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Role of Speckle Tracking Echocardiography in Assessing Anginal Chest Pain on Exertion

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ABSTRACT

Background: Left bundle branch block (LBBB) poses some restriction on coronary artery disease (CAD) diagnosis with noninvasive diagnostic modalities. **Objectives:** Evaluating the role of 2-D speckle tracking echocardiography (STE) in the diagnosis of CAD in patients with LBBB.

Patients and Methods: This was a single-center observational prospective study that lasted for 3 years. 80 patients with LBBB complaining of exertional chest pain underwent STE and coronary angiography (CA).

Results: 50 patients were put in group I, on exclusion of significant CAD. Group II had 30 patients having significant CAD on CA. Global longitudinal strain (GLS) of the left ventricle was higher in group II patients (p value of 0.0001). Also, time to peak strain in apical 2 chamber view (TTPS AP2), apical 3 chamber view (TTPS AP3) and apical 4 chamber view (TTPS AP4) were significantly higher among group II patients (p-value of 0.0001, 0.0001 and 0.0001 respectively). GLS can predict significant CAD using cutoff point of 11.4%, with sensitivity of 66% and specificity of 90% (p-value 0.0001). TTPS AP2 can predict significant CAD using cutoff point of 399.5 milliseconds (ms), with a sensitivity of 90% and specificity of 58% (p value 0.0001). TTPS AP3 can predict significant CAD using cutoff point of 385.5 ms, with a sensitivity of 73.3% and specificity of 72% (p-value of 0.0001). TTPS AP4 can predict significant CAD using cutoff point of 377.5 ms, with sensitivity of 90% and specificity of 52% (p-value of 0.0001).

Conclusion: STE could be valuable in the assessment of LBBB patient with suspected CAD.

Keywords: Global longitudinal strain (GLS), Left bundle branch block (LBBB), Speckle tracking echocardiography (STE), Time to peak strain (TTPS), Coronary artery disease (CAD), Coronary angiography (CA).

INTRODUCTION

Ischemic heart disease (IHD) has always been and still is on the top of the list of causes of death worldwide [(1)]. In Egypt it reached183.59 deaths per 100,000 in 2019, constituting 32.39% of all age deaths in that year, strikingly surpassing the global percentage [(2)]. Coronary supply demand mismatch leads to ischemia at the level of myocytes in addition to the conduction system, leading to impaired contractility and increased left ventricular filling pressure [(3)], and various conduction abnormalities such as left bundle branch block [(4)].

Left bundle branch is formed of a trunk and three fascicles. After passing through the fascicles, the electric impulse spreads through the dense Purkinje network to myocardial cells [(5, 6)]. Any total interruption at any level of that circuit being in the left bundle main trunk, both fascicles or even extensive ischemia of the myocardium and the Purkinje network in the territory of the left bundle, with intact proximal part of the left bundle and its branches will result in a LBBB pattern in the ECG. LBBB may occur as a result of stretching, a degenerative processes, infiltration like amyloidosis or fibrosis like Lenegre's disease affecting conduction system [(7)], or it may be a sign of ischemic heart disease. LBBB may occur in the absence of any of the above-mentioned conditions [(8, 9)] and it may be explained by a genotype theory that may be supported by some recent evidence [(10)].

Studies suggest that LBBB or intraventricular conduction delay can predict increased mortality. Another study suggested that LBBB morphology is a strong predictor of sudden arhythmic death [(11)]. Bearing that in mind, a patient with LBBB morphology should be thoroughly investigated to

address treatable causes if present. As the first step of assessing a patient with chest pain on exertion is noninvasive tests. In case of LBBB, the characteristic ST/T wave changes poses a restriction on some of these modalities. It renders detection of ST changes in stress ECG difficult to interpret [(12)]. Myocardial perfusion by nuclear imaging in the presence of LBBB may show heterogenous regional tracer uptake not indicative of ischemia or fibrosis. With exercise stress having higher rate of false positive septal perfusion defects than vasodilator stress testing [(13)]. This may be related to dyskinesia, decreased septal thickness compared to lateral wall [(14)] or due to functional septal hypoperfusion [(15)]. Another study concluded that it is lateral hyper-perfusion rather than reduced septal flow [(16)].

Deformation imaging echocardiography is proposed to overcome the limitations of the above-mentioned modalities, as a noninvasive objective measure to regional and global myocardial functions [(17)]. Speckle tracking echocardiography assesses myocardial function and transitional movement by measuring strain and strain rate , and is relatively angle independent [(18)]. Pain whether acute or chronic setting in the presence of risk factors for ischemic heart disease, GLS can detect subclinical myocardial damage early [(19)].

LBBB causes desynchrony of LV contraction and hence systolic dysfunction. Early septal activation during the isovolumetric (pre-ejection) phase pushing blood towards relaxed lateral wall, enhancing lateral wall contraction according to starling law pushing blood back to septum displacing it towards the right ventricle resulting in septal flash motion in the mid ejection phase (originally described in M-mode as septal peaking) [(20)].

The interaction between the septum and free wall leads to apical rocking or shuffle [(21)]. This desynchrony is accounted for as wasted work with one third of septal work contribution being lost and is considered as a burden on the lateral wall.

LBBB by speckle tracking echocardiography has characteristic strain segments curves, showing early peak basal and/or mid septal contraction and simultaneous basal and/or mid lateral wall stretching that occurs within 70% of the ejection phase. Then, the lateral wall peak contraction occurs after the ejection phase marked by the aortic valve closure [(22)].

PATIENTS

We collected one hundred Patients with left bundle branch block (LBBB) on electrocardiography (ECG) complaining of chest pain or anginal equivalent on exertion and suspected to have coronary artery disease (CAD). Of the 100 patients, only 80 patients were enrolled, as some of the patients didn't proceed to coronary angiography (CA) and some had poor acoustic window or disconnected ECG on STE.

Inclusion criteria: Chest pain or anginal equivalent and suspected to have CAD. Left bundle branch block pattern in resting ECG.

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Exclusion criteria:

Suboptimal 2D image quality. Established atrial fibrillation. Hemodynamically significant valvular lesion. Cardiomyopathy. Reduced ejection fraction. Regional wall motion abnormalities at rest other than that characteristic to LBBB. Previous PCI or CABG. Previous MI.

MEDTHODS

Speckle tracking echocardiography was performed using Philips epic 7 ultrasound machine to measure left ventricular global longitudinal strain (GLS) by averaging 18 segments from apical two (AP2), apical three (AP3), and apical four (AP4) chamber views and time to peak strain measured from beginning of QRS on ECG to the peak strain of each segment.

The average of the TTPS of the 6 segments of every apical view was reported individually as time to peak strain in AP2 view (TTPS AP2), AP3 view (TTPS AP3) and AP4 view (TTPS AP4) measured in milli seconds. CAD was considered significant if CA revealed a reduced left main stem luminal diameter by more than 50%, or reduced luminal diameter of left anterior descending, left circumflex or right coronary arteries by more than 70%.

Ethical approval:

Each patient enrolled in the study gave an informed consent to participate in this study. The Egyptian Ethical Committee of Medical Sciences approved this research. This work has been carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis: SPSS 2 2nd edition was used to run the statistical analysis. Quantitative variables were presented as mean and standard deviation.

Comparison between the two study groups by Mann Whitney U tests and student T tests according to normality testing was done. Categorical variables were presented in frequency and percentages.

Sensitivity analysis was conducted to predict incidence of significant CAD to set the optimal cutoff point for this prediction. Receiver curve of characteristic showed that area under the curve for predicted outcomes. Significant p value ≤ 0.05.

RESULTS

CA results split the recruited patients into two groups, according to the presence of significant CAD. Group I comprised 50 patients without significant CAD. Group II comprised 30 patients diagnosed with significant CAD accounting for 37.5% of the total number of included patients.

Table (1) showed the general characteristics of the patients. Age was higher among group II (p-value of 0.008). There was no statistically significant difference between groups in terms of gender (P=0.468), diabetes (p-value 0.36), hypertension (p-value 0.273), dyslipidemia (p-value 0.525), family history (p-value 0.678) and smoking (p-value 0.062).

Regarding the echocardiographic parameters in the two groups, GLS was significantly higher in group II patients (Figure 1) (p-value of 0.0001). Also, TTPS AP2, TTPS AP3 and TTPS AP4 were significantly higher among group II patients (Figures 2-4) (p-value of 0.0001, 0.0001 and 0.0001 respectively) as shown in table (2).

Sensitivity analysis showed that GLS can predict significant CAD using cutoff point of 11.4%, with sensitivity of 66% and specificity of 90% (p-value of 0.0001). Sensitivity analysis also showed that TTPS AP2 can predict significant CAD using a cutoff point of 399.5 ms, with sensitivity of 90% and specificity of 58% (p-value of 0.0001). TTPS AP3 can predict significant CAD using cutoff point of 385.5 ms, with sensitivity of 73.3% and specificity of 72% (p-value of 0.0001). TTPS AP4 can predict significant CAD using a cutoff point of 377.5 ms, with sensitivity of 90% and specificity of 52% (p-value of 0.0001).

Age, by regression analysis was an independent predictor of significant CAD after other risk factors adjustment with a p-value of 0.034 and OR 1.16. While, lower GLS is a predictor of absence of significant CAD with a p-value 0.0001 and OR 0.456.

Table (1): Comparison of demographics and clinical characteristics according to presence of significant CAD

		Group I		**Group II**		**p-value**	
		Mean ±SD/ count	Range/ percent	Mean ±SD/ count	Range/ percent		
Age in years		55.8 ±7.6	38-69	60.8 ±6.6	48-72	**0.008**	**S**
Gender	Male	16	32%	12	40%	0.468	NS
	Female	34	68%	18	60%		
Diabetes	No	35	70%	18	60%	0.36	NS
	Yes	15	30%	12	40%		
Hypertension	No	28	56%	13	43.30%	0.273	NS
	Yes	22	44%	17	56.70%		
Dyslipidemia	No	27	54%	14	46.70%	0.525	NS
	Yes	23	46%	16	53.30%		
Family history	Negative	38	76%	24	80%	0.678	NS
	Positive	12	24%	6	20%		
Smoking	No	41	82%	19	63.30%	0.062	NS
	Yes	9	18%	11	36.70%		

S: significant, NS: non-significant.

Table (2): Comparison of speckled tracking echocardiography findings according to presence of significant CAD

	Group I				Group II				P value	
	Min	Max	Mean	SD	Min	Max	Mean	SD		
GLS (%)	-3.1	-19.6	-12.1	3	-5.2	-13.2	-9	2	**0.0001**	**S**
TTPS AP2 ms	162	488	381.7	60.4	370	502	447.8	41.9	**0.0001**	**S**
TTPS AP3 ms	213	467	359.7	49.4	305	471	402.5	37.5	**0.0001**	**S**
TTPS AP4 ms	171	477	367.1	57.4	342	480	420.6	39.9	**0.0001**	**S**

GLS: global longitudinal strain, TTPS AP2: time to peak strain in apical 2 chamber view, TTPS AP3: time to peak strain in apical 3 chamber view, TTPS AP4: time to peak strain in apical 4 chamber view, ms: milli seconds.

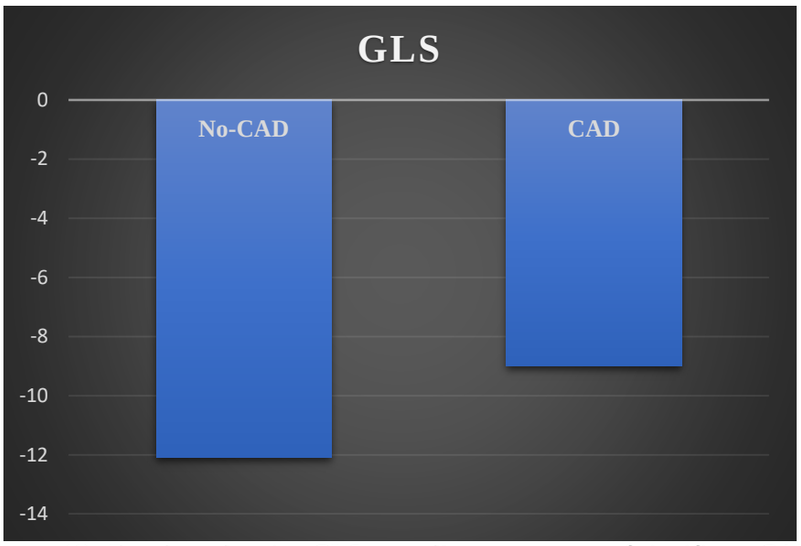

Figure (1): Bar chart showing GLS according to presence of significant CAD.
GLS: global longitudinal strain.

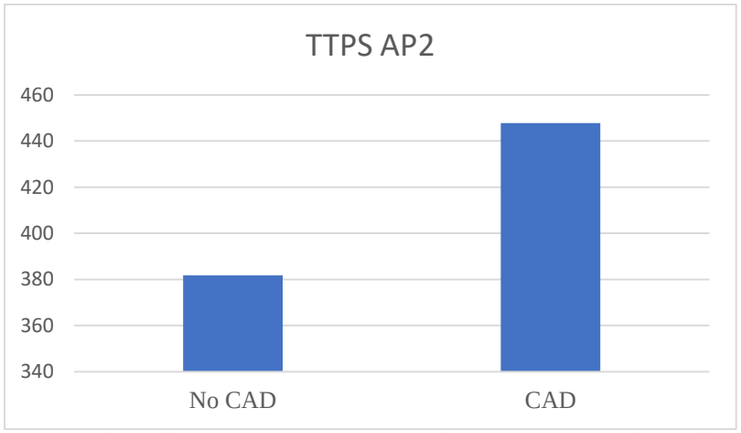

Figure (2): Bar chart showing TTPS AP2 according to presence of significant CAD
TTPS AP2: time to peak strain in apical 2 chamber view. Values are in milli seconds.

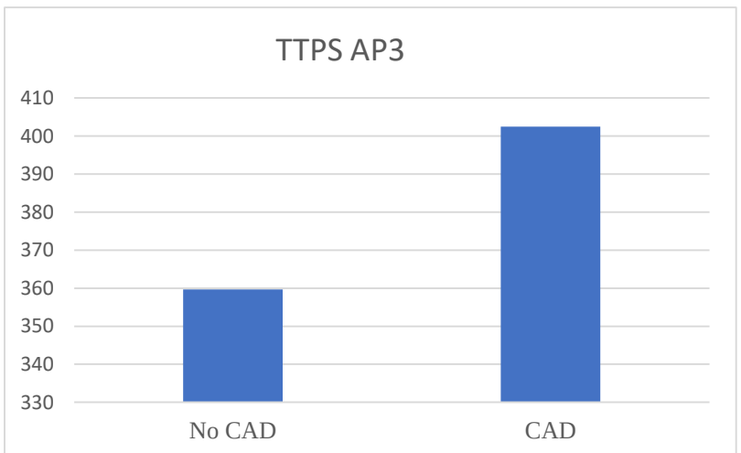

Figure (3): Bar chart showing TTPS AP3 according to presence of significant CAD
TTPS AP3: time to peak strain in apical 3 chamber view. Values are in milli seconds.

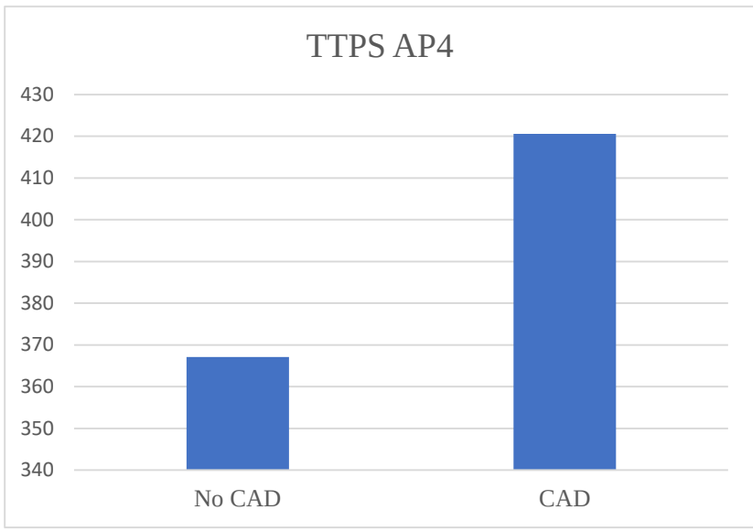

Figure (4): Bar chart showing TTPS AP4 according to presence of significant CAD
TTPS AP4: time to peak strain in apical 4 chamber view. Values are in milli seconds.

DISCUSSION

Patients presenting with chest pain on exertion or any other anginal equivalent such as dyspnea should be assessed properly to choose the appropriate investigation. Noninvasive modalities should be used first to assess the need for CA.

As the assessment of LBBB patients with chest pain for ischemia is difficult due to the various limitations posed by the LBBB on different imaging modalities as discussed earlier, we wanted to assess the role of speckle tracking echocardiography technique in diagnosing CAD in LBBB patients. As per **Moustafa *et al.*** [23] GLS measured by 2D speckled tracking echocardiography can be used to detect the presence and the extent of CAD. We wanted to test if that was also possible in patients with LBBB pattern in ECG. GLS and time to peak strain in two chamber three chamber and four chamber views (TTPS AP2, TTPS AP3 and TTPS AP4 respectively) were obtained and corelated to the results of CA concerning the presence of significant coronary artery stenosis.

In our study 50 patients (making up 62.5% of the patients) had no significant CAD (Group I) and 30 patients had significant CAD (Group 2). This is in agreement with a study that reports that LBBB is not always accompanied by epicardial coronary disease [8, 9].

Nevertheless, such patients have a higher risk of adverse outcomes, this mandates investigating them thoroughly to manage any treatable condition accompanied by the LBBB. Finding the right investigation to omit performing unnecessary coronary angiographic procedures would be of a huge benefit [24].

In our study age was higher among group II patients. This is concordant with **Nabati *et al.*** [25]**.** It seems that age is an independent predictor for significant CAD after adjustment for other risk factors with a p-value of 0.034 and OR 1.16. However, there was no significant difference between groups in regarding gender, hypertension, dyslipidemia, diabetes, smoking or family history. Unlike **Nabati *et al.*** [25] in whom their work, all the above-mentioned risk factors were statistically significant between their two groups. This may be attributed to the fact that our study group of age was lower than theirs. Also, patients with worse cardiovascular events like reduced ejection fraction, previous MI, previous PCI or CABG were excluded from our study.

In our study, GLS was shown to be a good indicator to rule out significant CAD with p value 0.0001 and OR 0.456. STE showed that GLS was significantly higher in significant CAD group (worse systolic function) than non-significant CAD group measuring -9 ± 2 and -12.1 ± 3 in the two groups respectively, with a p-value of 0.0001. This agrees with **Nabati *et al.*** [25] and **Abdulsalam *et al.*** [26] though with different values. This may be attributed to difference between vending machines and also due to exclusion of cases with dilated cardiomyopathy or previous myocardial infarction from our work.

Worse GLS among group II patients showed that STE was able to detect subtle impairment in systolic function. This agrees with **Klaeboe *et al.*** [27] where they concluded that ejection fraction (EF) though is widely used as a measure for systolic function, has many limitations and inaccuracies and that GLS makes a good candidate for accurately assessing systolic function. We found out that GLS could predict significant CAD using cutoff point of 11.4%, with sensitivity of 66% and specificity of 90% (p value 0.0001).

The delay in myocardial segments to reach peak strain in the presence of CAD was reflected as higher TTPS AP2, TTPS AP3 and TTPS AP4 values among Group II patients. This agrees with **Nabati *et al.*** [25]. This is justified, as ischemia affects cardiac myocytes as well as the heart conduction system, slowing down the electric impulse flow across the myocardium of LBBB patients even more prolonging left ventricular time to peak strain [7]. TTPS AP2 could predict significant CAD using cutoff point of 399.5 ms with sensitivity of 90% and specificity of 58% (p value 0.0001). TTPS AP3 could predict significant CAD using cutoff point of 385.5 ms with sensitivity of 73.3% and specificity of 72% (p value 0.0001). TTP AP4 could predict significant CAD using cutoff point of 377.5 ms with sensitivity of 90% and specificity of 52% (p value 0.0001).

Though such results are promising regarding the use of GLS and TTPS as a tool to exclude CAD in LBBB without the need to perform invasive CA, precise cut off point values should be taken cautiously as it is related to a certain software and is also obtained from a small sample size.

CONCLUSION

Diagnosis of CAD disease in patients with LBBB by non-invasive modalities has many limitations. Left ventricular GLS and TTPS obtained by speckle tracking echocardiography offers an objective tool that has good sensitivity for detection of CAD in patients with LBBB.

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