Iranian Heart Journal; 2021; 22 (1)

Original Article

Possible Advantages of Deferred Percutaneous Coronary Intervention in ST-Elevation Myocardial Infarction Patients With Moderate-to-High Thrombus Burden

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ABSTRACT

Background: Primary percutaneous coronary intervention is the standard of care for ST-elevation myocardial infarction (STEMI). However, the proper management of the culprit artery with residual moderate-to-high thrombus burden after the initial restoration of flow is still unclear.

Methods: One hundred patients with STEMI underwent primary percutaneous coronary intervention, through which the operators managed to establish thrombolysis in myocardial infarction (TIMI) II–III flow with minimal manipulation but with residual moderate-to-high thrombus burden in the culprit artery. The patients were categorized into 2 equal groups. Group A consisted of patients who underwent immediate stenting, and Group B was comprised of patients for whom the intervention was deferred. After 24 to 48 hours, coronary angiography was repeated in Group B, and stenting was done when needed. The patients had pre-discharge echocardiography and were followed for 4 weeks for major adverse cardiac events (MACE); additionally, echocardiography was repeated 1 month after discharge

Results: There was no difference between the 2 groups regarding the TIMI flow of the culprit artery at the end of the revascularization procedure. There was a significant difference between the groups concerning the need for coronary stenting, which was lower in the deferral group (100% of the patients had stents in Group A vs 58% in Group B; $P = 0.000$). No significant difference was observed between the immediate and the deferral groups apropos the in-hospital morbidity/mortality or left ventricular function. At follow-up, there was no difference between the 2 groups vis-à-vis MACE and left ventricular function.

Conclusions: Deferred stenting is beneficial in reducing the need for stenting and the associated mortality/morbidity. ***(Iranian Heart Journal 2021; 22(1): 26-32)***

KEYWORDS: STEMI, Primary PCI, Deferred PCI

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Received: May 29, 2020 **Accepted:** July 5, 2020

The management of acute ST-elevation myocardial infarction (STEMI) is still under the umbrella of research given that plenty of areas are awaiting answers. Proper management and right decisions should be based on solid evidence derived from clinical trials. During primary percutaneous coronary intervention (PCI), moderate-to-high thrombi may be found occluding the culprit artery partially or totally. Thrombus grading scales are essential tools used for the qualification and quantification of thrombus burden.[1]

Our aim was to investigate whether deferring the stenting of the culprit artery after PCI and restoring thrombolysis in myocardial infarction (TIMI) II–III flow with minimal manipulation but with residual moderate-to-high thrombus burden in patients presenting with STEMI for 24 to 48 hours could improve the outcome compared with immediate stenting.

METHODS

Data Sources and Patient Collection

Between July 2017 and July 2018, a total of 3475 patients with STEMI were admitted to Ain Shams University hospitals, Dar Al Fouad, and As-Salam International Hospitals. Of this total, we enrolled 100 patients who fulfilled the inclusion criteria of the study protocol. Informed oral or written consent of the patients and approval of the Ethics Committee of Ain Shams University were obtained according to the ethical guidelines of the 1975 declaration of Helsinki as revised in 2008.

Eventually, 330 records were selected and 69 were eliminated since they met the exclusion criteria (Fig. 1).

Selection Criteria and Data Extraction

This was an observational nonrandomized case-control study conducted on 100 patients with STEMI who were referred for primary PCI and fulfilled the following inclusion criteria: hospital arrival within 12 hours of MI symptoms, establishment of TIMI II–III flow without stenting and with minimal acute manipulation but with the culprit artery showing residual moderate-to-high thrombus burden, initial coronary angiography showing TIMI II–III flow in the culprit artery and moderate-to-high thrombus burden, and hemodynamic stability. We excluded patients outside the pre-specified age range, patients with low thrombus burden on their initial coronary angiography, patients with low thrombus burden after minimal acute manipulation with percutaneous transluminal coronary angioplasty (PTCA) balloons with or without thrombus aspiration catheters, patients with failure to achieve TIMI II–III flow in the culprit vessel despite PTCA ballooning or thrombus aspiration catheter use, and patients with hemodynamic instability.

Thrombus burden was graded according to the TIMI Thrombus Scale Grade.[1] **Grade 0**: no angiographic evidence of thrombus; **Grade I**: angiographic features suggestive of thrombi with decreased contrast density, haziness of the contrast, irregular lesion contours, or a smooth convex meniscus at the site of a total occlusion; **Grade II**: a definite thrombus present in multiple angiographic projections with marked irregular lesion contours with a significant filling defect (greatest dimension of the thrombus < 1/2 the vessel diameter); **Grade III**: a definite thrombus in multiple angiographic views (with the greatest dimension from > 1/2 to < 2 the vessel diameter); **Grade IV**: a definite large thrombus (greatest dimension > 2 the vessel diameter); and **Grade V**: a definite complete thrombotic occlusion in a vessel with a convex margin that stains with the contrast and persists for several cardiac cycles. High thrombus burden was considered to be grades of 3 to 5.

The patients were divided into 2 groups of 50 each. Group A was comprised of patients who underwent primary PCI and immediate stenting, and Group B consisted of patients for

whom the procedure was deferred for 24 to 48 hours and who received treatment with dual antiplatelet and glycoprotein IIb/IIIa receptor antagonists (25 μg/kg bolus and 0.15 μg/kg/min maintenance infusion of tirofiban or 180 μg/kg bolus and 0.5 μg/kg/min of eptifibatide). Thrombus aspiration was used for some patients in both groups if PTCA ballooning failed to restore TIMI II to TIMI III flow. All the patients had pre-discharge echocardiography for the assessment and were followed for 4 weeks after discharge for major adverse cardiac events (MACE). MACE was defined as having 1 or more of the following events: mortality; morbidity (readmission); stroke; chest pain (its duration and the Canadian Cardiovascular Society [CCS] Angina Score); heart failure symptoms including New York Heart Association (NYHA) classification of dyspnea, orthopnea, and paroxysmal nocturnal dyspnea; arrhythmias; any other cardiac symptoms; and revascularization on other coronary vessels.

All the patients received dual antiplatelets, including clopidogrel, in addition to aspirin. Heparin or low-molecular-weight heparin (enoxaparin) was administrated according to the clinical situation of each patient. Statins, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, and beta-blockers were added or continued for the post-PCI medical therapy of the entire study population as guided by the condition of the patient.

Outcomes

All the patients had pre-discharge echocardiography. The procedure was repeated 4 weeks later, and the patients were followed for 4 weeks after discharge for MACE, including all-cause mortality, MI, target vessel revascularization, and hospitalization for congestive heart failure. The data were compared between the 2 groups.

Statistical Analysis

The sample size was calculated based on the STATA 10 program. The outcomes were analyzed via the intention-to-treat module. *P value*s were calculated to determine the significance of the compared items. Descriptive statistics were carried out by calculating the number and percentage for the categorical data and mean±SD for the continuous variables. The continuous variables were tested via the Student *t*-test. The categorical variables were compared using the χ^2 test. The least significant level was set at a *P value* of less than 0.05 ($P > 0.05$: nonsignificant; $P < 0.05$: significant; and $P < 0.01$: highly significant).

RESULTS

The baseline demographic data showed nonsignificant differences between the 2 study groups regarding all the risk factors, except for age (54.22 ± 9.35 y in Group A vs and 58.6 ± 11.68 y in Group B; $P = 0.041$) and family history (80.0% of Group A vs 58.0% of Group B; $P = 0.017$. The duration of chest pain before presentation to the emergency department was not statistically significantly different between the 2 groups with an average duration of 4 hours ($P = 0.719$). There was a nonsignificant difference between Group A and Group B as regards hemodynamics at presentation (heart rate [$P = 0.139$], systolic blood pressure [$P = 0.408$], and diastolic blood pressure [$P = 0.735$]).

In Group A, there were 30 patients with anterior STEMI, 17 with inferior STEMI, and 3 with lateral STEMI. In Group B, there were 21 patients with anterior STEMI, 23 with inferior STEMI, and 6 patients with lateral STEMI.

At the end of the revascularization, procedure, there were no statistically significant differences between the groups in terms of the TIMI flow of the culprit artery

(TIMI III flow in 84% of Group A vs 86% of Group B; *P* = 0.114) and the degree of myocardial blushing (Grade III in 42% of Group A vs 43% of Group B; *P* = 0.114).

No procedure-related complications, including dissection, perforation, and cardiac arrest, were recorded in either group.

The most striking finding was the number of stents needed in both groups; there was a highly significant difference between the groups as regards the need for stent deployment in the culprit lesion in that it was lower in the deferral group (50 [100%] patients had coronary stents in Group A vs 29 [58.0%] patients in Group B; *P* = 0.000).

Post-procedural electrocardiography (ECG) changes showed a highly significant difference between the 2 groups, favoring immediate PCI insofar as the resolution of STEMI to more than 70% occurred in 96% of the patients in Group A and only 68% of those in Group B (*P* = 0.000).

Echocardiography, performed 1 month after hospital discharge to assess left ventricular function and mitral regurgitation, revealed no significant differences between the 2 groups.

Table 1: Post-PCI results

Post-PCI Results		Group A n = 50	Group B n = 50	Test Value	*P value*	Sig.
TIMI flow post culprit lesion	I	0 (0.0%)	3 (6.0%)	4.345*	0.114	NS
	II	8 (16.0%)	4 (8.0%)			
	III	42 (84.0%)	43 (86.0%)			
Degree of myocardial blushing	I	0 (0.0%)	3 (6.0%)	4.345*	0.114	NS
	2	8 (16.0%)	4 (8.0%)			
	3	42 (84.0%)	43 (86.0%)			
Creatinine level	Mean±SD	0.99 ± 0.32	1.13 ± 0.36	-1.252•	0.217	NS
	Range	0.7 – 2.1	0.6 – 1.7			
Hemoglobin level	Mean±SD	14.42 ± 3.72	12.99 ± 2.67	1.450•	0.153	NS
	Range	6.8 – 30.3	7.3 – 16.6			
Complications	No	50 (100.0%)	47 (94.0%)	3.093*	0.079	NS
	Yes	0 (0.0%)	3 (6.0%)			
In-hospital mortality	No	50 (100.0%)	47 (94.0%)	3.093*	0.079	NS
	Yes	0 (0.0%)	3 (6.0%)			
Resolution of STEMI to more than 70%	No	2 (4.0%)	16 (32.0%)	13.279*	0.000	HS
	Yes	48 (96.0%)	34 (68.0%)			

*, χ^2 test; •, Independent *t*-test
PCI, Percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction; NS, Nonsignificant; S, Significant; HS, Highly significant

Table 2: Echocardiography 1 month after discharge and the results concerning LV function and MR

		Group A n = 50	Group B n = 50	Test Value	*P value*	Sig.
EF	Mean±SD	51.72 ± 13.53	51.68 ± 8.23	0.017•	0.986	NS
	Range	19 – 84	29 – 66			
MR	No	38 (76.0%)	27 (57.4%)	8.443*	0.077	NS
	Trivial	0 (0.0%)	2 (4.3%)			
	Mild	8 (16.0%)	16 (34.0%)			
	Moderate	2 (4.0%)	2 (4.3%)			
	Severe	2 (4.0%)	0 (0.0%)			

*, χ^2 test; •, Independent *t*-test
PCI, Percutaneous coronary intervention; LV, Left ventricle; MR, Mitral regurgitation; EF, Ejection fraction; NS, Nonsignificant; S, Significant; HS, Highly significant

DISCUSSION

The management of acute STEMI is still under the umbrella of research given the extent of areas awaiting answers. Proper management and right decisions should be based on solid evidence derived from clinical trials. During primary PCI, moderate-to-high thrombi may be found occluding the culprit artery partially or totally. Thrombus grading scales are essential tools used for the qualification and quantification of thrombus burden.

We sought to investigate whether the deferral of the stenting of the culprit artery after PCI and the restoration of TIMI II–III flow with minimal manipulation but with residual moderate-to-high thrombus burden in patients presenting with STEMI for 24 to 48 hours could improve the outcome compared with immediate stenting.

The first important trial to address the safety and efficacy of the deferred stenting strategy was the Randomized Trial of Deferred Stenting Versus Immediate Stenting to Prevent No- or Slow-Reflow in Acute ST-Segment Elevation Myocardial Infarction (DEFER-STEMI). The study assessed whether deferred stenting might reduce no-reflow and salvage the myocardium in primary PCI for STEMI. It was a prospective randomized controlled parallel-group trial on patients with STEMI enrolled at a single center between March 11, 2012, and November 21, 2012.[2]

In our study, deferred stenting did not carry any additive value as regards enhancing the postprocedural intracoronary flow or myocardial blushing in the culprit vessel over immediate stenting in the setting of STEMI. These findings are concordant with those reported by Jianzhong et al,[3] who showed no significant differences in the incidence of no-reflow or slow-reflow between deferred stenting and immediate stenting.

These findings do not chime in with other randomized controlled trials that have shown lower rates of no-reflow in the deferral group and concluded that in high-risk STEMI patients, deferred stenting in primary PCI reduces no-reflow and increases myocardial salvage.[2, 3, 9, 13, 15]

In the current study, echocardiography at 1 month after hospital discharge demonstrated no significant differences between the 2 groups vis-à-vis left ventricular ejection fraction and mitral regurgitation; nevertheless, deferred stenting was associated with an increase in the long-term left ventricular ejection fraction in multiple observational studies ($P = 0.001$).[3, 14, 16]

We observed no significant differences in the rates of MACE between the 2 study groups, which is in line with the results of other studies with respect to major bleeding, MI, and target vessel revascularization.[3, 14, 16]

Our comparison of MACE at 1 month's follow-up between the 2 study groups revealed no statistically significant differences; this is consistent with data collected from various meta-analyses.[3, 10, 11, 14, 16]

Our primary endpoints included in-hospital mortality and morbidity. Despite 3 deaths in the deferral group, there was no statistically meaningful difference between the 2 study arms. All 3 patients had cardiac arrest early following the initial coronary angiography; the mode of arrest was noted to be ventricular tachycardia degenerating into resistant ventricular fibrillation with failure to restore sinus rhythm. Our assessments of cardiac enzyme levels and ECG at the time showed marked re-elevations in the biomarkers and the ST-segment on ECG, raising the possibility of re-infarction as the precipitating insult that initiated the unfortunate event. This finding is consistent with data derived from a famous trial, which indicated that deferred stenting at the time of primary PCI in patients with STEMI was not

superior for adverse cardiovascular outcomes to immediate stenting (which is the conventional practice). In addition, the trial showed that routinely deferred stenting was associated with a higher risk of target vessel revascularization, possibly because stenting at the time of the second procedure at 48 hours was deemed unnecessary in 15% of the patients (compared with 3% in the conventional management arm).[17]

The most striking finding in our study was the number of stents used for the culprit artery, with the figure being lower in the deferral group: 50 (100%) patients had coronary stents in Group A in contrast to only 29 (58.0%) patients in Group B (P = 0.000). This finding is consistent with the results of the DANAMI-3-DEFER trial, which reported that 15% of the deferred stenting group did not need culprit artery stenting as opposed to 3% of the immediate stenting group.

In light of the evidence gathered in this observational study, we conclude that deferring primary stenting has no superiority to conventional stenting at the time of primary PCI with respect to procedural complications, in-hospital mortality, short-term follow-up of MACE, and left ventricular function. Be that as it may, the only possible benefit of deferred stenting is the lower number of patients needing stents in the infarcted arteries, with a higher possibility of avoiding coronary stenting and its possible associated immediate and late complications.

We recommend that future investigations be undertaken on the possible management of culprit arteries with residual moderate-to-high thrombus burden after the restoration of TIMI II–III flow following minimal initial interventions by balloon or aspiration catheter in STEMI patients treated by primary PCI. Additionally, research needs to be conducted on different imaging modalities and their efficacy in discriminating patients who really need stenting from those who do not with a view to avoiding unnecessary coronary stenting.

CONCLUSIONS

Deferring PCI in our STEMI patients with moderate-to-high thrombus burden did not affect TIMI flow at the end of the procedure, in-hospital morbidity/mortality, or short-term MACE. Deferred stenting is beneficial in reducing the need for stenting and the associated mortality/morbidity.

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