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RESEARCH ARTICLE

USE OF DOBUTAMINE STRESS ECHOCARDIOGRAPHY TO ASSESS MYOCARDIAL VIABILITY BEFORE PCI IN TOTAL OCCLUSION OF CORONARY ARTERY IN A TERTIARY CARE CENTRE

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Abstract

Dobutamine stress echocardiography has significant advantages in our country due to its wide availability, portability, low cost and safety. This study was conducted with the aim to assess myocardial viability by Dobutamine Stress Echocardiography (DSE) before PCI in total occlusion of coronary artery. This study confirms that a biphasic response to dobutamine is highly predictive of postoperative recovery of regional contractile function (100% at 6th week follow-up). This studies provide evidence that, at low doses, inotropic stimulation with P- receptor agonists will result in an increase in LV function in areas of viable myocardium but not in areas of myocardial necrosis.

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Introduction:-

Assessment of myocardial viability gained popularity following the publication of a meta-analysis by Allman et al.¹ This study showed a 79% reduction in mortality in patients who underwent revascularization with evidence of viability compared to those who did not undergo any intervention. Few other pooled analyses were also subsequently published that showed benefit of revascularization in patients with viable myocardium. Viability testing therefore, came into practice to guide patient selection for revascularization in many centres worldwide.²

Echocardiography evaluates LV function and abnormalities of regional wall motion. Dysfunctional segments with a resting end diastolic wall thickness of lesser than six mm are thought to reflect areas with significant scar or non-viable segment. These segments generally do not improve after revascularization.³ Dysfunctional segments can be classified into viable or non-viable status with the help of stress echocardiography. Stress can either be physiologically induced e.g. treadmill test or pharmacological intervention such as dobutamine. Low dose Dobutamine Stress Echocardiography (DSE) is used for evaluation of viability.⁴ Dobutamine is given at a dose of 5-10 µg/kg body weight/min and contractility of the dysfunctional segments is measured in comparison to rest.⁵

¹Allman KC. Noninvasive assessment myocardial viability: Current status and future directions. Journal of Nuclear Cardiology 2013;20(4):618-37.

²Van Assche LMR, Kim HW, Kim RJ. Cardiac Mr For The Assessment Of Myocardial Viability. Methodist DeBakey Cardiovascular Journal. 2013;9(3):163- 168

³Borreguero LJJ, Ruiz-Salmerón R. Assessment of Myocardial Viability in Patients Before Revascularization. Rev Esp Cardiol. 2003;56:721-33.

⁴Zaglavara T, Haaverstad R, Cumberledge B, Irvine T, Karvounis H, Parharidis G et al. Dobutamine stress echocardiography for the detection of myocardial viability in patients with left ventricular dysfunction taking β blockers: accuracy and optimal dose. Heart. 2002;87(4):329-335.

⁵Bach DS, Armstrong WF. Dobutamine stress echocardiography. Am J Cardiol 1992;69:2:90H-96H.

Contractility will recuperate in hibernating myocardium while there will be no response in non-viable myocardium. Dobutamine stress echocardiography has significant advantages in our country due to its wide availability, portability, low cost and safety.

This study was conducted with the aim to assess myocardial viability by Dobutamine Stress Echocardiography (DSE) before PCI in total occlusion of coronary artery. The safety, efficacy and the prognostic importance of DSE has been evaluated in this study. The findings from this study will be used to assess the value of DSE for assessing myocardial viability with respect to the Indian scenario.

Aims and Objectives:-

To study the safety and efficacy of Dobutamine Stress Echocardiography (DSE) for assessment of myocardial viability before PCI in total occlusion of coronary artery.

Methodology:-

This observational study is conducted in the Department of Cardiology, D.Y Patil Hospital, Nerul, Navi Mumbai. 50 consecutive patients admitted in the Department of Cardiology, D.Y. Patil Hospital, Nerul, Navi Mumbai fitting the inclusion criteria of the study.

Inclusion Criteria

1. All patients aged 18 years or more
2. Patients who had impaired LV function
3. Patients with single vessel disease with CTO
4. Multi vessel disease coronary artery disease with at least one vessel having CTO

Exclusion Criteria

1. Patients not willing to participate in the study
2. Acute myocardial infarction /unstable angina of < 3 months duration
3. Coexistent significant valve disease
4. Coronary anatomy unsuitable for complete revascularisation
5. Other surgical procedures scheduled in addition to CABG
6. Any contraindication to DSE

Dobutamine stress echocardiography (DSE) Procedure

Two-dimensional transthoracic echocardiography was performed in combination with graded dobutamine infusion after obtaining informed. Consent. Dobutamine was administered intravenously by an infusion pump, starting at 5 µg/kg body weight per min for 5 min (first stage), advancing to 10 µg/kg per min for 5 min (second stage) and increasing by 10 µg/kg per min every 3 min up to a maximum of 40 µg/kg per min (stage 4). In patients not achieving 85% of their gender- and age-predicted maximal heart rate and with no symptoms or signs of myocardial ischemia, atropine (starting with 0.25 mg, increasing to a maximum of 1 mg) was administered intravenously at the end of stage 5, whereas dobutamine was continued. The test was prematurely terminated in the presence of horizontal or downsloping ST segment depression 0.2 mV 80 ms after the J point, ST segment elevation in non-Q leads, serious cardiac arrhythmias, significant chest pain, reduction in systolic blood pressure 40 mm Hg from that at rest, systolic blood pressure 90 mm Hg, hypertension (systolic blood pressure 220 mm Hg) or any side effect regarded as being due to dobutamine. A new wall motion abnormality was considered an interruption criterion only if it was severe and extensive. Betaloc was available and used (1 to 5 mg intravenously) to reverse the effects of dobutamine or dobutamine-atropine combination if these effects did not revert spontaneously and quickly. Repeat Transthoracic echo was done after one month in patients who underwent pci.

DSE Interpretation

Two-dimensional echocardiography was performed with a commercially available imaging system equipped with a 2.5- MHz probe, and the continuously monitored images were recorded on videotape at rest and during the final minute of each stage. Echocardiographic images were analysed off-line and a consensus was achieved by two cardiologists who had no knowledge of the exercise ECG data. For the wall motion analysis, the left ventricle was divided into 16 segments (30) and each segment was scored using a 4-point scale: 1 normal; 2 hypokinesia; 3 akinesia; 4 dyskinesia. A wall motion score index was derived both at rest and at peak stress by averaging the sum

of the individual's scores by the number of the segments. A test was considered positive in case of new or worsened wall motion abnormalities. However, akinesia becoming dyskinesia was not considered a criterion for positivity because this can be due to passive stretching phenomena rather than to "active" ischemia (31). Residual myocardial ischemia in the infarct zone or in the remote zone was evaluated according to the theoretic maximal risk area (32).

All patients were treated according to the institutional protocol for management total occlusion of coronary artery. Coronary angiography was performed and eventually myocardial revascularization procedures based on clinical grounds or on the response at DSE electrocardiography.

Statistical Analysis

The descriptive and analytical statistics was done. The data was analysed using statistical software (IBM SPSS V20.1, IBM Corporation, Armonk, NY, USA).

Table 1:- Angiographic data of the study population.

Variables	n	%
Approach		
Left Femoral Artery	0	0.0
Right Femoral Artery	14	28.0
Right Radial Artery	36	72.0
Ejection Fraction (%)		
Normal	0	0.0
Mild (>45)	17	34.0
Moderate (25-45)	27	54.0
Severe (<25)	8	16.0
Vessel Affected		
Single	12	24.0
Multiple	38	76.0
Calcification		
Present	16	32.0
Absent	34	68.0
LAD Type		
I	1	2.0
II	8	16.0
III	41	82.0
Dominance		
Left	14	28.0
Right	31	62.0
Both	5	10.0
LIMA		
Normal	50	100.0
Abnormal	0	0.0
RIMA		
Normal	49	98.0
Abnormal	1	2.0

The right radial artery was used as the approach for conducting angiography in 36 patients (72%) and the right femoral artery was used in 14 patients (28%). Seventeen (34.0%) patients had mild EF, 27 (54%) patients had moderate EF and 8 (16%) patients had severe EF. Thirty-eight patients (76%) had multiple vessel involvement and 12 patients (24%) had single vessel involvement. Calcification was seen in 34 patients (68%). Forty-one patients (82%) had LAD type III, 8 patients had (16%) LAD type II and 1 patients (2%) had LAD type I. Thirty-one patients (62%) showed right side dominance, with 14 patients (28%) having left side dominance with 5 (10%) patients having dominance on both the sides. Almost all patients showed LIMA and RIMA normal except one subject (2%) having abnormality in RIMA.

Table 2:- Dobutamine Stress Echocardiography (DSE) data of the study population.

Variables	n	%
Resting		
RWMA	50	100.0
Low Dose		
Improves	23	46.0
No Change	27	54.0
Peak Dose		
No Change	27	54.0
Sustained Improvement	6	12.0
Worsen	17	34.0
Test		
Positive	23	46.0
Negative	27	54.0
Territory		
LAD	33	66.0
RCA	10	20.0
Lcx	7	14.0

All the patients had regional wall motion abnormality (RWMA) at rest. At low doses of dobutamine, 23 patients (46%) showed improvement and 27 patients (54%) had no change. At peak doses of dobutamine, 27 (54%) patients showed no changes, 6 (12 %) showed sustained improvement and 17 (34%) showed biphasic response(worsening).Dobutamine Stress Echocardiography (DSE) test was positive for 23 (46%) and negative for 27 (54%) of the study patients.The DSE identified compromised vascular supply in LAD territory in 33 patients (66%), in RCA territory in 10 patients (20%) and in LCx territory in 7 patients (14%).

Table 3:- Complication occurring during Dobutamine Stress Echocardiography (DSE) test in the study population.

Variables	n	%
Chest Pain		
Present	6	12.0
Absent	44	88.0
Arrhythmias		
Present	4	8.0
Absent	46	92.0

During Dobutamine Stress Echocardiography (DSE) test, some of the patients encountered hard events. Chest pain was experienced by 6 (12%) patients and arrhythmias by 4 (8.0%) of the study patients.

Table 4:- Details of follow-up (6 weeks) patients.

Variables	n	%
Angioplasty		
Successful	18	78.2
Not-successful	5	21.8
EF Improvement on Echocardiography		
Present	12	66.6
Absent	6	33.4
EF Improvement Patient		
Monophasic during DSE	0	0.0
Biphasic during DSE	12	100.0

All patients underwent angioplasty after DSE analysis. Out of this only 5 (21.8%) were unsuccessful and rest all (18, 78.2%) were successfully conducted. Angiography was done at 6thweek following successful angioplasty and 66.6%

i.e. 12 patients showed improvement in ejection fraction. All these 12 patients which showed improvement in ejection fraction had biphasic response during DSE procedure.

Results & Discussion:-

In the present study all 23 patients underwent angioplasty after DSE analysis. Echocardiography was done at 6th week following successful echocardiography and 66.6%

i.e. 12 patients showed improvement in ejection fraction. All these 12 patients which showed improvement in ejection fraction had biphasic response (biphasic, defined as improvement at low dose and worsening at peak stress) during DSE procedure. This study confirms that a biphasic response to dobutamine is highly predictive of postoperative recovery of regional contractile function (100% at 6th week follow-up). This relation can be explained by the presence of viable tissue in a dyssynergic segment subtended by a critically stenotic coronary artery, exhibiting an inotropic response to low dose dobutamine and ischemia at high dose dobutamine provoked by the increased rate–pressure product and flow mal-distribution. In the present study, the majority of segments demonstrating such a biphasic response recovered in contractile function after revascularization. Our findings are in accordance with data reported by Afridi et al.⁶ and Cornel JH et al.⁷

Many previous studies have reported estimates for myocardial viability tested by DSE and its prognosis. Sicari et al.⁸ used dobutamine stress echocardiography in a multicenter prospective and non-randomized study. In the study, a total of 778 patients were assessed 12 ± 5 days after uncomplicated first MI. Myocardial viability emerged as the most important predictor of spontaneous events (reinfarction, unstable angina and death). An event rate of 18.8% was reported in patients with viability in the infarct region compared to only 10.0% in patient w/o viability during a mean follow-up of nine months. But there was no significant difference reported in the survival rate. Of all the patients with a positive dobutamine stress echocardiography twenty eight percent were revascularized during follow up compared with fifteen percent DSE negative patients. Previtali et al.⁹ used DSE in a non-randomized, multicenter, prospective, study in which a total of 152 patients were assessed 9 ± 5 days after uncomplicated first acute MI treated with thrombolysis within 6 hrs. After a mean follow up of 15 months, ischemia and viability or viability alone discovered early after treatment was associated with 46% event rate, whereas patients showing no viability in the infarct zone had a better prognosis with 20% event rate of unstable angina, reinfarction and death. Both the groups had equal revascularization procedures performed.

In a non-randomized, single-centre, prospective study by Salustri et al.¹⁰ found similar results in 245 patients after a mean follow up of 17 months. Patients showing viability (with or without ischemia) 6-14 days after their first uncomplicated acute MI determined by dobutamine stress echocardiography experienced a 23% event rate compared to 11% in patients without viability in the infarct area (unstable angina, reinfarction and death).

During dobutamine stress echocardiography test procedure, some of the study participants encountered adverse events. Chest pain was experienced by 6 (12%) patients and arrhythmias by 4 (8.0%) of the study patients. In contrast to our study, no major complications were observed during DSE procedure in a study conducted by Previtali M et

⁶Afridi I, Kleiman NS, Raizner AE, Zoghbi WA. Dobutamine echocardiography in myocardial hibernation: optimal dose and accuracy in predicting recovery of ventricular function after coronary angioplasty. *Circulation* 1995;91:663–70.

⁷Cornel JH, Bax JJ, Elhendy A, Maat APWM, Kimman GP, Geleijnse ML, et al. Biphasic response to dobutamine predicts improvement of global left ventricular function after surgical revascularization in patients with stable coronary artery disease: Implications of time course of recovery on diagnostic accuracy. *J Am Coll Cardiol* 1998;31:1002–10.

⁸Sicari R, Picano E, Landi P, Pingitore A, Bigi R, et al. Prognostic value of dobutamine-atropine stress echocardiography early after acute myocardial infarction. Echo Dobutamine International Cooperative (EDIC) Study. *J Am Coll Cardiol* 1997;29:254-260.)

⁹Previtali M, Fève R, Lanzarini L, Cavalotti C, Klersy C. Prognostic value of myocardial viability and ischemia detected by dobutamine stress echocardiography early after acute myocardial infarction treated with thrombolysis. *J Am Coll Cardiol* 1998;32: 380-386.)

¹⁰Salustri A, Ciavatti M, Seccareccia F, Palamara A. Prediction of cardiac events after uncomplicated acute myocardial infarction by clinical variables and dobutamine stress test. *J Am Coll Cardiol* 1999; 34: 435-440.

al.¹¹In their study, limiting side effects leading to the interruption of dobutamine stress echocardiography test procedure occurred in 5% patients and this included increase in systolic BP to 230 mmHg in 5 patients, symptomatic hypotension in 1 patient and symptomatic sustained ventricular tachycardia in 1 patient.

Dobutamine stress echocardiography is all aspects is an operator dependent procedure, which is not so with other imaging methods like radionuclide scan or MRI. This is one chief reason that in spite of better accuracy of dobutamine stress echocardiography than other techniques, the study and data can become misleading in inexperienced hands. Image acquisition and image quality are other critically important issues. Studies are uninterpretable if the same imaging planes are not compared or if the left ventricle is inadequately visualised. Small left ventricular size also poses a problem due to the smaller endocardial circumference over which a wall motion abnormality detection become difficult. An ischemia based technique has its inherent limitations to identify single and multi-vessel disease and also to recognise ischemia within areas of abnormal resting wall motion. False negative results can be seen for single vessel disease and LCx territory lesions as for this sensitivity dips down to as low as sixty-fivepercent.¹²¹³¹⁴

Conclusion:-

Dobutamine stress echocardiography is a practical method for the non-invasive assessment for significant coronary artery disease in patients physically unable to exercise. In the absence of a baseline myopathy or prior coronary intervention, it is a sensitive and specific test for the detection of coronary artery disease.

The present study comprised of patients with total occlusion of coronary artery. The Dobutamine Stress Echocardiography (DSE) was used to assess myocardial viability before PCI in these patients. This study confirms that a biphasic response to dobutamine is highly predictive of postoperative recovery of regional contractile function (100% at 6th week follow-up). This studies provide evidence that, at low doses, inotropic stimulation with P-receptor agonists will result in an increase in LV function in areas of viable myocardium but not in areas of myocardial necrosis. Dobutamine stress echocardiography, with a graduated infusion of the p-receptor agonist dobutamine, is well-suited to provide functional information at incremental levels of inotropic stimulation. The differential response at low doses, of dobutamine infusion can be used to distinguish viable (but dysfunctional) from necrotic myocardium and establish tissueviability.

In a clinical setting of a developing country like India dobuamine stress echocardiography can prove to be the best alternative to other expensive tests like Cardiac Magnetic Resonance (CMR) imaging, Positron Emission Tomography (PET), Single Photon Emission Computed Tomography (SPECT) and Computed Tomography (CT). DSE has significant advantages due to its wide availability, portability, low cost and safety. The results of this study supports the use of DSE to detect myocardial viability in patients with total occlusion of coronary artery.

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