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Evaluation of Patients with Myocardial Infarction Undergoing Percutaneous Coronary Intervention (PCI) Using Low Dose Dobutamine Stress Echocardiography

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Background: *Coronary artery disease (CAD) is a spectrum of heart diseases which has the highest mortality in the world. Dobutamine stress echocardiography (DSE) has emerged as a versatile and simple tool to assess myocardial function and has been used extensively to determine myocardial viability and predict reversibility of ischemia induced reduction in functional parameters.*

Aim of study: *assess the function and viability of ischemic myocardium of left ventricle (LV) before and after percutaneous coronary intervention (PCI) by using low dose dobutamine stress echocardiography (LDDSE) and to know the usefulness of low dose dobutamine (LDD) test in detecting the viable ischemic LV area.*

Method: *DSE was performed in 30 Iraqi patients (mean age **39-74** years; mean ejection fraction **45.8±7.96**%) with previous myocardial infarction (MI) (ischemia before more than 30 days) who were referred to Ibn Al-Bitar Specialized Center for Cardiac Surgery in Iraq-Baghdad for evaluation of LV myocardial function and viability and possible need for coronary angiography Between October 2016 to June 2018. Visual assessment of the regional LV systolic function was performed at the time of examination using a 17-segment model of the LV. The scores of all segments are summed to obtain the LV wall motion score (WMS) which is divided by the number of scored segments to obtain a wall motion score index (WMSI).*

Viability was predicted by WMS if function augmented during LDDSE. Regional and global functional recovery was defined by side-by-side comparison of echocardiographic images before and (3-6) months after revascularization.

Result: *there was significant decrease in WMSI from (1.9±0.33) before dobutamine to (1.69±0.3) after dobutamine. Then there was a significant relative increase in WMSI from (1.69±0.30) after giving 5 μg/kg/min dobutamine to (1.78±0.31) after giving 10 μg/kg/min dobutamine (P value 0.003). While there were no significant differences in WMSI after low dose dobutamine (1.69±0.3) with the same parameters 3-6 months after PCI (1.64±0.38). Also there were significant improvements of LV function after doing PCI as assessed by WMSI and EF.*

Conclusion: *WMSI during DSE is valuable tool to assess ischemic LV function and to evaluate its viability and predict of LV function improvement after doing PCI for the diseased artery.*

Key words: *Left ventricle, dobutamine stress echocardiography, wall motion score index, ejection fraction and percutaneous coronary intervention.*

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I. Introduction

Coronary artery disease (CAD) is a spectrum of heart disease which has the highest mortality in the world. Systolic LV function is an important predictor of outcome and its precise assessment remains of great importance for the choice of treatment in populations with MI (1). Echocardiography remains the most commonly used comprehensive cardiac imaging modality and is often the first test of choice for assessing cardiac structure and function (2).

DSE has emerged as a versatile and simple tool to assess myocardial function and has been used extensively to determine myocardial viability and predict reversibility of ischemia induced reduction in functional parameters. Dobutamine is a synthetic catecholamine (resulting from the modification of the chemical structure of isoproterenol) that causes both inotropic and chronotropic effects through its affinity for β1, β2, and α receptors in the myocardium and vasculature. Because of differences in affinity, the cardiovascular effects of dobutamine are dose dependent that has predominant inotropic (increase contractility) effects when used at lower doses (less than 10 μg/kg/min) via its effect on β1-adrenergic receptors in the heart followed by a progressive chronotropic response at increasing doses. Dobutamine also has effects on β2-adrenergic and α1- adrenergic receptors, leading to a balanced effect on the peripheral vasculature at lower doses (3).

Aim of study: assess the function and viability of ischemic myocardium of LV before and after PCI by using LDDSE and to know the usefulness of LDD test in detecting the viable ischemic LV area.

Subjects and Method

Thirty patients (mean age **39-74 years; 28** were men; mean ejection fraction (EF) **45.8±7.96**%) with old MI (ischemia before more than 30 days ago) and regional wall motion abnormality with or without L dysfunction who were referred to Ibn Al-Bitar Specialized Center for Cardiac Surgery in Iraq-Baghdad were included in a prospective cohort study between October 2016 to June 2018 and consent form were taken from each subject.

Echocardiography

Baseline Two dimensional (2D) echocardiographic examination was performed before dobutamine infusion in all patients by using a GE (Vivid E9) ultrasound machine equipped with the 2.5 MHz S5-1 transducer including standard 2D apical four- and two-chamber view (4C, 2C).

LV ejection fraction (EF) was computed using the Simpson biplane method from 2C and 4C apical views.

LVEF= ((LVEDV-LVESV)/LVEDV)*100% (2)

Dobutamine Stress Echocardiography (DSE)

On completion of the baseline echocardiographic study, the four standard views were obtained in digital format using stress echocardiograph software,

Patients were prepared for standard stress testing, Intravenous access is obtained and LDDSE was performed. (LDD) ((No.1 Biochemical Pharmaceutical Co., Ltd. Shanghai, China) infusion was administered using automated infusion pump (TE331, Terumo, Japan). Dobutamine was delivered intravenously using 3 minutes staged protocol starting from 5 μg /kg/min for 3 minutes, then 10 μg /kg/min for another 3 minutes period, then 3 minutes recovery without dobutamine.

The LV was divided into 17-segment model according to the standards of the American Heart Association (AHA). Images were obtained from apical five, four & two chamber views, and were stored digitally at rest, at 5 μg/kg/min and at 10 μg/kg/min LDD for analysis (4).

Patients were continuously monitored by electrocardiogram (ECG) and blood pressure (by cuff method) measurements during LDD test.

Dobutamine infusion was intended to be terminated if one of the following indications had occurred:

- Severe chest pain or intolerable side effects.
- 85% of age-related maximum predicted heart rate.
- ST-segment elevation >1 mm in leads without a Q wave
- Horizontal ST-segment depression > 2 mm in any lead.
- Significant ventricular or supraventricular arrhythmias.
- Uncontrolled systemic hypertension ≥ 180/110 mmHg or Hypotension (5).

Visual assessments of LV function

Visual assessment of the regional LV systolic function was performed at the time of examination using a 17-segment model of the LV. Each segment was analyzed individually and scored on the basis of its motion and systolic thickening. According to the recommendations of the American Society of Echocardiography and European Association of Cardiovascular Imaging (6), each of 17 LV segments wall motion was scored semiquantitatively as:

1 is given for normokinesia or hyperkinesias,
2 for hypokinesia,
3 for akinesia, and
4 for dyskinesia or aneurysm

WMSI was calculated both in resting conditions and during stress and represents an integrated (although simple and easy to obtain) measurement of the extent and severity of ischemia.

WMSI is computer independent (visual assessment) and obtainable within a few seconds.

The segmentation of the LV also represents the anatomical background for rapid (real-time) semi-quantitative assessment of wall motion. Numerical values can be assigned to any segment corresponding to the degree of wall motion abnormality.

Myocardial response to Dobutamine

All stress echocardiographic diagnoses can be easily summarized in four equations centered on regional wall function and describing the fundamental response patterns: normal, ischemic, viable, and necrotic.

The corresponding stress echocardiography patterns are displayed as follow:

- normal response, a segment is normokinetic at rest and normal or hyperkinetic during stress.
- In the ischemic response, the function of a segment worsens during stress from normokinesis to dyssynergy.
- In the viable response, a segment with resting dysfunction improves during stress.
- In the necrotic response, a segment with resting dysfunction remains fixed during stress. A resting akinesia that becomes dyskinesia during stress reflects a purely passive, mechanical phenomenon of increased intraventricular pressure developed by normally contracting walls and should not be considered a true active ischemia. It is conceptually similar to the increase in ST-segment elevation during exercise in patients with resting Q waves (7).

Revascularization and Follow-Up

The indication for coronary angiography in the study subjects was determined by the clinical judgment of the referring providers including all the patients with abnormal DSE with viable myocardium. The detailed for coronary artery anatomy, including the location and the severity of stenosis were derived from our cardiac catheterization laboratory database in Ibn-Albitar Cardiac Center.

All patients underwent coronary diagnostic angiography and subsequent revascularization after dobutamine stress test. Significant coronary artery disease was defined as >70 % luminar diameter stenosis in at least one of the three major coronary arteries (2).

Follow-up 2D echocardiography was performed (3-6) months after revascularization. Segments with resting dysfunction that were adequately revascularized we deemed viable if regional function had improved on side-by-side comparison with pre PCI results.

II. Results

The General characteristics of the study groups

Table (1) showed baseline characteristics of 30 patients illustrating the mean age and gender also the number of patients presented with the risk factors including hypertension, diabetes mellitus, hypercholesterolemia and smoking.

Table (1): Baseline characteristics of the study group

Variable		Value
Age (years)	**Mean ± SD**	**53.97±9.31**
	Range	**39-74**
Gender	**Male**	**28 (93.3%)**
	Female	**2 (6.7%)**
Hypertension	**Present**	**24 (80.0%)**
	Not present	**6 (20.0%)**
Diabetes mellitus	**Present**	**10 (33.3%)**
	Not present	**20 (66.7%)**
Hypercholesterolemia	**Present**	**22 (73%)**
	Not present	**8 (27%)**
Smoker	**Present**	**18 (60%)**
	Not present	**12 (40%)**

Dobutamine echocardiography and visual assessment of ischemic LV

WMSI were measured before and after 5 μg/kg/min dobutamine as shown in table (2). We noticed that there was significant decrease in WMSI before dobutamine from (1.9±0.33) to (1.69±0.3) after dobutamine.

Table (2): Comparison between patients in the study group at rest and after 5 μg/kg/min dobutamine

Parameter	before 5 μg/kg/min dobutamine (at rest)	After 5 μg/kg/min dobutamine	P value
WMSI	**1.9±0.33**	**1.69±0.3**	**<0.001∗**

All parametric data expressed in the mean and standard deviation (SD)

∗ P value less than or equal to 0.05 was considered as statistically significant

WMSI=wall motion score index

Regarding table (3) which revealed that there was a significant increase in WMSI from (1.69±0.30) after giving 5 μg/kg/min dobutamine to (1.78±0.31) after giving 10 μg/kg/min dobutamine (P value 0.003).

Table (3): Comparison between patients in the study group after giving 5 μg/kg/min and after 10 μg/kg/min dobutamine

parameter	After 5 μg/kg/min dobutamine	After 10 μg/kg/min dobutamine	P value
WMSI	**1.69±0.30**	**1.78±0.31**	**0.003∗**

All parametric data expressed in the mean and standard deviation (SD)

∗ P value less than or equal to 0.05 was considered as statistically significant

WMSI=wall motion score index

Table (4) which showed that there were no significant differences in WMSI after low dose dobutamine (1.69±0.3) with the same parameters (3-6) months after PCI (1.64±0.38).

Table (4): Comparison between patients in the study group after giving 5 μg/kg/min dobutamine and after doing PCI

Parameter	After 5 μg/kg/min dobutamine	After PCI	P value
WMSI	1.69±0.3	1.64±0.38	0.243

All parametric data expressed in the mean and standard deviation (SD)
WMSI=wall motion score index

As showed by table (5) there was significant differences in WMSI and EF before and after PCI.

Table (5): Comparison between patients in the study group before and (3-6) months after PCI using different parameters of echocardiography

Parameters	Before PCI	After PCI	P value
WMSI	1.9±0.33	1.64±0.38	<0.001*
EF%	45.8±7.96	54.7±7.2	<0.001*

WMSI=wall motion score index
EF= ejection fraction.

III. Discussion

The mean age of the study population was 53.97±9.31 years and most of them were men. Eighty percent of the patients had hypertension and about (33.3%) are diabetics. Seventy four percent have their total cholesterol >250 mg /dl and 60% were smoker. These findings were expected in those ischemic heart disease patients as the mentioned risk factor is common in these selected patients (8).

Revascularization has become an important therapeutic strategy for patients with old MI. However, the prognosis is dependent on the ratio of viable muscles (VM). Therefore, preprocedural identification of VM segments of the impaired myocardium is mandatory (9).

WMSI reflects the magnitude of myocardial damage and total extent of wall motion abnormalities. It has been described that a combined analysis of LVEF and WMSI seems preferable to the measurement of LVEF alone. The presence of hypercontractile segments may limit the reduction in systolic function measured by LVEF without limiting it when measured with WMSI since it is based on the contractility of each segment and scores equal the hypercontractile and normal segments. The main difference between WMSI and LVEF is that the WMSI rates equally normokinesia and hyperkinesia, avoiding the compensation that hypercontractile segments make on the dysfunctional ones in the measurement of LVEF and therefore assessing more directly the intensity and extent of the myocardial damage (10).

From our results we noticed that there were significant increases in global ischemic LV functions as assessed by WMSI after giving a baseline dose of dobutamine (5 μg/kg/min), then a significant relative decrease in LV functions after giving a second dose of dobutamine (10 μg/kg/min) (biphasic response which is defined as increased contractility in resting dysfunctional myocardium at low dose but deterioration of contractility at peak doses due to demand/supply mismatch that leads to ischemia), these results were considered as an indicator of viable ischemic myocardial segments because dobutamine is an adrenoreceptor agonist, and a low dose can improve myocardial systolic function by enhancing coronary blood flow and these results are in agreement with Joyce et al., 2015 who found that the hallmark of viability assessment with DSE is the identification of contractile reserve, defined as resting myocardial dysfunction that recruits in response to inotropic stimulation with dobutamine (11).

Also Lang et al; 2016 stated that myocardium that is dysfunctional at rest but improves in response to low-dose dobutamine (less than 20 μg/kg/min) is considered to be viable (12).

And by comparing the results of WMSI after giving LDD with that after doing PCI, it was noticed that there were no significant differences in values, this mean that dobutamine test is a valuable indicator test for viability. This is similar to conclusion of Allman et al., 2002 who demonstrates a strong association between myocardial viability on noninvasive testing and improved survival after revascularization in patients with chronic CAD and LV dysfunction (13).

The use of WMSI can give use an idea about the regional and global LV wall functions at the same time, this measurement is very useful to assess the possible improvement and viability for LV region supplied by the culprit diseased artery.

Then we followed up those groups within 3-6 months after PCI, this time limit was used to avoid as possible, the effect of the DES-ISR (drug eluting stent-in stent restenosis), (Restenosis was defined by quantitative coronary angiography as the recurrence of 50% diameter narrowing in a coronary segment that had previously been dilated), and giving the time for enabling the detection of those segments of viable myocardium that recovered slowly. This time limit was used also by Pleva et al., 2018 who stated that the presence of DES-ISR can appear from 6–9 months after the PCI intervention (14).

IV. Conclusion

WMSI during DSE is valuable tool to assess ischemic LV function and to evaluate its viability and predict of LV function improvement after doing PCI for the diseased artery.

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