Research Article

Impact of Revascularization Strategy on the Infarct Size During Coronavirus Disease-2019 Pandemic

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Abstract

There are no published studies that evaluate the different ST elevation myocardial infarction (STEMI) treatment strategies employed during the coronavirus disease (COVID-19) pandemic. Our aim is to determine the extent of infarct size between 1): Patients treated with thrombolysis and 2): Patients treated with primary percutaneous coronary intervention (PCI) after confirming negative for the Gene Xpert polymerase chain reaction (PCR) test for COVID-19 (pPCI after PCR). The latter implies a delay of approximately 60 minutes in an emergency department before transfer to a catheterization laboratory.

METHODS: *This is a single-center retrospective study including patients who underwent revascularization for acute STEMI during the COVID-19 pandemic (between January 1, 2020 and June 15, 2020) at Mohammed bin Khalifa Cardiac Centre in the Kingdom of Bahrain. Endpoints of interest were the following parameters that reflect the extent of myocardial damage and can be used to estimate the infarct size nearly as measured by cardiac magnetic resonance: neutrophil to lymphocytes ratio, Creatine phosphokinase, Creatine kinase–myocardial band, Troponin-I, Ejection fraction, Wall motion score index, and Determine score, which is the sum total of leads with [Q waves×2]+[fragmented QRS]+[T wave inversion].*

RESULTS: Out of 80 patients presented with acute STEMI during the study period, 91.25% were males. The Thrombolysis group reported significantly higher occurrence of inferolateral myocardial infarctions (7.5% vs. 2.5%, p = 0.027) and diabetes mellitus (67.5% vs. 42.5%, p = 0.042) compared to the pPCI after PCR group. Based on time from the onset of chest pain to presentation to emergency department, we observed a trend of treating patients presented within 3 hours with thrombolysis (mean time 3.2±2.2) and those with more than 3 hours chest pain duration with pPCI after PCR (mean time 5.2±4.4), but this difference was statistically not significant. Furthermore, the Thrombolysis group recorded significantly lower creatinine levels [70.3(±15) vs. 88.6(±31.5), p = 0.001] and higher HbA1C level, as well, [7.6(±2.5) vs. 6.9(±2.2), p = 0.040] compared to pPCI after PCR**.** Comparing the two groups, none of the outcome parameters that we pre-selected to define the extent of myocardial infarction were statistically significant.

CONCLUSION: *pPCI after PCR for acute STEMI in the context of the COVID-19 pandemic remains superior to thrombolysis because the size of infarct was not adversely affected by the extra time taken to secure the staff and workplace prior to coronary intervention.*

KEYWORDS: *Coronavirus disease-2019, ST elevation myocardial infarction, primary percutaneous coronary intervention, thrombolysis, GeneXpert test, polymerase chain reaction.*

ABBREVIATIONS AND ACRONYMS

CK-MB: Creatine kinase – myocardial band

COVID-19: Corona virus disease 2019

CPK: Creatine phosphokinase

EF: Ejection fraction

MKCC: Mohammed bin Khalia Cardiac Centre

NLR: Neutrophil to lymphocytes ratio

PCR: polymerase chain reaction

pPCI after PCR: Primary percutaneous coronary intervention after negative geneXpert PCR test for COVID-19

STEMI: ST elevation myocardial infarction

WMSI: Wall motion score index

Introduction

Coronary artery disease is an important cause of death around the world and acute ST-elevation myocardial infarction (STEMI) is its dangerous presentation with high morbidity and mortality **(1).**

Several studies have shown that primary percutaneous coronary intervention (pPCI) performed by experienced operators reduces STEMI related complications, mainly mortality, reinfarction and stroke **(2).** Furthermore, for hospitals without onsite PCI services, transport of STEMI patients to a PCI center is superior to thrombolysis under specific circumstances **(3).**

pPCI is preferred if the medical contact-to-balloon time is less than 90 min and the delta time (i.e. medical contact-to-balloon time minus medical contact-to-thrombolysis time) is less than 60 min, or if there are other reasons (e.g. contraindications to thrombolysis, symptom onset of more than 3 hours or high-risk STEMI as in cardiogenic shock). Thrombolysis is preferred for STEMI patients with less than 3 hours of chest pain, if the medical contact-to-balloon time is more than 90 min or the delta time is more than 60 min **(2,3).**

Currently, no published studies are evaluating different STEMI treatment strategies during COVID-19 pandemic. Many Chinese hospitals recommended thrombolysis in STEMI patients of unknown COVID-19 status or pPCI only after the patient had a negative GeneXpert PCR test. Our cardiac Centre and many institutions worldwide adopted this guideline during the COVID-19 crisis **(4).** The GeneXpert test is molecular testing which allows pPCI but with a delay of almost 90 minutes from presentation to the emergency department **(4).**

We could not compare hard endpoints like mortality due to under-power (small sample size) so we decided to compare the extent of infarction based on certain parameters in blood sample, ECG and echocardiogram that reflect infarct size, which is the strongest determinant of post-myocardial infarction chronic left ventricular systolic function and of long-term adverse volumetric changes that occur in response to a depressed ejection fraction (EF). Early determination of infarct size following Acute STEMI is therefore key to assessing the future risk of patients and instructive for optimization of therapeutic strategies.

Methods

This is a single-center retrospective study including patients who underwent revascularization for acute STEMI during the COVID-19 pandemic (between January 1, 2020, and June 15, 2020) at Mohammed bin Khalifa Cardiac Centre (MKCC) in the kingdom of Bahrain.

All patients were treated based on the on-call interventional cardiologist's discretion either with thrombolysis at emergency department (ER) or pPCI after confirmation of negative GeneXpert PCR test for COVID-19 (pPCI after PCR).

GeneXpress test is a real-time polymerase chain reaction (RT-PCR) test that utilized for the qualitative detection of nucleic acid from the SARS-CoV-2 in the nasopharyngeal swab, nasal swab, or nasal wash/aspirate specimen which implies a delay of pPCI for about 60 minutes to obtain the sample, send it to COVID-Lab, processing time and transfer of the patient from ER to CathLab once COVID-19 ruled out.

Endpoints of interest were the following parameters that reflect the extent of myocardial infarction: neutrophil to lymphocytes ratio (NLR), Creatine phosphokinase (CPK), Creatine kinase – myocardial band (CK-MB), Troponin-I, Ejection fraction (EF), Wall motion score index (WMSI)

and Determine score which is the total of leads with [Q waves×2]+[fragmented QRS]+[T wave inversion]).

The data were analyzed using IBM SPSS 25 where the categorical variables (dichotomous and ordinal) were summarized calculating the categories' frequencies and percentages. Continuous variables were summarized by calculating the mean and the standard deviation (Mean (±SD)). The significance of the difference between any categories was examined by the Chi-square test or the Fisher's exact test (An extension of Chi-square test for 2x2 tables) armed with Mote Carlo simulation of 10000 samples to obtain a more precise estimate of the p-value.

For exploring the relationship between an independent categorical and a dependent continuous variable (e.g.: revascularization strategy and serum NLR level), a Monte Carlo simulated Mann-Whitney test was used considering the test assumptions and the sample size. The significance of any relationship or a difference was established using Alpha 0.05 as a cut-off point.

Results

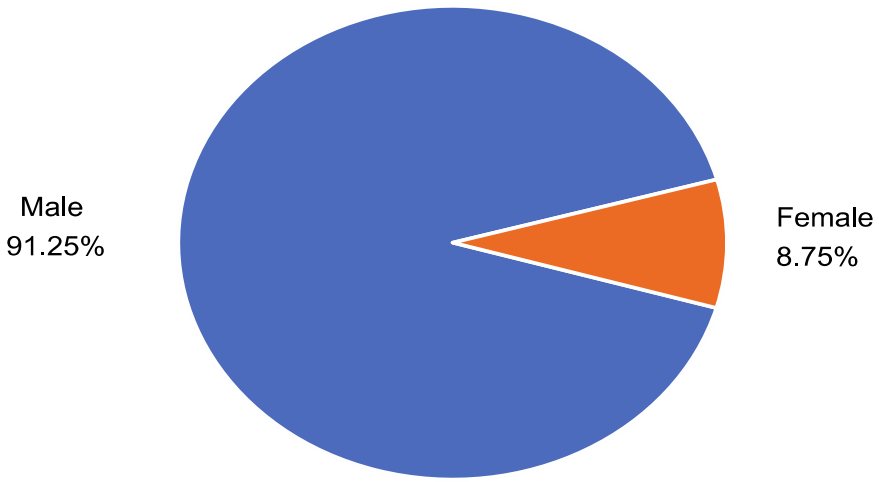

Figure 1. Gender distribution among acute STEMI patients treated during COVID-19 pandemic.

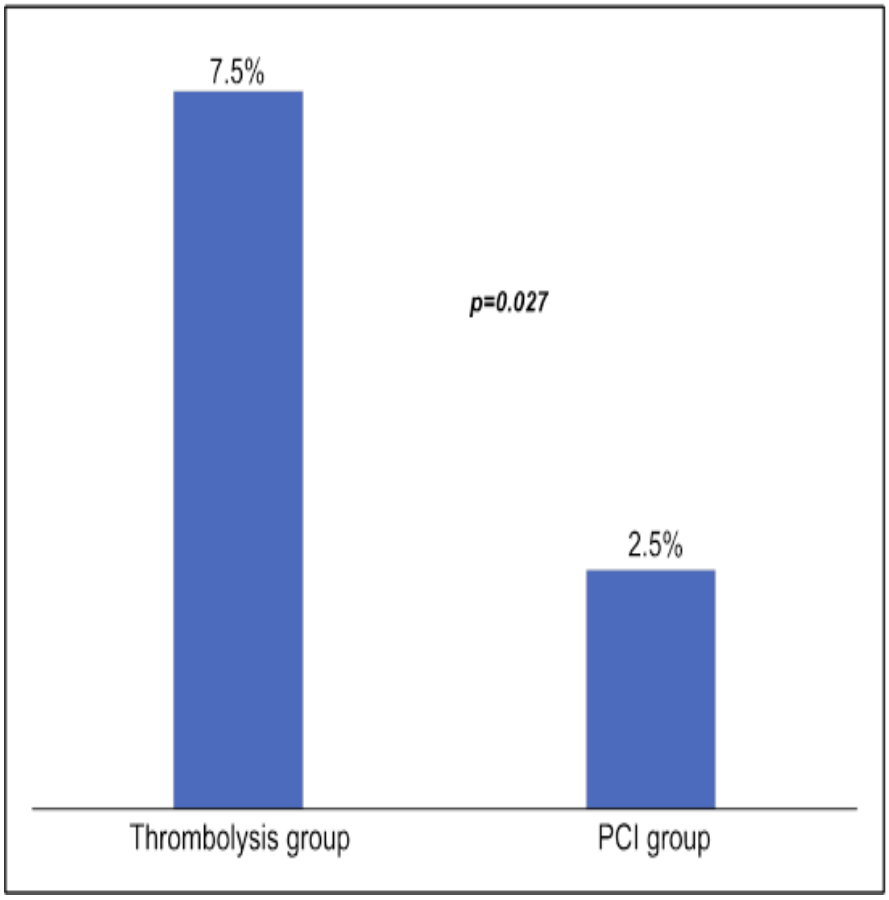

Figure 2. Prevalence of acute inferolateal STEMI in the two groups (pPCI after PCR vs. Thrombolysis)

Our study showed that out of 80 patients presented with acute STEMI during the study period of the COVID-19 pandemic; 91.25% were males (**Figure 1)**. The two groups did not differ significantly in terms of the baseline characteristics except that the Thrombolysis group reported a significantly higher occurrence of inferolateral myocardial infarctions compared to the pPCI after PCR group (7.5% vs. 2.5%, p=0.027) (**Figure 2)**.

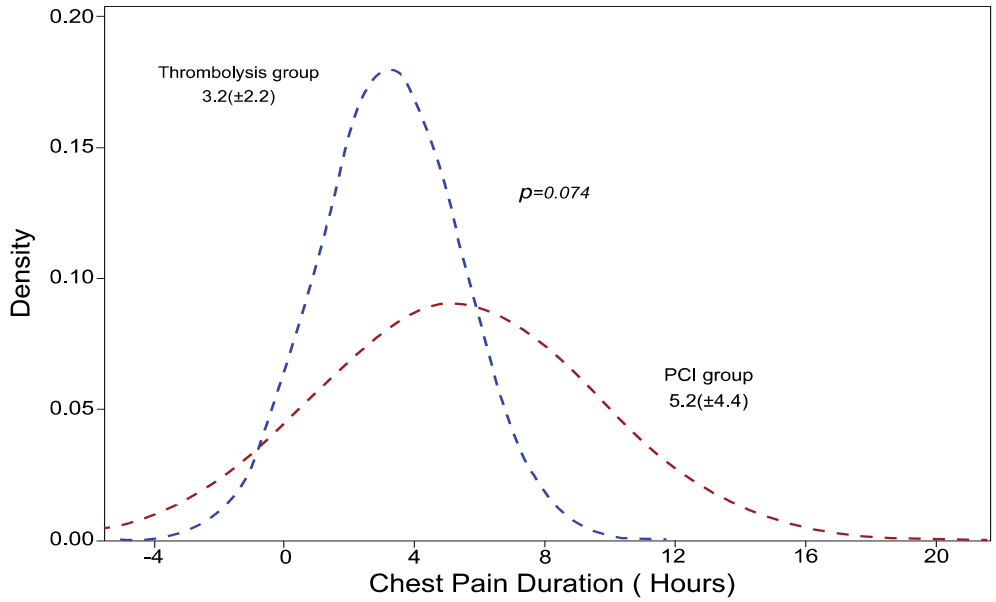

Figure 3. Duration from the onset of chest pain till presentation to the emergency department in the two groups (pPCI after PCR vs. Thrombolysis)

Besides, the prevalence of Diabetes mellitus among the thrombolysis group was significantly higher than those treated with pPCI after PCR (67.5% vs. 42.5%, p=0.042). Time from onset of chest pain to presentation to ER showed a trend of treating patients presented within 3 hours with thrombolysis (mean time 3.2 ±2.2) and those with more than 3 hours chest pain duration with pPCI after PCR (mean time 5.2 ±4.4), but this difference was statistically not significant (**Figure 3)**.

The two groups did not differ significantly across most of their laboratory findings except for their levels of Creatinine and HbA1C. Thrombolysis group recorded significantly lower Creatinine level on average when compared to their pPCI after PCR counterparts 70.3(±15) vs. 88.6(±31.5), p=0.001) and higher HbA1C level on average as well (7.6(±2.5) vs. 6.9(±2.2),

p=0.040). However, despite their statistical significance, these differences remain very small. The full analysis of the baseline characteristics of the study population is depicted in **Table 1.**

Variable		Thrombolysis	Primary PCI	P-value
Demographics				
Age (Years), mean (±SD)		53.2(±10.4)	56.8(±11.3)	0.148
Male gender, n. (%)		38(95%)	35(87.5%)	0.469
Clinical diagnosis				
Chest pain duration (Hours), mean (±SD)		3.2(±2.2)	5.2(±4.4)	0.074
Site of ST elevation Myocardial Infarction (STEMI)	Anterior, n. (%)	13(32.5%)	15(37.5%)	0.787
	Anterolateral, n. (%)	11(27.5%)	6(15%)	0.985
	Inferior, n. (%)	8(20%)	11(27.5%)	0.868
	Inferoposterior, n. (%)	3(7.5%)	6(15%)	0.454
	Inferolateral , n. (%)	3(7.5%)	1(2.5%)	*0.027*
	Inferopoterolateral, n. (%)	1(2.5%)	0	-
	Lateral, n. (%)	1(2.5%)	1(2.5%)	0.999
	True posterior, n. (%)	0	0	-
	Isolated right ventricular, n. (%)	0	0	-
Clinical variables				
Diabetes Mellitus, n. (%)		27(67.5%)	17(42.5%)	*0.042*
Hypertension, n. (%)		21(52.5%)	19(47.5%)	0.823
Hyperlipidemia, n. (%)		25(62.5%)	19(47.5%)	0.261
Smoking, n. (%)		15(37.5%)	23(57.5%)	0.117
Coronary artery diseases, n. (%)		4(10%)	6(15%)	0.737
Cerebrovascular accident, n. (%		0	2(5%)	0.494
Peripheral vascular diseases, n. (%)		0	0	-
Chronic obstructive airway disease, n. (%)		0	0	-
Dialysis, n. (%)		1(2.5%)	0	0.999
Laboratory investigations				
Hemoglobin g/dl, mean (±SD)		14.7(±1.5)	14.1(±1.8)	0.102
White blood cells x10^9/L, mean (±SD)		11.3(±3.2)	10.6(±4.2)	0.153
Platlets x10^9/L, mean (±SD)		248.7(±71.1)	261.2(±98.2)	0.526
Creatinine mmol/L, mean (±SD)		70.3(±15)	88.6(±31.5)	0.001
Low density lipoprotein (LDL) mmol/L, mean (±SD)		3.5(±0.9)	3.3(±1.1)	0.305
Hemoglobin A1c %, mean (±SD)		7.6(±2.5)	6.9(±2.2)	0.040

Table 1. Baseline characteristics of study population

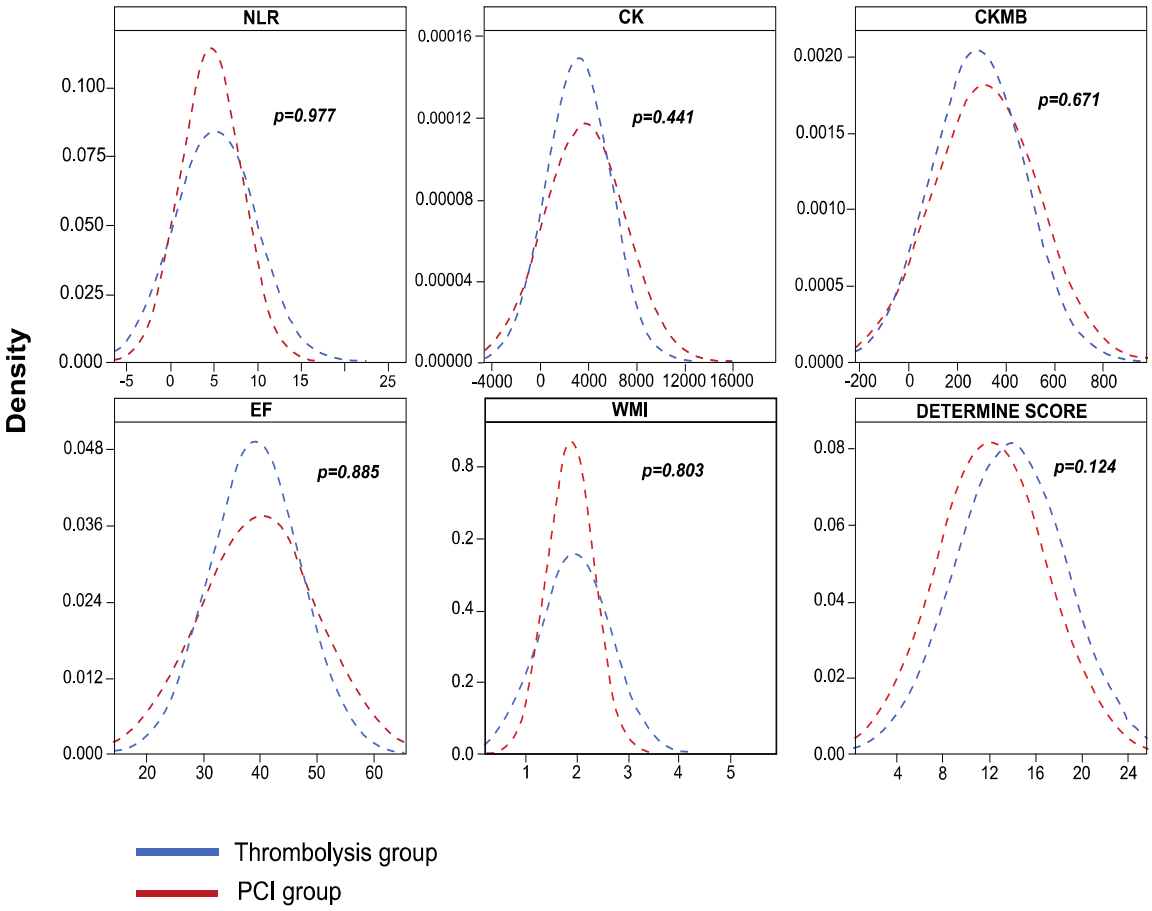

Figure 4. Comparison of parameters illustrating the extent of myocardial infarction between the two groups (pPCI after PCR vs. Thrombolysis)

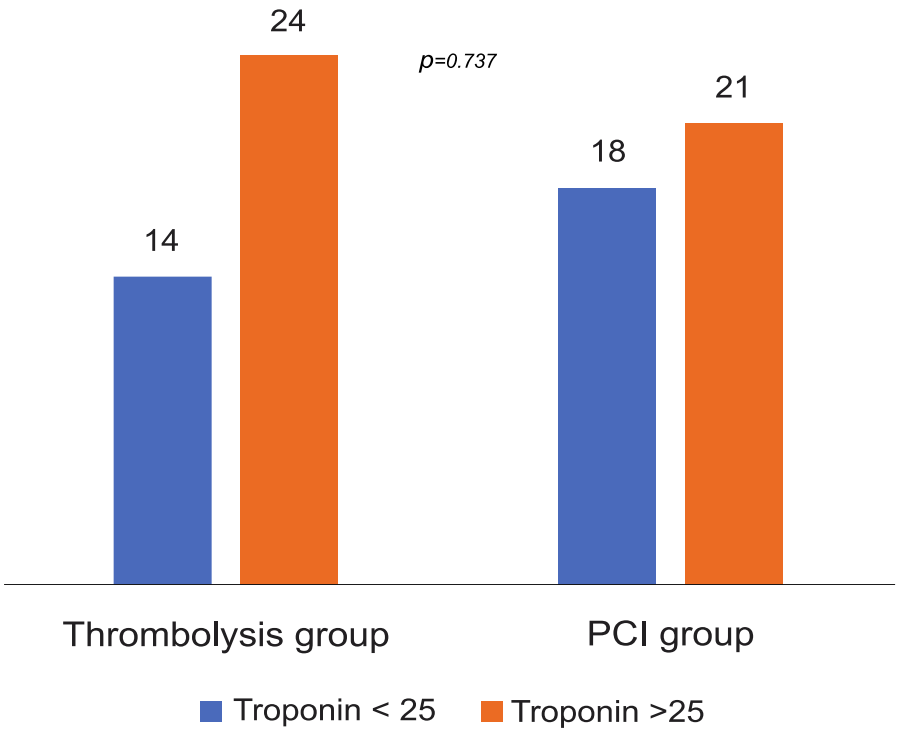

Figure 5. Comparison of Troponin-I level between the two groups (pPCI after PCR vs. Thrombolysis)

None of the outcome parameters that we pre-selected to define the extent of myocardial infarction was statistically significant comparing the two groups. All the observed differences were most likely ingenuine as confirmed with the Mote Carlo simulated Mann-Whitney test for (NLR, CK, CK-MB, EF, WMSI) and independent samples T-test for Determine score **(Figure 4)**. As for

Troponin levels, the simulated Chi-square test showed no significant difference between the two groups **(Figure 5).** Summary of differences in parameters reflecting the size of the infarct is depicted in **Table 2.**

Variables	Thrombolysis	Primary PCI	P-value
Neutrophil to lymphocyte ratio (NLR), mean (±SD)	8.4(±22.4)	4.7(±3.5)	0.980
Creatine phosphokinase (CPK) u/L, mean (±SD)	3175(±2667)	3689.4(±3389)	0.441
Creatine kinase-MB (CK-MB) u/L, mean (±SD)	284.7(±194)	316.2(±220)	0.671
Troponin-I >25 ng/mL, n. (%)	24(63.2%)	21(53.8%)	0.737
Ejection fraction (EF), mean (±SD)	39.3(±8.1)	40(±10.6)	0.885
Wall motion index (WMI), mean (±SD)	1.9(±0.7)	1.9(±0.5)	0.803
DETERMINE SCORE, mean (±SD)	13.8(±4.9)	12.2(±4.9)	0.142

Table 2. Thrombolysis versus primary percutaneous Intervention after GeneXpert test based on parameters that reflect the size of infarction.

Discussion

In our study, the percentage of females presented with acute STEMI during the COVID-19 pandemic was significantly lower than males (91.25 vs. 8.25%, P < 0.001), which may reflect COVID-phobia as they were reluctant to come to the hospital with a fear of getting infected with COVID-19 and hence we may see more cases of ischemic left ventricular failure among females after the pandemic.

Furthermore, the overall number of cardiac patients that attended our cardiac center during the COVID-19 pandemic was decreased compared to the non-COVID-19 period. We reported a 32% reduction in STEMI cases in comparison to the same period last year. A Spanish study that recorded visits from 71 hospitals of the STEMI care network in Spain reported a 40% reduction in patients treated with primary PCI **(5).** Another study revealed a 38% reduction in cardiac catheterization procedures that were diagnosed as STEMI in 9 high volume centers in the United States **(6).** Tam et al. reported significant delay in the number of patients with STEMI seeking medical care in Hong-Kong, China, after the measures taken by the institution of infection

control **(7).** Similar observations have been reported in a study of 19 public primary PCI centers in Austria, where a lower rate of admitted and therefore treated patients with ACS was reported **(8).**

Infarct size depends mainly upon ischemic time duration and proportionately related to short and long-term survival and adverse cardiovascular events in patients presented with STEMI **(9).** The same study by Tam et al. showed a 4-fold increase in median time from symptoms onset to first medical contact (from 82.5 to 318 min), and more than 2-fold increase in median time from door to device (from 84.5 to 110 min) **(7,10,11).** In our study, the time from onset of chest pain to the first presentation to the emergency department showed a trend of treating patients presented early < 3 hours with thrombolysis (mean time 3.2 ±2.2) and pPCI for those presented with more than 3 hours chest pain (mean time 5.2 ±4.4).

Furthermore, 7.5% of patients with inferolateral MI were found in the thrombolysis group compared to 2.5% in pPCI after PCR group (P = 0.027), which reflects that inferior STEMI patients had less access to pPCI during COVID-19, this may be attributed to the fact that it is less prognostically relevant compared to anterior wall STEMI.

Different parameters were well established to gauge the infarct size as CPK, CK-MB, Troponin-I, EF and WMSI **(12).** Recently, accumulating evidence has demonstrated the strong link between high NLR and increased morbidity and mortality in a wide range of cardiovascular diseases, including STEMI **(13,14).** Chen et al. showed a strong association of NLR with myocardial damage (CK-MB) and a negative association with cardiac contractility (Ejection fraction and fractional shortening) thus high NLR strongly predicts the severity of myocardial damage and extent of infarction **(15).**

Electrocardiogram (ECG) is an inexpensive tool to measure the infarct size. Daniel et al. revealed that the presence and extent of Q waves, fragmented QRS, and T wave inversions on ECG are independently associated with an increase in infarct size. DETERMINE score is calculated from the number of leads with these markers and can be used to estimate the infarct size nearly as well as measured by cardiac magnetic resonance (CMR) and the addition of the DETERMINE score to LVEF improved infarct size estimation significantly **(16).**

None of the outcome parameters that we pre-selected to define the extent of myocardial infarction (NLR, CK, CK-MB, Troponin-I, EF, WMSI and Determine score) was statistically significant comparing the two groups. All the observed differences were most likely ingenuine and thus revascularization with primary percutaneous coronary intervention after negative GeneXpert

PCR test for coronavirus disease-19 was not associated with an adverse event in term of the extent of infarction and should remain considered as the gold standard and first policy for revascularization during COVID-19 pandemic, if applicable.

Conclusion

pPCI after PCR for acute STEMI in the context of the COVID-19 pandemic remains superior to thrombolysis because the size of infarct was not adversely affected by the extra time taken to secure the staff and workplace prior to coronary intervention.

Limitations

The relatively small sample size and retrospective design precluded more extensive characterization of the population and analysis of hard endpoints.

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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