Indian Heart Journal xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Indian Heart Journal

journal homepage: www.elsevier.com/locate/ihj

Original Article

Examination of the appropriate timing of reperfusion therapy for recent myocardial infarction: a Japanese single-center retrospective study☆,☆☆

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ARTICLE INFO

Article history:
Received 3 June 2016
Accepted 28 June 2017
Available online xxx

Keywords:
Recent myocardial infarction
Percutaneous coronary intervention

ABSTRACT

Background: The various guidelines clearly mention the treatment strategies for in patient of acute myocardial infarction (MI) presenting more than 24 h from symptom onset (recent myocardial infarction, RMI). However, the appropriate timing of reperfusion for RMI is unclear.
Methods: We retrospectively evaluated 525 consecutive MI patients who underwent percutaneous coronary intervention (PCI) in our hospital between January 2008 and December 2012.
Results: Sixty RMI patients were more frequently associated with cardiac complications such as myocardial rupture (3.3% vs. 0%; $p < 0.01$), ventricular septal rupture (3.3% vs. 0.4%; $p < 0.05$), and congestive heart failure (15% vs. 2.6%; $p < 0.001$) than 272 consecutive ST-elevation myocardial infarction (STEMI) patients. Of the 60 RMI patients, 33 (55.0%) underwent PCI within 7 days (early-PCI group) and 27 (45.0%) underwent PCI after 7 days (late-PCI group). Left ventricular ejection fraction measured by echocardiography at second hospital day was similar between the groups. The early-PCI group was more significantly associated with cardiogenic shock and heart failure and more frequently required intra-aortic balloon pumping (24.2% vs. 3.7%; $p < 0.05$) than the late-PCI group. There were no significant differences in 30-day mortality, cardiac complications, and major cardiac events during long-term follow-up (12–36 months) between the groups.
Conclusion: RMI patients had a higher incidence of cardiac complications than AMI patients. Clinical outcomes were similar between patients undergoing early revascularization and those undergoing late revascularization, although the former group included a higher proportion of patients with severe cardiac failure.

1. Introduction

Prognosis in ST-elevation myocardial infarction (STEMI) is reportedly inversely related to delay in reperfusion, and current guidelines recommend an early invasive strategy for high-risk non-ST-elevation acute coronary syndrome (NSTEACS) patients.[1–4] The various guidelines clearly mention the treatment strategies for in patient of acute myocardial infarction (MI) presenting more than 24 h from symptom onset (recent myocardial infarction, RMI).[5,6] However, the appropriate timing of reperfusion for RMI is unclear. So, we retrospectively investigated the difference of clinical outcome between the RMI patients underwent PCI within 7 days after admission and those who underwent PCI after more than 7 days after admission.

2. Methods

2.1. Study population

We retrospectively collected data from 525 consecutive MI patients in our hospital between January 2008 and December 2012. MI patients complicated with cardiopulmonary arrest out of the hospital (n = 33) and having the left main trunk culprit lesion (n = 23) and chronic total occlusion (CTO) lesions in a non-infarct-

☆ This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.
☆☆ The authors report no financial relationships or conflicts of interest regarding the content herein.
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http://dx.doi.org/10.1016/j.ihj.2017.06.015

related artery (n = 28) were excluded. MI was defined according to the "third universal definition of myocardial infarction" proposed by the Writing Group on behalf of the Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction.[7] Acute MI (AMI) was defined as MI diagnosed within 24 h from symptom onset, and recent MI (RMI) was defined as MI diagnosed after 24 h from symptom onset. Diagnostic ST-elevation is defined as new ST-elevation at the J point in at least 2 contiguous leads ≥2 mm (0.2 mV) in men or ≥1.5 mm (0.15 mV) in women in leads V_2–V_3 and/or of ≥1 mm (0.1 mV) in other contiguous chest or limb leads. This study included 381 AMI patients (including 272 STEMI patients) and 60 RMI patients. All RMI patients were Q wave MI.

The demographic, clinical, and angiographic characteristics of the patients as well as in-hospital and 30-day outcomes were investigated. Cardiogenic shock on admission was defined according to the following clinical criteria used in the SHOCK trial[8]: hypotension was defined as a systolic blood pressure of <90 mmHg for at least 30 min or the need for supportive measures to maintain the systolic blood pressure at ≥90 mmHg, and end-organ hypoperfusion was defined as cold extremities or a urine output of <30 mL/h and a heart rate of ≥60 beats/min.

2.2. In-hospital management

Coronary angiography (CAG) was performed immediately after the diagnosis of MI in all patients. PCI was performed as soon as possible in all AMI patients. In RMI patients, PCI for the culprit lesion was performed at the operator's discretion, depending on patient consent, the requirement for evaluation of coexisting diseases, and cardiac failure treatment before PCI. PCI in all patients was performed using intravascular ultrasound (IVUS). If attenuated plaques or massive thrombi were detected by IVUS or CAG, we performed thrombus aspiration and distal protection before stent implantation. A thrombus was defined as an intraluminal lobulated mass with evidence of blood flow (microchannels) within the mass, mobility, and a sparkling or scintillating appearance.[9] An attenuated plaque was defined as a hypoechoic plaque with deep ultrasound attenuation without calcification or a very dense fibrous plaque.[10]

CTO was defined as total occlusion of the artery lumen without anterograde flow or with flow (anterograde or retrograde) through collateral vessels in an artery other than the culprit artery. Door-to-balloon time was defined as the time between patient arrival at our hospital and the beginning of the mechanical reperfusion procedure. Door time was defined as the time of patient arrival at our hospital, indicated by the moment they took a number to be evaluated (before the patient was checked-in in that hospital area), which was automatically recorded by the information system. Balloon time was defined as the time of the first angioplasty balloon inflation or the first aspiration with an aspiration thrombectomy device. After the intervention, all patients were admitted to a coronary care unit. The patients underwent transthoracic echocardiography on day 1 after admission, and left ventricular ejection fraction (LVEF) was measured using the biplane method of discs (modified Simpson's rule). Left ventricular (LV) volume was measured in the apical 4-chamber and 2-chamber views. Serum creatine kinase isoenzyme levels were measured at baseline and at 3, 6, 9, 12, and 24 h after PCI.

2.3. Medications

All AMI and RMI patients received a loading dose of aspirin (200 mg) and clopidogrel (300 mg). During the procedure, intravenous unfractionated heparin was administrated to maintain an activated clotting time of 250–300 s, and the postprocedural use of intravenous unfractionated heparin was left to the operator's discretion in AMI patients. In all RMI patients, unfractionated heparin was administered as an intravenous bolus of 60 IU/kg (maximum, 4000 IU), followed by an infusion of 12 IU/kg/h (initial maximum, 1000 IU/h) that was adjusted to maintain an activated partial thromboplastin time of 1.5–2.0 times the control value. The intravenous infusion was administered for at least 48 h. All AMI and RMI patients took the statins, β-blockers and angiotensin converting enzyme inhibitors(ACEIs)/angiotensin receptor blockers(ARBs) as soon as possible after emergency CAG and primary PCI. There were no patients treated with fibrinolysis before primary PCI in the current study.

After discharge, aspirin was used indefinitely, clopidogrel was continued for at least 12 months, and other medications (e.g., statins, β-blockers, angiotensin-converting enzyme inhibitors) were used according to the current guidelines.[2]

2.4. Statistical analysis

All data were analyzed retrospectively. Categorical variables were expressed as numbers and percentages, and continuous variables were expressed as mean ± standard deviation. After testing for normal distribution, differences were compared using the unpaired Student's *t*-test, χ^2 test, or Fisher's exact test, as appropriate. Time-to-survival outcomes were analyzed using the Kaplan–Meier method. Cases were censored when death was observed. In order to compare time-to-survival outcomes between STEMI and RMI groups, *P*-values were calculated using the Cox regression stratified by matched pairs. All statistical analyses were performed with EZR (Saitama Medical Center, Jichi Medical University, Japan),[11] which is a graphical user interface for R (The R Foundation for Statistical Computing, version 2.13.0). More precisely, it is a modified version of R commander (version 1.6–3) designed to add statistical functions frequently used in biostatistics. A two-tailed *p*-value of <0.05 was considered statistically significant.

3. Results

3.1. RMI vs. STEMI

The 381 AMI patients included 272 STEMI patients and 109 non-STEMI patients. After propensity matching the remaining population (n = 120 [n = 60 RMI and n = 60 STEMI]), peak creatinine kinase level, creatinine clearance, and LVEF measured by echocardiography at second hospital day were significantly lower in the RMI group than in the STEMI groups (Table 1). However, there were no significant differences in 30-day mortality and the frequency of requiring intra-aortic balloon pumping (IABP) and cardiogenic shock between the RMI group and STEMI group. Moreover, there were no significant differences in the puncture site after PCI between the RMI group and STEMI group. After propensity score matching, prognosis during 5-year follow up of RMI patients was significantly poorer than STEMI patients (hazard ratio, 4.04; 95% confidence intervals, 1.76–9.26) (Fig. 1).

3.2. Early reperfusion vs. late reperfusion

Of 60 RMI patients, 33 (55.0%) underwent PCI within 7 days (early-PCI group) and 27 (45.0%) underwent PCI after 7 days (late-PCI group). The LVEF measured by echocardiography at second hospital day was similar between the groups. The early-PCI group was more significantly associated with cardiogenic shock and heart failure and more frequently required IABP (24.2% vs. 3.7%; $p < 0.05$) than the late-PCI group. Blood transfusion was performed more frequently in the early-PCI group than in the late-PCI group, although this difference was not significant (21.2% vs. 11.1%;

Please cite this article in press as: Y. Mizuguchi, et al., Examination of the appropriate timing of reperfusion therapy for recent myocardial infarction: a Japanese single-center retrospective study, Indian Heart J (2017), http://dx.doi.org/10.1016/j.ihj.2017.06.015