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A Randomized Trial of Deferred Stenting Versus Immediate Stenting to Prevent No- or Slow-Reflow in Acute ST-Segment Elevation Myocardial Infarction (DEFER-STEMI)

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Objectives The aim of this study was to assess whether deferred stenting might reduce no-reflow and salvage myocardium in primary percutaneous coronary intervention (PCI) for ST-segment elevation myocardial infarction (STEMI).

Background No-reflow is associated with adverse outcomes in STEMI.

Methods This was a prospective, single-center, randomized, controlled, proof-of-concept trial in reperfused STEMI patients with ≥1 risk factors for no-reflow. Randomization was to deferred stenting with an intention-to-stent 4 to 16 h later or conventional treatment with immediate stenting. The primary outcome was the incidence of no-/slow-reflow (Thrombolysis In Myocardial Infarction ≤2). Cardiac magnetic resonance imaging was performed 2 days and 6 months after myocardial infarction. Myocardial salvage was the final infarct size indexed to the initial area at risk.

Results Of 411 STEMI patients (March 11, 2012 to November 21, 2012), 101 patients (mean age, 60 years; 69% male) were randomized (52 to the deferred stenting group, 49 to the immediate stenting). The median (interquartile range [IQR]) time to the second procedure in the deferred stenting group was 9 h (IQR: 6 to 12 h). Fewer patients in the deferred stenting group had no-/slow-reflow (14 [29%] vs. 3 [6%]; p = 0.006), no reflow (7 [14%] vs. 1 [2%]; p = 0.052) and intraprocedural thrombotic events (16 [33%] vs. 5 [10%]; p = 0.010). Thrombolysis In Myocardial Infarction coronary flow grades at the end of PCI were higher in the deferred stenting group (p = 0.018). Recurrent STEMI occurred in 2 patients in the deferred stenting group before the second procedure. Myocardial salvage index at 6 months was greater in the deferred stenting group (68 [IQR: 54% to 82%] vs. 56 [IQR: 31% to 72%]; p = 0.031].

Conclusions In high-risk STEMI patients, deferred stenting in primary PCI reduced no-reflow and increased myocardial salvage. (Deferred Stent Trial in STEMI; NCT01717573) (J Am Coll Cardiol 2014;63:2088–98) © 2014 by the American College of Cardiology Foundation

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Primary percutaneous coronary intervention (PCI) with stenting immediately after coronary reperfusion salvage procedures jeopardizes myocardium, improves prognosis, and is the current standard of care for acute ST-segment elevation myocardial infarction (STEMI) (1,2). No-reflow is defined as an acute reduction in myocardial blood flow despite a patent epicardial coronary artery (3). The pathophysiology of no-reflow involves microvascular obstruction

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secondary to distal embolization of clot, microvascular spasm, and thrombosis (3). No-reflow occurs in ~10% of cases of primary PCI and is associated with patient characteristics such as advanced age and delayed presentation and coronary characteristics such as a completely occluded culprit artery and heavy thrombus burden (3–7).

No therapies have been shown to prevent no-reflow, and when it occurs, treatment by administration of vasodilator drugs (8) and intra-aortic balloon counterpulsation therapy is empirical (2,3,8,9). The rationale for our intervention was to avoid the potential adverse effects of immediate stenting when the likelihood of no-reflow might be greatest. Deferred stent implantation might allow time for reduction in coronary thrombus burden and recovery of microvascular function such that the likelihood of no-reflow is reduced. We hypothesized that after initial coronary reperfusion and normalization of coronary blood flow, brief deferral of stenting might reduce the occurrence of no-reflow compared with usual care with immediate stenting and increase myocardial salvage. We investigated this hypothesis in a real-life clinical setting involving STEMI patients treated with primary PCI.

Methods

Trial design. We performed a prospective, randomized, controlled, parallel group trial in STEMI patients enrolled at a single center between March 11, 2012, and November 21, 2012. The trial was a proof-of-concept trial nested in a larger prospective cohort study (10).

Participants and eligibility criteria. Patients at risk of no-reflow were selected if radial artery access was used and ≥1 of the following inclusion criteria were met: 1) clinical history (3–7) that included myocardial infarction, increased age (i.e., 65 years of age or older), duration of symptoms >6 h; 2) culprit coronary artery abnormalities (3–7) including an occluded artery (Thrombolysis In Myocardial Infarction [TIMI] flow grade 0/1 [11]) at initial angiography, heavy thrombus burden (TIMI grade 2 or higher [12]), long lesion length (≥24 mm), small vessel diameter (i.e., ≤2.5 mm); 3) clinical signs of acute microvascular injury after initial reperfusion (3–7) with persistent ST-segment elevation >50%.

The exclusion criteria were 1) the absence of normal (TIMI flow grade 3) coronary blood flow after initial reperfusion with aspiration thrombectomy with or without balloon angioplasty. The residual severity of the culprit stenosis was not relevant to participation provided TIMI flow grade 3 was evident; 2) cardiogenic shock; 3) a contraindication to magnetic resonance imaging (MRI) (e.g., permanent pacemaker); 4) inability to give informed consent.

Abbreviations and Acronyms

ECG = electrocardiogram
IQR = interquartile range
MRI = magnetic resonance imaging
PCI = percutaneous coronary intervention
STEMI = ST-segment elevation myocardial infarction
TIMI = Thrombolysis In Myocardial Infarction

Setting. Consecutive STEMI patient admissions were screened for these inclusion and exclusion criteria. During ambulance transfer to the hospital, the patients received 300 mg aspirin, 600 mg clopidogrel, and 5000 IU unfractionated heparin (2,9). Catheter laboratory management is described in the Online Appendix.

Informed consent. Witnessed informed consent was verbally obtained after coronary reperfusion in eligible patients in the cardiac catheter laboratory. When the patient returned to the Coronary Care Unit, a patient information sheet approved by the local ethics committee was provided, and written informed consent was then obtained. The patients who were not randomized were included in a registry.

Randomization, implementation, and blinding. Randomization took place immediately after obtaining verbal consent using a Web-based computer tool with a concealed random allocation sequence provided by the independent clinical trials unit and implemented by the catheter laboratory physiologist. Randomization was on a 1:1 basis between usual care with immediate stenting and deferred stenting.

Interventions. The deferred PCI strategy involved an intention-to-stent 4 to 16 h after initial coronary reperfusion. This time interval was based on a balance between competing benefits and risks. A short minimum period (4 h) was adopted, given our concern about the theoretical time-related risk of coronary reocclusion. In practice, a guideline of at least 8 h was recommended for the deferred PCI to permit the beneficial effects of reperfusion and antithrombotic therapies and so that all patients could be treated between 7:00 AM and 11 PM during the first 24 h of admission to ensure that the second procedure occurred at a time that facilitated a rest period for the patient and the staff. Finally, an upper limit of 16 h was set to minimize any prolongation of the hospital admission.

The treatment protocol for deferred patients included transfer to the Coronary Care Unit, continuous intravenous infusion of glycoprotein IIb/IIIa inhibitor therapy (tirofiban 0.15 μg/kg/min) and administration of subcutaneous low molecular weight heparin (enoxaparin 1 mg/kg every 12 h) for up to 16 h. The radial artery sheath used for PCI was retained or removed according to operator and patient preference. Arterial blood pressure and the radial sheath site were monitored in the Coronary Care Unit. All patients also