

***Incremental prognostic value of left ventricular mechanical dyssynchrony
assessment in patients with first acute anterior myocardial infarction
and its correlation with infarct size and clinical outcome***

Thesis submitted for partial fulfillment of MD degree in Cardiology

By

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INTRODUCTION

After successful reperfusion therapy in the hyperacute stage of acute myocardial infarction (MI), dysfunctional myocardial segments subtended by the infarct-related artery can follow two different natural courses: functional recovery or irreversible remodeling. Predicting functional recovery or remodeling remains an elusive goal of echocardiography (1).

The clinical importance of LV (left ventricular) remodeling was emphasized by White et al., who demonstrated that patients who died during follow-up after myocardial infarction had significantly larger LV volumes and lower left ventricular ejection fraction (LVEF) than survivors. As a consequence, early identification of patients with LV remodeling after myocardial infarction is of vital importance (2).

Several variables have been identified to predict an increase in LV volume and a decrease in LV ejection fraction after an acute MI. These include infarct size (3,4), anterior location (5), cardiac enzyme index (6), transmural extent of infarction (7), patency of infarct-related artery (8), end-systolic volume (ESV) (2), microvascular obstruction (9) and mitral deceleration time (10). However, these are interrelated risk factors and each measure reflects a different aspect of the disease state and none can currently be considered as definitive (11).

It has been demonstrated that LV dyssynchrony seems to be of considerable importance for response and prognosis after CRT (cardiac resynchronization therapy). Importantly, reverse remodeling of the LV more frequently occurs in patients with substantial LV dyssynchrony at baseline. In addition, patients with LV reverse

remodeling after CRT have a better prognosis than those without LV reverse remodeling (12-14).

Presumably LV dyssynchrony after acute myocardial infarction results in LV dilatation. Experimental and clinical reports have demonstrated that dyssynchrony results in decreased cardiac output, slowed relaxation rates, and reduced peak filling velocity, as well as increased myocardial energy demand (15-17). Furthermore, dyssynchronous contraction itself may result in redistribution of myocardial fiber strain and blood flow (18,19) and may be associated with abnormalities of myocardial perfusion (20,21). Abnormal patterns of contraction and myocardial stretch are likely to increase mechanical loading and myocardial work which could potentially impair functional recovery after ischemic injury and may negatively influence the contractility of residual viable myocardium, thus further impairing LV function (22).

Zhang et al. emphasized the significant impact of acute myocardial infarction on regional myocardial contractility and systolic LV synchronicity early in the course, even in the absence of QRS widening or bundle-branch block. They also concluded that the degree of LV systolic dyssynchrony was significantly larger in patients with anterior infarction compared to inferior infarction (11).

In a study published in 2010, Shin SH et al. have concluded that the contractile pattern may be an important determinant of post-myocardial infarction prognosis independently of global and regional contractile function. However, further studies are needed to support this hypothesis (23).

AIM OF THE STUDY

To assess the prognostic value of left ventricular mechanical dyssynchrony by tissue doppler after successful primary percutaneous intervention in patients with first acute anterior myocardial infarction and its correlation with infarct size, remodeling and clinical outcome.

PATIENTS AND METHODS

This study will be conducted on 50 patients admitted to Ain Shams University hospital and Ain Shams University Specialized Hospital (ASUSH) with acute anterior ST-segment elevation myocardial infarction (STEMI) who will undergo primary percutaneous intervention (PCI). Echocardiographic assessment of LV mechanical dyssynchrony of the patients will be compared with that obtained from 30 age- and gender-matched healthy subjects with no history of cardiovascular disease or systemic illness, with normal physical examination, electrocardiogram and echocardiographic examination.

Inclusion criteria:

Patients with anterior STEMI with symptom onset within the last 6 hours who are eligible for primary intervention for a totally occluded left anterior descending artery (LAD).

Exclusion criteria:

Patients who have one or more of the following will be excluded from the study:

1. Patients with cardiogenic shock or cardiac arrest.
2. Patients with left main disease or with concomitant significant lesion(s) in left circumflex and/or right coronary arteries.
3. Patients suffering from uncontrolled arrhythmia during the echocardiographic study.

4. Patients suffering from previous myocardial infarction.
5. Administration of primary thrombolysis prior to PCI.
6. Failed trial of successful reperfusion (TIMI “Thrombolysis In Myocardial Infarction” flow grade less than III).
7. Patients with pacemaker or CRT (cardiac resynchronization therapy) implanted before or after the index event.
8. Patients with previous history of dilated, hypertrophic or restrictive cardiomyopathies.
9. Patients with rheumatic heart disease with significant valvular stenosis or regurgitation.
10. Patients in which obtaining adequate two-dimensional echocardiographic images is not possible or in which there is improper visualization of the endocardium.

Methods:

- All eligible patients admitted to the coronary care unit with first acute anterior STEMI will receive 300 mg Aspirin, 600 mg clopidogrel prior to primary PCI, which is going to be performed according to the standard techniques. The goal will be to achieve TIMI flow grade 3 with less than 10% residual stenosis. Patients with unsuccessful reperfusion will be excluded from the study. All the patients will be subjected to the following:

1. Thorough history taking with special emphasis on:

- a. Age

- b. Risk factors for coronary artery disease (Hypertension, Diabetes mellitus and its duration, smoking status, dyslipidemia, family history and obesity).
- c. Onset of chest pain.
- d. Previous history of coronary artery disease (chronic stable angina, previous acute coronary syndrome, coronary angiography, percutaneous or surgical revascularization).
- e. Previous pacemaker or CRT implantation.

2. Thorough clinical examination with special emphasis on:

- a. Accurate assessment of vital data.
- b. Signs of cardiac pump failure or other complications of acute myocardial infarction.

3. Twelve lead surface electrocardiogram (ECG):

- a. Recorded on admission for assessment of:
 - Site of infarction.
 - Presence of complications as conduction abnormalities or arrhythmias.
 - QRS duration.
- b. Recorded 90 minutes after passage of the first wire during primary PCI.

4. Procedural data:

- Detecting door-to-balloon time.
- TIMI flow grade.

5. Creatine Kinase(CK), and Creatine Kinase-myocardial band(CK-MB):

Measured on admission and every 8 hours for 24 hours to detect peak enzymatic elevation.

6. Standard transthoracic two-dimensional echocardiographic examination done within 48 hours of admission:

M-mode , two-dimensional, tissue doppler as well as pulsed and continuous Doppler flow across the different heart valves in all the standard views will be done with particular emphasis on

- a. Left ventricular end diastolic and endsystolic diameters (LVEDD, LVESD) using short axis parasternal window at the level of papillary muscles.
- b. Left ventricular end diastolic and endsystolic volumes using biplane Simpson's method (LVEDV, LVESV).
- c. Left ventricular ejection fraction using biplane Simpson's method.
- d. Mitral regurgitation; its presence and severity.
- e. Left atrial diameter in parasternal short axis view; left atrial volume index.
- f. Wall motion score index.
- g. Calculate E/E'(mitral peak early filling velocity/peak mitral lateral annular velocity in early diastole).

7. Echocardiographic assessment of left ventricular mechanical dyssynchrony encompassing:

- a. M-mode to assess septal-to-posterior wall-motion delay (SPWMD).
- b. Color-coded tissue doppler imaging will be performed (in both MI and control groups) in order to:

- i. Calculate the time-to-peak systolic velocity (Ts) of twelve segments of the left ventricle (the six basal and six middle segments).
- ii. Calculate the systolic dyssynchrony index (Ts-SD) which is the standard deviation of the Ts of the twelve segments of the left ventricle mentioned above.

8. **Gated SPECT (single photon emission CT) study** will be done before discharge to determine the final infarct size using a Gamma camera system (Philips Medical Systems) after intravenous injection of Tc-99m .

9. **Follow-up:**

All the patients will be kept on aspirin, clopidogrel (for at least 3 months), statin, angiotensin-converting enzyme inhibitor (ACEI) and beta-blocker (BB) according to their tolerance with 6-month follow-up for:

- a. MACE (major adverse cardiac events) within the 6 month follow up period which include : mortality, reinfarction, rehospitalization and ischaemic target lesion revascularization.
- b. Occurrence of LV remodeling assessed by echocardiography.

Statistics

All data will be gathered, tabulated and statistically analyzed using a commercially available statistical software package and the results will be thoroughly discussed.

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