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## **ORIGINAL ARTICLE**

# Does high-dose intracoronary adenosine improve regional systolic left ventricular function in patients with acute myocardial infarction?



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#### **KEYWORDS**

Acute myocardial infarction; Adenosine; Primary PCI; Echocardiography; Tissue Doppler imaging **Abstract** *Background:* Reperfusion injury limits the beneficial effects of primary percutaneous coronary intervention (PCI) in the setting of acute myocardial infarction (AMI). Adenosine limits reperfusion injury in animal models.

*Objective:* Is to study the effects of high-dose intracoronary adenosine administration in the setting of primary PCI on coronary blood flow and regional left ventricular function.

Methods: Sixty patients with a definite diagnosis of ST elevation AMI within 6 h from the onset of chest pain were randomly allocated to receive adenosine (6 mg) or saline placebo (on a 1:2 ratio) as an adjunct to primary PCI with assessment of TIMI flow, TIMI myocardial blush grade (MBG), and occurrence of no-reflow. Systolic (S) wave velocity was recorded at the mitral annulus in the territory of the infarct related artery using pulsed-wave tissue Doppler within 24 h from admission and one week after PCI.

Results: Both groups showed no significant difference in terms of age, sex, risk factors, infarct location, and distribution of coronary artery disease. The adenosine group showed a higher incidence of TIMI III flow (95% vs. 65%, p < 0.03), a higher incidence of MBG 2-3 (95% vs. 67.5%,

Abbreviations: AMI, acute myocardial infarction; CK, creatine kinase; CTFC, corrected TIMI frame count; LV, left ventricular; MBG, myocardial blush grade; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction; TDI, tissue Doppler imaging

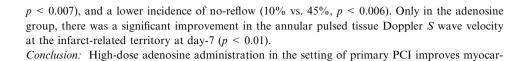
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dial perfusion and regional left ventricular systolic function.



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#### 1. Introduction

Early reperfusion of the ischemic myocardium by thrombolytic agents is effective in reducing mortality from acute myocardial infarction. However, better results, including further reduction in mortality and recurrence of ischemia, can be achieved with direct percutaneous transluminal coronary angioplasty.<sup>1</sup>

Unfortunately reperfusion is followed by morphological and functional changes that result in tissue damage known as reperfusion injury. Reperfusion injury results from several complex and interdependent mechanisms that involve the production of reactive oxygen species, alterations in intracellular calcium handling, endothelial cell dysfunction, altered myocardial metabolism, and activation of neutrophils, platelets and complement. Reperfusion injury is manifested as stunned myocardium, reversible microvascular injury, and lethal myocyte necrosis.<sup>3</sup>

Adenosine has been studied extensively as a cardioprotective agent. It antagonizes many of the biochemical and physiological mechanisms implicated in the ischemia reperfusion injury. It has been shown to replenish high energy phosphate stores in endothelial cells and myocytes, to inhibit oxygen free radical formation, to inhibit neutrophil activity, to participate in myocardial ischemic preconditioning, and to improve microvascular function,4 thereby reducing post-ischemic ventricular dysfunction, myocyte necrosis and apoptosis, and infarct size. An intracoronary bolus of adenosine 30–60 µg is recommended for prevention and treatment of no-reflow by the ESC guidelines for the treatment of STEMI (class IIb; level of evidence C). A small open-label clinical study has shown that intracoronary administration of 4 mg of adenosine is safe in patients with acute myocardial infarction, with favorable effects on TIMI flow grade, incidence of no-reflow, left ventricular function, and clinical course.

Encouraged by this data, we thought of studying the effects of high-dose intracoronary adenosine immediately before initial balloon inflation on coronary blood flow and regional left ventricular systolic function in acute myocardial infarction. In the design of the present study, we attempted to address some of the methodological limitations of earlier trials. First, we used tissue Doppler imaging (TDI) to assess the improvement in regional LV systolic function because it offers an objective measure to quantify regional LV function. Second, we administered the study drug sub-selectively to the ischemic myocardium. Third, we used a very high dose of adenosine, and last, we administered the intracoronary adenosine before initial balloon dilatation.

## 1.1. Objectives

The aim of this work is to study the effects of high-dose intracoronary adenosine administration in the setting of primary PCI on the coronary blood flow and regional left ventricular systolic function.

#### 1.2. Methodology

#### 1.2.1. Study population

This study included 60 patients referred to the Ain Shams University Hospital for primary PCI within 6 h from the onset of acute myocardial infarction.

Inclusion criteria were symptoms of chest pain lasting at least 20 min, not relieved by sublingual nitrates, and an ECG showing ST segment elevation > 0.1 mV in two or more limb leads or > 0.2 mV in two or more contagious precordial leads, or presumed new left bundle branch block. Presentation should be within 6 h from the onset of chest pain. The patient must have native coronary artery disease with TIMI flow from 0-2.

Exclusion criteria were hypersensitivity or contraindication to heparin, aspirin, or contrast media, receiving thrombolytic therapy, severe asthma, high grade AV block, or cardiogenic shock (systolic blood pressure (SBP) < 80 mmHg sustained for > 30 min, unresponsive to fluids, or SBP < 100 mmHg with vasopressors and/or requirement for intra-aortic balloon pump). Patients with spontaneous reperfusion (TIMI III flow at diagnostic coronary angiography) were excluded.

1.2.1.1. Study design. Eligible patients were randomly allocated (1:2) to receive adenosine or saline placebo. The study was approved by the medical ethics committee of our institution and all patients gave an informed consent before the procedure.

#### 2. Methods

### 2.1. Standard 12-leads electrocardiogram

The 12-lead ECG obtained on admission and after reperfusion was investigated for the degree of ST segment deviation from isoelectric line, which was measured manually to the nearest 0.5 mm in every lead at 0.08 s after J-point using preceding TP segment as a baseline. The magnitude of ST segment resolution was expressed as a percentage of initial ST elevation.

## 2.2. Invasive procedure

All patients received heparin (5000 IU), aspirin (150 mg), and clopidogrel (300 mg). The patients were subjected to diagnostic coronary angiogram through a femoral approach. PCI was performed using the standard technique for the culprit lesion only. After giving an additional bolus of heparin (5000 units), the obstruction of the infarct related artery was crossed with a 0.014 inch guidewire. An over-the-wire balloon was positioned at the level of the obstruction. The wire was pulled out, and

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