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Myocardial Strain Analysis by 2-Dimensional Speckle Tracking Echocardiography in Patients with Suspected Coronary Artery Disease

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ABSTRACT

Background: segmental and global longitudinal peak systolic strain can detect the presence, severity, and extension of coronary artery disease (CAD) in suspected CAD patients.

Objective: To evaluate the role of myocardial strain by 2-dimensional speckle tracking echocardiography in patients with suspected CAD and normal LVEF without rest segmental wall motion abnormalities

Methods: segmental and global longitudinal peak systolic strain was done in seventy-four suspected CAD patients with normal echocardiographic study then correlated to the coronary angiography findings for each patient.

Results: 18.5 was global longitudinal strain (GLS) cut off can detect CAD with AUC of 0.791, sensitivity of 82.4%, specificity of 70.2%, PPV of 71.2% and NPV of 93%. There was significant relation between CAD presence and GLS with mean value of 19.94 ± 2.68 and 16.77 ± 2.87 for non-significant and significant CAD respectively. Means of GLS were 14.88 ± 2.09, 16 ± 2.66, 18.25 ± 2.62 and 19.94 ± 2.68) for 3 CAD, 2 CAD, 1 CAD and normal results respectively (p value <0.001). GLS discriminated well between LM stenosis and non- LM stenosis (13 ± 0.71 and 16.7 ± 1.91 respectively, p<0.001). Segmental longitudinal systolic strain can localize the affected vessel with p value < 0.001 and our study showed positive relation between GLS and LVEF and inverse relation between GLS and syntax score (p<0.001).

Conclusion: Global and segmental longitudinal strain assessed by 2D-STE at rest in suspected CAD even without apparent wall motion abnormalities can diagnose CAD earlier and can predict which patient at higher risk. Also, it can identify how many vessels affected and localize CAD with accepted sensitivity and specificity.

Keywords: CAD, Global & segmental longitudinal strain, Coronary angiography.

INTRODUCTION

Transthoracic echocardiography is performed for suspected CAD patients. However, a lot of patients with ischemic heart disease (IHD) do not exhibit rest wall motion abnormalities especially without structural heart disease or history of myocardial infarction [(1)].

While, stress ECG is widely available but has limited sensitivity and specificity [(2)].

Myocardial perfusion imaging techniques have good diagnostic accuracy, but radiation, cost, and lack of availability are considered a major limitation [(3)].

It is also possible to do physical/pharmacological stress echocardiography with good sensitivity and specificity in comparison with myocardial perfusion imaging, but this method needs great experience with associated side effects limiting its common use [(4)].

The last European Society of Cardiology (ESC) guidelines recommended using cardiac computed tomography (CCT) for younger patients who have chest pain and low to intermediate clinical likelihood of CAD due to its greater anatomic information and high negative predictive value. However, CCT disadvantages are less availability, costs, and a need of a well-trained team [(5)].

Global longitudinal strain (GLS) is non-invasive and easy way to detect early signs of myocardial dysfunction as cause of CAD. Hence selecting patients for coronary angiography as longitudinally subendocardial fibers are more suffering in case of CAD. So, studying the global and segmental longitudinal strain is sensitive for detection of presence localization and extension of coronary artery disease [(6)].

PATIENTS AND METHODS

Our study performed in Zagazig University hospitals cardiology department. Patients.

Inclusion criteria: seventy four Patients with suspected CAD and normal LVEF without rest segmental wall motion abnormalities who had high clinical likelihood of CAD, patients with symptoms in spite of tolerated maximal medical anti ischemic treatment, patients with inconclusive non-invasive testing patients with typical angina at minimal effort and high-risk features on non-invasive testing.

Exclusion criteria: Patients with ECG changes consistent with transmural MI, LV systolic impairment, significant valvular heart disease, marked myocardial hypertrophy, significant ventricular arrhythmia, pacemaker insertion, BBB and those with poor echocardiographic image.

On admission to the hospital, all patients agreed by written consent for the research work up that included the following:

1- Meticulous medical histories included the basic patients' data like age, sex, body mass index, and any cardiovascular risk factors and previous current management and chest pain analysis

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2- Careful clinical examination (vital signs –general examination –local cardiac examination).

3- Laboratory investigations to assess risk factors.

4- Standard 12- leads resting ECG to assess the rhythm, the presence of ischemia and or presence of old MI or LBBB.

5- Chest X-ray (P-A view) can detect cardiothoracic ratio and pleural effusion.

6- Conventional echocardiographic by using 2D, m-mode and Doppler study to assess LV wall thickness, LVEDD, LVESD ,LVEDV.LVESV, systolic & diastolic functions, LVEF (measured by modified Simpson method), evidence of ischemic mitral regurgitation, pericardium, ascending aorta and pulmonary artery pressure.

7- Longitudinal Strain Imaging was performed before coronary angiography. After adjusting the frame rate between 60 and 90/second and ECG tracing to detect AVC at end of t wave and breath hold. Three apical views (apical long axis, 2- and 4-chamber) were selected with good image quality and were kept for offline longitudinal strain analysis, by selecting the AFI software and identifying the region of interest either by machine or manually if the endocardium tracing was not proper. Each view gave its GLS, at the end average GLS was obtained with bull s eye map with colour code column graded from normal red to severely diseased blue segments **(7).**

8- Coronary angiography was performed for all patients. Multiple angulated views of each coronary artery were obtained. An experienced operator who was unaware to the echocardiographic findings data analyzed the coronary angiographic results. Coronary stenosis considered significant when ≥ 50 % in left main or ≥ 70 % in a major branch vessel. Each coronary artery was assigned to the corresponding myocardial segment, then syntax score was calculated. Syntax score (SS) was divided into below 22 is low risk and above 32 is high risk and in between is intermediate risk. The syntax score can assess CAD anatomy and complexity, aid revascularization strategy decision making and as a prognostic tool for long term morbidity and mortality used mainly in LM and multivessel CAD **(9)**.

Ethical approval: Informed consents were obtained from all patients. The study was approved by IRB of Faculty of Medicine, Zagazig University and conducted in accordance with the Declaration of Helsinki.

Statistical analysis

The results data were analyzed using IBM SPSS software package version 20.0**. (**Armonk, NY: IBM Corp**).** Qualitative results were expressed as number and percent. The quantitative results were expressed by using range (minimum and maximum), mean and standard deviation, median and interquartile range (IQR). P value ≤ 0.05 is considered significant. Both Chi-square test categorize variables, and compare between different groups and One-way ANOVA test used for normally distributed quantitative variables, to compare between more than studied groups. Receiver operating characteristic (ROC) curves defined the diagnostic accuracy of GLS to various events, as shown by AUC and the 95 percent Confidence Interval (CI) for each event (CI). It was shown that the "optimum cutoff point" was evaluated by Confidence Interval (CI) for each event.

RESULTS

Seventy-four suspected CAD patients with normal echocardiographic study were selected with inclusion and exclusion criteria. All demographic/risk factors/echo and 2DSTE (global/segmental longitudinal strain) data were correlated with angiographic results. Table (1) demonstrated that the participating subjects mean age was 54.24 ±7.78 years with their age range between 37 to 69 years, females were 28 (37.8%) and 46 males (62.2%) and the mean of the BMI of the studied subjects was 27.36 ± 3.72 with range of 20.8 - 33.5). Also, this table demonstrated that there was 36 diabetic patients (48.6%), 48 hypertensive patients (64.9%), 43 dyslipidemic patients (58.1%), 24 smokers (32.4%) and 10 patients had family history of CAD (13.5%). Additionally, the mean of LVEDVI of the participating patients was 51.07 ± 3.92 ml/m^2 with range of 44.9 – 74.5 ml/m^2, the mean of LVESVI was 32.53 ± 5.1 ml/m^2 with range of 27.1 – 35.6 ml/m^2 and the mean of participating patients LVEF was 61.12% ± 4.59 with range of 53-71. This table demonstrated that among the participating patients there were 17 without significant CAD (23%) and 57 with significant CAD (77%). There were 28 participating patients (37.8%) with one vessel affected, 12 participating patients (16.2%) with two vessels and 17 with three vessels (23%). According to lesion site, there were 5 participating patients with LM (6.8%), 57 patients with LAD (77%), 24 patients with LCX (32.4%) and 22 patients with RCA (29.7%).

Table (1): The clinical /Echo/Angio 74 patients' baseline data

Age Mean ± SD.	**54.24 ± 7.78**	
Female	**28**	**37.8**
Male	**46**	**62.2**
BMI Range	**20.8 – 33.5**	
BMI (kg/m^2)	**27.36 ± 3.72**	
Diabetes mellitus	36	48.6
Hypertension	48	64.9
Dyslipidemia	43	58.1
Smoking	24	32.4
Family history of CAD	10	13.5
LVEDVI Mean ± SD	**51.07 ± 3.92**	
LVESVI Mean ± SD	**32.53 ± 5.1**	
EF Mean ± SD	**61.12 ± 4.59**	
CAD Presence	**No.**	**%**
Non-significant	**17**	**23.0**
23.0	**57**	**77.0**
CAD lesion distribution		
Normal	**17**	**23.0**
One vessel	**28**	**37.8**
Two vessels	**12**	**16.2**
Three vessels	**17**	**23.0**
CAD Lesions localization		
LM	**5**	**6.8**
LAD	**57**	**77.0**
LCX	**24**	**32.4**
RCA	**22**	**29.7**

Table (2) demonstrated presence of statistically significant correlation between GLS and CAD.

Table (2): Relation between CAD detection and GLS

	Presence		**test**	**P**
	Non-significant	**Significant**		
GLS				
Mean ± SD.	**- 19.94 ± 2.68**	**-16.77 ± 2.87**	**t= 4.051**	**<0.001***

Using GLS, it was shown that at 18.5, it can discriminate between non-significant from significant CAD with sensitivity of 82.4%, specificity of 70.2%, PPV of 71.2%, NPV of 93% and AUC of 0.791 (Table 3 and figure 1).

Table (3): GLS discrimination between non-significant and significant CAD (n = 74) by ROC curve

	AUC	**p value**	**95% C.I**		**Cut off#**	**Sensitivity**	**Specificity**	**PPV**	**NPV**
			L.L	**U.L**					
GLS	**0.791**	**<0.001***	**0.661**	**0.921**	**-18.5**	**82.4**	**70.2**	**71.2**	**93.0**

Fig (1): GLS discrimination between non-significant and significant CAD (n = 74) by ROC curve.

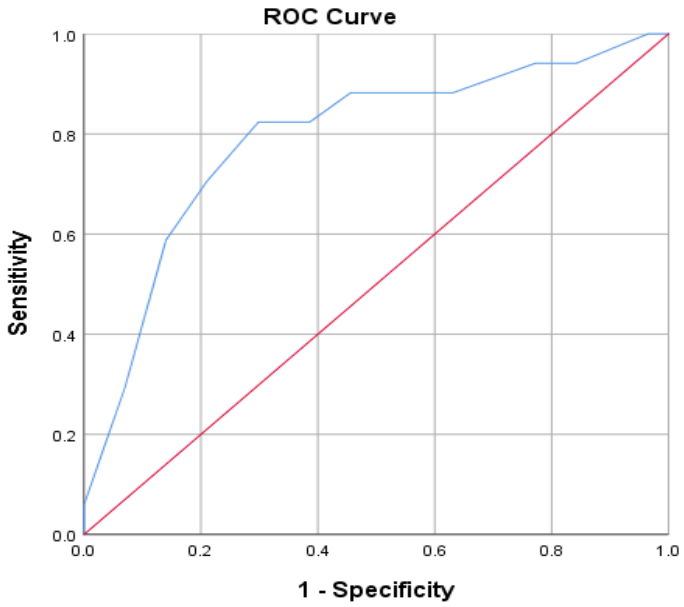

Table (4) demonstrated that there was high statistically significant inverse relation between CAD extension and LVGLS, the more affected CAD the lower LVGLS value.

Table (4): Relation between CAD extension and GLS

	CAD Extension				**Test**	**P**
	Normal	**One vessel**	**Two vessels**	**Three vessels**		
GLS						
Mean ± SD.	**-19.94 ± 2.68**	**-18.25 ± 2.62**	**-16 ± 2.66**	**-14.88 ± 2.09**	**F= 13.571**	**<0.001***

Table (5) demonstrated that SLS can discriminate LM from non-LM by these values 13 ± 0.71 and 16.7 ± 1.91 respectively (p value <0.001).

Table (5): Relation between (LM and non-LM lesion and SLS (segmental longitudinal strain)

Segmental longitudinal strain	**LM**	**Non LM**	**F-test**	**P value**
Mean ± SD	-13 ± 0.71	-16.7 ± 1.91	F= 3.68	0.015*

SD: Standard deviation, F: One-way ANOVA test, Statistically significant at $p \leq 0.05$

P: p value for comparing between studied groups

Table (6) demonstrated that segmental longitudinal peak systolic strain (SLPSS) at 16.5, it can identify LM lesions with AUC of 0.759, sensitivity of 79.4%, specificity of 95.0%, PPV of 97.0% and NPV of 70.2%. Using SLPSS, it was shown that at cut off of 18.5, it can identify LAD lesions with AUC of 0.791, sensitivity of 87.4%, specificity of 73.2%, PPV of 70.2% and NPV of 89%. Also, SLPSS at cut off of 18.5, can identify LCX lesions with AUC of 0.783, sensitivity of 81%, specificity of 91.7%, PPV of 93.5% and NPV of 80.2%. Using SLPSS at cut off of 18.5, can identify RCA lesions with AUC of 0.841, sensitivity of 85.7%, specificity of 95.5%, PPV of 96.8% and NPV of 78.8%.

Table (6): Roc curve analysis for the use of segmental longitudinal peak systolic strain (SLPSS) to discriminate allocate lesions (n = 74)

	AUC	p value	95% C.I		Cut off#	Sensitivity	Specificity	PPV	NPV
			L.L	U.L					
LM	0.759	0.054	0.652	0.867	16.5	79.4	95.0	97.0	70.2
LAD	0.791	<0.001*	0.661	0.921	18.5	87.4	73.2	76.2	89.0
LCX	0.783	<0.001*	0.680	0.886	18.5	81.0	91.7	93.5	80.2
RCA	0.841	<0.001*	0.749	0.934	18.5	85.7	95.5	96.8	78.8

Table (7) This table demonstrates that DM .dyslipedmia ,smoking and family history of CAD are independent predictors for CAD.

Table (7): multivariate logistic regression analysis

	B	S.E	P value	95% C.I	
				Lower	Upper
Age	-0.045	0.049	0.362	-0.143	0.053
Sex	-0.923	0.738	0.216	-2.398	0.552
BMI	0.106	0.097	0.282	-0.089	0.300
DM	-0.197	0.722	0.004	-1.639	1.245
HTN	-0.608	0.783	0.441	-2.172	0.957
Dys-lipidemia	-0.647	0.761	0.006	-2.168	0.873
Smoking	-1.945	0.816	0.020*	-3.574	-0.315
Family history of CAD	-0.043	1.142	0.007	-2.322	2.237

Among participating subjects there were 17 patients without CAD (23%) with syntax score (SS) equal 0, syntax scores were low less than 22 (54%) for 40 patients, while intermediate and high syntax scores (>22)(23%) were recorded for 17 patients. Our study demonstrated inverse relationship between GLS and syntax score (p value < 0.001). GLS in subjects without CAD, low SS and intermediate to high SS was (–19.94, 18.25 and-13.8, respectively) (p value < 0.001).

Table (8): Syntax score and GLS

	SYNTAX Score										
	NO CAD			Low SS			Intermediate & High SS			P Value	Significance
	Mean	Median	SD	Mean	Median	SD	Mean	Median	SD		
GLS	**19.94**	**19.99**	**2.68**	**18.25**	**18.41**	**2.62**	**13.8**	**14.01**	**1.7**	**<0.001**	**Significant**

DISCUSION

2DSTE advantages for the CAD evaluation are noninvasive, easy, available, low costs, angle independent, rapid diagnosis with segmental localization of CAD and it can differentiate between many different diagnoses with bull eye-specific patterns. While, the pitfalls are lack of standardization and fixed cutoff values, operator dependence, lack of accuracy in tachycardia and lower spatial resolution than other imaging methods [8].

Seventy-four suspected CAD patients with normal echocardiographic study were selected with inclusion and exclusion criteria. All demographic/risk factors/echo and 2DSTE (global/segmental longitudinal strain) data were correlated with angiographic results. Our participating patients mean age was 54.24 ± 7.78 with their age range of 37-69 years, among them there were 28 females (37.8%) and 46 males (62.2%). The mean BMI was 27.36 ± 3.72 with range of 20.8-33.5. Also, there were 36 diabetic patients (48.6%), 48 hypertensive patients (64.9%), 43 dyslipidemic patients (58.1%), 24 smokers (32.4%) and 10 patients had family history of CAD (13.5%). Also, our research demonstrated the strong relation between CAD presence and risk factors except for hypertension.

Our study concluded that there was no statistically significant relation between CAD presence and baseline data. Also, there was strong significant relation between CAD presence and extension and presence of individual risk factors such as diabetes mellitus, dyslipidemia with high LDL, smoking and positive family history of CAD with significant P value. While, in hypertensive patients there was no significant relation with presence and extension of CAD.

Our study concluded that there was statistically significant relation between GLS and risk factors except for hypertension, age, BMI and sex. Also, our research showed statistically significant correlation between GLS and CAD presence. **Radwan *et al.* [9]** showed that both study groups had the same risk factors. **Moustafa *et al.* [10]** demonstrated that no strong correlation between demographic and risk factors and GLS in their study. Our research demonstrated that the mean of LVEDVI of the participating patients was 51.07 ± 3.92 ml/m^2 with range of 44.9 – 74.5 ml/m^2, the mean of LVESV was 32.53 ± 5.1 ml/m^2 with range of 27.1 – 35.6 ml/m^2 and the mean of LVEF was 61.12 ±4.59% with range of 53-71%. Our study concluded that there was high statistically significant inverse relation between CAD extension and LVEF and positive relation between CAD extension and LVEDVI and LVESVI, the more affected CAD the lower LVEF value and higher LVEDVI and LVESVI.

Also, our study concluded that there was high statistically significant inverse relation between CAD extension and LVGLS, the more affected CAD the lower LVGLS value. Echocardiographic data of our study showed statistically significance in term of LVEDVI, LVESVI, LVEF and coronary angiography results regarding normal, single CAD, two-CAD, and three CAD groups (p <0.001, p <0.001, and p <0.001, respectively). **Radwan *et al.* [9]** study concluded the presence of CAD associated with lower LVEF and good correlation between LVEF and GLS also. **Biering-Sørensen *et al.* [11]** study proved that no significant relation between CAD presence and LVEF or LV internal dimension. In addition, **Montgomery *et al.* [12]** concluded that there was good correlation between LVEF and global longitudinal strain, while **Gaibazzi *et al.* [13]** proved that there was inverse relationship between LVEF and LVEDD.

Coronary angiographic results showed that 17 patients had normal coronary angiography, while other 57 patients had significant CAD. 28 patients of examined patients had one CAD (37.8%), while 12 patients (16.2%) had two-vessel CAD, the remaining 17 patients (23%) suffered from three-vessel CAD. LAD lesions, which consisted of a part of single, double or triple/multivessel disease were recorded in 57 patients (77%). LCX lesions, which consisted of a part of single, double or triple/multivessel disease were present in 24 patients (32.4%). RCA lesions, which consisted of a part of single, double or triple/multivessel disease were present in 22 patients (29.7%). LM lesions, which consisted as a part of single, double or triple/ multivessel disease were recorded in 5 patients (6.8%).

Our research concluded that GLS cut off at 18.5 can discriminate between non-significant and significant CAD with AUC of 0.791, sensitivity of 82.4%, specificity of 70.2%, PPV of 71.2%, and NPV of 93%. Also, there was significant correlation between CAD presence and GLS with mean values of 19.94 ± 2.68 and 16.77 ± 2.87 for non-significant and significant CAD respectively. Also, there was inverse relation between number of the diseased vessels and GLS values, as mean GLS values were 19.94 ± 2.68, 18.25 ± 2.62, 16 ± 2.66 and 14.88 ± 2.09 for normal, non-significant CAD, two CAD and three CAD respectively (p value <0.001). While, GLS can discriminate LM from non-LM by these values 13 ± 0.71 and 16.7 ± 1.91 respectively (p value <0.001). Also, in our research segmental longitudinal peak systolic strain (**SLPSS)** at 16.5, it can identify LM lesions with AUC of 0.759, sensitivity of 79.4%, specificity of 95.0%, PPV of 97.0% and NPV of 70.2%. Using **SLPSS,** it was shown that at cut off of 18.5, it can identify LAD lesions with AUC of 0.791, sensitivity of 87.4%, specificity of 73.2%, PPV of 70.2% and NPV of 89%. Also, **SLPSS** at cut off of 18.5 can identify LCX lesions with AUC of 0.783, sensitivity of 81%, specificity of 91.7%, PPV of 93.5% and NPV of 80.2%. Using **SLPSS,** cut off of 18.5 can identify RCA lesions with AUC of 0.841, sensitivity of 85.7%, specificity of 95.5%, PPV of 96.8% and NPV of 78.8%. Our study concluded that there was strong statistically significant relation between lesion localization and SLS and GLS that can discriminate LM from non-LM by these values (13 ± 0.71 and 16.7 ± 1.91 respectively, p value <0.001). Our study is in agreement with **Bar *et al.* [14]**, which showed that GLS for no CAD, one CAD, two CAD and three CAD can discriminate LM from non-LM (p<0.001). **Bar *et al.* [14]** demonstrated that mean GLS at -18.4 can discriminate between significant and non-significant CAD with 74% sensitivity and 58% specificity. Also, **Radwan *et al.* [9]** showed that mean GLS values of – 18.65 ± 0.79, -15.13 ± 0.68, - 12.25 ± 0.09 and -9.1±1.94 for normal, one CAD, two CAD and three CAD respectively (p<0.001) can discriminate LM from non-LM (by the values of 14.41 ± 1.27 and 17.1 ± 1.91 respectively (p<0.001).

Our study is in agreement with **Billehaug *et al.* [15]** who concluded that global longitudinal strain was decreasing substantially with CAD severity. Also, they concluded that measurement of the global longitudinal strain had modest diagnostic accuracy in prediction of the CAD, diastolic dysfunction and haemodynamics. **Farsalinos *et al.* [16]** measured GLS mean in different Echo machines and concluded that measurement of the GLS between different machines had the same mean with different SD.

Among participating subjects, there were 17 (23%) patients without CAD with syntax score (SS) equal 0, syntax scores were low (< 22) for 40 (54%) patients, while intermediate and high syntax scores (>22) were recorded for 17 (23%) patients.

Our study demonstrated inverse relationship between GLS and syntax score (p value < 0.001). GLS in subjects without CAD, low SS and intermediate to high SS were –19.94, -18.25 and -13.8 respectively (p value < 0.001). These results match well with **Bar *et al.* [14]**. **Vrettos *et al.* [17]** concluded that there was negative relation between SS

and GLS. While **Moustafa *et al.* [10]** study showed that there was a negative correlation between GLS and SS and it was statistically insignificant for low SS (p value 0.05) but highly significant for intermediate and SS (with p value 0.001). We observed that previous studies, which showed different cutoff values for the global longitudinal strain in detection of CAD and this can be explained by type of the echo machine and package software for each machine as well as patients' demographic risk factors and clinical conditions including the hemodynamics and echo data including the diastolic function. So, our study recommends to standardize GLS software for all echo machines to increase the clinical utility of the strain modalities in daily practice by fixing the GLS cut of value in cardiac diseases regardless of the used echo machine.

STUDY LIMITATION

1- The study did not include a large number of patients and was single center study.
2- Other strain parameters like radial, transverse, circumferential, twist and torsion not included in this study due to lack of definitive standardization and the fact that longitudinal fibres is the most affected in case of CAD.
3- The study took in consideration only the anatomical significance of the lesion not the functional significance of the lesion, so it is recommended to add FFR or iwFR in the coming studies.

CONCLUSION

Global and segmental longitudinal peak systolic strain evaluated by speckle tracking echocardiography at rest in suspected CAD even without apparent wall motion abnormalities can diagnose CAD earlier, and can predict patients at higher risk also it can identify how many vessels were affected and localize CAD with good sensitivity and specificity.

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