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ORIGINAL ARTICLE

Impact of Short First Medical Contact to Device Time on Final TIMI Blush Grade in Primary PCI

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ABSTRACT

Background: Greater first medical contact to device time has been observed to adversely effects the outcome of primary PCI. European Society of Cardiology (ESC) recommends a maximum of 90 min delay in FMC to device time. However, the effect of the FMC to the device time on the myocardial reperfusion (TIMI blush grade) is not assessed yet.

Objective: To investigate the effect of the FMC to the device time on the TIMI blush grade of the STEMI patients who underwent primary PCI.

Methodology: It was a prospective study consisting of 445 STEMI patients of Punjab Institute of Cardiology, Lahore, fulfilling the entry criteria in this study in the time period from January 2020 up to January 2022. The patients were divided into two study groups: those with FMC-D interval of < 90 min or short group and those with FMC-D interval of ≥ 90 min or the long group. TIMI blush grade was taken as the primary clinical endpoint whereas MACE at the 30 day follow up were taken as the secondary endpoints. Comparison of the clinical and peri-procedural outcomes was done among the two groups by SPSS.

Results: The mean FMC-D time was 77.3 ± 32.1 minutes in short FMC-D time group and 117.1 ± 12.5 minutes in long FMC-D time group ($p < 0.01$). At the duration of 30 days, individuals in the long group showed significantly higher rates of MACE (14.2% vs 3.9%, $p = 0.0002$). Higher cardiac death rate was the driving force behind the noted difference (7.1% vs 1.2%, $p = 0.002$).

Conclusion: First medical contact to device time does not significantly impact the final TIMI blush grade in patients underwent PCI. Patients in whom the delay of treatment is < 90 minutes have significantly lower rates of MACE at the 30 days duration.

Keywords: First medical contact, TIMI blush grade, PCI, STEMI, FMC-D time.

INTRODUCTION

Primary percutaneous coronary intervention (PCI) has taken the form of being the most used strategy of reperfusion in chronic and acute coronary artery disease. Excellent outcome for the ST-segment elevation myocardial infarction (STEMI) is related to the primary PCI due to being better than fibrinolytic therapy in the reduction of stroke, death and reinfarction.[1-3]

Restoration of the patency of the culprit artery in due time and thus myocardial salvage remains the principal objective of the PCI in STEMI patients. Nevertheless, prompt execution of the PCI remains the deciding factor for its efficiency because a strong correlation exists between mortality and the delay in the first medical contact (FMC) with the device times.[4] The updated guidelines suggests FMC to the balloon time to be under 90 mins of duration for patients being presented to a hospital capable of PCI and for the hospital not capable of PCI, the duration is 120 min.[5] Numerous hospitals lack catheterization laboratory and so process of transferring the patient to a hospital capable of PCI might be related to long delays in the reperfusion.[6-8]

In the modern day practice, normal range (Thrombolysis In Myocardial Infarction [TIMI] flow grade 3) of the epicardial flow of blood in culprit artery can be achieved in around 90% of the total cases.[9] Nevertheless, restoration of perfusion of the tissue at the myocardium level in around one out of every three patients is not achieved, [9,10] even following a successful PCI, because of impaired microvascular blood flow, and such patients have limited benefits of the reperfusion.[11] Prolonged ischemic duration has been observed to be related to greater area of the microvascular obstruction.[12,13] Observational studies of larger scale researched on the association among myocardial perfusion and ischemic duration, but these studies precede the use of the antiplatelet therapy and stents in a routine manner,[14] only consisted of results based on a single-center,[15] or there was lack of core laboratory analysis. Furthermore, following STEMI, numerous factors can influence the clinical outcomes. Among those factors one is time delays. On the basis of data acquired from the larger registries, guidelines presented by European Society of Cardiology (ESC) in 2012 set the quality targets clearly for the STEMI networks, with recommendations of <90 min delays from the FMC and <12hr delay from the onset of symptoms to the primary PCI in all the patients diagnosed with STEMI.[16] The guidelines presented in 2017 further endorsed the significance of the delays that are system dependent with recommendation of primary PCI under 90 min duration of the diagnosis and under 60 min in situations where the patient is presented directly to primary PCI center. When delay greater than 120 min occurs between the diagnosis and the reperfusion, fibrinolysis is recommended.[16] Nonetheless, data is scare on effect of the FMC to the device time on the microvascular reperfusion. TIMI myocardial perfusion grading (TMP) is a method that is both cost-effective and easily available for the quantification of myocardial perfusion at PCI procedure ending which provides crucial information beyond the epicardial flow.[17] We, thus, investigated effect of the FMC to the device time on the myocardial reperfusion from the prospective study of the primary PCI in patients with STEMI by the use of TIMI blush grade.

MATERIALS AND METHODS

It was a prospective study consisting of 445 STEMI patients of Punjab Institute of Cardiology, Lahore, fulfilling the entry criteria in this study in the time period from January 2020 up to January 2022. Every participant in the study was asked to provide informed consent and in case of the inability of the patient to do so, their relatives were asked for the informed consent prior to angiogram. Review board of the institution approved our study.

Every consecutive patient where diagnosis of AMI was suspected under the duration of 12hr of the onset of symptoms who were suggested to go to name of institute to undergo pPCI were eligible for the study. Following inclusion criteria was defined 1) usually occurring anginal pain that lasts for duration of >30 min, 2) ST-segment elevation of the value >0.2 mV in two contiguous leads of ECG at least. Regardless of infract vessel, probable thrombolytic therapy and the hemodynamic status, every patient was considered prior to the intervention. Patients who failed to be diagnosed with STEMI along with patients who were not able to provide the written consent or were unwilling to participate in the study as well as the follow up, were not made part of the study. Baselines characteristics for both the procedure and patients were collected along with the time delays

Extraction of all the data was done from the questionnaire Performa that was prefilled which included demographics of the patients and variables including onset of the symptoms upon arrival to the hospital, gender, door to the balloon time, age, culprit vessel, risk factors and length of the lesion, etc. Calculation of the TIMI flow frequency was carried out as TIMI 0, TIMI I, TIMI II, and TIMI III which are defined as: TIMI 0 flow defining no perfusion to myocardium following occurrence of occlusion of the coronary artery (perfusion without the penetration), TIMI I flow, when the distal coronary bed fills incompletely because of faint antegrade flow (partially occurring perfusion), TIMI II flow being defined as sluggish or delayed flow of the blood but distal coronary bed fills up completely (partially occurring reperfusion); and TIMI III flow, normal flow of blood in coronary artery where distal bed fills up completely.

Assessment of the TMP grading in culprit artery was carried out upon the ending of PCI procedure. Following intracoronary injection of glycerol trinitrate (200 µg), coronary angiography was carried out in two different projections, envisioning periphery of infract related artery (IRA). Final angiographies permitted contrast media to wash in and also wash out of microvasculature. Definition of TMP grades was acquired using method provided by Gibson et al. [18]: TMP grade 0 being no contrast entering microvasculature (no blush); TMP grade 1 defining slow entry of the contrast into microvasculature but failure to exit it; TMP grade 2, delay in both entry as well as exit of the contrast in microvasculature; TMP grade 3 defining contrast entering and exiting normally from microvasculature (blush).

FMC was detailed as initial contact of the patient with any of the health services such as primary care. For the patients who were initially attended by national service for medical emergency, definition of FMC was done as time of arrival of ambulance or any other medical emergency vehicle at the location of the patient. FMC to the device time was noted as arrival time of the first encountered medical facility/personnel to first coronary balloon dilatation being initiated. The patients were divided into two groups: FCM to device time ≤ 90 mins (short) and FMC > 90 mins (long). Successful epicardial perfusion was noted upon achieving TIMI flow grade 3 and the 2/3 MBG grade was taken as successful microcirculatory reperfusion.

The primary endpoint of this study are final TIMI blush grade and the secondary end point include major adverse cardiac events (MACE) at 30 days follow-up.

Statistical analysis: Data was statistically analyzed using the SPSS V 20.0 (SPSS Inc, Chicago, IL, USA). Expression of the continuous variables was done as median with interquartile range (IQR) or mean ± standard deviation. Expression of categorical variables was done as percentages and counts. For the continuous variables, checking of the histograms was done for the normal distribution. Comparison of clinical outcome as well as procedural and baseline characteristics was done among the patients having delay from the first medical contact to the device (FMC-D) of less than 90 min (short) with the patients where FMC-D was greater than 90 min (long) for the univariate analysis, by the use of chi-square test for the categorical variables, continuous variables with normal distribution were subjected to unpaired t-test whereas non-parametric tests like Mann-Whitney U-test or Wilcoxon rank sum test were used for the continuous variables having non-normal distribution.

RESULTS

The current study consisted of 445 subjects. Subjects were separated into two groups on the basis of FMC-D delay: patients getting treated before the 90 min (“short” group; n = 205) and patients with a delay of ≥90 minutes (“long” group, n = 240). Table 1 depicts the baseline characteristics. All the subjects of the study were considered for the primary PCI. None of the subjects received thrombolysis therapy. Mean of the age was noted to be 63 ± 12 years which was found to be significantly lower in short group compared to the long group (61.3 ± 12.2 vs 65.9 ± 11.8, p = 0.0001), 74.6 % (n = 332) were men (short: 74.1% (n = 152) vs long: 75% (n = 180), p = 0.835). Diabetes mellitus was found to be in 17.6% (n = 38) of subjects in short group and in 22.9% (n = 55) of subjects in long group (p = 0.167). Patients with family history were equally distributed in both groups (short: 20.5% (n = 42) vs long group: 22.1% (n = 53), p = 0.681). No other baseline variable was found to be statistically different between the groups

Table 1: Baseline characteristics of the patients of both the study groups

Variable	Short (n = 205)	Long (n = 240)	p-value
Age (mean ± SD)	61.3 ± 12.2	65.9 ± 11.8	0.0001*
Gender, n (%)			
Male	152 (74.1%)	180 (75 %)	0.83
Female	53 (25.8 %)	60 (25 %)	
BMI (mean ± SD)	26.8 ± 4.2	27.3 ± 4.2	0.21
Risk factors, n (%)			
Smoking	95 (46.3%)	105 (43.7%)	0.58
Diabetes mellitus	38 (17.6%)	55 (22.9%)	0.16
Hypertension	100 (48.8%)	108 (45%)	0.42
Dyslipidemia	75 (36.6%)	95 (39.6%)	0.51
Family history	42 (20.5%)	53 (22.1%)	0.68
No. of vessels involved n (%)			
Single vessel	83 (40.5%)	89 (37.1%)	0.44
Two vessels	70 (34.1%)	77 (32.1%)	
Three vessels	52 (25.4%)	74 (30.4%)	
Infarct related artery, n (%)			
Left anterior descending (LAD)	92 (44.9%)	103 (42.9%)	0.60
Right coronary artery (RCA)	88 (42.9%)	98 (40.8%)	
Left circumflex (LCX)	23 (11.2%)	34 (14.2%)	
Left main (LM)	2 (0.97%)	5 (2.08%)	

*Statistically significant

Overall, the median FMC-D time was noted to be 95 ± 19 minutes. The mean FMC-D time was 77.3 ± 32.1 minutes in short FMC-D time group and 117.1 ± 12.5 minutes in long FMC-D time group (p < 0.01). Moreover, the pre-procedural and post-procedural characteristics of patients of both groups are given in Table 2. No significant difference was observed between the two groups with respect to post procedural TIMI blush grade.

Table 2: Pre-procedural and post-procedural characteristics of the patients

Variable	Short (n = 205)	Long (n = 240)	p-value
FMC to device time (min), mean ± SD	77.3 ± 32.1	117.1 ± 12.5	< 0.01*
Baseline TIMI flow grade			
0/1	164 (80%)	197 (82.1%)	0.57
2/3	41 (20%)	43 (17.9%)	
Final TIMI flow grade			
0/1	2 (0.97%)	3 (1.2%)	
2	12 (5.9%)	21 (8.7%)	0.48
3	191 (93.2%)	216 (90%)	
Final TIMI Myocardial Blush Grade			
0/1	9 (4.4%)	7 (2.9%)	
2	26 (12.7%)	32 (13.3%)	0.70
3	170 (82.9%)	201 (83.7%)	

*Statistically significant

Table 3 depicts the clinical outcomes. At the duration of 30 days, individuals in the long group showed significantly higher rates of MACE (14.2% vs 3.9%, p = 0.0002). Higher cardiac death rate was the driving force behind the noted difference (7.1% vs 1.2%, p = 0.002).

Table 3: Major adverse cardiac events observed in both the groups after the procedure

Variable	Short (n = 205)	Long (n = 240)	p-value
MACE at 30 days	8 (3.9%)	34 (14.2%)	0.0002*
Death	3 (1.5%)	10 (4.2%)	0.09
Cardiac death	4 (1.2%)	17 (7.1%)	0.002*
Nonfatal MI	0 (0%)	1 (0.41%)	0.35
Repeat procedure	1 (0.48%)	6 (2.5%)	0.08

*Statistically significant

DISCUSSION

Despite how the time delay in the treatment of the STEMI patients by the thrombolytic therapy is shown to have a prognostic role,[19,20] its role remains controversial in the primary angioplasty patients.[20-22] In the collective analysis of every randomized trials comparing the primary angioplasty and thrombolysis, it was noted by Zijlstra et al. [20] that the mortality observed a linear increase with the time delay only in the individuals getting treated by the thrombolysis therapy, whereas relative stability was noted for the individuals receiving primary angioplasty treatment. Cannon et al. [22] conducted a study consisting of 27,080 subjects who were undergoing the primary angioplasty and noted association of the mortality with only door to balloon time but not with onset to the balloon time. Occurrence of no relationship among the mortality and ischemic time in the primary angioplasty might be associated with low risk profile of the subjects being made part of the randomized trials.[20] Moreover, a number of studies have associated first medical contact to device time with the gender, clinical outcome of the patients and MACE.[4,23-29] However, no study up till now has reported the effect of FMC-D time on the final myocardial blush grade of the patients. Recent recommendations from the guidelines of the AHA/ACC STEMI propose primary PCI as suggested reperfusion strategy in the cases where FMC-D time is ≤ 90 minutes for the individuals getting directly transported by the emergency medical systems (EMS) to PCI hospital or when FMC-D time is ≤ 120 minutes for the individuals initially getting transferred to non-PCI (STEMI referral) hospital.[30] Taking into consideration the medical facilities and number of cardiac centers present around Pakistan, the present study was conducted by diving the patients into two groups based on their FMC-D time at a cutoff point of 90 mins. To the best of our knowledge, the current study is the first one to report impact of FMC-D time on myocardial final blush grade as indicative of reperfusion after PCI.

According to our study findings, FMC-D time does not significantly impact the final TIMI blush grade of the patients, which is accordance with the findings of Mazhar et al. [31] who compared the no-reflow and normal flow groups and based on final TIMI flow at the end of the procedure and found to association between reperfusion and FMC-D time. The possible explanation behind this may be a limitation of the study that not very long FMC-Device time (117.1 ± 12.5) was observed even in the patients of group long FMC-D time compared to that of the short one, which may affect the relationship between time delay and blush grade, which warrants a large multi-center study.

Moreover, we noted that increased age is significantly related to the delay in the treatment exceeding the duration of 90 minutes (p = 0.0001). Similarly, in a study consisting of 3832 individuals, Ruiz et al. noted age to be an independent predictor in the >120 minutes FMC-R delay.[32] Several factors might have played their role in this. Primarily, frequency of atypical symptoms increase with increasing age, so STEMI diagnosis becomes more difficult.[33] Furthermore, elderly patients have a harder time communicating with first medical responders. Other than that, frailty and presence of comorbidities extend the duration from diagnosis to the treatment.[34] Finally, in the patients of very old age, conventional treatment options are considered more compared to the primary PCI before the activation of established network pathways of STEMI.

The evidence of fewer mid-term as well as long term MACE is ample in the individuals in whom the FMC-D or door to balloon times were short.[28,35] In current analysis, although we did not find the significant association between FMC-D and final blush grade, nevertheless, we noted MACE rates in the individuals where FMC-D delay was <90 minutes to be significantly lower compared to the patients where the delay exceeded 90 minutes, which is in line with the previous studies.[4,28,35] Lower rates of occurrence of the cardiac deaths in the initial 30 days was the driving factor behind this difference.

Lastly, our study demonstrates that delay of <90 minutes in the treatment was noted in roughly 46% of the individuals who received treatment between year 2020 and year 2022. In is indicated that short time delay proved beneficial in the clinical outcomes.[35] Therefore, all STEMI networks must ultimately try to achieve optimal treatment delays. Furthermore, it is not clear if much improvement can be made in this regard in the extensively rural areas, remote from the centers capable of PCI, areas where there is limited access to the primary healthcare facilities. Undeniably, feasibility remains a primary issue in the current context. Wide number of variables play their role in overall delay in the treatment from onset of the symptoms to the reperfusion. Modulation of the component that is dependent on the patient i.e., utilizing the time from the onset of symptom to initial medical contact can be done via public service announcements.

CONCLUSION

First medical contact to device time does not significantly impact the final TIMI blush grade in patients underwent PCI. Advanced age extends the revascularization delay following initial medical contact in the STEMI patients. Patients in whom the delay of treatment is <90 minutes have significantly lower rates of MACE at the 30 days duration.

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