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Value of global longitudinal peak systolic strain derived by 2-D speckle tracking in detection of obstructive coronary artery disease

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Abstract

Background:

Early detection of obstructive coronary artery disease (CAD) using Peak Systolic global longitudinal strain derived by 2-D Speckle Tracking in patients with chronic stable angina.

75 patients with chronic stable angina were enrolled in this cross sectional study, (Mean age was 56.69 ± 6.96 y, 35 were males), 42.7 % were diabetic and all patients were assessed by thorough history taking, clinical examination,12 lead surface ECG, conventional, speckle Echocardiography and coronary angiography in Mansoura specialized medical hospital from march 2017 to October 2017

Results:

Statistically significant decrease was found in GLS-Avg values in patients with obstructive CAD when compared to patients with normal coronary angiography ($p<0001$) and in patients with 3 or more risk factors when compared to patients with one or two risk factors ($p=0.014$),

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And when syntax score was increasing among patients with obstructive CAD a significant decrease in median GLS-Avg values was noted ($p<0.001$), but when regional systolic strain values were compared to affected coronary arteries no significant difference was found ($p=0.844$) i.e almost identical correlation between affected segments by speckle tracking and obstructed arteries by coronary angiography.

Multivariate logistic regression analysis showed that GLS-Avg was found as a predictor for CAD disease in patients with chronic stable angina ($p=0.028$ with odds ratio 31.4 and 95% CI (1.85-535))

ROC curves were established and cutoff value was determined for GLS-Avg as -16 with 89.8% sensitivity and 100% specificity

Conclusion:

longitudinal strain derived by speckle tracking can be used as non-invasive simple test for evaluation of patients with chronic stable angina and as a predictor for presence or absence of obstructive CAD

Keywords: Speckle Tracking – Coronary artery disease – Coronary Angiography – Syntax score.

Declarations:

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Mansoura Faculty of Medicine (IRB code MS 17.01.70). This study was carried out in accordance with the rules of the Helsinki Declaration. Informed written consent was obtained from all the participants

Consent for Publication

Not applicable

Availability of Data and Materials

All data generated or analyzed during this study available from the corresponding author on reasonable request

Competing Interests

The authors have nothing to disclose

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Authors Contributions

1st Author MA: Data Collection, Paper formulation

2nd Author MY: Design of the work

3rd Author MW: Analysis and interpretation of data, Paper Editing

All authors have read and approved the manuscript

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Not Applicable

Background

One of the most common causes of death worldwide is ischemic heart disease (IHD). IHD has a wide range from being asymptomatic to myocardial infarction (MI) and may lead to sudden cardiac death. (1)

Despite presence of many imaging tools and provocative tests for noninvasive assessment of coronary artery disease (CAD), noninvasive identification of patients with CAD continues to be a clinical challenge as only 35 % of patients who undergo coronary angiography show obstructive CAD.(2)

Echocardiographic deformation imaging tools especially that measures strain rate and strain have been validated for evaluation of various myocardial disorders even if the resting 2-D echocardiography shows normal function, it can detect subclinical affection of the myocardium.(3)

Changes in the intraventricular pressure and affection of coronary circulation have direct effect on longitudinal muscle fibers of the myocardium so, impairment of the longitudinal fibers function occurs first. As a result, measurement of longitudinal strain and strain rate may be sensitive in subclinical assessment of LV dysfunction (4)

As known that intermittent ischemic attacks may lead to subtle forms of myocardial dysfunction, Average Global longitudinal peak systolic strain (GLS-Avg) derived by Two Dimensional Speckle Tracking Echocardiography (2D-STE) can be used as a tool for early detection of these subtle forms especially in patients with severe or critical coronary artery stenosis with high sensitivity (5).

The aim of this study was early detection of obstructive CAD in patients with chronic stable angina (CSA) disease using peak Systolic GLS-Avg Derived by 2-D Speckle Tracking.

Patients and methods

- **Study population**

The study was case control study and conducted on 75 consecutive patients with CSA who were admitted to Mansoura specialized hospital in the period between November 2017 and March 2018 for elective coronary angiography

- **Inclusion criteria:**

Patients complaining of typical ischemic chest pain according to AHA criteria with normal 12 lead electrocardiogram (ECG) and average 2-D transthoracic ECHO with normal resting segmental wall motions

- **Exclusion criteria:**

Patients with ischemic changes in ECG, or abnormal RSWMs in 2-D TTE, Patients with previous MI (STEMI&NSTEMI) or with previous coronary artery bypass grafting or percutaneous intervention and Patients with ventricular paced rhythm or with valvular heart disease.

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❖ **Ethics statement**

All procedures were performed as recommended by the guidelines. Data were analyzed anonymously. The study was explained to all patients and they gave oral informed consent.

❖ **Methodology**

All patients were subjected to the following: Through history has taken, full general and local examination & investigations included: 12 leads ECG, 2-D STE and coronary angiography

- **2-D conventional ECHO:**

Patients were examined by a commercially available system (Vivid 9, General ElectricVingmed, Horton, Norway) in left lateral position. Data acquisition in apical &parasternal views. M-mode, 2D strain images were done and saved in cine-loop.

- **2-D speckle tracking ECHO with GLS -Avg :**

Segmental longitudinal peak systolic strain was measured in all views between aortic valve opening and closing for the 6 basal, 6 midventricular and 5 apical segments. The average longitudinal peak systolic strain of these segments will be calculated automatically to provide GLS -Avg.

- **Coronary angiography:**

Findings obtained from coronary angiography include location of lesions, number of vessels affected. Severity of coronary lesions: defined as > 70% of diameter stenosis considered significant, > 2 major epicedial coronary vessels are called multi vessel diseases. Left main coronary artery diseases: defined as ≥50% of coronary artery narrowing in left main artery. Syntax score: to assess the severity of the CAD by evaluation the number of coronary vessel affected, dominance, and location of lesions, complexity like calcifications, tortuosity, bifurcation, disease, long lesion and the presence of thrombus. It can be calculated through syntax score website(http://www.syntaxscore.com)

Statistical analysis

The collected questionnaires were subjected to revision, and the collected data were coded, processed and analyzed using SPSS program for Windows (version 22).One-sample Kolmogorov-Smirnov test is used to test the data normality.

Qualitative data are represented in percentage and numbers. Chi-square test is used to compare categorical variables.

Results

❖ **Descriptive data:**

Mean age was 56.69 ± 6.96 y, 46.7 % were males, 64% were obese with mean BMI 31.77 ± 4.31 (Figure 1)

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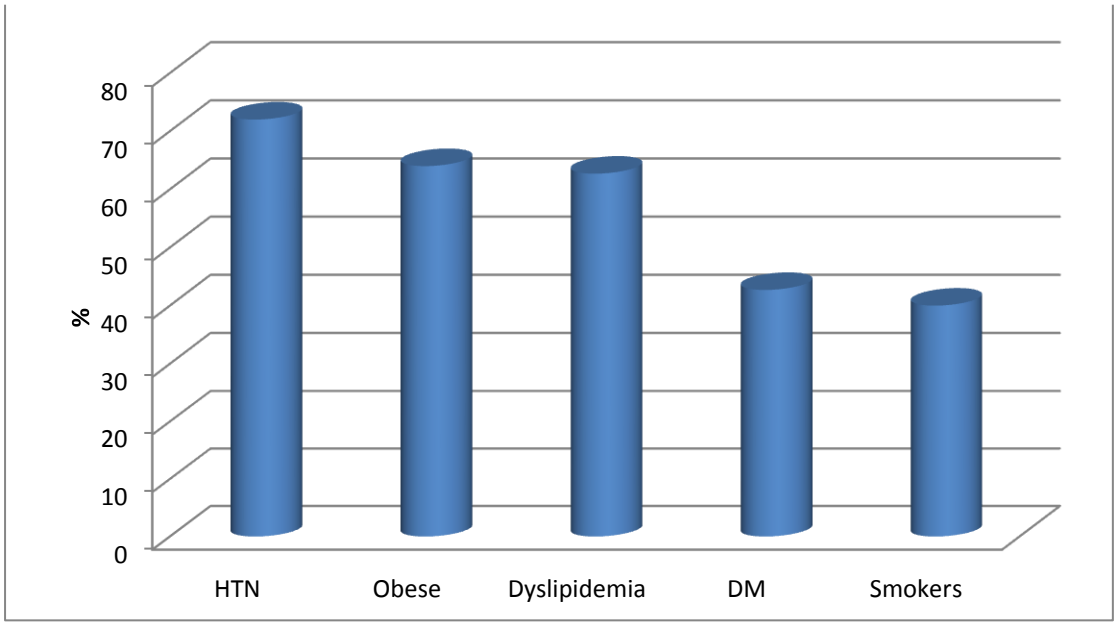

Figure 1 relation demographic and clinical data of the studied group

40% were smokers, 72% were hypertensive patients and 62.7% had a history of dyslipidemia. (Table 1)

Diabetic patients were 42.7% of the study population with median duration of diabetes about 8 years (Table 1).

Table 1 **shows relation demographic and clinical data of the studied group**

Variables	**Study group (n=75)**	
Age/years		
Mean ± SD	56.69±6.96	
Min-Max	42-72	
BMI		
Mean ± SD	31.77±4.31	
Min-Max	25-44	
Sex		
Male	35	46.7%
Female	40	53.3%

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Obesity		
Non obese	*27*	*36.0%*
Obese	*48*	*64.0%*
DM	32	42.7%
HTN	54	72.0%
Duration of HTN Median (Min-Max)	6 (0-20)	
Smokers	30	40.0%
Dyslipidemia	47	62.7%
Positive family history	41	54.7%

57.3% of patients presented with CSA class II, while 20% presented with class I and 22.7% presented with class III (Table 2).

Table 2 Shows relation between angina class and angio description.

Variables	**Study group (n=75)**	
	No	%
Angina class		
1	15	20.0%
2	43	57.3%
3	17	22.7%
Angio description		
No	16	21.3
Single vessel	37	49.3
two vessels	14	18.7
Three vessels	3	4.0
LM with other vessels	5	6.7

78.7% of the patients had obstructive coronary lesions, 49.3% had single vessel affection,

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18.7% had 2 vessels affection, 4% had 3 vessels affection and 6.7% had left main disease. Among 75 patients, 18% had normal coronary angiography and normal GLS-Avg values while 78% of patients had obstructive CAD and abnormal GLS-Avg values (Figure 2).

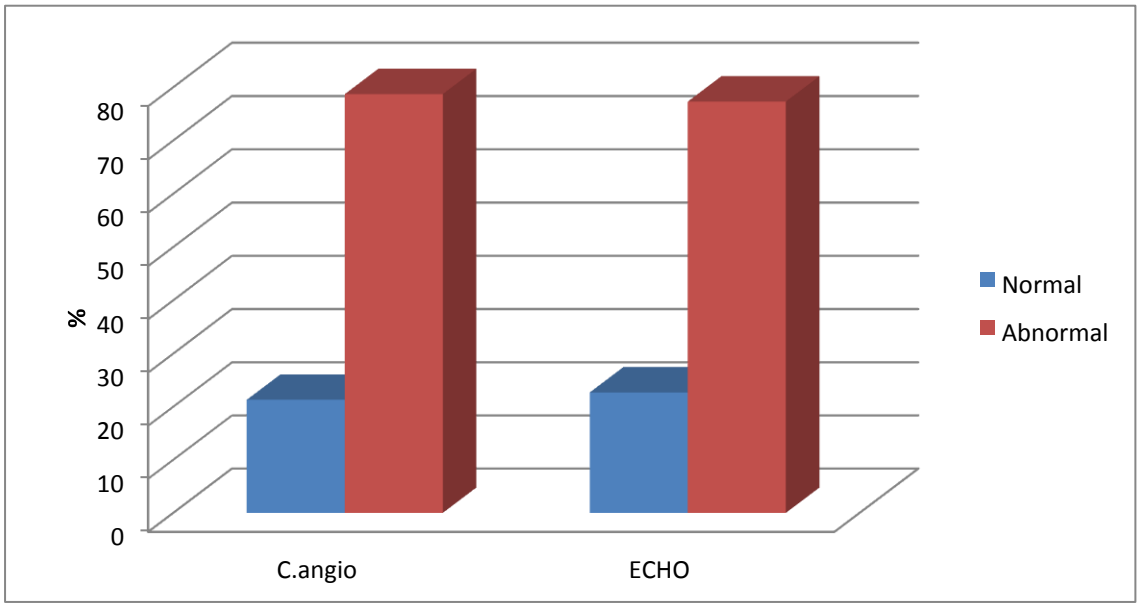

Figure 2 relation between ECHO results and coronary angiography results

❖ **Comparative data:**

GLS-Avg values were compared between patients with obstructive CAD and patients with normal coronary angiography and statistically significant decrease in values of GLS-Avg was found in patients with obstructive CAD with a cutoff value of -16 (p<0001) (Table 3).

Table 3 shows relation between coronary angiography and GLS-Avg

GLS-Avg	Coronary angiography		t-test	p-value
	Normal (n=16)	**Abnormal (n=59)**		
pMean SD	-19.02±1.57	-15.59±1.53	3.74	<0.001**
Min-Max	-21: -17	-18 : -10		

*significant p <0.05, **highly significant p<0.001

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Z: Mann Whitney test, χ^2 : chi square test, highly significant p <0.001,* significant p <0.05**

When GLS-Avg values were compared to the number of traditional risk factors for IHD, statistically significant difference in the values of GLS-Avg was found in patients with 3 or more risk factors versus patients with one or two risk factors (p=0.014) (Figure 3).

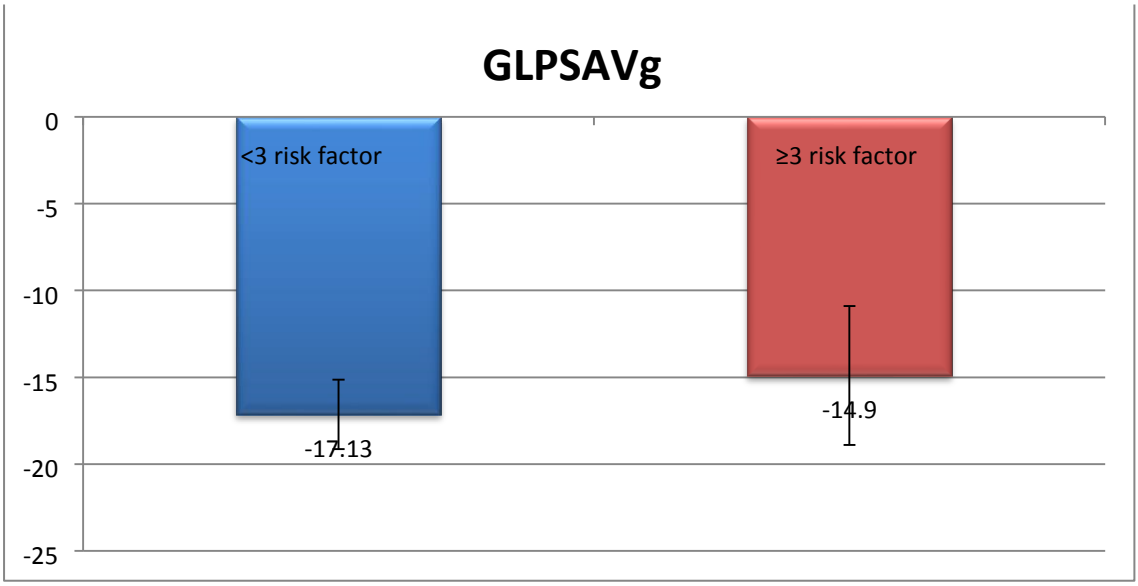

Figure 3 relation between No of risk factors and GLS-Avg values

And when syntax score was increasing among patients with obstructive CAD, a significant decrease in median GLS-Avg values was noted (p<0.001) (Table 4)

Table 4 shows relation between GLS-Avg and syntax score

syntax.score	GLS-Avg		**Mann-Whitney**	**p-value**
	≤-16	>-16		
median (min-max)	3 (0-9)	15 (8-36)	7.188	<0.001**

*significant p <0.05, **highly significant p<0.001

Test used: test :Mann–Whitney *U* test

LAD territory was affected in 26 patient in coronary angiography but was affected in only 25 of them by ECHO, While RCA territory was affected in 24 patient by coronary angiography and was affected in all the 24 patients by ECHO., however that LCX territory was affected in 25 patient in coronary angiography but was affected in only 23 of them by ECHO. (Table 5 & Figure 4)

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Table 5 shows relation between territory affected by ECHO and by coronary angiography.

	territory affected by coronary angiography		territory affected by ECHO	
	No	%	No	%
LAD	26	42.6	25	40.9
RCA	24	39.3	24	39.3
LCX	25	41.0	23	37.7

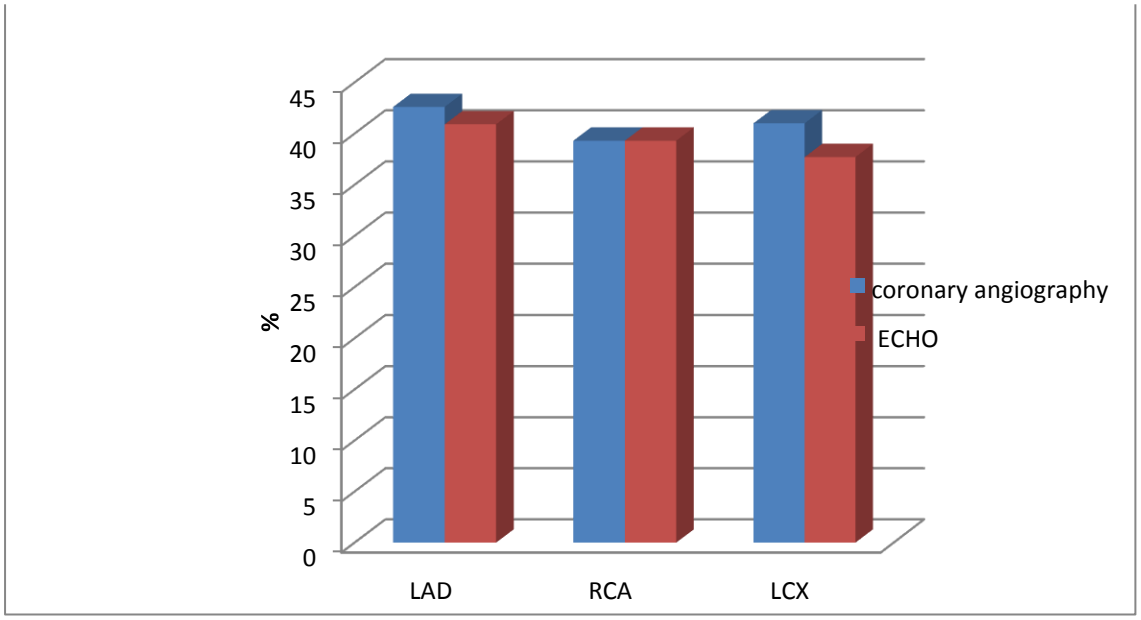

Figure 4 relation between territories affected by ECHO and by coronary angiography.

When univariate and multivariate logistic regression analyses were established among patients with abnormal coronary angiography GLS-Avg was found as a predictor for obstructive CAD in patients with CSA (p=0.028 with odds ratio 31.4 and 95% CI (1.85-535)) Finally, ROC curves were established for the relation between GLS-Avg and results of coronary angiography revealed 100% specificity for GLS- Avg to detect patients who have CAD by coronary angiography with a cutoff value of -16 and found to have 94.9% sensitivity

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for GLS-Avg to rule out CAD in patients with normal coronaries by coronary angiography with cutoff value of -17.1. (Table6)

Table 1 results of sensitivity and specificity of GLS- Avg by ROC curve.

AUC	95% Confidence Interval		Cut off	Sensitivity	Specificity	PPV	NPV	Accuracy
	Lower Bound	Upper Bound						
0.982	0.958	1.006	-17.1	94.9%	93.8%	98.2%	83.3%	94.7%
			-16.0	89.8%	100%	100%	72.7%	92%

Discussion

CAD is one of the biggest health problems worldwide. Coronary angiography is the gold standard method for evaluation of coronary anatomy and to guide their treatment either by intervention or medical treatment. (2)

There are many advances that occurred in echocardiography in the last fifteen years, this provided methods for analysis of different types of myocardial strains using STE that allows for quantitative evaluation of LV function with a high level of accuracy (6).

Therefore, we performed this study to evaluate whether measurement of GLS-Avg values derived by 2-D STE could predict obstructive CAD confirmed by coronary angiography.

18% of patients had normal GLS-Avg by speckle tracking and normal arteries by coronary angiography, while 78 % of patients had abnormal GLS-Avg by speckle tracking and were found to have coronary lesions by angiography. Only 4% of patients who had normal GLSAvg were found to have abnormal coronary angiography.

There was statistically significant correlation between decreased values of the GLS-Avg and presence of obstructive CAD by coronary angiography with a cutoff value of -16 (Provided that there is associated decrease in the longitudinal strain of group of segments "territory".

This finding was consistent with the hypothesis of Rostamzadeh et al., 2015 who stated that longitudinal myocardial deformation has a good predictive value for diagnosis of obstructive CAD.(7)

Radwan et al., 2017 also reported that GLS-Avg measurement by 2D STE is an accurate & sensitive method for prediction of presence and severity of obstructive CAD. (8)

Moustafa et al., 2017 also described that patients who had normal resting LV function and proved to have severe CAD angiographically, could be discovered by presence of decreased GLS-Avg values in STE.(9)

Farokhnejad et al., 2015 opinion came in favor of the pre about the role of deformation parameters derived by STE in diagnosis obstructive CAD in patients with CSA.(10)

In patients with normal LV function and normal resting segmental wall motion by 2-D Echo, (Kimura K., et al , 2012) proved that prediction of obstructive coronary artery disease can be done using measurement of GLS-Avg by STE.(11)

We verified that longitudinal strain measurement is a good negative test as only 4% of patients who had normal longitudinal strain were found to have abnormal coronary angiography however 96% of patients who had normal GLS-Avg were found to have normal coronary angiography, so it is considered as a good test to rule out presence of obstructive CAD , thus we can mostly avoid coronary angiography for patients with normal GLS-Avg .

Also, Fahim, M., et al.2015, declared that patients who are suspected to have CSA could be differentiated from others who have normal coronaries by analysis of the parameters of deformation using STE. (12)

This was also described by Ogunyankin, K., et al. 2010 who correlated values of GLS-Avg with coronary angiography and found that they can aid in detection of patients with normal coronary arteries. (13)

Radwan et al., 2017 , argued this result and declared that global strain is not a good negative test to rule out presence of obstructive CAD. (8)

In the same way, Ingvild Billehaug et al, 2015 , corroborated that GLS-Avg is a good test for detection of obstructive CAD and can be used only for detection of ischemic patients, otherwise it cannot be used to exclude CAD.(14)

We also found that reduced global systolic strain associated with reduced strain in group of segments(territory), are significantly correlated to coronary artery lesions discovered by coronary angiography, i.e.100% of patients who had reduced strain values in segments related to Right Coronary Artery(RCA), were found to have a stenotic lesion in RCA angiographyically, while 96% of patients who had reduced strain values in segments related to Left Anterior Descending artery(LAD), were found to have a stenotic lesion in LAD angiographyically, otherwise only 92% of patients who had reduced strain values in segments related to Left Circumflex Coronary artery(LCX), were found to have a stenotic lesion in LCX angiographyically.

So, we found that systolic strain has the highest specificity for detection of obstructive CAD in RCA followed by LAD and LCX In those patients.

These results were supported by Vrettos, A., et al. 2016 , who correlated the global longitudinal peak systolic strain with the site and severity of coronary artery lesions assessed by coronary angiography. (15).

This relation between segmental longitudinal strain values reduction by STE and site of coronary artery lesion by coronary angiography is also declared by Moustafa, S., et al. 2017 (9).

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While, Montgomery, D., et al. declared that abnormal myocardial deformation at rest identifies significant CAD especially for LAD stenosis. (16)

The relation between GLS-Avg in study patients and syntax score derived from coronary angiography was also studied and we found significant inverse relationship between syntax score and GLS-Avg In low, intermediate and high syntax scores.

And when GLS-Avg values were correlated to syntax score, statistically significant difference in values of GLS-Avg was found in patients with syntax score 0-9 versus patients with score 8-36 ($p<0.001$).

Vrettos, A., et 2016, study supported our results as they suggested that GLS-Avg may be of value in detection of patients who have high syntax score on coronary angiogram. There was an inverse correlation between GLS-Avg and syntax score assessed by coronary angiography.(15)

However Moustafa, S., et al. 2017 proved that there is inverse correlation between syntax score & GLS-Avg that was significant with high and intermediate scores only but found to be insignificant for low syntax score. (9).

The relation between number of risk factors for CAD (HTN, DM and Smoking) and values of GLS-Avg was also studied and we found a significantly inverse relationship between number of risk factors and values of GLS-Avg ($p<0.014$)

And when GLS-Avg values were correlated to the number of traditional risk factors for CAD, statistically significant difference in the values of GLS-Avg was found between patients with 3 or more risk factors versus patients with one or two risk factors.

This was also reported by Conte, L., et al., 2013 who measured the degree of longitudinal fibers dysfunction by STE in diabetic and obese patients and found reduction in GLS-Avg in those patients. (17)

Finally we established univariate and multivariate logistic regression and a ROC curve for the relation between GLS-Avg and results of coronary angiography.

They revealed 100% specificity for measurements of GLS-Avg to detect patients with CAD by coronary angiography. Among patients who had abnormal coronary angiography, GLSAvg ($p<0.028$) and family history ($p<0.05$) were found as strong predictors for obstructive CAD in patients with CSA.

The results expand our understanding of the association between GLS-Avg and CAD and support the clinical applications of STE in evaluation of coronary angiography indications.

Study limitations

Firstly, the sample size was relatively inadequate to continue significant sub-groups analysis so we need a larger study for confirmation of our results and increase its reproducibility.

Secondly, we focused only on normal and significantly obstructive results of coronary angiography ignoring other results such as non-significant lesions or non-obstructive CAD as coronary ectasia.

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Thirdly, image limitations in patients with poor ECHO window in whom we couldn't obtain an image of high quality to do speckle tracking, lead to loss of large number of patient sample.

Finally, we didn't take in account the effect of systemic diseases such as HTN and DM on values of longitudinal strain during its correlation with coronary angiography.

Conclusion

Speckle tracking is effective in predicting presence or absence of CAD in patients with CSA and in prediction of affected vessels based on the distribution of segments affected in longitudinal strain. Thus, speckle tracking can be used as non-invasive test for patients with CSA and others who are suspected to have CAD.

Recommendations

Therefore, we recommend the routine use of longitudinal strain derived by speckle tracking as non-invasive simple test for evaluation of patients with CSA and as a predictor for presence or absence of obstructive CAD.

Declarations:

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Mansoura Faculty of Medicine (IRB code MS 17.01.70). This study was carried out in accordance with the rules of the Helsinki Declaration. Informed written consent was obtained from all the participants

Consent for Publication

Not applicable

Availability of Data and Materials

All data generated or analyzed during this study available from the corresponding author on reasonable request

Competing Interests

The authors have nothing to disclose

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Authors Contributions

1st Author MA: Data Collection, Paper formulation

2nd Author MY: Design of the work

3rd Author MW: Analysis and interpretation of data, Paper Editing

All authors have read and approved the manuscript

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