19 are still unknown. Compared to venous thromboembolism, arterial thrombus formation is more likely to be due to platelet activation and/or endothelial dysfunction.

Some data on other viruses, such as influenza, suggest that an acute respiratory infection could lead to an inflammatory state and/or changes in the hemodynamic layer affecting the coronary plaque causing it to rupture and leading to a myocardial infarction [33].

Often, COVID-19 infection can be completely asymptomatic. The SARS-CoV-2 virus, causing a systemic inflammatory response leading to endothelial and hemostatic activation, including platelet activation and a coagulation cascade, could be one of the reasons that would explain, at least in part, the increase in coronary TB in patients with STEMI following the advent of COVID-19 [34].

Therefore, in the future, when the mechanisms that increased thrombogenicity during SARS-CoV-2 disease become clearer, there may be a more specific therapeutic approach to better manage this disease.

Conclusions

In patients presenting with STEMI in the COVID-19 era, there was a strong signal towards increased coronary thrombotic loads; further research is therefore needed to understand the mechanism leading to increased thrombotic burden in patients with SARS-CoV-2 infection. However, this was not correlated with worse clinical outcomes. It is necessary to establish a COVID-19 status in all cases of STEMI, and it remains important to choose the benefit of the aggression of antithrombotic therapy in selected cases.

References

1. Levi M, Thachil J, Iba T, Levy JH (2020) Coagulation abnormalities and thrombosis in patients with COVID-19. Lancet Haematol 7: e438-e440.
2. Seitz R, Gürtler L, Schramm W (2021) Thromboinflammation in COVID-19: can α2-macroglobulin help to control the fire? J Thromb Haemost 19: 351-354.

3. Lippi G, Sanchis-Gomar F, Favaloro EJ, Lavie CJ, Henry BM (2021) Coronavirus disease 2019–associated coagulopathy. Mayo Clin Proc 96: 203-217.

4. Bikdeli B, Madhavan MV, Jimenez D, Chuich T, Dreyfus I, et al. (2020) COVID-19 and thrombotic or thromboembolic disease: implications for prevention, antith- trombotic therapy, and follow-up. J Am Coll Cardiol 75: 2950-2973.

5. Nougier C, Benoit R, Simon M, Desmurs-Clavel H, Marcotte G, et al. (2020) Hypofibrinolytic state and high thrombin generation may play a major role in SARS-COV2 associated thrombosis. J Thromb Haemost 18: 2215-2219.

6. Bachler M, Bösch J, Stürzel DP, Hell T, Giebl A, et al. (2021) Impaired fibrinolysis in critically ill COVID-19 patients. Br J Anaesth 126: 590-598.

7. Zanza C, Racca F, Longhitano Y, Piccioni A, Franceschi F, et al. (2021) Risk management and treatment of coagulation disorders related to COVID-19 infection. Int J Environ Res Public Health 18:1268.

8. Mitrovic M, Sabljic N, Cvetkovic Z, Pantic N, Dakic AZ, et al. (2021) Rotational thromboelastometry (ROTEM) profiling of COVID-19 patients. Platelets 32: 690-696.

9. Benvenuto D, Giovanetti M, Ciccozzi A, Spoto S, Angeletti S, et al. (2020) The 2019-new coronavirus epidemic: evidence for virus evolution. J Med Virol 92: 455-459.

10. Connors JM, Levy JH (2020) COVID-19 and its implications for thrombosis and anticoagulation. Blood 135: 2033-2040.

11. Greinacher A, Selleng K, Mayerle J, Palankar R, Wesche J, et al. (2021) Anti-platelet factor 4 antibodies causing VITT do not cross-react with SARS-CoV-2 spike protein. Blood 138: 1269-1277.

12. Levi M, Van der Poll T, Ten Cate H (2006) Tissue factor in infection and severe inflammation. Semin Thromb Hemost 32: 33-39.

13. Sebag SC, Bastarache JA, Ware LB (2011) Therapeutic modulation of coagulation and fibrinolysis in acute lung injury and the acute respiratory distress syndrome. Curr Pharm Biotechnol 12: 1481-1496.

14. Nakamura S, Nakamura I, Ma L, Vaughan DE, Fogo AB, et al. (2000) Plasminogen activator inhibitor-1 expression is regulated by the angiotensin type 1 receptor in vivo. Kidney Int 58: 251-259.

15. Tiede A, Sachs UJ, Czwalinna A, Wirwitzke S, Bikker R, et al. (2021) Prothrombotic immune thrombocytopenia after COVID-19 vaccination. Blood 138: 350-353.

16. Greinacher A, Thiele T. Warkentin TE, Weisser K, Kyrle PA, et al. (2021) Thrombotic Thrombocytopenia after ChAdOx1 nCov-19 Vaccination. N Engl J Med 384: 2092-2101.

17. Schultz NH, Sørvoll IH, Michelsen AE, Munthe LA, Lund-Johansen F, et al. (2021) Thrombosis and Thrombocytopenia after ChAdOx1 nCoV-19 Vaccination. N Engl J Med 384: 2124-2130.

18. Scully M, Singh D, Lown R, Poles A, Solomon T, et al. (2021) Pathologic Antibodies to Platelet Factor 4 after ChAdOx1 nCoV-19 Vaccination. N Engl J Med 384: 2202-2211.

19. Datta P, Zhang F, Dordick JS, Linhardt RJ (2021) Platelet factor 4 polyanion immune complexes: Heparin induced thrombocytopenia and vaccine-induced immune thrombotic thrombocytopenia. Thromb J 19: 66.

20. Iwakura K, Ito H, Kawano S, Shintani Y, Yamamoto K, et al. (2001) Predictive factors for development of the no-reflow phenomenon in patients with reperfused anterior wall acute myocardial infarction. J Am Coll Cardiol 38: 472-477.

21. Sianos G, Papafaklis MI, Daemen J, Vaina S, Van Mieghem CA, et al. (2007) Angiographic stent thrombosis after routine use of drug-eluting stents in ST-segment elevation myocardial infarction: the importance of thrombus burden. J Am Coll Cardiol 50: 573-583.

22. Fukuda D, Tanaka A, Shimada K, Nishida Y, Kawarabayashi T, et al. (2003) Predicting angiographic distal embolization following percutaneous coronary intervention in patients with acute myocardial infarction. Am J Cardiol 91: 403-407.

23. Oxley TJ, Mocco J, Majidi S, Kellner CP, Shoirah H, et al. (2020) Large-vessel stroke as a presenting feature of Covid-19 in the young. N Engl J Med 382: e60.

24. Bangalore S, Sharma A, Slotwiner A, Yatskar L, Harari R, et al. (2020) ST-segment elevation in patients with Covid-19: a case series. N Engl J Med 382: 2478-2480.

25. Merkler AE, Parikh NS, Mir S, Gupta A, Kamel H, et al. (2020) Risk of ischemic stroke in patients with coronavirus disease 2019 (COVID-19) vs patients with influenza. JAMA Neurol 77: 1-7.

26. Bilaloglu S, Aphinyanaphongs Y, Jones S, Iturrate E, Hochman J, et al. (2020) Thrombosis in hospitalized patients with COVID-19 in a New York City health system. JAMA 324: 799-801.

27. Sianos G, Papafaklis MI, Serruys PW (2010) Angiographic thrombus burden classification in patients with ST-segment elevation myocardial infarction treated with percutaneous coronary intervention. J Invasive Cardiol 22: 6B-14B.

28. Van't Hof AWJ, Liem A, Suryapranata H, Hoorntje JC, De Moer MJ, et al. (1998) Angiographic assessment of myocardial reperfusion in patients treated with primary angioplasty for acute myocardial infarction: Myocardial blush grade. Circulation 97: 2302-2306.

29. Schaaf MJ, Mewton N, Rioufol G, Angoulvant D, Cayla G, et al. (2016) Pre-PCI angiographic TIMI flow in the culprit coronary artery influences infarct size and microvascular obstruction in STEMI patients. J Cardiol 67: 248-253.

30. Tiede A, Sachs UJ, Czwalinna A, Werwitzke S, Bikker R, et al. (2021) Prothrombotic immune thrombocytopenia after COVID-19 vaccination. Blood 138: 350-353.

31. Aldujeli A, Hemadeh A, Briedis K, Tecson KM, Rutland J, et al. (2020) Delays in Presentation in Patients With Acute Myocardial Infarction During the COVID-19 Pandemic. Cardiol Res 11: 386-391.

32. Beyrouti R, Adams ME, Benjamin L, Cohen H, Farmer SF, et al. (2020) Characteristics of ischaemic stroke associated with COVID-19. J Neurol Neurosurg Psychiatry 91: 889-891.

33. Kwong JC, Schwartz KL, Campitelli MA, Chung H, Crowcroft NS, et al. (2018) Acute myocardial infarction after laboratory confirmed influenza infection. N Engl J Med 378: 345-353.

34. Masi P, Hekimian G, Lejeune M, Chommeloux J, Desnos C, et al. (2020) Systemic inflammatory response syndrome is a major contributor to COVID-19-associated coagulopathy: insights from a prospective single center cohort study. Circulation 142: 611-614.