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Correlation of Acute Change in Left Ventricle End diastolic Pressure after Primary Percutaneous Coronary Intervention with cardiac biomarkers in Patients with ST Segment Elevation Myocardial Infarction

Thesis* Submitted *by

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ACC	American College of Cardiology
ACS	Acute coronary syndrome
AHA	American Heart Association
AMI	Acute myocardial infarction
ANP	Atrial natriuretic peptide
ASE	American Society of Echocardiography
ATP	Adenosine Triphosphate.
BNP	Brain natriuretic peptide
BP	Blood pressure
Ca^{2+}	Calcium ion
CABG	coronary artery bypass grafting
CAD	Coronary artery disease
CHF	Congestive heart failure
CK	Creatine Kinase
COP	cardiac output
CRP	C-Reactive protein
CTFC	The Corrected TIMI Frame Count
cTnI	Troponin I
CVS	Cerebrovascular stroke
ECG	electrocardiography
ESC	*European Society of Cardiology*
EDV	End diastolic volume
EF	Ejection fraction
ESV	End systolic volume
FBS	Fasting Blood Sugar
FH	Family history
GP	Glycoprotein
HDL	High-density lipoprotein
HF	Heart failure
HTN	Hypertension
IHD	Ischemic heart disease
LA	Left atrium
LAD	Left Anterior descending
LBBB	left bundle branch block
LCX	Left circumflex artery.
LDL	Low density lipoprotein
LVEDP	left ventricle end-diastolic pressure
LV	Left Ventricle
LVEF	left ventricular ejection fraction
LVSD	left ventricular systolic dysfunction
LVSF	left ventricular systolic function

MACE	Major Adverse Cardiovascular end points.
MBG	Myocardial Blush Grade
MRI	magnetic resonance imaging
MVD	Multivessel Disease.
PCI	Primary percutaneous intervention
PPCI	primary percutaneous coronary intervention
PT	Prothrombin Time
PTCA	Percutaneous transluminal coronary angioplasty
P value	Probability value
RBS	Random Blood Sugar.
RCA	Right Coronary Artery
RR	Relative risk
RV	Right ventricle
SPECT	single-photon emission computed tomography
STEMI	ST segment elevation myocardial infarction
TDI	tissue Doppler imaging
TFGs	TIMI Flow Grades
TIMI	Thrombosis In Myocardial Infarction
TL	thrombolysis
TMPG	TIMI Myocardial Perfusion Grade
UA	Unstable angina
Vp	velocity propagation

Contents

Introduction

ST segment elevation myocardial infarction (STEMI) constitutes 40% of all acute myocardial infarctions (AMI), which continues to be a significant public health problem in both developed and developing counties (1).

Primary percutaneous intervention (PCI) is now classified as class I indication in STEMI in the Guidelines of the European Society of Cardiology (ESC) (2).

Reperfusion therapy is the cornerstone of the treatment of patients with acute ST elevation myocardial infarction (STEMI) (3). Many randomized clinical trials have shown that primary percutaneous coronary intervention (PCI) is superior to thrombolytic therapy in the treatment of patients with STEMI (4).

The aim of reperfusion therapy for many years has focused on achieving epicardial artery patency at the site of the occlusive thrombus. It is now possible, through advances in interventional techniques and adjunctive pharmacological treatment, to achieve TIMI (Thrombosis In Myocardial

Infarction) grade 3 epicardial flow (normal) in 95% of patients(5,6).

Despite this achievement, mortality, although declining, still remains high **.** This is possibly because despite restoration of TIMI grade 3 flow, 40% of patients do not achieve microvascular flow, which should be the goal of reperfusion therapy (7).

Successful primary PCI within 3–24 hours of the onset of chest pain has been associated with improved LV systolic function at a mean follow-up period of 22 months (8).. Other studies of primary PCI have also reported improved LV systolic function compared to thrombolysis (9).

In acute myocardial infarction (MI), decreasing compliance of the left ventricle is directly associated with prognosis(10). In patients with ST segment elevation MI (STEMI), left ventricular filling pressure increases(11,12).

Early improvement of perfusion after MI will improve left ventricle function and decrease the infarction area, thus decreasing mortality(13,14). The efficacy of reperfusion treatment may be shown indirectly with electrocardiography (ECG), by regression of ST elevation, but there is a need for methods to

demonstrate left ventricle and microvascular function improvement[15] .

Primary percutaneous coronary intervention (PCI) is regarded as the best reperfusion model in STEMI. PCI may be used to show hemodynamic changes in the left ventricle or to measure left ventricle end-diastolic pressure (LVEDP) for evaluation of reperfusion efficacy and success.

studies have now demonstrated a robust association between BNP or NT-proBNP and the short- and long-term risk of death across the spectrum of non-ST-elevation ACS,[16-18]. including patients without myocardial necrosis or clinical evidence of heart failure. In some patients with ACS, elevated levels of BNP directly reflect the degree of left ventricular dysfunction resulting from acute myocardial infarction. However, the strong association between levels of BNP/NT-proBNP and mortality among patients without measurable myocyte necrosis (i.e., release of cardiac troponin) indicate that the level of BNP may reflect the extent or severity of the ischemic insult, even when irreversible injury has not occurred.[18]

These findings suggest that transient ischemia may induce BNP synthesis and release in proportion to the severity of myocardial ischemia. As such, BNP adds a new dimension to

our ability to quantify the consequences of acute myocardial ischemia.

Aim of the work

The aim of this study is to assess the value of LVEDP measurement **before and after restoration of coronary artery patency** in the cath lab, in the setting of primary PCI, in predicting the success of reperfusion among patients with STEMI undergoing primary PCI and correlating the LVEDP change with the peaking of cardiac enzymes,ST segment resolution,chest pain relief, LV dysfunction and with the change in the level of BNP before and after primary PCI.

Chapter 1 Diastolic dysfunction in Acute Coronary Syndrome

[A] HISTORY:

Left ventricular diastolic function plays an important role in myocardial performance[19]. Events that occur during diastole are crucial to effective systolic function; defects in lusitropy (the ability of the myocytes to relax) have been implicated as an early sign of the development of congestive heart failure[20]. The lusitropic state is influenced by both biochemical and biomechanical events (active relaxation) in addition to the biophysical properties of the heart (passive stiffness)[21] .

To demonstrate the importance of assessment of left ventricular end-diastolic pressure (LVEDP) in patients presenting with acute myocardial infarction (STEMI), we will try to focus on the diastolic side of the hemodynamics of the heart.

[B] INTRODUCTION:

As pointed out by Henderson in 1923, diastolic relaxation of the heart is a vital factor and not merely the passive stretching of a rubber bag (22).

Normal LV diastolic function refers to the capacity to fill and maintain stroke volume without a compensatory increase of atrial filling pressure, either in rest or during exercise.

Events that precipitate diastole include both active (intramyocardial) and passive (extramyocardial) mechanisms [21].

Active events that occur within cardiac myocytes include:

- ✧ Ca2+ regulation.
- ✧ myofilament structure and function alteration.
- ✧ neurohormonal activation.

Passive events that influence relaxation include: Changes in early diastolic load and afterload [23].

[C] DEFINITIONS OF DIASTOLE:

1. Physiological diastole:

The term Diastole is derived from two Greek words, to send apart "expand". Physiological diastole commences as left ventricular pressure starts to fall after the peak of ejection phase and extends to the onset of isovolumetric contraction with the term protodiastole being applied to the early part of the relaxation phase-from when aortic flow begins to fall until aortic valve shuts (24).

2. Cellular diastole:

At the cellular level diastole can be considered as beginning when ATP hydrolyses and actin–myosin cross bridges become unlinked

allowing for sarcomeric relaxation. This is integrally related to decreasing intracellular concentrations of calcium owing to enhanced sarcoplasmic reuptake of calcium.

Like systole, diastole is an active process. Dysfunction at the cellular level is mediated principally viadecreased ATP hydrolysis and/or impaired uptake of the intracellularcalcium. Additionally,in the case of regional ischemia, there may be regional cellularimpairment such that the heart ceases to function as a syncytium (24).

3. Mechanical diastole:

Diastole is considered to begin when the pressurewithin the left ventricle begins to fall duringthe isovolumic relaxation phase. This would occur after a significantnumber of myocardial cells had entered cellular diastole andin a metabolically active process. The left ventricular pressurewill continue to fall rapidly, with opening of the mitral valveoccurring when the left ventricular pressure falls below theleft atrial pressure (24).

4. Clinical diastole:

In contrast, cardiological diastole is demarcated by the heart sounds and extends from closure to the aortic valve (A2) to the start of the first heart sound (M1) with the term protodiastole being applied to the early phase of rapid filling, the time when third heart sound can be heard (25).

5. Electrocardiographic diastole:

On an electrocardiogram, diastole is the period between the end of the T wave and the beginning of the QRS complex (26).