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Deferred Stenting as an Alternative Strategy for Management of ST-Elevation Myocardial Infarction with Significant Thrombus Burden

M. Nadeem Attar[1*], Ibrahim Bader[1], Michael F. Dorsch[1], Ben D. Tyrrell[1], Raymond Leung[1], Neil Brass[1], William Hui[1] and Po Kee Cheung[1]

[1]Department of Cardiology, C. K. Hui Heart Centre, Royal Alexandra Hospital Foundation, 10240, Kingsway, Edmonton, AB T5H 3V9, Canada.

Authors' contributions

This work was carried out in collaboration between all authors. Author MNA designed the study, wrote the protocol, and wrote the first draft of the manuscript. Authors IB and MFD managed the literature searches and analyses of the study performed. Authors RL, NB and WH managed the experimental process. Authors BDT and PKC carried out angiography review and data analysis. All authors read and approved the final manuscript.

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Short Research Article

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ABSTRACT

Objectives: We evaluate a deferred stenting strategy following intense antithrombotic and antiplatelet therapy as an alternative to primary percutaneous coronary intervention with immediate stenting in ST-Elevation myocardial infarction (STEMI) patients with large thrombus burden.
Methods: We identified all consecutive patients where a deferred stenting strategy was chosen as initial management strategy. Baseline characteristics, clinical outcomes and complications were collected from local and provincial databases. Procedural characteristics were evaluated from detailed review of angiograms.
Results: Between June 2011 and March 2014, thirty eight patients were treated with a deferred stenting strategy. TIMI thrombus grade scale 4 or 5 on the initial angiogram was seen in 82% of cases. Immediate thrombectomy or balloon angioplasty was performed in 25 out of 38 patients to

**Corresponding author: Email: nadattar@hotmail.com, nadattar@hotmail.com;*

restore flow. Aggressive antithrombotic (86% heparin) and antiplatelet (100% Eptifibatide and 100% dual antiplatelet therapy) was administered. No emergency repeat catheterisation was required. Thirty six patients had a relook angiogram. No further coronary intervention was required in 12/36 (33%) of patients, 23/36 (64%) patients received at least one stent and one patient was sent for coronary bypass surgery. No major bleeding occurred. One patient treated with deferred stenting died at 2 months from stent thrombosis. No other major adverse cardiovascular events occurred.

Discussion: In our experience deferred stenting is safe and has the potential to reduce no reflow and thereby reduce infarct size.

Keywords: Deferred stenting; primary percutaneous coronary intervention; st-elevation myocardial infarction; glycoprotein 2b/3a inhibitors.

1. INTRODUCTION

Primary Percutaneous Coronary Intervention (PPCI) reduces the risk of reinfarction and mortality in patients with ST-Elevation Myocardial Infarction (STEMI) - [1]. PPCI with stent placement has Class 1A recommendation by ACC/AHF guidelines [2].

Microvascular obstruction (MVO) or no-reflow phenomenon is an established complication of coronary reperfusion therapy for acute myocardial infarction. No Reflow phenomenon, also known as microvascular obstruction (MVO), has been defined as a patency restoration of an epicardial infarct-related coronary artery without complete microvascular reperfusion [3] and is associated with greater myocardial injury. There are at least two mechanisms of the no-reflow phenomenon- capillary injury and microvascular embolism [4]. Coronary microvasculatures are often damaged irreversibly due to myocardial ischemia and reperfusion. In clinical settings, PPCI may accelerate embolization of plaque gruels and microthrombi to the microvessels, which further reduces tissue perfusion. Angiographically visible distal embolization is seen in 6.3% [5] after PPCI in an unselected contemporary population with STEMI and is associated with adverse outcomes. A higher incidence of 15.2% of distal embolization has been reported previously [6]. There have been attempts to use distal protection devices or adjunct thrombectomy to prevent distal embolization. Distal protection devices have not proved to be effective [7], and in TASTE trial, thrombectomy did not affect outcomes in STEMI [8]. These mechanical adjuncts might not have had the desired beneficial effect due to a large thrombus burden in a proportion of unselected STEMI patients undergoing PPCI with immediate stenting. The no-reflow zone expands during the first few hours of reperfusion suggesting an element of reperfusion injury [9]. The extent of the no-reflow zone correlates with infarct size, and it has additional prognostic information [4]. Aggressive antiplatelet therapy with aspirin, clopidogrel / Ticagrelor, and/or platelet glycoprotein IIb/IIIa receptor inhibitors is a promising adjunctive therapy for improving tissue perfusion. ADMIRAL trial [10] provided preliminary evidence that intravenous glycoprotein IIb/IIIa inhibitor-abciximab is associated with a high incidence of TIMI-3 flow and with an 80% reduction in adverse cardiac events compared with control among acute MI patients undergoing PPCI.

On restoring TIMI flow in STEMI either mechanically or spontaneously, presence of large thrombus burden can potentially be attenuated by a period of intense antiplatelet and antithrombotic therapy. Deferring stent implantation following the index procedure might then allow time for reduction in coronary thrombus burden, recovery of microvascular circulation and reduce the likelihood of no-reflow.

Our study aims to evaluate whether it is safe to defer stent implantation once epicardial flow is restored and a large thrombus is revealed.

2. METHODS

In a high volume, single centre study we identified all consecutive patients where a deferred stenting strategy was chosen. Between June 2011 and January 2014, thirty eight STEMI patients where deferred stenting strategy was utilized were studied retrospectively. Patients referred for PPCI due to chest pain and ≥0.2 mV ST-segment elevation in ≥2 contiguous electrocardiographic leads with a stable thrombolysis in myocardial infarction (TIMI) flow 3 obtained either spontaneously or after balloon dilatation and/or thrombectomy of an occluded IRA were included. Patients who underwent stent implantation at index PPCI procedure, those with

absence of TIMI flow 3 after initial reperfusion and cardiogenic shock were excluded. Baseline characteristics and clinical outcomes as well as complications were collected from local and provincial databases. Total thrombus burden was measured as per TIMI thrombus grade scale- 0 to 5 and coronary blood flow was recorded as per TIMI flow -0 to 3. Procedural characteristics were evaluated from detailed review of the angiograms by two experienced interventional cardiologists.

2.1 Index Procedure: Coronary Angiogram +/- Adjunct PCI

All patients were pretreated with Aspirin 325 mg, Clopidogrel 600 mg or Ticagrelor 180 mg, and weight based unfractionated heparin (UFH). Glycoprotein IIb/IIIa receptor blocker – Eptifibatide (Integrelin) was administered during the PCI procedure (bolus and infusion for 36 to 72 hours). Patients with unstable lesions or impaired blood flow of the IRA at admission had an acute PCI performed using wire introduction, thrombus aspiration using the 6Fr Export AP aspiration catheter (Medtronic, Minneapolis, MN, USA), or Pronto V4 Extraction Catheter (Vascular Solutions, Minneapolis, USA) and/or dilation in the lesion with an undersized balloon (1.5 or 2.0 mm in diameter). In patients with TIMI flow 3 at admission, consideration was given as to whether PCI was necessary to obtain a stable blood flow. At the end of the procedure, Eptifibatide infusion was continued and was combined with UFH infusion or Low molecular weight heparin -Enoxaparin subcutaneously. Six patients were treated with Eptifibatide infusion alone without UFH or Enoxaparin at the discretion of the experienced operator.

2.2 Second Procedure: Re-Angiography/ Intervention

A repeat angiography was planned 36 to 72 hours after the primary procedure, and stent implantation was performed in the culprit lesion in cases with a residual diameter stenosis >40% visually. Clopidogrel 75 mg daily or Ticagrelor 90 mg bd for one year and Aspirin indefinitely were prescribed for all patients.

2.3 Events and Definitions

TIMI flow and TIMI thrombus grade of the IRA were evaluated independently by two experienced cardiologists. In addition, thrombus burden at the start of the second procedure was compared with that at the end of the first procedure. The clinical course was evaluated in all patients during an 8 to 30-month follow-up period. We recorded the occurrence of major bleedings and the occurrence of major adverse events (MACE) defined as cardiac death, recurrent myocardial infarction and clinically driven target lesion revascularization (TLR). Any death not clearly attributable to a non-cardiac cause was classified as cardiac.

2.4 Statistical Analysis

Demographic and clinical data was entered on an Excel spreadsheet. Statistics was performed using SPSS 11.5 package.

3. RESULTS AND DISCUSSION

3.1 Index Procedure

Thirty eight consecutive STEMI patients underwent deferred stenting strategy. In thirteen patients (34%), TIMI 3 flow was seen spontaneously in IRA and no immediate PCI was performed. PCI with thrombectomy+/-balloon dilatation was performed in twenty five patients (66%) with TIMI flow <3. Demographic characteristics of the study patients are outlined in Table 1.

3.2 Second Procedure

Thirty six patients underwent repeat angiogram+/-intervention. One patient with tortuous, aneurysmal arteries and another who was an 89-year-old male with a degenerated vein graft were stable to be discharged and did not undergo the second procedure. Thirty five patients (97%) had TIMI flow 3 at repeat angiogram and one patient (3%) had TIMI flow 2 with thrombus and was successfully stented following thrombectomy. As a result of the second procedure twenty three patients (64%) had stents implanted, one patient (3%) had CABG and twelve patients (33%) did not require stents. Angiographic data illustrating changes in thrombus grade and TIMI flow is shown in Table 2.

We adopted a simple approach for risk stratification by grading the thrombus burden. Greater thrombus burden and an occluded culprit artery are both associated with large infarct size [11] and an adverse prognosis [2,12]. Patients with an initial evidence of successful reperfusion and a large thrombus burden were selected for intention-to-stent strategy with 36 to 72 hours of intense antiplatelet and antithrombotic therapy

(mean 66 hours). A shorter duration of 4-16 hours of antiplatelet and antithrombotic treatment has been used in a recent study [13] and in another study [14]; the duration of the therapy was 12 to 16 hour. In our study 33% patients did not require stents at the second procedure as compared to 38% of patients not receiving stent (because of residual stenosis of <30% and no visible thrombus) in a study by Kelbæk et al. [14].

Glycoprotein IIb/IIIa inhibitor therapy is an evidence-based antithrombotic treatment [2,12] and was included in therapeutic strategy to reduce thrombus burden before stent implantation in the deferred stenting group [12]. On Index angiogram, the thrombus burden was grade 4 or 5 in thirty one (82%) and grade 3 in seven (18%) of the patients. We compared the thrombus burden between the index and the second procedure. On repeat angiogram thrombus had dissolved in twenty five (69%) and visible thrombus was seen in only eleven (31%) of the patients. In this study, there was significant reduction in the proportion of patients with angiographic evidence of thrombus at the start of the second versus the first procedure (31% vs. 100%; $p < 0.0001$). The proportion of patients with angiographic evident thrombus at the beginning of second procedure was much lower in our study (31%) than that seen in a recent trial-62.7% [13]. This finding is likely due to prolonged Eptifibatide infusion (mean of 66 hours) in our study as compared to the other trials of deferred stenting [13,14]. Although Eptifibatide increases the risk of bleeding, no major bleeding occurred. This may be probably because radial artery access was used in 84% of our patients.

Deferred stenting in PPCI reduces no-reflow and increases myocardial salvage as compared to conventional PPCI with immediate stenting [13]. Cardiac MRI was performed in the study by Carrick et al. [13] and by Kelbæk et al. [14] to assess myocardial salvage. Of all the available modalities, Cardiac MRI provides the most comprehensive assessment of MVO [15]. We did not perform Cardiac MRI to evaluate myocardial salvage or MVO. Echocardiogram was performed pre-discharge and average ejection fraction of 50% indicates smaller/limited myocardial damage in our study group.

3.3 Clinical Events

Patients were followed up for 8 to 30 months. No MACE occurred during the hospital stay. No bleeding complications requiring blood transfusion were observed in hospital. One patient treated with deferred stenting died at 2 months of follow-up from definite stent thrombosis, two patients had clinically indicated repeat cardiac catheterization – one at 9 months and the other at 12 months. No new problems were identified and medical management was continued. The stents in both of these patients were patent with minimal instent restenosis. No other major adverse cardiovascular events occurred.

Table 1. Baseline characteristics of the study patients

Base line characteristics n=38	
Age , years	**57 (33 to 89)**
Sex, % males	84%
Smoking history	64%
Diabetes mellitus	19%
Hyperlipidemia	36%
Hypertension	44%
Family history	14%
Ethnicity –Caucasians	63%
- Native Americans	24%
- South Asians	8%
-Chinese	5%
Infarct type -Inferior	63%
-Anterior	24%
-Anterolateral	5%
-Inferoposterior	5%
-Posterolateral	3%
Infarct related artery- Right coronary artery	47%
-Left anterior descending artery	24%
-Left circumflex artery	8%
-Left main stem	5%
-Saphenous vein graft	16%
Average peak troponin I, µg/l	23
Mean hemoglobin, g/l	112
Mean creatinine, µmol/l	79
Mean ejection fraction	50%

Table 2. Procedural characteristics: TIMI flow and thrombus burden

	Index procedure, n=38		Second procedure n=36	
	Pre	**Post**	**Pre**	**Post**
TIMI flow 3, % of patients	34%	100%	97%	100%
Thrombus score, Δ-value (mean)	4.3	2.6	0.9	-

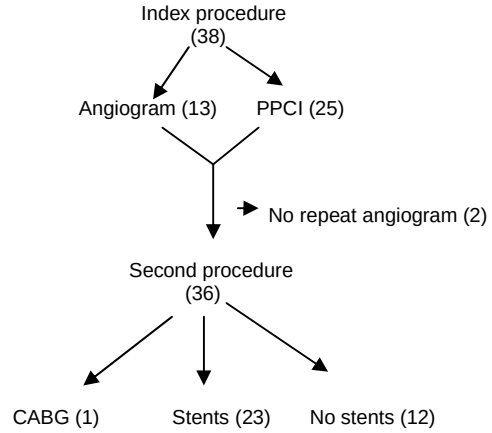

Fig. 1. Outcome of procedures. Number of patients shown in brackets

3.4 Limitations

This is a retrospective study in a single centre and there was no comparable control group. It reflects real life practice by highly experienced operators. However, these findings need confirmation in a large, randomized multicentre clinical trial or meta analysis of several smaller trials.

4. CONCLUSION

A systematic review [16], supports the notion that deferred stenting may be safe in appropriately selected STEMI patients. In our experience deferred stenting strategy appears to be safe and a sizable proportion of the patients did not require stent implantation. The study confirms previous findings in the field and is incremental.

The efficacy of deferred stenting is likely to be greatest in patients at the highest risk of no-reflow with a large thrombus burden and it should be considered a treatment option in this subset of patients.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Approval for the study was obtained from Research and Ethics Committee of Royal Alexandra Hospital. All authors hereby declare that the study has been approved by the local ethics committee and has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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