ORIGINAL RESEARCH

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Role of Left Ventricular Speckle Tracking Imaging in Detection of Coronary Artery Disease in Non-Diabetic Patients

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Abstract

This study aimed to determine the role of global longitudinal strain (GLS) in early diagnosis and detection of severity of coronary artery disease (CAD) in non-diabetic patients with preserved left ventricular ejection fraction (EF) without regional wall motion abnormalities presented with chronic coronary syndrome, and to identify the role of territorial longitudinal strain (TLS) in detection of the affected coronary artery. We enrolled 60 non-diabetic patients with suspected CAD who underwent resting echocardiography and speckle tracking imaging and subsequently coronary angiography then results were correlated together. Patients with family history of CAD (68.3%), hypertension (68.3%), smokers (43.3%), and dyslipidemia (81.6%). All participants had normal left ventricular systolic function with mean EF of 64.02±6.15% and no regional wall motion abnormalities at rest. Patients were classified angiographically according to the number of the diseased vessels into: 3 vessels disease (43.3%), 1-2 vessels disease (35%), and normal coronary angiography (21.7%) with GLS mean values of -13.69±1.94%, -15.4±1.74%, and -18.80±2.14%, respectively. There was a negative significant correlation between GLS values and the number of diseased vessels (P=0.001). The values of TLS were significantly lower in myocardial regions supplied by stenotic arteries than those supplied by non-stenotic arteries. Mean TLS values for stenotic left anterior descending, left circumflex, and right coronary arteries were -15.51±3.19, -13.06±2.90, -13.27±2.60 with P=0.011, 0.001, and 0.001, respectively. Speckle tracking derived GLS is an effective non-invasive method in predicting presence and severity of CAD and in locating the affected vessels based on the distribution of segments affected in TLS.

Keywords

Left ventricular, Non-diabetic patients, Coronary artery disease, 2D speckle tracking, Strain imaging

Imprint

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1. Introduction

Coronary artery disease (CAD) is a major and growing health problem. Accurate and rapid diagnosis is crucial , as it can help in selecting the proper management plan whether medical treatment or coronary revascularization, thus, improves the prognosis of those patients [1]. Conventional echocardiography at rest provides limited information in the diagnosis of CAD. Thus, stress test is usually required as non-invasive diagnostic method for detection of coronary artery stenosis; however, both exercise and pharmacological stress testing could carry a risk of cardiovascular events. So, the development of a non-invasive and quantitative method for detecting coronary artery stenosis without a stress test would be ideal [2]. Recent studies reported that strains by 2D speckle tracking imaging could be used to assess the deformation of the myocardial ischemia area and thus to detect CAD but the diagnostic accuracy is still under search [3], Myocardial strains were found to be affected independently by diabetes mellitus (DM), so the presence of DM may affect the diagnostic accuracy of Global longitudinal strain (GLS) in detecting CAD [4].

2. Material and Method

The present study included 60 non-diabetic patients with suspected CAD who were collected prospectively and admitted to Banha university hospital. All of them underwent resting echocardiography and subsequently coronary angiography by operators who are blinded to the echocardiographic results.

2.1 Key inclusion criteria:

Non-diabetic Patients referred to the Cath lab with Suspected CAD: with high pre-test probability accord-

ing to 2019 ESC guidelines for diagnosis and management of chronic coronary syndromes [5] and/or patients with high risk of CAD according to SCORE (systematic coronary risk estimation) risk chart, that predicts 10 years risk of fatal CAD [6].

2.2 Key exclusion criteria:

Patients with recorded history of DM; or diagnosed as having DM during hospitalization [7], patients who had regional wall motion abnormalities detected by resting echocardiography, reduced left ventricular ejection fraction (LVEF), severe valvular stenosis or regurgitation, suboptimal angiographic or echocardiographic images, the presence of permanent pacemaker, arrhythmias such as atrial fibrillation and frequent premature complexes that may affect the analysis of the images, presence of left bundle branch block or right bundle branch block, patients with history of coronary revascularization (including coronary artery bypass grafting and percutaneous coronary intervention), acute ST segment elevation myocardial infarction (STEMI), patients with conditions mandating immediate complete revascularization as cardiogenic shock of electrical instability, and finally patients with associated co morbidities (liver failure, renal failure, and malignancy).

2.3 Study methods:

All participants were subjected to:

2.3.1 Full history taking, complete clinical examination,12-lead ECG, Laboratory investigations:

Lipid profile (low density lipoprotein, high density lipoprotein, total cholesterol, and triglycerides), serum creatinine, and HBA1c

2.3.2 Transthoracic Echocardiography:

The echocardiographic examination was performed for all patients before coronary catheterization using ultrasound EPIQ 7C system, equipped with the X5-1 probe (Philips Medical Systems, Andover, MA, USA.

2.3.2.1 Two-dimensional Echocardiography:

Interventricular septum (IVS) and left ventricular posterior wall thickness (LVPW), LV end-diastolic dimensions (LVEDD), and left atrial (LA) dimensions (at end-systole) were obtained from the parasternal long-axis view, LVEF using M-mode and by biplane SIMPSON methods [8], left ventricular end systolic (ESV) and End diastolic (EDV) volumes, mitral E-wave and A-wave velocities and the E/A ratio, and mitral annulus TDI E velocity to obtain E/E' ratio.

2.3.2.2 Two-dimensional Speckle Tracking Echocardiography:

Image Acquisition:

Two-dimensional gray scale images of three consecutive cardiac cycles for each of three standard apical (two-, three-, and four-chamber) views were saved at a frame rate of between 40 and 60 fps, during breath holding, With stable ECG tracing.

Speckle Tracking analysis:

An investigator who was blinded to the angiographic results conducted the strain analysis off-line by using commercially available software (Philips Medical Systems, EPIQ 7C, Q LAB 10).

The LV endocardial border was traced throughout the cardiac cycle automatically and was adjusted manually in case of poor tracking. The tracking quality was ascertained visually and segments with inadequate tracking were rejected.

After manual adjustment of the region of interest width and shape, the software automatically divides the region of interest into 6 segments, with the possibility of further manual correction.

Once the region of interest was optimized, the software generated strain curves for each selected myocardial segment. From these curves, the operator obtained regional and global strain. (By averaging values observed in all segments) [9].

The strain analysis was summarized in a color-coded bull's eye display with a conventional 17-segment LV model.

Global longitudinal strain is defined as the average value of the 17 segmental PSLSs, and segmental longitudinal strain (basal, mid- or apical segments) is defined as the average value of PSLSs of the corresponding six segments (five segments for the apex). In addition, TLS (territorial longitudinal strain) is the average of the corresponding segmental PSLSs based on the perfusion territories of the 3-epicardial coronary arteries [left circumflex artery (LCX), left anterior descending artery (LAD) and right coronary artery (RCA)] in the 17-segment LV model [10].

2.3.3 Coronary angiography:

Coronary angiography was performed to all patients within days after echocardiography was completed. Two experienced angiographers, blinded to patient's clinical information and echocardiography results, scored the angiograms with regard to the location and the severity of stenosis of the major 3-epicardial coronary arteries as defined by the American Heart Asso-

ciation classification, the severity of coronary stenosis was expressed as a percentage of the vessel narrowing, Stenosis with ≥50% will be considered significant.

CAD disease was defined according to number of the diseased vessels, and the degree of stenosis as following:

Critical CAD was defined as stenosis ≥ 70% in ≥1 epicardial coronary artery (or ≥50% in LM).

3-vessel CAD was defined as stenosis ≥70% in at least one epicardial vessel and concomitantly ≥50% in other 2 epicardial vessels.

One- or two-vessel CAD was defined as stenosis ≥70% in one or two vessels and <50% in another vessel(s).

2.4 Statistics:

The collected data were tabulated and analyzed using SPSS program (version 24.0). For presentation of numerical (parametric data), mean and standard deviation were used to describe both central tendency and dispersion of the data. In case of categorical (non-parametric data), number and percentages were used for description. Independent sample t-test was used to compare numerical data between two different groups. Chi-square test for categorical data. P-value of less than 0.05 was used as an accepted level of significance to denote significant difference between groups.

3. Results

The study included 60 patients; 35 males (58.3%) and 25 females (41.7%), with mean age was 54.67±9.40 years, mean body mass index was 28.92±4.79. As regard to risk factors of the studied patients there were 41 patients (68.3%) who had family history for CAD, 41 patients (68.3%) had hypertension; 26 (43.3%) smoker patients, and 49 (81.6%) patients had dyslipidemia, as shown in table 1.

Table 1
Patients characteristics and risk factors

Age	Range	32 – 71
	Mean ± SD	54.67 ± 9.40
Body mass index	Range	22.1 – 40.2
	Mean ± SD	28.92 ± 4.79
Sex	Male (%)	35 (58.3%)
	Female (%)	25 (41.7%)
Family History	No (%)	19 (31.7%)
	Yes (%)	41 (68.3%)
Hypertension	No (%)	19 (31.7%)
	Yes (%)	41 (68.3%)
Smoking	No (%)	34 (56.7%)
	Yes (%)	26 (43.3%)
Dyslipidemia	No (%)	11 (18.3%)
	Yes (%)	49 (81.6%)

The entire studied group had laboratory investigations including: LDL that showed elevated trend among the whole group (mean 122.42 ± 29.15 mg/dl), HDL, TG (triglycerides), TC (total cholesterol), Creatinine, and HbA1c (table 2).

Table 2
Laboratory findings

	Range	Mean ± SD
LDL	61 – 180	122.42 ± 29.15
HDL	27 – 89	42.53 ± 10.78
TG	50 – 308	162.50 ± 71.91
Creatinine	0.46 – 1.33	0.83 ± 0.25
HbA1c	5 – 6.2	5.73 ± 0.34
TC	74 – 280	197.42 ± 43.41

LDL: low density lipoprotein, HDL: high density lipoprotein, TG: triglycerides, TC: total cholesterol

Table 3 shows the current medications taken by the studied group.

Table 3
Medications

	Number	%
ASA	56	93.3
ACEI/ARB	35	58.3
Statin	52	86.7
Beta blocker	44	73.3
Ca channel blocker	5	8.3
Nitrates	26	43.3

ASA: aspirin, ACEI: angiotensin converting enzyme inhibitor, ARB: angiotensin receptor blocker

Basic echocardiographic examinations were done to all the participants before having coronary angiography, all participants had a normal left ventricular systolic function (EF % mean value was 64.02±6.15 %) with no regional wall motion abnormalities at rest. Basic diameters as IVS diameter, LVEDD, LVESD, LVPW, LA, EDV, ESV, E/A ratio and E/E' ratio were measured as shown in table 4.

Table 4
Conventional Echocardiographic parameters

	Range	Mean ± SD
IVS	0.7 – 1.6	1.13 ± 0.22
LVEDD	3.5 – 6.3	4.91 ± 0.58
LVESD	2.2 – 4	3.11 ± 0.43
LVPW	0.6 – 1.3	0.85 ± 0.17
EF%	50 – 77	64.02 ± 6.15
LA	3 – 5.5	4.11 ± 0.50

	Range	Mean ± SD
E/A	0.5 – 3.2	1.07 ± 0.42
E/E' Medial	6 – 25	11.07 ± 4.13
E/E' Lateral	4.6 – 17.4	7.66 ± 2.68
EDV	31 – 137.7	77.49 ± 23.95
ESV	19.7 – 91.5	37.95 ± 16.85

IVS: interventricular septum, LVEDD: left ventricular end-diastolic dimension, LVESD: left ventricular end-systolic dimension, LVPW: left ventricular posterior wall, EF: ejection fraction, LA: left atrium, EDV: end-diastolic volume, ESV: end-systolic volume

Mean value of global longitudinal peak systolic strain (GLPSS) in 3 vessels disease group was (-13.69±1.94%), in 1-2 vessel disease group was (-15.4±1.74%), and in the control group was (-18.80±2.14%), apparently there was statistically significant difference between the 3 groups (p =0.001) as shown in table 5.

Table 5
Global longitudinal peak systolic strain (GLPSS)

		Range	Mean ± SD	F. test	P value		
Global Strain %	**3 Vessel**	-18 – -10.9	-13.69 ± 1.94	30.709	0.001*	P1	0.004*
	1–2 Vessel	-19.3 – -13	-15.40 ± 1.74			P2	0.001*
	Control	-22.2 – -14.9	-18.80 ± 2.14			P3	0.001*

P1: between 3 vessel &1-2 vessel disease, P2: between 3 vessel & control, P3: between 1-2 vessel & control, *Significant

There was a negative significant correlation between the global strain values and the number of diseased vessels, the more diseased vessels the less negative the strain values, with P value=0.001 and r value=0.674 (table 6).

Table 6
Correlation between global strain and the number of the diseased vessels

GLOBAL Strain (GLPSS)%	**Number of vessels**	
	R	P
	-0.674	0.001*

TLS % mean value in LAD disease was (-15.51 ± 3.19%), and when compared to those with normal LAD (-17.78 ± 2.71%) in any of the three groups, we found that there was a statistically significant difference (p value 0.011) as shown in table 7.

Table 7
Territorial peak left anterior descending artery longitudinal strain

TLS Strain %	LAD disease	Normal LAD
Range	-21.8 – -8	-23.1 – -14.2
Mean ± SD	-15.51 ± 3.19	-17.78 ± 2.71
T. test	2.636	
P. value	0.011*	

TLS: territorial longitudinal strain, LAD: left anterior descending artery, *Significant

When comparing global longitudinal peak systolic strain of the LCX territory (TLS%) between those with LCX disease (-13.06 ± 2.90 %) to those with normal LCX (-17.48 ± 2.90%) in any of the three groups, there was a statistically significant difference in the means (p value 0.001) as shown in table 8.

Table 8
Territorial peak left circumflex artery longitudinal strain

TLS Strain %	LCX disease	Normal LCX
Range	-19.1 – -4	-21.6 – -9.6
Mean ± SD	-13.06 ± 2.90	-17.48 ± 2.90
T. test	5.736	
P value	0.001*	

TLS: territorial longitudinal strain, LCX: left circumflex artery, *Significant

When comparing global longitudinal peak systolic strain of the RCA territory (TLS%) between those with RCA disease (-13.27 ± 2.60 %) to those with normal RCA (-17.21 ± 2.41) in any of the three groups, there was a statistically significant difference in the means (p value 0.001) as shown in table 9.

Table 9
Territorial peak right coronary artery longitudinal strain

TLS Strain %	RCA disease	Normal RCA
Range	-19.24 – -8	-25.6 – -13.0
Mean ± SD	-13.27 ± 2.60	-17.21 ± 2.41
T. test	6.084	
P value	0.001*	

TLS: territorial longitudinal strain, CA: right coronary artery, *Significant

4. Discussion and Conclusions

Conventional echocardiography at rest provides little information on the presence of coronary artery disease. Therefore, the aim our study was to determine the rule of GLS in the early diagnosis and detection

of severity of CAD, in non-diabetic patients presented with chronic coronary syndrome and preserved LV ejection fraction without regional wall motion abnormalities.

As proven in other studies that diabetes can affect the diagnostic accuracy of GLS [11] we have excluded diabetic patients from our cohort.

Regarding other risk factors like positive family history which represents (68.3%), smoking (43.3%) and dyslipidemia (81.6%) there were no studies confirming its direct effect on GLS, in contrary to hypertension (68.3%) which was proved to have a direct effect on impairment of the GLS [12].

Interestingly, it was found that in the very first stages of hypertension, it is possible for a patient to show regional alterations while GLS remains in the normal values [13], so hypertension wasn't excluded from our study and patients were controlled on medical treatment including ACEi/ARBs, Beta blocker, and Ca channel blockers (58.3%, 73.3%, 8.3%, respectively).

Regarding to speckle tracking imaging results we found that GLS declined incrementally with increased severity of CAD (the severity of coronary stenosis and the number of stenotic vessels) with statistically significant negative correlation as the GLS was mostly impaired in patients with 3-vessel CAD (-13.69±1.94 %) compared with control and one or two vessel disease patients (-18.80 ± 2.14% and -15.40 ±1.74 %, respectively) and this comes in concordance with Moustafa et al. [14] and Hubbard et al. [15]. Also, Bakhoum et al. [16] declared that patients who are suspected to have chronic stable angina could be differentiated from others who have normal coronaries by analysis of the parameters of deformation using STE also they declared that strain values are more decreased with increased severity of CAD.

Another important finding in our study results is the predictive value of TLS% in locating stenotic coronary artery. As we found that the values of TLSs were significantly lower in myocardial regions supplied by stenotic arteries than in those by non-stenotic arteries. Mean TLS% value for stenotic LAD, LCX and RCA were (-15.51±3.19, -13.06±2.90, -13.27±2.60) with P values=0.011, 0.001, and 0.001, respectively.

These results come in favor with Montgomery et al. [4], Biering-Sørensen et al. [17], and Yang et al. [18], in contrary with Zuo et al. [19], and Hanekom et al. [20] results which found that the diagnostic accuracy of TLS was unsatisfactory this may be explained by larger sample volume in both studies than ours as we had limitations in the elective procedures during COVID 19 pandemic.

List of abbreviations:

CAD	coronary artery disease
DM	diabetes mellitus
EDV	end diastolic volume
EF	ejection fraction
ESV	end systolic volume
GLPSS	global longitudinal peak systolic strain
GLS	global longitudinal strain
HDL	high density lipoprotein
IVS	interventricular septum
LA	left atrium
LAD	left anterior descending artery
LCX	left circumflex artery
LDL	low density lipoprotein
LVEDD	left ventricle end-diastolic dimensions
LVEF	left ventricular ejection fraction
LVPW	left ventricular posterior wall
RCA	right coronary artery
SCORE	systematic coronary risk estimation
SD	standard deviation
STEMI	ST segment elevation myocardial infarction
TC	total cholesterol
TG	triglycerides
TLS	territorial longitudinal strain

Statement on Ethical Issues:

We obtained ethical approval from the Ethics Committee of the Faculty of Medicine, Banha University, Banha, Egypt and informed written consents from the study participants.

Conflict of Interest:

None declared.

Authors' Contributions:

SK defined the aim of research and the design of experiment. SK and MA carriedout the experiments. MH participated in the design of the study and performed the statistical analysis. HA coordinated and helped to draft the manuscript. All authors read and approved the final manuscript

Case Example:

RCA territorial strain (TLS%) measured -13%, in a patient whose C/A revealed CTO RCA

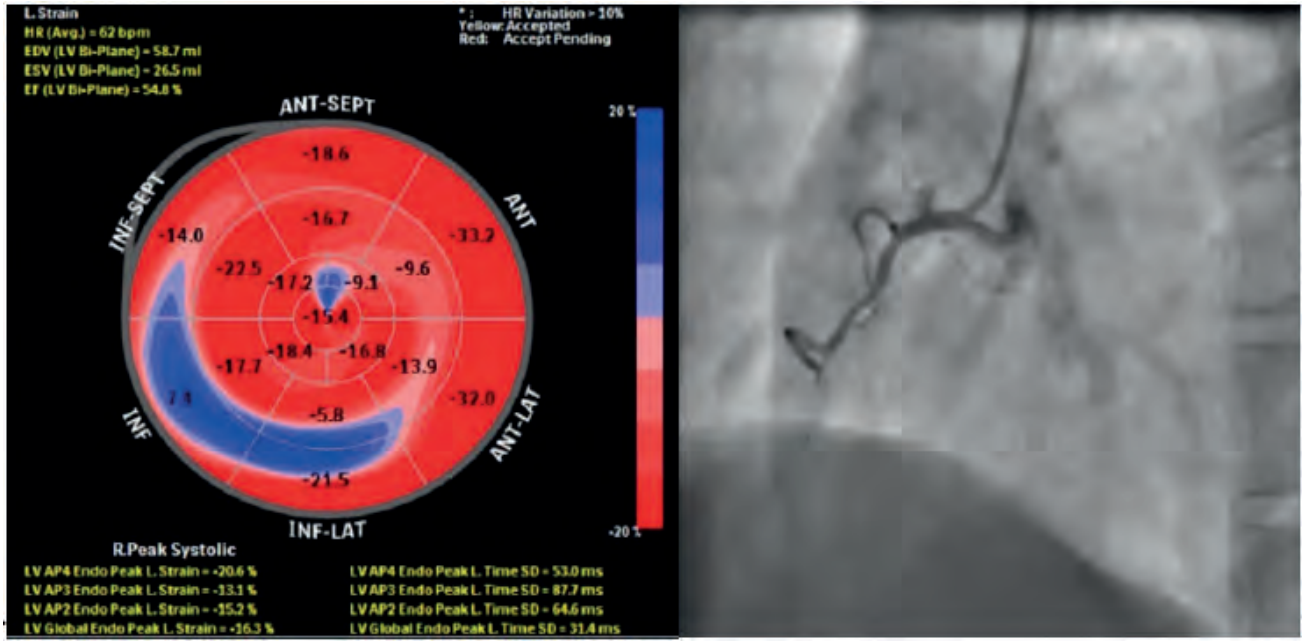

Figure 1. left panel showing 17 segments bull's eye, right panel: coronary angiography of the same patient showing CTO RCA.

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