Original articles

Value of two-dimensional speckle-tracking echocardiography for diagnosing significant coronary stenosis in patients with negative dobutamine stress echocardiography

Nguyen Thi Ngoc[1], Nguyen Anh Vu[2*], Do Thien Toan[3], Nguyen Le Hoang Minh[4]

[1]Cardiology Center, Tam Anh General Hospital, Ho Chi Minh City

[2]Department of Internal Medicine, Hue University of Medicine and Pharmacy

[3]Department of Geriatrics, Kien Giang General Hospital

[4]Cardiovascular Center, Hue University of Medicine and Pharmacy Hospital

***Corresponding author:** Nguyen Anh Vu; Email: navu@huemed-univ.edu.vn
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Abstract

Background: Detection of regional wall motion abnormalities during dobutamine stress echocardiography (DSE) is challenging and dependent on individual interpretation, which may reduce sensitivity and accuracy while increasing the false-negative rate. Two-dimensional speckle-tracking echocardiography (STE) during DSE is a highly sensitive method with the potential to detect false-negative cases among patients with negative DSE results.

Aim: This study assessed the value of global longitudinal strain (GLS) and regional longitudinal strain (RLS) by two-dimensional STE to detect significant coronary stenosis (SCS) among patients with negative DSE.

Methods: This cross-sectional study applied two-dimensional STE to 68 patients with negative DSE. They had stable angina suspected of chronic CAD according to the diagnostic criteria of the ESC 2024 and the Ministry of Health of Vietnam 2023. STE findings were compared against selective coronary angiography (DSA) and multi-slice computed tomography (MSCT).

Results: In the early recovery, GLS and RLS reached highest value. GLS reached AUC = 0.968 and Sensitivity = 84.4%, Specificity = 97.2% at GLS > -16.5%; RLS/LAD reached AUC = 0.863 and Sensitivity = 84.6%, Specificity = 83.3% at RLS/LAD > -16.7%; RLS/RCA reached AUC = 0.863 and Sensitivity = 71.4%, Specificity = 80.6%; RLS/LCx reached AUC = 0.926 and Sensitivity = 90.0, Specificity = 83.3 at RLS/LCx > -12.6%.

Conclusions: GLS and RLS measured during the early recovery phase are valuable in the assessment of coronary artery stenosis. STE-derived strain parameters may provide additional diagnostic information for significant stenosis across all three coronary artery territories in patients with negative DSE.

Keywords*: Dobutamine stress echocardiography; speckle tracking echocardiography; global longitudinal strain; regional longitudinal strain; significant coronary artery stenosis.*

1. INTRODUCTION

Dobutamine stress echocardiography (DSE) is a tool for detecting and stratifying patients with a history of coronary artery disease (CAD) or those suspected of having CAD, offering numerous benefits due to its accessibility, and low cost [1]. The European Society of Cardiology (ESC) has designated Class I, Level of Evidence B for the assessment of suspected CAD using DSE [2]. Regional wall motion abnormalities (WMA) during DSE are a late manifestation of ischemia. Detection of WMA is challenging due to sub-optimal windows with tachycardia following stress. Therefore, DSE remains a subjective method due to the opinions of the individual performing the ultrasound and evaluating the results [3]. This challenge may reduce the sensitivity, accuracy and raise the false negative rate of DSE. Therefore, patients with negative DSE should be suggested for a higher sensitivity test. The 2D speckle-tracking echocardiography (STE) during DSE is not influenced by the subjectivity of the observer in the analysis of global longitudinal strain (GLS). A high sensitivity method to facilitate the early detection of regional dysfunction in the assessment of ischemia, distinguishing passive motion from true contractile impairment, and quantifying early changes in myocardial function. Therefore, STE has the potential to detect false negatives among patients with negative DSE. STE measures GLS, which is the recommended value for assessing coronary artery stenosis, with a normal value of -22% < GLS < -18% and an abnormal threshold of GLS > -16% [3, 4]. Currently, there is limited research utilizing STE to investigate myocardial ischemia.

The cut points and values of GLS and regional longitudinal strain (RLS) have not been extensively validated among patients with negative DSE. In this study, we assessed the value of STE to detecting significant coronary stenosis (SCS) among patients with negative DSE. The finding reflects the potential contribution of STE to identifying SCS in patient who may have been missed by DSE.

2. SUBJECTS AND METHODS

2.1. Design: A cross-sectional study was conducted from August 2023 to June 2025.

2.2. Subjects: The study population consisted of patients with stable angina suspected of having chronic CAD, according to the diagnostic criteria of the ESC 2024 [2] and the Ministry of Health of Vietnam 2023 [5].

2.3. Sampling criteria: The patient presented for evaluation at Tam Anh General Hospital, Ho Chi Minh City, with stable angina suspected of chronic coronary artery disease and was invited to participate in the study, provided they were at least 18 years of age. Patients with contraindications for dobutamine stress testing were excluded from the study, including those who are pregnant, with EF < 40%, asthma, severe valvular heart disease, hypertrophic cardiomyopathy, idiopathic cardiomyopathy, congenital heart disease, severe hypertension, cerebrovascular accident, cancer, atrioventricular block, persistent atrial fibrillation, and acute coronary syndrome. Patients with poor image quality that are difficult to process were also excluded from the study.

2.4. Sample size: Sample size was estimated to assess the sensitivity and specificity of myocardial deformation parameters (Equation 1). Assuming a sample distribution ratio between the two groups is 1:1, the type I error probability α = 0.05; sensitivity 95% (p = 0.95) or specificity 93% (p=0.93) [3]; margin of error d = 0.1. From that, the minimum sample size was estimated to be 26 patients for each group.

$$n \geq \frac{Z^2_{(1-\frac{\alpha}{2})}\, p\times(1-p)}{d^2} \qquad \textit{(Equation 1)}$$

2.5. Research process

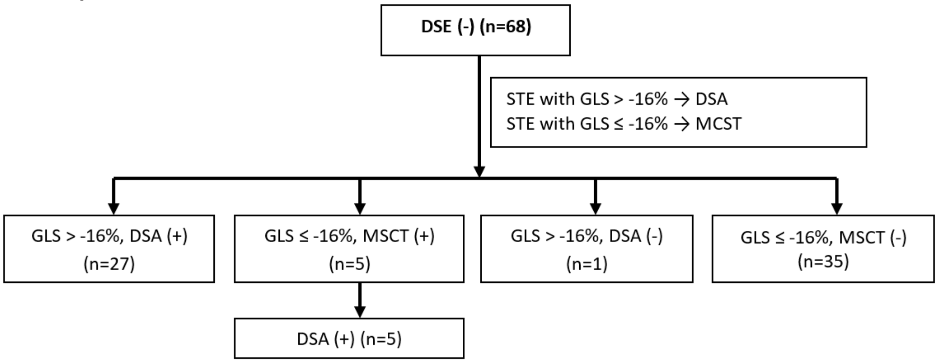


Figure 1. Study flow chart

A total of 68 patients with stable angina and DSE (-) were evaluated for STE, GLS and RLS. An elevation in GLS was observed in 28 patients, and DSA was subsequently indicated for definitive diagnosis in 27 patients with DSA (+) and 1 patient with no significant stenosis with DSA (-). A total of 40 patients with stable angina who did not exhibit a reduction in GLS were indicated for MSCT to exclude significant coronary stenosis. Among these, 35 patients had MSCT (-) results, the remaining 5 patients with MSCT (+) results underwent further evaluation with DSA, which confirmed significant stenosis DSA (+) (Figure 1).

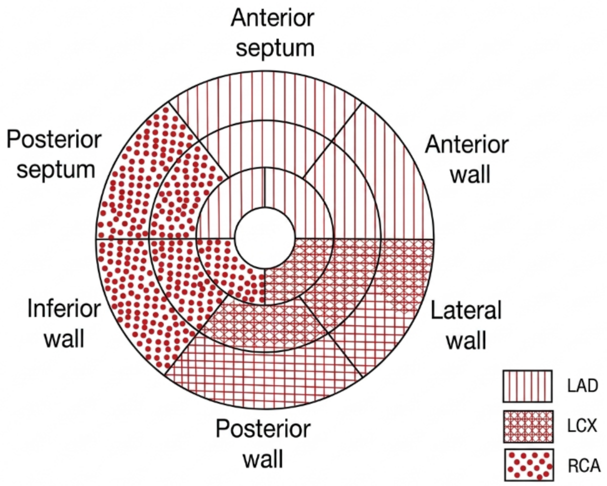
2.6. Assessments in research

Background characteristics including age, gender, diabetes, hypertension, current smoker, dyslipidemia, ejection fraction (EF), and tricuspid annular plane systolic excursion (TAPSE) were reviewed from patient records.

Coronary artery stenosis was defined based on DSA or MSCT according to the guidelines of the ESC in 2024. Significant coronary artery disease was defined as any of the following: (i) Stenosis ≥ 50% of the left main coronary artery, (ii) Stenosis ≥ 70% for other coronary arteries, (iii) Intermediate stenosis (50 - 70%) on DSA confirmed by invasive Fractional Flow Reserve (FFR) < 0.80 or Instantaneous Wave-Free Ratio (iFR) < 0.90. For coronary lesions of intermediate angiographic severity, the functional significance of stenosis was evaluated using invasive physiological assessment with FFR or iFR, in accordance with contemporary clinical practice guidelines.

DSE was performed according to the guidelines of the American Society of Echocardiography in 2020 and the tissue marking technique as per the guidelines of the ESC in 2019. Dobutamine was delivered in graded doses starting at 5 µg/kg/min and increasing at 3-minute intervals to 10, 20, 30 and 40 µg/kg/min. Endpoints for termination of the test include achievement of the target heart rate, hypotension, significant arrhythmia, severe hypertension, and intolerable symptoms. DSE (+) when there are new-onset angina, abnormal movement in at least two adjacent regions during the dobutamine infusion phase, significant changes in the electrocardiogram indicative of severe ischemia [1]. Only patients with DSE(-) were included in the STE analysis to assess the likelihood of false negative detection.

The STE images were recorded at rest, at dosage of 20 µg/Kg/min, peak, and early recovery (within 2 minutes post-dobutamine recovery). Tissue marking monitoring is performed at frame rate from 50 to 90 fps using EchoPAC on GE VIVID S70 (offline analysis). The left ventricle was divided into six myocardial segments in each cross-section, and the GLS was calculated as the average value of the apical longitudinal deformation of all segments at the end of systole [6]. RLS were calculated as the average of segmental strain values within the corresponding coronary artery territories, based on the 17-segment model of the left ventricle defined by the American Heart Association [7]. (Figure 2).



LAD: Left anterior descending artery
LCx: Left Circumflex Artery
RCA: Right coronary artery

Figure 2. Circumferential polar plot of the 17 myocardial segments derived by visual wall motion assessment and speckle tracking echocardiography, showing the definition of regions supplied by respective coronary arteries

"Source: Ilardi F, 2021" [7]

2.7. Data analysis

Data were analyzed using Stata version 17. Qualitative variables are described by frequency, percentage, and quantitative variables are described by mean ± standard deviation (Mean ± SD). Testing the proportion between groups using Fisher's exact test and comparing the means between groups using independent t-test. The values examined in this study include sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). Statistical tests are considered significant when $p < 0.05$.

2.8. Ethics in Research

The study was approved by the Ethics Committee of the University of Medicine and Pharmacy, Hue University, under approval number H2023/488.

3. RESULTS

3.1. Characteristics of the study sample

Table 1. Characteristics of the study sample

Characteristics		**Total number of samples (n = 68)**	**Significant stenosis (n=32)**	**No significant stenosis (n=36)**	**p**
Age, *Mean ± SD*		67.62 ± 11.68	71.38 ± 11.05	64.28 ± 11.33	0.011
Gender, frequency (%)	Male	32 (47.06)	15 (46.88)	17 (47.22)	1.000
	Female	36 (52.94)	17 (53.13)	19 (52.78)	
Diabetes, frequency (%)	Yes	19 (27.94)	14 (43.75)	5 (13.89)	0.008
	No	49 (72.06)	18 (56.25)	31 (86.11)	
Hypertension, frequency (%)	Yes	61 (89.71)	29 (90.63)	32 (88.89)	1.000
	No	7 (10.29)	3 (9.38)	4 (11.11)	
Current Smoking, frequency (%)	Yes	8 (11.76)	8 (25.00)	0 (0)	0.001
	No	60 (88.24)	24 (75.00)	36 (100)	
Dyslipidemia, frequency (%)	Yes	63 (92.65)	28 (87.50)	35 (97.22)	0.180
	No	5 (7.35)	4 (12.50)	1 (2.78)	
EF, Mean ± SD		69.36 ± 6.37	69.84 ± 6.02	68.87 ± 6.76	0.554
TAPSE, *Mean ± SD*		21.19 ± 2.46	20.81 ± 2.15	21.58 ± 2.72	0.219

EF: Ejection fraction; TAPSE: Tricuspid annular plane systolic excursion

The study included 68 patients with a mean age of 67.62 ± 11.68 years. The group with coronary artery stenosis had a mean age of 71.38 ± 11.05 years, compared to the no significant stenosis group, which had a mean age of 64.28 ± 11.33 years. There was a statistically significant difference between the two study groups with p=0.01. The male group consisted of 32 patients, with 15 patients (46.88%) exhibiting significant stenosis and 17 patients (47.22%) demonstrating no significant stenosis. A total of 36 female patients were included, comprising 17 patients (53.13%) with significant stenosis and 19 patients (52.78%) without stenosis; there was no difference between the two gender groups in the two study cohorts. The risk factors associated with diabetes, with p=0.008, and smoking, with p=0.01, showed a significant difference between the two study groups. EF and TAPSE did not differ between the two study groups, with p = 0.554 and p = 0.219.

3.2. The association of GLS and RLS with coronary artery disease among patients with negative DSE

GLS and RLS were different between the significant and no significant stenosis groups at the early recovery phase. The mean GLS was -14.08% in the significant stenosis group, whereas it was 19.91% in the no significant stenosis group (p < 0.001). GLS and RLS/LAD showed statistically significant differences between the two study groups across all stress phases (p < 0.05).

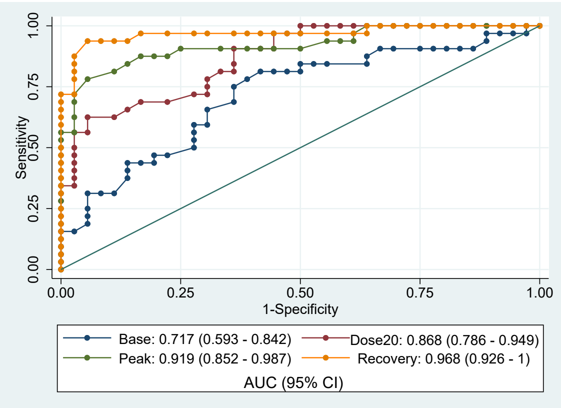
Table 2. Analysis of GLS and RLS in patients with stable angina pectoris undergoing dobutamine stress echocardiography with negative results

Strain *Phase*	**Significant stenosis** Mean% ± SD%	**No significant stenosis** Mean% ± SD%	**p***
GLS	(n = 32)	(n = 36)	
Rest	-18.03% ± 2.61%	-19.85% ± 1.92%	0.002
20 mcg/kg/min	-16.50% ± 6.72%	-21.81% ± 2.68%	< 0.001
Peak	-14.95% ± 2.63%	-19.68% ± 2.27%	< 0.001
Early recovery	-14.08% ± 2.61%	-19.91% ± 2.20%	< 0.001

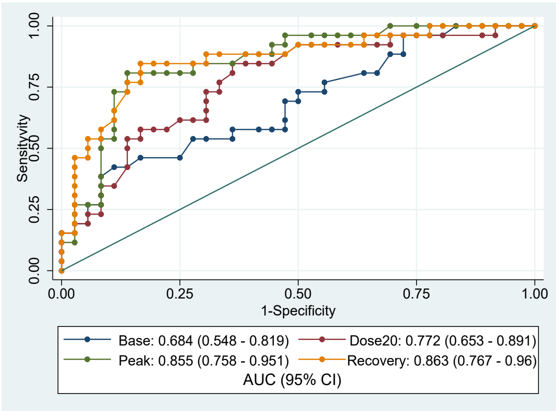
RLS/LAD	*(n = 26)*	*(n = 36)*	
Rest	-17.69% ± 3.72%	-20.14% ± 2.94%	0.005
20 mcg/kg/min	-16.84% ± 4.62%	-21.68% ± 4.86%	< 0.001
Peak	-12.32% ± 4.36%	-18.99% ± 4.71%	< 0.001
Early recovery	-11.66% ± 5.37%	-19.11% ± 4.10%	< 0.001
RLS/RCA	*(n = 14)*	*(n = 36)*	
Rest	-18.10% ± 4.95%	-18.85% ± 3.39%	0.542
20 mcg/kg/min	-18.64% ± 4.81%	-20.42% ± 4.21%	0.205
Peak	-15.91% ± 7.42%	-18.27% ± 4.87%	0.194
Early recovery	-13.29% ± 6.47%	-18.89% ± 3.67%	< 0.001
RLS/LCx	*(n = 10)*	*(n = 36)*	
Rest	-17.15% ± 5.81%	-18.72% ± 3.48%	0.286
20 mcg/kg/min	-15.03% ± 4.34%	-18.62% ± 4.75%	0.037
Peak	-11.08% ± 5.26%	-15.31% ± 5.48%	0.035
Early recovery	-6.80% ± 3.36%	-15.91% ± 4.87%	< 0.001

GLS: Global longitudinal strain; RLS: Regional longitudinal strain
LAD: Left anterior descending artery; LCx: Left Circumflex Artery
*RCA: Right coronary artery; * T-test*

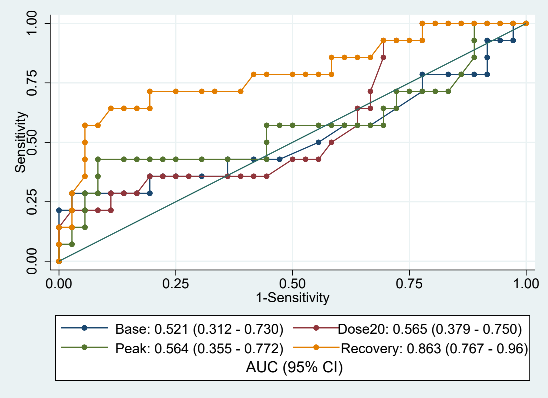
Analysis of the area under the ROC curve in the DSE (-) group indicated that the early recovery phase had the highest value (AUC=0.968) with a cutoff point for GLS > -16.5% (Sensitivity = 84.4, Specificity = 97.2) (Figure 3; GLS). Early recovery phase RLS has the highest value in assessing coronary artery stenosis by region. The AUC for the early recovery phase is 0.863 for the LAD branch, 0.863 for the RCA branch, and 0.926 for the LCx branch. In the DSE (-) sample, the RLS during the recovery phase achieved values with a specificity exceeding 80% across all branches; sensitivity was high for the LAD branch at 84.6% and for the LCx branch at 90%, while the RCA branch exhibited an acceptable sensitivity of 71.4% (Figure 3; RLS). Thus, RLS has demonstrated the potential to assess significant coronary artery stenosis regionally.

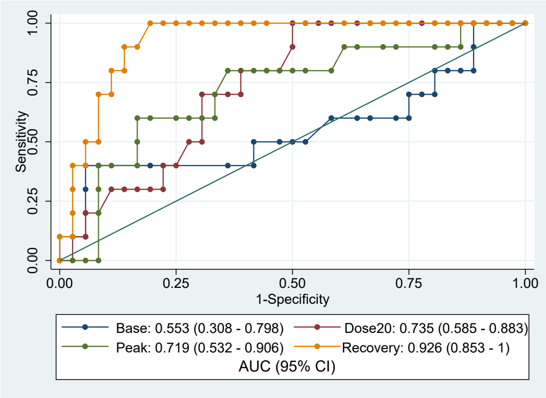


GLS
Peak stress: Cut-off > -16.8%
Sensitivity: 78.1 (CI 95%: 63.6 - 90.7)
Specificity: 94.4 (CI 95%: 85.5 - 99.3)
Early recovery: Cut-off > -16.5%
Sensitivity: 84.4 (CI 95%: 71.0 - 94.7)
Specificity: 97.2 (CI 95%: 90.3 - 99.9)



RLS/LAD
Peak stress: Cut-off > -16.2%
Sensitivity: 80.8 (CI 95%: 65.1 - 93.5)
Specificity: 83.3 (CI 95%: 70.5 - 93.6)
Early recovery: Cut-off > -16.7%
Sensitivity: 84.6 (CI 95%: 69.9 - 95.6)
Specificity: 83.3 (CI 95%: 70.5 - 93.6)





RLS/RCA
Peak stress: Cut-off > -13.6%
Sensitivity: 42.9 (CI 95%: 23.0 - 71.1)
Specificity: 91.7 (CI 95: 81.3 - 98.3)
Early recovery: Cut-off > -16.4%
Sensitivity: 71.4 (CI 95%: 49.2 - 91.6)
Specificity: 80.6 (CI 95%: 67.2 - 91.8)

RLS/LCx
Peak stress: Cut-off > -14.2%
Sensitivity: 80.0 (CI 95%: 55.5 - 97.5)
Specificity: 63.9 (CI 95%: 49.0 - 79.2)
Early recovery: Cut-off > -12.6%
Sensitivity: 90.0 (CI 95%: 69.2 - 99.8)
Specificity: 83.3 (CI 95%: 70.5 - 93.6)

Figure 3. The AUC for GLS and RLS in the study of coronary artery disease is significant in patients with stable angina who have a negative dobutamine stress echocardiography

Multivariable analysis showed that GLS was an independent predictor of coronary artery disease during both the peak and early recovery phases, with odds ratios (ORs) of 95.41 and 181.3, respectively (Table 3).

Table 3. Adjusted logisitic regression for factor assocated with coronary artery disease (n = 68)

Characteristics		**Peak stress**		**Early recovery**	
		OR (CI 95%)	**p**	**OR (CI 95%)**	**p**
GLS	> -16.5%	95.41 (10.49 - 867)	< 0.001	181.3 (17.99 - 1827)	< 0.001
	≤ - 16.5%	1		1	
Gender	Male	0.70 (0.14 - 3.59)	0.667	1.64 (0.23 - 11.7)	0.624
	Female	1		1	
Diabetes	Yes	3.48 (0.62 - 19.64)	0.159	5.70 (0.68 - 48.13)	0.110
	No	1		1	

4. DISCUSSION

4.1. Characteristics of the participants (Table 1)

The study included 68 patients with a mean age of 67.62 ± 11.68 years. The group with significant stenosis had an average age of 71.38 ± 11.05 years, compared to the no significant stenotic group, which had an average age of 64.28 ± 11.33 years. There was a statistically significant difference between the two study groups with p = 0.01. In the study conducted by Ilardi Federica [7], the mean age was 66.3 ± 8.2, with a p-value of 0.190, indicating no significant difference between the two study groups, similar to our findings. The male group consisted of 32 patients, with 15 patients [46.88%] exhibiting significant stenosis and 17 patients [47.22%] demonstrating no significant stenosis, similar to the findings in the male study conducted by Ilardi Federica [7]. A total of 36 female patients were studied, with 17 patients [53.13%] exhibiting significant stenosis, while 19 patients [52.78%] were no significant stenosis, p = 1.000; there was no difference between the two gender groups in the two study cohorts. The risk factors associated with diabetes, with p = 0.008, and smoking, with p = 0.01, show a significant difference between the two study groups. In our study, hypertension and dyslipidaemia showed no significant differences between the two groups with p = 1.000 and p = 0.248 compared to Ilardi Federica [7] p = 0.18 and p = 0.94, indicating no differences between the two groups. Ejection fraction did not differ between the two study groups, with p = 0.219 compared to Ilardi Federica [7] p = 0.14.

4.2. Analysis of global longitudinal strain in patients with stable angina pectoris undergoing dobutamine stress echocardiography with negative results (Table 2) (Figure 3).

The limitations of the echocardiographic stress test are dependent on the individual performing the procedure. We continue to perform myocardial tissue marking techniques in 68 cases with DSE [-]. We identified 36 no significant stenosis patients and 32 significant stenosis patients. At early recovery, the results showed that significant stenosis group was a higher GLS than no significant stenosis group [-14.08% ± 2.61% compared to -19.91% ± 2.20% with $p < 0.001$]. The analysis of the area under the ROC curve indicates that the early recovery has the highest value [AUC = 0.968]; sensitivity of 84.4% and specificity of 97.2% at cut-off GLS > -16.5%. According to the author Ragab Tamer M in 2025, the research findings indicate that GLS during the recovery phase in the group with significant coronary artery stenosis is higher than in the group without stenosis, with values of -15.5% ± 4% compared to -19.1% ± 3.1%, and a $p = 0.03$. In the recovery phase, the sensitivity of GLS was 95% and the specificity was 93% [8]. Following cessation of stress, myocardial perfusion may recover rapidly; however, myocardial contractile function does not immediately return to normal, a phenomenon known as post-ischemic stunning. As a result, wall motion may appear to normalize, whereas myocardial deformation remains impaired. Technical conditions during the recovery phase are also more favorable than at peak stress, including a gradual reduction in heart rate, improved image quality, and more stable frame-to-frame tracking [11].

4.3. Analysis of longitudinal strain (RLS) in patients with stable angina pectoris undergoing dobutamine stress echocardiography with negative results.

LAD branch: The study results indicate that the longitudinal strain values in the RLS/LAD region decreased during the early recovery [-11.66% ± 5.37% compared to -19.11% ± 4.10%, $p < 0.001$], with a significant difference observed between the two study groups. The authors Kamal Halessa and colleagues indicate that a resting left ventricular systolic function RLS of higher than -16.13% may suggest significant CAD with involvement of the left main coronary artery and three branches [9], similar to our findings when RLS during the early recovery phase is higher than -16.7%. In our study, we analysed the area under the ROC; in early recovery, a cutoff point of higher than -16.7% demonstrated a sensitivity of 84.6% and a specificity of 85.7%, with an AUC of 0.863.

RCA branch: With the value of strain in the RLS/RCA region during the early recovery, RLS/RCA increased [-13.29% ± 6.47% compared to -18.89% ± 3.67%, $p < 0.001$, AUC = 0.863], indicating a significant difference between the two groups. The RLS/RCA value at a threshold of > -16.4% has a sensitivity of 71.4% and 80.6%.

LCx branch: In the analysis of results, RLS/LCx increased during the recovery phase [-6.80% ± 3.36% compared to -15.91% ± 4.87 with $p < 0.001$, AUC = 0.92], indicating a statistically significant difference between the two groups. With a threshold of RLS > -14.2%, at peak stress, the sensitivity is 80% and the specificity is 63.9%. In the recovery phase, with a cutoff > -12.6%, the sensitivity is 60% and the specificity is 96.8%.

4.4. Study limitations

This study has several limitations that should be considered when interpreting the findings.

First, this was a single-center study, which limits generalizability. The findings are exploratory and require further validation using multi-center data.

Second, the sample size was small, particularly for the RLS analyses. Although several potential confounders were identified, including age, current smoking status, and diabetes, these factors could not be adequately controlled for in the analysis. Future studies should expand the sample size to enable RLS analyses and to allow adequate control for potential confounding factors.

Third, the reference standard for diagnosis was not uniform across the study population. DSA, the current gold standard, was applied to high-risk groups, including those with GLS > −16% or MSCT [+]. In contrast, patients with GLS < −16% were classified as having no significant stenosis if MSCT [−], without confirmation by DSA. This definition may be subject to verification bias and could have led to an overestimation of the diagnostic accuracy of STE. This reflects both practical and ethical considerations, as routine invasive coronary angiography cannot be justified for all patients with negative DSE results and normal strain parameters. Therefore, the reference standard was determined according to clinical risk stratification and the hospital's current practice. Patients with abnormal GLS underwent DSA, whereas those with normal GLS underwent MSCT as a non-invasive rule-out strategy. This approach reduces the invasiveness associated with DSA while still maintaining reliable negative diagnosis, given that MSCT demonstrated a specificity of 96.7% compared with DSA [10].

Fourth, intraobserver and interobserver variability analyses were not performed, which may limit the assessment of the reliability of STE-derived strain measurements.

5. CONCLUSION

GLS and RLS measured during the early recovery phase are valuable in the assessment of coronary artery stenosis. STE-derived strain parameters may provide additional diagnostic information for significant stenosis across all three coronary artery territories in patients with negative DSE.

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