INTRODUCTION

Large numbers of patients referred for evaluation of chest pain are unable to perform adequate, diagnostic exercise testing. In these patients, dobutamine stress echocardiography (DSE) represents an alternative, exercise –independent stress modality.

Dobutamine stress echocardiography is an accurate, non invasive technique in detecting CAD, its sensitivity, specificity and accuracy for the detection of CAD are 80%, 84% and 81% ***(Geleijnse et al., 1997).*** However, this approach is subjective and relies on operator experience and doesn’t attempt to define the distal ischemic substrate ***(Hoffmann et al., 1996).***

The current ASE guidelines recommend the interpretation of 15 DSE per month to maintain interpretation skills. This intensive exposure is not frequent, therefore, it was necessary to develop a more quantitative method to overcome the above mentioned limitations ***(Armstrong et al., 1988).***

Several new ultrasound techniques have been developed to quantify dobutamine stress, this includes tissue Doppler velocity imaging (TVI), its derivatives, regional strain/strain rate imaging (S/SR) and two-dimensional (2d) strain based on speckle tracing.

Regional Doppler tissue velocities in one area, however, are affected by motion in adjacent tissue and therefore might not differentiate between active contraction and passive motion. This might be the limitation of this technique ***(Edvardsen et al., 2001)*.**

Strain (change in length per unit length) reflects deformation of a structure and therefore directly describes the contraction/relaxation pattern of the myocardium ***(Mirsky et al., 1973)***.

Strain measurements exclude the effects from adjacent regions avoiding errors produced by translational motion and tethering ***(Weidemann et al., 2002)*.**

Myocardial strain may be measured using a variety of echocardiographic technique, the current era of myocardial strain measurement began with the measurement of SR from comparison of adjacent tissue velocities (tissue velocity imaging strain). Subsequently, strain has been measured using speckle tracking techniques using ultrasonic reflectors (speckles) within tissues that can be followed from frame to frame through the cardiac cycle.

Each of these methodologies presents its own clinical challenge ***(Marwick et al., 2006).***

AIM OF THE WORK

The aim of the present study to compare the feasibility and accuracy of two-dimensional strain derived from speckle –tracking and tissue velocity imaging (TVI) derived strain during dobutamine stress echocardiography in patient with ischemic heart disease.

DOBUTAMINE STRESS ECHOCARDIOGRAPHY

Introduction:

Continuous improvement in ultrasound techniques and image acquisition led to the development of a new non invasive test known as **stress echocardiography** which was first described in 1979 by Wann and colleagues ***(Wann et al., 1979)***.

It is based on the principle which states that during stress induced ischemia, the decrement in contractile function is directly related to decrease in regional subendocardial blood flow, a principle proposed by Gallagher ***(Gallagher et al., 1983)*** and by Ross ***(Ross, 1987).***

Dobutamine pharmacology:

Dobutamine is a synthetic catecholamine analog of dopamine that bind to beta 1 and beta 2 adreno receptors (in its dextro form) and to a lesser extent to alpha 1 postsynaptic adreno receptors (in its levo form) ***(Rufflo, 1987)*** it has a half life of 2 minutes and reach a steady state after 10 minute of continuous intravenous infusion, it is metabolized mainly in the liver ***(Hoffman et al., 1990).***

Hemodynamic effects:

Dobutamine increases coronary blood flow 6 fold in normal as well as diseased arteries ***(Rude et al., 1982)*** some experimental results indicates in severe coronary artery disease dobutamine can induce inhomogenous flow and subsequent ischemia ***(McGillem et al., 1988).*** Dobutamine has strong inotropic, lusitropic effect increasing cardiac output by 52%, mean arterial pressure by 25%, heart rate by 10% and relaxation velocity by 41% ***(Lunkerheimer et al., 1992)*** patient who experience ischemia during DSE has decrease in stroke volume without increase in end-diastolic pressure.

These findings which contrast to response to ischemia induced by exercise or atrial pacing stress test is explained by absence of increase venous return during dobutamine administration ***(Pierard LA, et al., 1989).***

DSE protocol and interpertation:

Most echocardiography laboratories use a standard protocol for evaluation of coronary artery disease (CAD) ***(Geleijnse et al., 1997)*** in all patients after obtaining consent and after 3 hours being fasting, basal blood pressure, heart rate, ECG and 2-dimensional echo are performed then dobutamine is infused with a mechanical pump infusion is initiated at 5 µg/kg/min, and the dose increased every 3 min to 10, 20, 30, and finally 40 µg/kg/min. If 85% of the age-predicted maximal heart rate is not achieved, atropine is given (0,25 mg /min with a maximum of 1 mg) until the target heart rate is achieved or one of the end point is achieved.

Standard end-points were used, including termination of the protocol, development of severe angina or other intolerable symptoms, development of hypertension (systolic pressure >230 mmHg and or diastolic pressure>120 mmHg), symptomatic hypotension, serious arrhythmia, or extensive ischaemia denoted by wall motion abnormalities involving at least 2 contagious segments and assessed by an expert observer. A positive test is defined by a new or worsening wall motion abnormality. In segments with a resting wall motion abnormality, the biphasic response was used to define ischaemia.

Assessment of wall motion abnormalities:

Wall motion abnormalities can be assessed semi-quantitatively by means of visual inspection or quantitatively with the aid of computerized system ***(Nidrof et al., 1994)***.

Left ventricle is divided into 16 segment according to American Society of Echocardiography ***(Schiller et al., 1989)*** a new American Heart Association (AHA) LV segmentation model (17 segment) has been proposed ***(Cerqueira et al., 2002)*** (figure 1) wall motion is reported according to numerical classification in which: **normal (1)**: uniform increase in endocardial excursion and thickening, **hypokinesia (2)**: denoted by reduced < 5 mm inward systolic wall motion and delayed contraction, **akinesia (3)**:absence of inward motion and thickening and **dyskinesia (4)**: systolic thinning and outward systolic endocardial motion ***(Eddy et al., 1994)***.

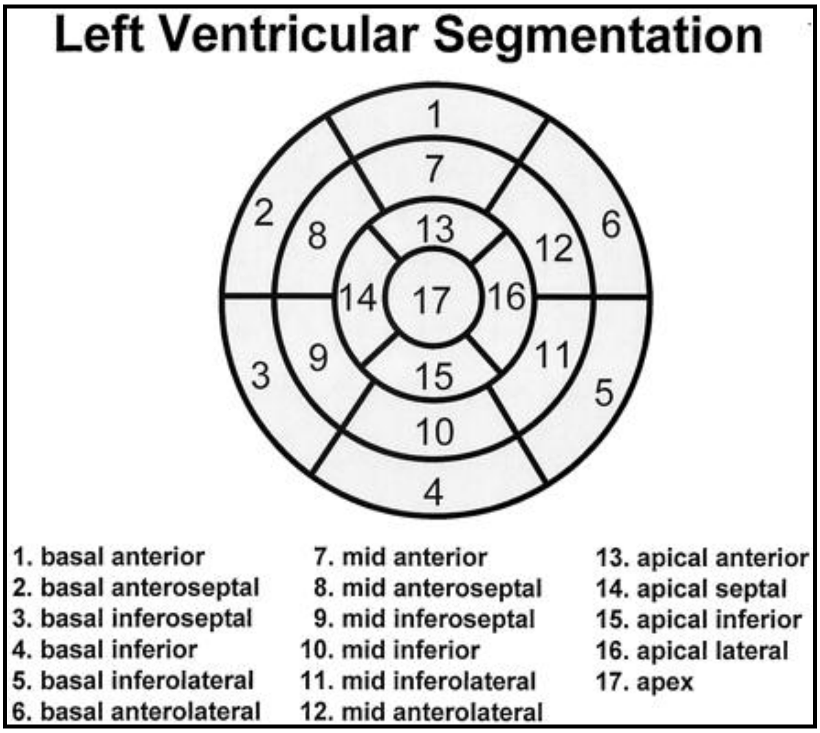

Fig. (1): Typical bull eye representation used for reporting the modes of 17 myocardial segments ***(Cerqueira et al., 2002).***

Wall motion segmental index (WMSI):

It is computed by dividing the sum of the segment scores by the number of interpreted segment. WMSI of one is normal and any increase in the score reflect worsening of wall motion. Interpretation of stress echocardiographic tests by an echocardiographer without specific training severely underestimates the diagnostic potential of this technique. One hundred stress echocardiographic studies are more than adequate to build the individual learning curve and reach the plateau of diagnostic accuracy that the test can yield ***(Picano et al., 1991).***

Safety and side effects of DSE:

The most common side effect seen during DSE is listed in the following table ***(Mertes et al., 1993)***.

Table (1): Incidence of side effect during DSE

Side effect	**Incidence %**
Typical coronary chest pain	17-23%
Arrhythmia	11-35%
Atypical chest pain	8%
Dyspnea	2-5%
Hypotension	0-27%
Nausea	0-10%
Total incidence of side effects	26-35%

Less serious side effects including tremor, nervousness, hypotension and hypertension response. hypotension may be caused by ischemia, dynamic outflow tract obstruction or from the vasodilator effect of dobutamine in combination with a small hyperdynamic left ventricle and low stroke volume.

Application of DSE:

DSE in clinical practice should be reserved to patient who can not exercise due to certain illness (COPD, obesity, neuromuscular, neurological or orthopedic illness), advanced age or lack of motivation to exercise.

DSE is used in the following:

1- Detection and localization of CAD in patient with chest pain, dyspnea on exertion or as preoperative assessment in non cardiac surgery.

2- Cardiac risk stratification in post myocardial infarction patient as well as pre and postcoronary revascularization.

3- Evaluation of myocardial viability.

4- Non -ischemic heart disease

1- Detection and localization of CAD

The accuracy of exercise echocardiography has been examined in numerous studies ***(Segar et al., 1992; Marcovitz et al., 1992; Hoffman et al., 1993; Marwick et al., 1993; Previtali et al., 1993)*** and summarized in table (2). As the threshold level of WMA required to define a positive study has varied, there has been the expected inverse relationship between sensitivity and specificity, with specificity being lowest in the studies reporting the highest sensitivity to be highest in studies with lower sensitivity.

Table (2): Sensitivity and specificity of DSE for detection of CAD in several studies.

Author	Patient No	Stenosis	Sensitivity	Specificity
Segar	85	>50%	95	82
Marcovitz &Armstrong	141	>50%	96	66
Hoffman	66	>70%	79	81
Marwic	217	>50%	72	83
prevital	80	>50%	79	83

As with all other imaging modalities, the sensitivity for detection of patients with single-vessel disease has been lower than sensitivity for detection of patients with multivessel disease. Although the sensitivity for identifying patients with multivessel disease is high, it is not uncommon to understate the number of diseased vessels. Specific accuracy for identification of coronary lesions in the LAD, versus that in the posterior circulation (RCA and LCX coronary arteries), has been investigated in several studies. Although the overall accuracy for detecting patients with coronary disease has been equivalent, the ability to precisely identify an obstruction in the LAD has exceeded that for the posterior circulation. The underlying basis for this phenomenon probably relates to the greater ease with which the LAD territory is visualized versus the occasional problematic visualization of the posterior endocardium, as well as the greater amount of myocardium perfused by the anterior circulation. Additionally, because of the overlap between the right coronary artery and circumflex coronary artery territories, precise separation of these territories has been problematic ***(Wilim et al., 2005).***

2- Cardiac risk assessment

Preoperative risk assessment: Cardiac risk assessment before major non cardiac surgery is an important clinical challenge. The most important clinical predictors of cardiac death and nonfatal myocardial infarction are previous infarction, angina, heart failure (HF), and diabetes mellitus (DM). Patients with one or more of these risk factors generally warrant further risk assessment. Because the majority of patients being evaluated for major surgical procedures, especially vascular, cannot adequately exercise, pharmacologic stress testing is preferred. Dobutamine stress testing has been shown to improve risk stratification of patients before vascular or nonvascular surgery ***(Poldermans et al., 1995; Das et al., 2000; Boersma et al., 2001).***

A low ischemic threshold during stress testing (at a heart rate <70% of the age-predicted maximal heart rate)is the strongest predictor of cardiac events. Based on recent meta-analyses, the prognostic power of stress echocardiography is similar to or exceeds that seen with radionuclide testing ***(Shaw et al., 1996; Kertai et al., 2003).***

B- Patients with known or suspected CAD:

DSE has been shown to have significant prognostic power ***(Chuah et al., 1998; Marwick et al., 2001; Sicari et al., 2003).*** A greater extent of WMA, dilation of the LV at maximal stress, and a low threshold at which ischemia develops all predict a worse outcome. A normal dobutamine stress echocardiogram carries a low spontaneous cardiovascular event rate (usually <1.5%/year) ***(Wilim et al., 2005).***

C- ***Post-acute myocardial infarction prognosis****:*

Identification of high-risk patients after an acute myocardial infarction is possible by using clinical features such as recurrent post-infarction angina, older age, heart failure, and cardiogenic shock. Absence of these clinical characteristics, however, does not necessarily predict a low subsequent risk. With stress echocardiography, the presence of residual or remote ischemia is detected as stress-induced WMA. After infarction, worsening ventricular function with stress confers a worse prognosis. In evaluating a group of patient with acute myocarsial infarction who received thrombolytic therapy, Smart and co –authors reported 76% positive predictive value and 74 % negative predictive value of DSE for the presence of multivessel disease

(Geleijnse et al., 1997; Carlos et al., 1997; Picano et al., 1998; Sicari et al., 2002).

D-Assessment of PCI results:

DSE may be a valuable tool in early assessment of PCI, stress ECG has low sensitivity in single vessel disease and exercise scintigraphy usually reveals a fixed defect at sites nourished by dilated artery ***(Hirzel et al., 1981; Manyari et al., 1988).***

Akosah and coworker demonstrated an immediate improvement in regional myocardial function after successful angioplasty in their patients ***(Akosah et al., 1993)***

E- Assessment of myocardial viability:

Chronic systolic ventricular dysfunction does not necessarily imply irreversible myocardial injury. Indicators of myocardial viability have included contractile reserve to inotropic stimulation and preserved myocardial thickness, as well as intact myocardial perfusion and metabolism. Several studies have shown the utility of DSE in the evaluation of myocardial viability. Incremental infusion of dobutamine elicits an augmentation of regional function in dysfunctional segments that is predictive of recovery of function after revascularization ***(Afridi et al., 1995; Bax et al., 2001).*** The use of high-dose in addition to low-dose dobutamine unmasks differences in contractile reserve, with significant implications for both recovery of function after revascularization and prognosis.

Dysfunctional myocardium shows one of four responses to dobutamine:

1) Biphasic response: augmentation at a low dose followed by deterioration at a higher dose

2) Sustained improvement: improvement in function at a low dose that persists or further improves at higher doses 3) worsening of function, without contractile reserve; and 4) no change in function. Sensitivity for recovery of function ranges between 74% and 88%, with a specificity between 73% and 87% ***(Bax et al., 2001).*** Combination of the types of responses to dobutamine (e.g., any contractile reserve) increases the sensitivity of DSE with a slight decrease in specificity for predicting recovery of function. Studies that have compared determination of viability with DSE and radionuclide studies have shown slightly higher sensitivity and lower specificity for radionuclide techniques ***(Quershi et al., 1997)***.

Myocardial thickness also is an indicator of myocardial viability. Myocardium that is thin (6 mm) has a very low likelihood of viability and recovery of function after revascularization (negative predictive value of 93%). A combination of contractile reserve during DSE and preserved myocardial thickness (>6 mm) yields the best diagnostic accuracy for echocardiography in predicting recovery of function ***(Cwajg et al., 2000).***

Contraindication of DSE: It includes critical aortic stenosis, hypertrophic cardiomyopathy, uncontrolled conditions: arterial hypertension, arrhythmia ischemia, congestive heart failure, hemodynamic instability and electrolyte imbalance

Comparison of DSE and other modalities: During upright isotonic exercise, the hemodynamic response of the cardiovascular system resembles that recorded during dobutamine infusion except for greater increase in blood pressure and heart rate in addition to evaluation of functional capacity ***(Vuille et al., 1994).***

In comparing DSE and stress electrocardiogram for detection of CAD various investigator reported a sensitivity 79% Vs 63% specificity 79% Vs 72% and accuracy 77% Vs 63% respectively ***(Ryan et al., 1987; Martin et al., 1992).***

Both DSE and thallium 201 scintigraphy have a high sensitivity {about 90%} and specificity {about 80%} for detecting CAD ***(Warner et al., 1993).***