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# RESEARCH
# ROLE OF DOBUTAMINE STRESS ECHOCARDIOGRAPHY AND LONGITUDINAL SPECKLE TRACKING IN DETECTION OF UNDERLING ISCHEMIA IN PATIENTS WITH DILATED CARDIOMYOPATHY IN COMPARISON WITH CORONARY ANGIOGRAPHY

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**Abstract:**

**Background:** Dilated cardiomyopathy is the most common cardiomyopathy and one of the important causes of death. Low dose dobutamine and 2D –longitudinal speckle tracking echocardiography is an interesting method for noninvasive assessment of underlining ischemia.

**Objective:** ToDetermine the validity and performance of low dose dobutamine stress test and longitudinal speckle tracking in detection of underling ischemia in Dilated cardiomyopathy in comparison to coronary angiography .

**Patients and Methods:** A cross sectional study was Conducted from January 2018 to May 2019.`included patients with dilated cardiomyopathy (EF <40%) and elective coronary angiography was done one week prior 2D-longitudinal speckle tracking –low dose dobutamine stress echocardiograph.

**Results:** Total 60 patients were included in the study ,male 43(71.7%),female 17(28.3%),mean age (54.8±8.1).Mean ejection fraction was 37.5 ± 3.1% ranging from 30 – 40%, while mean GLS was -8.7 ± 2.4 ranging from (-15.4) – (-2.3) .41.7% of all patients had LBBB ,45% were smokers, 55% were hypertensive, and 55% were diabetics, all patients completed the dobutamine infusion without significant adverse events.

Overall, 83.3% had positive coronary angiographic findings (critical stenosis), in which 78.3% were LAD, 53.3% had LCX, and 66.7% had RCA .Assessment of myocardial ischemia using 2D LV longitudinal speckle tracking showed that; 80% had LAD, 71.7% had LCX and 73.3% had RCA involvement.

According to kappa analysis for agreement between 2D LV longitudinal speckle tracking, low dose dobutamine stress echocardiography and coronary angiography; there was almost perfect agreement in terms of detecting ischemia in LAD vessels, moderate agreement in LCX vessels and substantial agreement for RCA vessels.

**Conclusion:** The current study reveals overall moderate to substantial agreement between 2D longitudinal speckle –low dose dobutamine stress echocardiography with coronary angiography, in detection underling ischemia of dilated cardiomyopathy. Revealing a good diagnostic performance, while diagnostic validity ranged from good to

excellent ability (depending on the involved vessels) to predict ischemia, also had high sensitivity(100%) and good specificity(70%) in detection of underling ischemia

***Background :***The availability of an accurate, inexpensive, and non-invasive test for assessing the myocardial ischemia is critical factor to determine the clinical decision-making and prognostic evaluation. 2D-Longitudinal speckle tracking –Dobutamine stress echocardiography which is available, noninvasive, low cost in the detection of ischemia comprise with gold stander in detection of ischemia (coronary angiography) in the setting of myocardial LV dysfunction, enables revascularization to improve left ventricular function for a favorable prognosis[(1)].***Methods':Study design:*** After prior approval from the department of health care cardiology Center, verbal informed consent taken from patients, after the patient did elective coronary angiography, given appointment about one week later to 2D-longitudinal speckle track-low dose dobutamine stress echocardiography. The cross sectional observational study period was from January 2018 to May 2019.

***Inclusion criteria:*** Patients age more than 18 years with Global LV dysfunction <40 (ESC 2016) [(2)] undergoing Elective Coronary angiography.

***Exclusion criteria:*** Recent acute coronary syndrome (ACS) i.e. less than four weeks, Moderate to severe valvular heart disease and Recent serious arrhythmias (e.g. VT, VF, AT, etc.).Any patients fit to the criterions of DCM, offered coronary angiography then scheduled for 2D echocardiography, longitudinal speckle tracking and low dose dobutamine stress echo (5-10 μg/kg/minute), all the procedures done in the catheterization unit and echocardiography unite.

The study included patients with dilated cardiomyopathy and coronary angiography. positive coronary angiography findings depend on (i.e. visual assessments by interventional cardiologist). If there is a stenosis more than 50% in left main stem coronary artery (LMS) or if the stenosis more than 70% in the right coronary artery (RCA), left anterior descending coronary artery (LAD), or left circumflex artery (LCX) [(3)].all these patients offered echocardiography.

Evaluation of risk factors of CAD like smoking, diabetes mellitus, hypertension, body mass index and family history of CAD (i.e. for male age <55 years, while for female age <65 years [(4)]).

***Types of investigations used:***

***Conventional 2D echocardiography:*** Evaluation of LV function using conventional LV EF using Linear M. mode cursor at the tips of mitral valve leaflets in Para sternal long axis view, LV septal wall thickness was measured from left ventricular side leading endocardial edge of septum to right ventricular side leading endocardial edge of septum, LV end diastolic septal wall thickness value of ≥ 10 mm was considered to be hypertrophied taken in parasternal long axis view on M mode trace. Regional wall motion abnormality was assessed using apical long axis view for assessment of antero-septal and posterior-lateral wall basal, mid, apical segments LV 4C view for septal and lateral wall basal, mid, apical segments. LV 2C view for anterior and inferior wall.

***Two-dimensional longitudinal speckle tracking analysis:*** Using available 2D strain software (GE E 9), acquisition of 3 apical views; apical 3 chamber, 4 chamber, & 2 chamber views was done, all images were taken at end expiration, to avoid LV apical for shortening ,and reducing sector width & depth was used to increase frame rate for better image resolution. All images were digitally stored at a high frame rate (>63 frames/s, mean 70 ± 12). Region of interest was localized at LV endocardial border 2 at base, and one apical to include the entire myocardium at end systolic frame. The software algorithm automatically segmented the LV into six equidistant segments and selected suitable speckles in the myocardium for tracking. The software algorithm then tracked the speckle patterns on a frame-by-frame basis using the sum of absolute difference algorithm. Finally, the software automatically generated LV strain profiles for each of the six segments of each view, from which end-systolic strain was measured. The average value of strain at each level (basal, middle, and apical) and global strain obtained using Bull eye model measuring peak regional & global LV longitudinal strain of 17 LV segments was calculated [(3)].

All measurements were preformed off-line on a dedicated workstation Using available 2D strain software (GE E9). Longitudinal strain was computed using 2D-speckle-tracking analysis by automated function imaging (AFI). For strain processing, the peak of the R-wave on the electrocardiogram was used as the reference time point for end-diastole and segments with poor-quality tracking were manually discarded. GLS was only computed from patients with >92% of segments adequately tracked (≥15 segments for a 17-segment model). Given the average value of –17 ± 0.1% for normal GLS, any value assessed by AFI less than −16% was considered as impaired GLS [(3)].

Thorough correlation of LV regional longitudinal impairment with Coronary territories was evaluated in all patients , Value of regional longitudinal strain less than −16% were considered to be abnormal and diagnostic of CAD if it involve more than 3 segments in same coronary territories [(3)].

***Low dose dobutamine longitudinal speckle tracking echocardiography:***
Low dose dobutamine infusion (5 to10 mic/kg/min)was given according to protocol dobutamine infusion,5mic/kg/min over 3 min then longitudinal speckle tracking image obtained and evaluated for any significant improvement or worsing impaired(more than 3 segment within coronary territory) in LV segment which means nonviable or significant coronary artery stenosis may be help to confirm coronary artery ischemia, also 10mic/kg/min given over 3min reevaluated by longitudinal speckle tracking [(5)].

***Coronary angiography:***
Coronary angiography was done for all patients using standard protocol and the diagnosis of CAD was defined if there is stenosis more than 50% in left main stem coronary artery(LMS) and if the stenosis more than 70% in the right coronary artery(RCA), left anterior descending coronary artery ( LAD ) and circumflex artery (CX)[(3)].

**Results:** IN the current study total sample was (60 patients) mean age of patients was 54.8 ± 8.1 years, with male to female ratio of 2.5:1,other dataas in table 1, all patients completed the dobutamine infusion without significant adverse events.Regarding distribution of echocardiographic data of study group Mean ejection fraction was 37.5 ± 3.1% ranging from 30 – 40%, while mean GLS was -8.7 ± 2.4 ranging from (-15.4) – (-2.3), as illustrated in table.2.Overall, Thedistribution of coronary angiography findings for involvedarteries, 83.3% had positive coronary angiographic findings (stenosis), in which 78.3% were LAD, 53.3% had LCX, and 66.7% had RCA, as illustrated in table.3.Assessment of ischemia using 2D LV longitudinal strain speckle tracking showed that; 86.7% had LAD, 78.3% had LCX and 78.3% had RCA involvement, as illustrated in table.4.

According to kappa analysis for agreement between 2D LV longitudinal strain – speckle tracking and coronary angiography; there was moderate to substantial agreement (since kappa between 0.60 – 0.8) in terms of detecting ischemia in all the vessels, with high SN (sensitivity) 100%, good SP (specificity) 70.0%, high PPV (94.3%) and NPV (100%),as illustrated in figure .1.

According to kappa analysis for agreement between lowdose dobutamine stress2D LV longitudinal stain – speckle tracking and coronary angiography; there was moderate to substantial agreement (since kappa between 0.60 – 0.8) in terms of detecting ischemia in all the vessels, with high SN (sensitivity) 100%, good SP (specificity) 70.0%, high PPV (94.3%) and NPV (100%),as illustrated in figure 2.

**Table.1: demographic and clinical characteristics**

| Variable | Value |
|---|---|
| **Number** | 60 |
| **Age (years), mean ± SD** | 54.8 ± 8.1 |
| **Gender, n (%)** | |
| **Female** | 17 (28.3%) |
| **Male** | 43 (71.7%) |
| **BMI (kg/m$^2$)** | 31.5 ± 3.4 |
| **Smoker, n (%)** | 27 (45.0%) |
| **Hypertension, n (%)** | 33 (55.0%) |
| **DM, n (%)** | 33 (55.0%) |
| **Family Hx of CAD, n (%)** | |
| **Negative** | 54 (90.0%) |
| **Positive** | 6 (10.0%) |

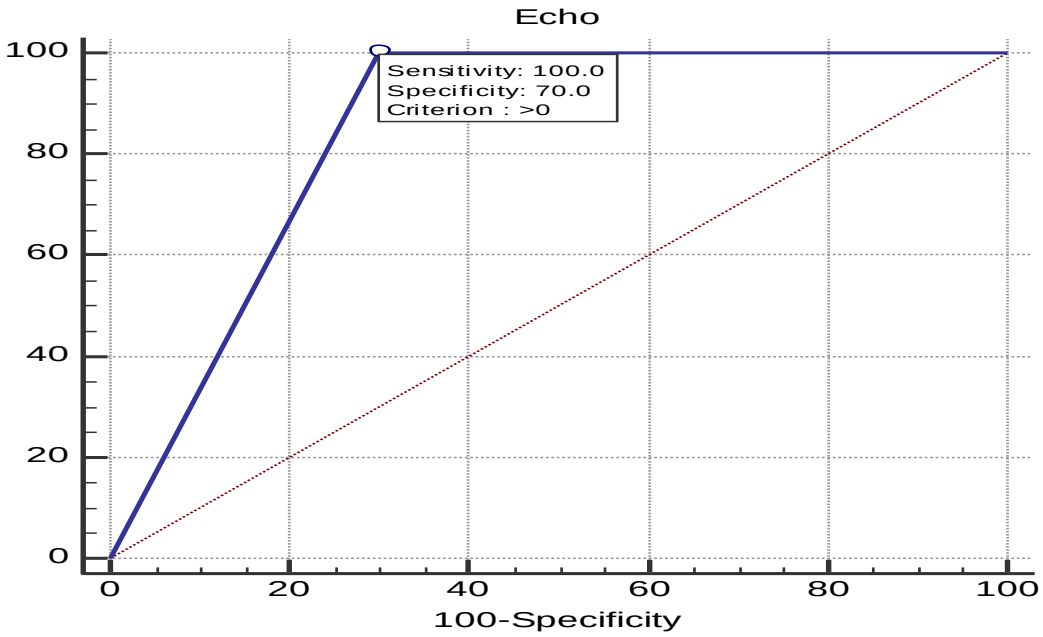
**Table.2: Distribution of echocardiographic data of study group**

| Variable | Value |
|---|---|
| **Number** | 60 |
| **EF (%), mean ± SD** | 37.5 ± 3.1 |
| **GLS, mean ± SD** | -8.7 ± 2.4 |

EF: ejection fraction, GLS: global longitudinal strain

**Table.3:Distribution coronary angiography findings for involved arteries**

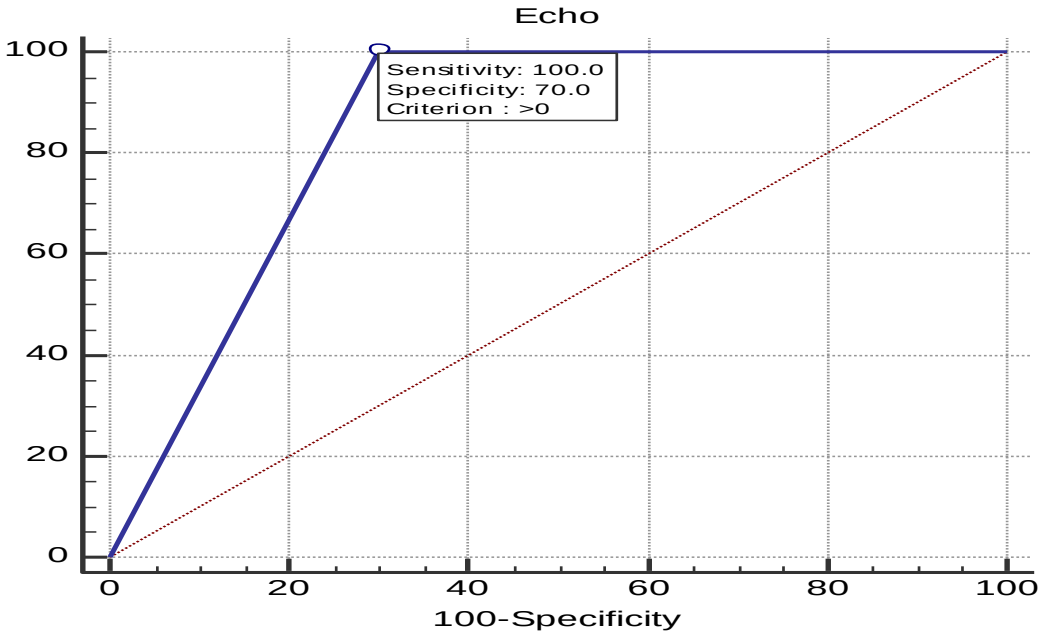
| critical lesion per coronary arteries | Value |
|---|---|
| **Overall** | 50 (83.3%) |
| **LAD** | 47 (78.3%) |
| **LCX** | 33 (55.0%) |
| **RCA** | 40 (66.7%) |




| Echo | Angiography | | Kappa | P. Value |
|---|---|---|---|---|
| | Stenosis | No stenosis | | |
| **Ischemia** | 50 | 3 | 0.795 | < 0.001 |
| **No ischemia** | 0 | 7 | | |

**AUC = 0.85**
**Sensitivity = 100.0%**
**Specificity = 70.0%**
**Positive LH = 3.33 (index of suspicion +20%)**
**INegative LH < 0.01 (index of suspicion -45%)**
**PPV = 94.3%**
**NPV = 100.0%**

**Figure.1: ROC curve of 2D LV longitudinal speckle tracking in the detection of ischemia**




| LDD-STE | Angiography | | Kappa | P. Value |
|---|---|---|---|---|
| | Stenosis | No stenosis | | |
| **Ischemia** | 50 | 3 | 0.795 | <0.001 |
| **No ischemia** | 0 | 7 | | |

**AUC = 0.85**
**Sensitivity = 100.0%**
**Specificity = 70.0%**
**Positive LH = 3.33 (index of suspicion +20%)**
**Negative LH < 0.01 (index of suspicion -45%)**
**PPV = 94.3%**
**NPV = 100.0%**

**Figure.2: ROC curve of low dose dobutamine stress and 2D LV longitudinal speckle tracking in the detection of ischemia**

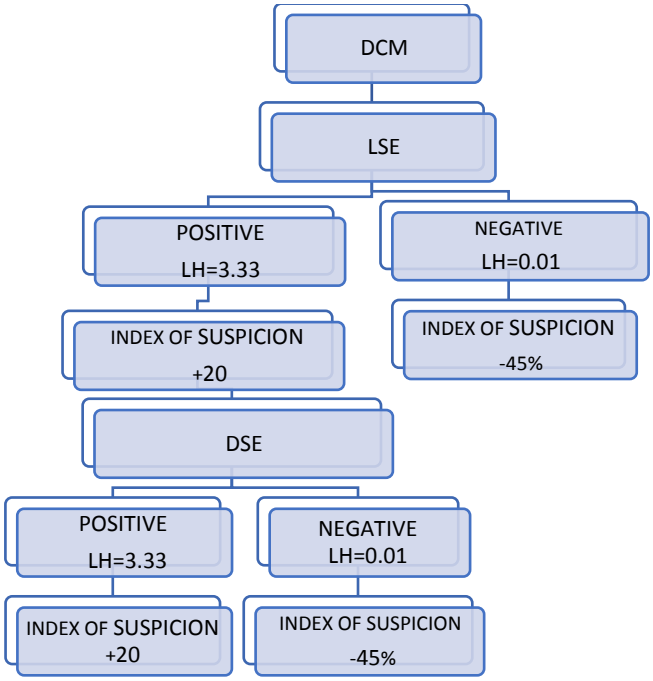



**Figure.3: Algorithm for diagnosis myocardium ischemiain DCM**

**Discussion:**In the current study was examined patients with global LV dysfunction (i.e. EF<40%), who underwent 2D speckle tracking and low dose The dobutamine stress for assessment of myocardial ischemia.
In the current study mean LVEF which is similar to Bansal et al study with LVEF 35.2% ±10.8[(6)], and similar to Ismail et al study with LVEF was 35% ± 8 [(8)], while for Wang et al study LVEF 43.24±5.71 which is slightly higher than ours data which could be explained by the inclusion criteria was LVEF <50 [(7)],. Indicating the primary inclusion criteria of these three studies is similar.
In the current study was assessed the three major arteries (LAD, LCX, and RCA), for assessment of LAD, the Sensitivity and Specificity was 100%, 61.5%, and for LCX theSensitivity and Specificity was 96.8% and 44.4%, and for assessment of RCA it was Sensitivity andSpecificity, 97.5% and 60.0%(because of LAD territory supply large area ,no wide anatomical variation as LCX territory 85%RCA dominant so LAD reveal high sensitivity and specificity vs to LCX was less). overall the agreement level between 2D STE and coronary angiography was moderate to substantial, overall sensitivity and specificity was 100% to70% respectively. IN Wang et al study, longitudinal strain (LS) and longitudinal strain rate (LSr) at rest had the following Sensitivity andSpecificity, 66.2%, and 68.9% for LS and 65.5% and 71.6% for LSr, respectively [(7)]. These values were lower than reported by current study.because in Wang et al study evaluated myocardium viability(positive test only to improvement LST+LDDSE) but current study (positive test to improvement and significant worse in LST segment as evaluated myocardial ischemia rather than viable myocardium However; the author state that both LS and LSr at rest were independent predictors of viable myocardium [(7)].
In Gong et al study they assessed (radial (RS), circumferential (CL) and longitudinal strain (LS) and strain rate (Sr) parameters), in terms of strain parameters they found that for RS the Sensitivity was 67%, and 48% Specificity, while for CS the Sensitivity was 73% and 67% Specificity, and for LS the Sensitivity was 67.8% and 63%. While for strain rate, the RSr had 65% Sensitivity and 49% Specificity, for CSr the Sensitivity was 67% and 64% Specificity, and for LSr the Sensitivity was 74% and 62%Specificity [(9)]. These values is somewhat lower than reported by our study.because in Gong et al study evaluated myocardium viability(positive test only to improvement LST+LDDSE) but current study (positive test to improvement and significant worse in LST segment as evaluated myocardial ischemia rather than viable myocardium

In Liu et al, they used 2D – STE for assessing the viability of the myocardium using layer specific STE; they reported the highest AUC for longitudinal strain (for endocardial layer) 0.767, 77.1% Sensitivity and 65.4% Specificity, which is lower than reported by our study [10].Because in Liu et al study evaluated myocardium viability(positive test only to improvement LST+LDDSE) but current study (positive test to improvement and significant worse in LST segment as evaluated myocardial ischemia rather than viable myocardium

Detection of ischemia when a coronary arterydisease is suspected is essential. Exercise anddobutamine stress echocardiography (DSE) arewell established for identifying inducible ischemia.Ischemia is defined by a regional reductionof myocardial thickening or abnormal wall motion. Myocardial ischemia can also provokea delayed onset and termination of systolicthickening. Unfortunately, the human eyehas insufficient temporal resolution to identifythese abnormalities in real time[11].

Semi-quantitative echocardiography is inexpensive, user-friendly and widely available forroutine examination and viable myocardium detection. However, it was limited by the experience of investigator, poor precision and reproducibility. STE is an algorithm, which provides objective and reproducible quantification of global and regional myocardial function and detection of viable myocardium[12].

Dobutamine is an adrenoreceptor agonist and improved myocardial systolic function by enhancing coronary blood flow at a low dose. To increase the sensitivity, and specificity, we selected the STE-LDDSE to detect myocardial viability. Li DY et al. confirmed that dobutamine infused at a rate of 10 μg/kg/min effectively improved the wall motion [13].

In the current study was assessed the three major arteries (LAD, LCX, and RCA) for detecting ischemia using STE-LDD against angiography, for assessment of LAD, the Sensitivity and Specificity was 100%, 61.5% (kappa = 0.715), and for LCX theSensitivity and Specificity was 97.0% and 37.0% (kappa = 0.359), and for assessment of RCA it was Sensitivity and Specificity, 97.5% and 65.0% (kappa = 0.535),overall the Specificity was 70.0% and 100% Sensitivity with overall agreement level between 2D STE-LDD and angiography was substantial (kappa = 0.795).In Wang et al study, STE-LDD had high SN and SP for detecting myocardial viability with 89% Sensitivity and 84% Specificity for LS and 90%Sensitivity and 88% Specificity for LSr[7].In Ismail et al study, they use STE – LDD to identify systolic strain and strain rate and analyzed 16 – segments in order to identify the optimal cut-off value to determine myocardial viability, for assessment of strain 10 segment showed good sensitivity and Specificity (around 80s%), while for assessment of strain rate 11 segments showed high Sensitivity and Specificity (around 90s%) [8], which is in agreement with our findings.InGong et al study, there was an improvement in STE-LDD compared to STE at rest, in which they reported 71% Sensitivity and 76% Specificity for RS and 70% Sensitivity and 77%Specificity for RSr. 88%Sensitivity and 87% Specificity for CS, also 86% Sensitivity and 86% Specificity for CSr. And finally, 86% Sensitivity and 87% Specificity for LS and 88% Sensitivity and 83% Specificity for LCr[9]. Which is in agreement with our findings. In multivariate logistic regressionanalysis demonstrated that LS and LSr superior toCS and CSr. Combining LS and LSr at LDDSE, the sensitivity,specificity and accuracy for the assessment ofviable myocardium to 89.8, 90.2 and 89.9 %, respectively [9].

lastly the current study reveal good sensitivity and specificity longitudinal speckle tracking-low dose dobutamine stress echocardiography to evaluated underling ischemia in dilated cardiomyopathy as in figure 3 algorithmwhich iscritical factor to determine the clinical decision-making and prognostic evaluation.

**Limitation of technique:**.1-the main problem with speckle tracking,however,is increasingly recognized. The lack of standardization. Each vendor of ultrasound equipment, or analysis software, has different algorithms, that will perform differently during analysis.in head to head comparisons, biases between analysis may be substantial, especially when when compared to an external reference[ 14] .

2-plane misplacement

3-arrythmias.

***Conclusion:*** In current study reveals overall moderate to substantial agreement between 2D-LST-DSE with coronary angiography, in detection underling ischemia of dilated cardiomyopathy. Revealing a good diagnostic performance, while diagnostic validity ranged from good to excellent ability (depending on the involved vessels) to predict ischemia, also had high sensitivity and good specificity in detection of underling ischemia.

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