IJC Heart & Vasculature 10 (2016) 8–12

Contents lists available at ScienceDirect

IJC Heart & Vasculature

journal homepage: http://www.journals.elsevier.com/ijc-heart-and-vasculature

Predictors and outcome of no-reflow post primary percutaneous coronary intervention for ST elevation myocardial infarction

Jawad Mazhar [a,*,1], Mary Mashicharan [a,1], Ahmad Farshid [a,b,1]

[a] The Canberra Hospital, Canberra, Yamba drive, Garran, ACT 2605, Australia
[b] Australian National University, Canberra, Australia

ARTICLE INFO

Article history:
Received 28 July 2015
Received in revised form 21 October 2015
Accepted 3 November 2015
Available online 6 November 2015

Keywords:
No-reflow
Slow coronary flow
Primary percutaneous coronary intervention
ST elevation myocardial infarction

ABSTRACT

Background: No-reflow (TIMI <3) during primary PCI (PCI) for STEMI occurs in 11–41% of cases, indicates poor myocardial tissue perfusion, and is associated with a poor outcome. We aimed to determine predictors and 12 month outcomes of patients who developed no-reflow.
Methods: We analysed the PCI database of The Canberra Hospital and identified 781 patients who underwent primary PCI during 2008–2012. Follow-up at 12 months was with letter, phone call and review of hospital records.
Results: No-reflow was observed in 189 patients (25%) at the end of the procedure. Patients with no-reflow were older (64 vs. 61 years, p = 0.03). No-reflow patients were more likely to have initial TIMI flow <3 (89% vs. 79%, p = 0.001), thrombus score ≥ 4 (83% vs. 69%, p = 0.0001), higher use of glycoprotein IIb/IIIa inhibitors (57% vs. 48%, p = 0.03) and longer median symptom to balloon time (223 min vs. 192 min, p = 0.004). No-reflow was an independent predictor of mortality (HR 1.95, CI 1.04-3.59, p = 0.037) during 12 month follow-up. On multivariate analysis, age > 60 years, thrombus score ≥ 4 and symptom to balloon time > 360 min were independent predictors of no-reflow. In 17% of cases of no reflow, it occurred only after stent insertion.
Conclusions: No-reflow occurred in 25% of STEMI patients undergoing primary PCI and was more likely with older age, high thrombus burden and delayed presentation. No-reflow was associated with a higher risk of death at 12 month follow-up.

1. Introduction

Primary percutaneous coronary intervention (PCI) is the reperfusion strategy of choice in restoring blood flow to the occluded coronary artery in patients with ST elevation myocardial infarction (STEMI) [1]. Impaired coronary flow (Thrombolysis in Myocardial infarction grade < 3) despite restoration of epicardial coronary artery patency in the absence of any spasm or dissection is known as no-reflow [2]. It is thought to be caused by a combination of ischemic endothelial injury that obstructs the capillary lumen, neutrophil accumulation, reactive oxygen species and distal embolization of atherothrombotic debris [2,3]. No-reflow occurs in 11–41% of STEMI patients treated by primary PCI and is associated with poor left ventricular function, adverse clinical events and death [2,3]. A number of clinical, serologic and angiographic parameters have been shown to be associated with no-reflow [3].

The results of clinical trials testing a number of treatment strategies for no-reflow have been conflicting and there is no definitive treatment of no-reflow once it has occurred [4–8]. In the absence of an effective treatment strategy, it is crucial to prevent no-reflow by knowing the predictors or risk factors of no-reflow. Previous studies have identified various predictors of no-reflow, which are different between studies, likely due to the differences in the populations being studied [2,3,9,10]. We aimed to identify the clinical and angiographic factors that predicted no-reflow in our contemporary cohort of consecutive patients with STEMI treated with primary PCI, and to determine the impact of no-reflow on mortality.

2. Methods

2.1. Study population

We reviewed the PCI database of The Canberra Hospital and identified 781 patients who presented as acute ST elevation myocardial infarction during 2008 to 2012. The creation and maintenance of the PCI registry was approved by the ACT Health Human Research Ethics Committee and all patients provided written consent for inclusion in the registry and follow-up. Demographic and procedural characteristics and the indication for the procedure were prospectively recorded and entered into the database. TIMI flow was measured retrospectively by a single experienced cardiologist who was blinded to the clinical data.

* Corresponding author at: Interventional Cardiology Fellow, Department of Cardiology, The Canberra Hospital, Garran, ACT 2605, Australia.
E-mail address: jawadmc2@gmail.com (J. Mazhar).
[1] This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

http://dx.doi.org/10.1016/j.ijcha.2015.11.002

The Canberra Hospital is the region's major public hospital, providing specialist and acute care to more than 700,000 people. We perform approximately 2000 diagnostic angiograms, 800 PCI and 150 primary PCI procedures per year.

2.2. Procedure

PCI procedures were performed through the femoral or radial artery using 6 Fr sheaths. All patients were treated with dual antiplatelet therapy including aspirin and either clopidogrel or prasugrel prior to the procedure. Aspirin was continued indefinitely and clopidogrel or prasugrel was recommended for 12 months. Intravenous heparin was administered to achieve an activated clotting time of 300 s. Adjunctive pharmacotherapy including the use of glycoprotein IIb/IIIa inhibitors and the type of stent were at the discretion of the interventional cardiologist. All patients underwent pre and post intervention ECG.

2.3. Assessment of coronary angiograms

All angiograms were reviewed by an experienced cardiologist blinded to the patients' outcome and follow-up status. Epicardial coronary blood flow was quantified visually using the Thrombolysis in Myocardial infarction (TIMI) flow grade classification [11]. Initial TIMI flow was assessed at the beginning of the procedure prior to wire insertion and final TIMI flow was assessed at the end of the procedure. No-reflow was defined as TIMI grade <3 at the end of the procedure in the absence of any coronary dissection or spasm. In the sub-group of patients that developed no-reflow, coronary flow was also assessed immediately before and after stent insertion in order to assess the influence of stent deployment on no-reflow. Coronary flow immediately before and after stent insertion was quantified by TIMI frame count in order to objectively determine any change in flow after stent insertion [11]. For this purpose, TIMI frame count (TFC) of >20 was defined as no-reflow. All angiograms were recorded at 15 frames/s.

Myocardial blush grading was not performed as most angiogram films were not acquired long enough to estimate the myocardial blush grade. Thrombus burden was estimated by using the thrombus scoring system proposed by the TIMI group [12].

2.4. Definitions and endpoints

The primary clinical endpoint for the study was all-cause mortality at 12 months. Other outcomes measured were re-infarction, stent thrombosis, transient ischemic attack (TIA) or cerebrovascular event (CVA), target lesion PCI, and coronary artery bypass grafting (CABG). MACE was defined as the composite of death, stent thrombosis, target vessel revascularization, re-infarction and stroke. Stent thrombosis was defined as definite stent thrombosis by angiography. MI was defined according to the third universal definition of MI [13]. Stroke was defined as a new focal neurological deficit following catheterisation or intervention lasting more than 24 h and confirmed by imaging. Cardiogenic shock was defined as a systolic BP <90 mm Hg or a requirement for inotropic therapy.

Symptom onset time was the time recalled by the patient as the onset of symptoms. First medical contact (FMC) was defined as the time of arrival of ambulance at the scene or patient arrival time at the first emergency department. Balloon time was defined as the time of first device used for reperfusion.

2.5. Data collection and follow-up

In-hospital clinical events were recorded by a research nurse prior to discharge. Long term follow-up was conducted by letter, phone calls and review of hospital records at 12 months. In case of adverse events, further details were obtained from the patient's medical records, physician or from other hospitals. We also obtained approval to access the Australian Institute of Health and Welfare National Death Index to obtain accurate data on vital status and date of death for our patients. We supplied the patients' name, date of birth and residential address and these parameters were matched with data on the national death index. We accepted a match when a patient on the national death index had the same name and date of birth as a patient in our registry.

2.6. Statistical analysis

Patients were categorised as having “normal flow” or “no-reflow” based on the final TIMI flow at the end of the procedure. The baseline clinical characteristics and procedural characteristics of the two groups were compared using the Student's t test for continuous variables and the chi-square test for categorical variables. Cox proportional hazard multivariate analysis was performed to determine predictors of death during follow-up. We also performed a multivariate analysis to determine predictors of no-reflow. Variables in the model included age > 60 years, gender, smoking status, diabetes mellitus, hypertension, cardiogenic shock, anterior MI, culprit vessel, thrombus score, three vessel disease, glycoprotein IIb/IIIa inhibitor use, use of >1 stent, total stent length, type B2/C lesion, symptom to first medical contact and symptom to balloon time. A p value <0.05 was considered significant. All statistical analyses were performed using SPSS Statistics for Windows, Version 22.0.

3. Results

Primary PCI was performed in 781 patients during 2008–2012. Seventeen patients were excluded for the following reasons; 1 patient had intravascular ultrasound (IVUS) and percutaneous coronary intervention (PCI) was not required, 12 patients had unsuccessful PCI, 4 patients did not have long term follow-up although they had no in-hospital adverse events. Therefore we had 764 patients with long-term follow-up for analysis. No-reflow was seen in 189 (25%) patients at the end of the procedure. The clinical characteristics of patients with final no-reflow or normal flow are shown in Table 1. Patients with no-reflow were older (64 ± 12 years vs. 61 ± 13 years, p = 0.02) and there was a trend for them to be less likely to be smokers (22% vs. 29%, p = 0.052).

The procedural characteristics are shown in Table 2. The normal flow and no-reflow groups were similar in terms of the culprit vessels involved, proportion of patients with three vessel disease (21% vs. 20%, p = 0.77) and total stent length per patient (24 ± 12 vs. 22.1 ± 11 mm, p = 0.06). Use of prasugrel (23% vs. 24%, p = 0.95) and drug eluting stents (22% vs. 22%, p = 0.96) was similar between the two groups. Balloon angioplasty alone was used more often in no-reflow group (10.6% vs. 2.6%, p = <0.0001). Patients with no-reflow were more likely to have initial TIMI flow of 0–1 (77% vs. 64%, p = 0.0007) and thrombus score ≥4 (83% vs. 69%, p = 0.0001). Glycoprotein IIb/

Table 1
Clinical characteristics of patients with normal flow and no-reflow.

	No-reflow n = 189 (25%)	Normal flow n = 575 (75%)	p value
Mean age (years)	64 ± 13	61.4 ± 13	0.023
Female sex	43 (23%)	131 (23%)	0.98
Diabetes	38 (20%)	97 (17%)	0.32
Hypertension	79 (42%)	236 (41%)	0.85
Smoker	42 (22%)	169 (29%)	0.052
Ex-smoker	36 (19%)	100 (17%)	0.61
Hyperlipidaemia	60 (32%)	171 (30%)	0.60
Family history of IHD	43 (23%)	154 (27%)	0.27
BMI	27.7 ± 5.4	27.2 ± 4.6	0.91
Prior PCI	27 (15%)	96 (17%)	0.42
Prior CABG	12 (6%)	22 (4%)	0.16

BMI = body mass index, CABG = coronary artery bypass graft, IHD = ischemic heart disease,
PCI = percutaneous coronary intervention.