



Original Article

The predictive value of speckle tracking during dobutamine stress echocardiography in patients with chronic stable angina

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ABSTRACT

Objective: Evaluation of the diagnostic value of speckle tracking echocardiography (STE) at rest and during dobutamine stress in predicting the presence and severity of coronary artery disease (CAD) in patients with chronic stable angina.

Methods: A total of 100 patients with chronic stable angina were evaluated using STE at rest and during dobutamine stress to detect the presence, severity, and number of affected coronary arteries. Then, the correlation with the SYNTAX score (SS) was analyzed.

Results: STE at stress showed better agreement with coronary angiography (CA) than dobutamine stress echocardiography (DSE) in detecting the presence of coronary artery stenosis (Kappa = 0.819, $p < 0.001$). STE at stress suggested involvement of the left anterior descending artery (LAD) with excellent agreement with CA (Kappa = 0.816, $p < 0.001$). For right coronary artery, STE at rest and stress showed good agreement with the CA results (Kappa = 0.775 and 0.858, respectively, $p < 0.001$), whereas for left circumflex artery, STE at rest and stress showed a fair agreement with the CA results (Kappa = 0.556 and 0.583, respectively, $p < 0.001$). Resting global longitudinal peak systolic strain (GLPSS) $\geq -15.2\%$ had the best diagnostic accuracy (sensitivity = 61.8%; specificity = 93.5%) in predicting SS > 22. Stress GLPSS $\geq -12.5\%$ had the best diagnostic accuracy (sensitivity = 82.4%; specificity = 78.3%) in predicting SS > 22.

Conclusion: Speckle tracking during DSE has high sensitivity and specificity for predicting the presence of CAD. It provides quantitative diagnostic information that decreases the false positive and false negative results of DSE.

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1. Introduction

Early detection and management of patients with known or suspected coronary artery disease (CAD) result in better outcomes and decreased mortality. Noninvasive imaging tests can help in determining the presence, extent, and severity of CAD and myocardial ischemia.¹

Dobutamine stress echocardiography (DSE) is a useful and applicable stress tool for assessment of the presence, site and severity of CAD. Its diagnostic accuracy seems comparable to other noninvasive stress modalities used in patients who are unable to exercise. In accordance with the 2012 ACC/AHA guidelines for the

diagnosis and management of patients with stable ischemic heart disease, pharmacological stress echocardiography is considered a class I recommendation for the assessment of ischemic patients with limited exercise capacity.²

Speckle tracking echocardiography (STE) is a new technique that allows calculation of segmental systolic strains. The longitudinal myocardial fibers are located subendocardially (the most susceptible area to ischemia). Therefore, measurements of the longitudinal systolic shortening motion are the most sensitive markers of CAD, especially in patients with moderate-to-severe coronary artery affection.³

Dobutamine stress STE is a promising imaging tool that permits the offline evaluation of myocardial velocities and deformation parameters, which provide important insights into the systolic and diastolic function of the heart in addition to the myocardial

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mechanics that explain other pathophysiological processes of the heart.⁴

The aim of the present study was to evaluate the diagnostic value of speckle tracking at rest and during DSE in predicting the presence, site and severity of CAD in patients with chronic stable angina.

2. Patients and methods

2.1. Study design and patients selection

A single center, cross-sectional study was carried out at Benha University Hospital, Egypt from January 2017 to November 2018 after approval from the ethics committee. This study enrolled patients with chronic stable angina and good left ventricular (LV) systolic function (LV ejection fraction [EF] \geq 50%) with no regional wall motion abnormalities (RWMA) at rest. An informed consent was taken from all patients.

Patients who developed chest pain with no RWMA, patients with nonconclusive test results, LVEF $<$ 50%, prior myocardial infarction, prior percutaneous coronary intervention or coronary artery bypass grafting, significant valvular heart disease or prosthetic valves, congenital heart disease, rhythm other than sinus rhythm, poor echocardiographic window, hypersensitivity to contrast agents or refusal to undergo coronary angiography (CA), and other comorbidities (severe renal impairment or advanced liver disease) were excluded from the study.

2.2. Echocardiography

All echocardiographic examinations were performed and recorded for offline analysis using a Philips EPIQ 7C, Release 1.7 (Philips Healthcare, Andover, MA, USA) machine with Q lab 10.4, an S5-1 probe and simultaneous electrocardiogram signal.⁵

2.2.1. Conventional echocardiography

A modified biplane Simpson's method in the apical four- and two-chamber views, as recommended by the American Society of Echocardiography (ASE), was used to calculate the LVEF.⁵

2.2.2. Dobutamine stress echocardiography

This procedure was performed using a standard protocol recommended by the ASE. All patients were informed to stop β -blockers and nitrates for at least 48 h before the test.⁶ The stress protocol was terminated if (1) the age predicted maximum heart rate (HR) was achieved (at least 85%), (2) the patient reported intense chest pain, (3) the systolic blood pressure increased to $>$ 230 mmHg, the diastolic blood pressure increased to $>$ 120 mmHg, or there was a drop in systolic blood pressure $>$ 20 mmHg.⁶ The wall motion score index (WMSI) was calculated in the 17-segment model of the left ventricle at each stage of the protocol, wherein myocardial segments were graded according to their wall motion as normokinetic = 1, hypokinetic = 2, akinetic = 3 or dyskinetic = 4. Any deterioration by one grade or more, from baseline to peak stress, in two or more contiguous segments was considered a positive test for myocardial ischemia.⁷

2.2.3. Speckle tracking echocardiography

Three consecutive end-expiratory cardiac cycles in the apical four-chamber, two-chamber and long axis views at high frame rates ($>$ 70 frames/sec), and harmonic imaging were obtained. STE analysis was performed offline on greyscale images of the LV obtained in these views. If the image quality was good the machine automatically traced the endocardial wall and in case if low quality image, semi-automated method was used by identification of 3

points (basal septal, basal lateral and apical). After that, the software automatically generated strain curves for different myocardial segments. Global longitudinal systolic strain (GLSS) was calculated as the mean strain of all 17 segments. Peak longitudinal strain parameters and their changes from rest to peak stress were estimated. A bull's eye diagram was then drawn from the data obtained from all myocardial segments. The diagnostic information of each trace was contained in a parametric color, labeling the qualitative and quantitative indices of myocardial wall motion.⁸

2.3. Coronary angiography

This procedure was performed for all patients by an expert cardiologist blinded to echocardiographic results in accordance with the Judkins technique. Significant stenosis was defined as stenosis \geq 50% for the left main and \geq 70% for the right coronary, left anterior descending (LAD) and circumflex arteries. Multivessel CAD was defined as significant stenosis in two or more vessels.⁹ The SYNTAX score (SS) was calculated using the online calculator (<http://www.syntaxscore.com>) by two experienced interventional cardiologists.

2.4. Statistical analysis

Data management and statistical analysis were performed using SPSS vs. 25 (IBM, Armonk, New York, United States). Numerical data were summarized as the means and standard deviations or medians and ranges. Categorical data were summarized as numbers and percentages. Rest and stress clinical and echocardiographic parameters were compared using a paired *t*-test. Using CA as the gold standard, diagnostic indices and agreement were calculated for DSE and STE at rest and at stress for the detection of affected coronaries, types and number of vessels affected. Before running comparisons between those with SS \leq 22 and those with SS higher than 22, numerical data were assessed for normality using normality tests and direct visualization methods. Numerical data were compared using the independent *t*-test, whereas categorical data were compared using the chi-square test. Echocardiographic parameters during rest and stress were compared using two-way repeated measures analysis of variance (mixed model) to test for significant interaction. Simple main effects were compared using posthoc comparisons with Bonferroni adjustment. Correlation analysis was performed between the SS and other parameters using Spearman's correlation. "r" is the correlation coefficient. It ranges from -1 to $+1$. -1 indicates a strong negative correlation, $+1$ indicates a strong positive correlation, and 0 indicates no correlation. Receiver operating characteristic (ROC) analysis was performed for prediction of the SS $>$ 22. The area under the curve (AUC) with 95% confidence interval (CI), best cutoff point, and all diagnostic indices were calculated. All *P* values were two-sided. *P* values $<$ 0.05 were considered significant.

3. Results

A total of 144 patients with chronic stable angina were scheduled for DSE for investigating suspected CAD. Forty-four patients were excluded (37 patients developed chest pain but without RWMA, and 7 patients could not complete the test ["nonconclusive test results"]). Eventually, 100 patients were enrolled in the present study. The study included 53 males (53%) with a mean age of 58 ± 5 years. Fifty-nine percent had diabetes mellitus, 61% were hypertensive, 30 patients 30% were smokers, and 15% had a positive family history of premature CAD.

3.1. Dobutamine stress echocardiography

The mean duration of the DSE study was 10 ± 2 min. Forty-seven patients (47%) reached the target HR, and 13 patients (27.7%) needed augmentation with atropine. Forty patients (40%) developed anginal pain, and 13 patients (13%) developed other complications in the form of palpitations, headache, and dizziness. Sixty-nine patients (69%) had abnormal DSE results suggestive of coronary artery involvement. Single vessel was found in 42 patients (60.9%), two vessels found in 17 patients (24.6%), whereas three vessels were present in 10 patients (14.5%). LAD was suggested in 51 patients (73.9%), left circumflex artery (LCX) in 19 patients (27.5%) and right coronary artery (RCA) in 36 patients (52.2%). Clinical and echocardiographic data (during rest and stress) are presented in (Table 1).

3.2. Speckle tracking echocardiography

Seventy-two patients (72%) had abnormal STE at rest suggestive of coronary artery stenosis, and normal findings were found in 28 patients (28%). Under stress, abnormal results suggestive of coronary artery stenosis increased in up to 78 patients (78%), and normal findings were found in only 22 patients (22%). Single vessel disease was found in 46 patients (63.9%) during rest and 45 patients (57.7%) during stress, two vessels disease diagnosed in 15 patients (20.8%) during rest and 18 patients (23.1%) during stress, three

vessels disease found in 11 patients (15.3%) during rest and 15 patients (19.2%) during stress. LAD involvement was described in 52 patients (72.2%) during rest, whereas 59 patients (75.6%) diagnosed during stress. LCX was found in 20 patients (27.8%) during rest and increased during stress to 24 patients (30.8%). RCA involvement was found in 37 patients (51.4%) during rest, whereas during stress it increased to 43 patients (55.1%). The STE parameters are shown in (Table 1).

The validity of DSE and STE (at rest and stress) with CA for detecting the presence of CAD, number of affected vessels and the affected territory illustrated in (Table 2)

3.3. Coronary angiography

Coronary angiography was performed on all patients. It revealed that 80 patients (80%) had significant coronary vessel disease, whereas 20 patients (20%) had normal coronary vessels. The SS for each patient was calculated. The patients with CAD were divided in accordance with their SS into group I (low SS ≤ 22) and group II (intermediate-high SS > 22) (Table 3).

The mean SS in group I was 13.8 ± 9.33 ranging from 0 to 22, whereas it was 35.15 ± 4.13 ranging from 27 to 39 in group II.

Male gender was significantly prevalent in group II, $p < 0.003$. There was no significant difference in age between the 2 groups ($p < 0.471$). Risk factors (diabetes mellitus, hypertension, smoking, dyslipidaemia and a positive family history of CAD) were highly prevalent in group II patients.

Resting echocardiography revealed no statistically significant difference between the two groups except for the global

Table 1
Clinical and echocardiographic data of the studied patients.

Variable	Rest	Stress	P value
Clinical data:			
Heart rate (bpm)	80 ± 15	145 ± 16	<0.001
Systolic blood pressure (mmHg)	123 ± 17	167 ± 10	<0.001
Diastolic blood pressure (mmHg)	81 ± 11	97 ± 10	<0.001
Conventional echocardiographic data:			
LVEDV (ml)	97 ± 12	105 ± 22	<0.001
LVESV (ml)	46 ± 8	37 ± 7	<0.001
LVEF (%)	57 ± 4	62 ± 5	<0.001
WMSI	1 ± 0	1.4 ± 0.2	<0.001
Speckle tracking echocardiography:			
GLPSS (%)	-17.1 ± 2.6	-13.2 ± 2.7	
Abnormal results	72 (72%)	78 (78%)	
Number of affected vessels:			
One	46 (63.9%)	45 (57.7)	
Two	15 (20.8%)	18 (23.1)	
Three	11 (15.3%)	15 (19.2)	
Affected vessels:			
LAD	52 (72.2)	59 (75.6)	<0.001
LCX	20 (27.8)	24 (30.8)	
RCA	37 (51.4)	43 (55.1)	
Dobutamine stress echocardiography:			
Abnormal results		69 (69)	
Number of affected vessels:			
One		42 (60.9)	
Two		17 (24.6)	
Three		10 (14.5)	
Affected vessels:			
LAD		51 (73.9)	
LCX		19 (27.5)	
RCA		36 (52.2)	

Values are mean \pm standard deviation or number (%).

LVEDV = left ventricular end-diastolic volume; **LVESV** = left ventricular end-systolic volume; **LVEF** = left ventricular ejection fraction; **WMSI** = wall motion score index; **GLPSS** = global longitudinal peak systolic strain; **LAD** = left anterior descending artery; **LCX** = left circumflex artery; **RCA** = right coronary artery.

Table 2
Validity of DSE and STE (at rest and stress) with CA for detecting the presence of CAD, number of affected vessels and the affected territory.

Variable	Sensitivity	specificity	PPV	NPV	Kappa	P value
Presence of CAD						
DSE	85%	95%	98.6%	61.3%	0.663	<0.001
STE at rest	86.3%	85%	95.8%	60.7%	0.620	<0.001
STE at stress	95%	90%	97.4%	81.8%	0.819	<0.001
Number of affected vessels						
Single vessel:						
DSE	73.2%	100%	100%	63.3%	0.633	<0.001
STE at rest	79.5%	85%	92.1%	65.4%	0.597	<0.001
STE at stress	93.2%	94.7%	97.6%	85.7%	0.854	<0.001
Two vessels:						
DSE	36.8%	90.9%	53.8%	83.3%	0.313	0.003
STE at rest	47.1%	94.1%	66.7%	87.7%	0.463	<0.001
STE at stress	75%	94%	75%	94%	0.69	<0.001
Multivessel:						
DSE	61.5%	97.7%	80%	94.4%	0.657	<0.001
STE at rest	69.2%	97.7%	81.8%	95.5%	0.716	<0.001
STE at stress	84.6%	95.4%	73.3%	97.6%	0.751	<0.001
The affected territory						
LAD affection:						
DSE	83.9%	90.9%	92.2%	91.6%	0.739	<0.001
STE at rest	83.9%	88.6%	90.4%	81.3%	0.719	<0.001
STE at stress	94.6%	86.4%	89.8%	92.7%	0.816	<0.001
LCX affection:						
DSE	60.9%	93.5%	73.7%	88.9%	0.579	<0.001
STE at rest	60.9%	92.2%	70%	88.8%	0.556	<0.001
STE at stress	69.6%	89.6%	66.7%	90.8%	0.583	<0.001
RCA affection:						
DSE	67.4%	90.7%	86.1%	76.6%	0.591	<0.001
STE at rest	78.3%	98.1%	97.3%	84.1%	0.775	<0.001
STE at stress	89.1%	96.3%	95.3%	91.2%	0.858	<0.001

DSE = dobutamine stress echocardiography; **STE** = speckle tracking echocardiography; **LAD** = left anterior descending artery; **LCX** = left circumflex artery; **RCA** = right coronary artery; **PPV** = positive predictive value; **NPV** = negative predictive value.

Table 3
Coronary angiography results.

Affected coronaries:	80 (80%)
Number of affected vessels:	
One	48 (60%)
Two	19 (23.8)
Three	13 (16.2)
Affected vessels:	
LAD	56 (70.0)
LCX	23 (28.8)
RCA	46 (57.5)
SYNTAX score	21 (0–39)

LAD = left anterior descending artery; LCX = left circumflex artery; RCA = right coronary artery.

longitudinal peak systolic strain (GLPSS), which was significantly lower in group II patients (-14.9 ± 1.9 vs. -17.2 ± 1.6 , $p < 0.001$).

DSE revealed significantly decreased LVEF (57 ± 4 vs. 64 ± 4 , $p < 0.001$) and GLPSS (-10.9 ± 1.8 vs. -13.5 ± 1.7 , $p < 0.001$) in group II. WMSI was significantly increased in group II patients (1.4 ± 0.2 vs. 1.3 ± 0.2 , $p < 0.004$). However, there was no statistically significant difference between the 2 groups with regard to both LV end-diastolic volume and LV end-systolic volume.

The ROC curve was used to assess the diagnostic value of GLPSS (%) at rest and stress in predicting SS > 22. The value of resting GLPSS $\geq -15.2\%$ had the best diagnostic accuracy (sensitivity = 61.8%; specificity = 93.5%) in predicting SS > 22, with an AUC of 0.827 (95% CI: "0.732 to 0.921"). The value of stress GLPSS $\geq -12.5\%$ had the best diagnostic accuracy (sensitivity = 82.4%; specificity = 78.3%) in predicting SS > 22, with an AUC of 0.837 (95% CI: "0.748 to 0.927") (Fig. 1).

There was a highly significant negative correlation between SS and GLPSS at rest and stress ($r = -0.555$ and -0.532 , respectively, P value of <0.001). In addition, there was a significant positive correlation between SS and absolute decrease in GLPSS from rest to stress ($r = 0.240$, $p < 0.016$). There was no significant statistical correlation between SS and changes in WMSI during stress ($r = 0.168$, $p < 0.136$). Fig. 2 illustrate the bull's eye of the LV longitudinal strain of one patient from our study.

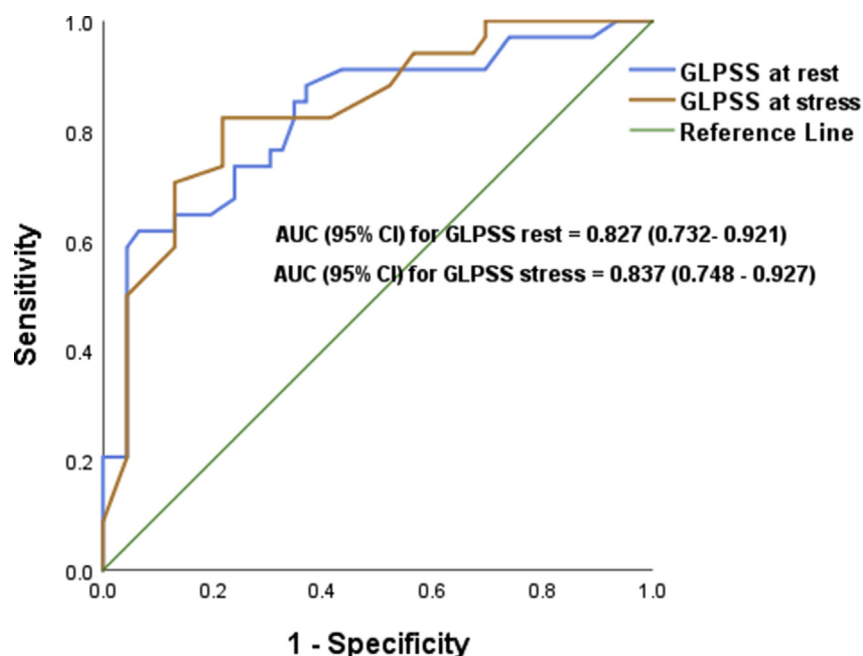


Fig. 1. ROC curve of GLPSS at rest and stress for predicting SYNTAX score >22. GLPSS = global longitudinal peak systolic strain; ROC = receiver operating characteristic.

4. Discussion

The findings of our study demonstrated that the measurement of GLPSS during DSE is an appropriate modality that provides quantifiable information for the detection of myocardial ischemia and for predicting the number and severity of affected vessels in patients with chronic stable angina. Only a few studies compared multiple echocardiographic parameters (DSE, STE at rest and during dobutamine stress) for assessment of the presence, site, and severity of CAD.

In the present study, DSE could predict the presence of CAD with 85% sensitivity and 95% specificity. While adding STE at stress increased the sensitivity for detecting CAD in patients with chronic stable angina with better agreement with CA (Kappa = 0.819, $p < 0.001$). These results were in agreement with those of Ng et al¹⁰ who found that the mean GLPSS at peak stress (84.2% sensitivity and 87.5% specificity) was comparable with the expert wall motion analysis (76.0% sensitivity and 92.2% specificity) and had significantly higher accuracy compared to circumferential and radial strains in detecting significant CAD. However, the combination of expert wall motion analysis and quantitative longitudinal systolic strain analysis had the highest diagnostic accuracy (100% sensitivity and 87.5% specificity).

Similarly, Aggeli et al⁸ reported that the variation in values of GLSS between rest and stress had 81% sensitivity and 72% specificity. Rumbinaitė et al¹¹ found that longitudinal strain had the best predictive value for significant coronary artery stenosis (sensitivity = 89.4%, specificity = 64.7%). Park et al¹² found that GLPSS at stress has 85% sensitivity, 92% specificity, 80% PPV and 94% NPV in predicting significant CAD. In contrast, DSE was found to have 48% sensitivity, 83% specificity, 52% PPV and 81% NPV.

In the present study, DSE had 81% sensitivity and 82% specificity for the detection of single-vessel disease. However, adding STE to DSE increased the sensitivity to 93.2% and the specificity up to 94.7%. The diagnostic value of adding STE to DSE was more sensitive ($p < 0.001$). For the detection of 2-vessel disease, STE at stress had more sensitive and specific values than DSE. DSE provided unique features to identify multivessel disease. However, adding STE at

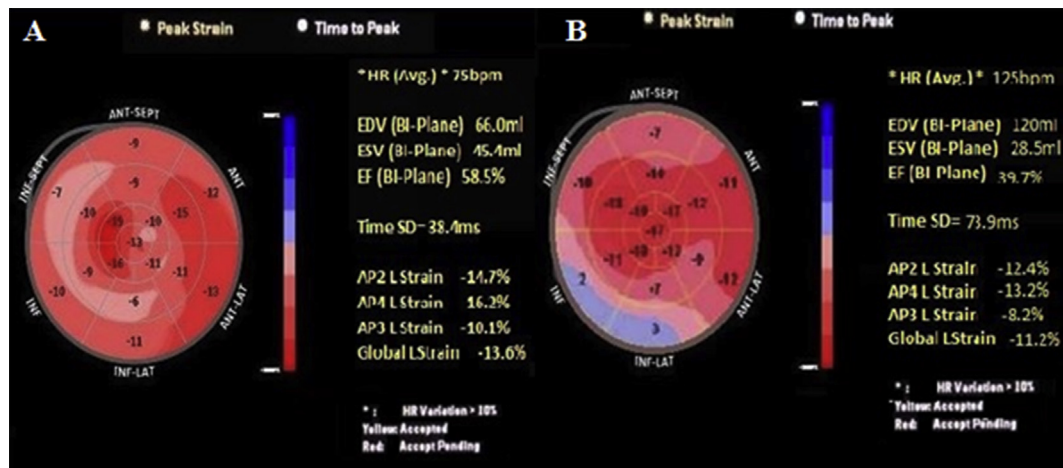


Fig. 2. Bull's eye of LV longitudinal strain of a patient with LAD and RCA lesion (SYNTAX score = 34) (A) at rest = -13.6% and (B) at stress = -11.2% . LAD = left anterior descending artery; RCA = right coronary artery; LV = left ventricular.

stress provided results that are more sensitive. This good sensitivity might be valuable in clinical practice for patients at intermediate to high risk, with the aim of decreasing false negative results, which may have a negative effect on outcome.

According to Choi et al.,¹³ 2D longitudinal strain could discriminate left main or multi-vessel disease from lesser CAD with 76% sensitivity and 74% specificity. Similarly, Hussein et al.¹⁴ revealed that the validity of longitudinal strain in detecting stenosis in different numbers of coronary arteries was good, and the best values were reported in the detection of three-vessels disease.

In our study, we studied the change in the regional longitudinal strain in accordance with the coronary arteries' supply territory.

STE at stress had excellent agreement with CA results for detecting LAD involvement and good agreement regarding RCA. However, it showed fair agreement with CA results for detecting LCX involvement. DSE had good agreement with CA results for detecting LAD involvement. However, it showed only fair agreement with CA results for detecting LCX and RCA involvement. This finding was consistent with that of Shah,¹⁵ who showed that the sensitivity of DSE in detecting LCX disease was 55%, which was lower than that for detecting LAD (80%) and RCA (76%).

Comparable results have been illustrated by Hanekom et al.,¹⁶ who showed that 2D STE during DSE can detect territorial lesions with excellent sensitivity for LAD (77% sensitivity and 79% specificity) exceeding that for LCX (71% sensitivity and 66% specificity) and RCA (65% sensitivity and 56% specificity). The lower diagnostic accuracy that was reported in the posterior circulation might be attributed to tracking problems in the posterolateral segments. Hussein et al.¹⁴ showed that stress GLSS was a good predictor for the presence of significant LAD stenosis with 93.8% sensitivity and 75% specificity compared with those of CA.

In the present study, male gender and cardiac risk factors were significantly prevalent in patients with $SS > 22$. Resting echocardiography revealed no statistically significant difference between the 2 groups except for GLPSS, which was significantly lower in those with $SS > 22$.

According to Choi et al.,¹³ patients with CAD and high SS had a significantly lower GLPSS at rest. In addition, Shimoni et al.¹⁷ reported that GLSS was significantly lower among patients with a high SS. Bakhom et al.¹⁸ showed that GLSS decreased incrementally with increasing severity of CAD defined by an increasing number of stenotic coronary vessels.

In our study, the value of resting GLPSS $\geq -15.2\%$ and stress GLPSS $\geq -12.5\%$ had the best diagnostic accuracy in predicting

$SS > 22$. This finding was consistent with that of Vrettos et al.,¹⁹ who illustrated that a GLPSS cutoff value of -13.95% predicts the detection of a high SS among patients with suspected CAD. Similarly, Moustafa et al.²⁰ showed that there was a negative correlation between GLPSS at rest and the SS that was significant in both high and intermediate scores and nonsignificant for a low SS with a cutoff value of -13.7 for predicting a high SS. In addition, Radwan and Hussein²¹ showed that GLSS decreased incrementally with increasing severity of CAD and that the risk of multi-vessel disease increased with decreasing GLSS. The optimal GLSS cutoff value for detecting significant CAD was -15.6% .

5. Conclusion

STE during DSE has a high sensitivity and specificity in predicting the presence of CAD in patients with chronic stable angina. It provides quantitative diagnostic information that decreases the false positive and false negative results of DSE. In addition, there is a highly significant strong correlation between GLPSS measured at rest and that measured during DSE in predicting the SS value.

6. Study limitation

It was single-center study with relatively small number of patients. So larger multicentre studied with large number of patients are needed to further evaluate the use of speckle tracking during dobutamine stress echocardiography. As all patients were in sinus rhythm, no conclusion can be drawn on patients with atrial fibrillation or other arrhythmias.

Conflict of interest

None declared.

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