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Value of S'-wave Dispersion of Mitral Annular Tissue Velocity in Predicting the Presence of Significant Coronary Artery Stenosis

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Abstract: ***Background: Coronary artery disease (CAD) is a paramount cause of death. Global and regional left ventricular (LV) systolic function is an important non-invasive marker of CAD. Using tissue Doppler imaging (TDI), we can visualize and measure the low velocities generated by myocardium which are: S'-wave, E'-wave, and A'-wave. However, the cutoff values for systolic and diastolic velocities are still unclear. We aimed to examine the value of the S'-wave dispersion of TDI derived mitral annular velocities for the prediction of angiographically significant coronary artery stenosis. Methods: We included 120 patients with symptoms suggesting CAD in the study. We excluded patients with previous myocardial infarction, atrial fibrillation, significant valvular disease, and congestive heart failure. All patients had undergone full history taken and clinical examination; complete 12-leads electrocardiography, echocardiographic with assessment of LV systolic and diastolic dimensions, fraction of shortening, ejection fraction, and Doppler derived mitral valve velocities; TDI with measuring of S'-wave, S'-wave dispersion, E'-wave, A'-wave and E'/A' ratio of the septal, lateral, anterior and inferior walls; and coronary angiography. Lesions with ≥ 70% narrowing in major epicardial artery or ≥ 50 % narrowing in the left main coronary artery were considered significant. Patients were classified into two groups according to the presence or absence of significant coronary stenosis. Results: Clinical and conventional echocardiographic measures were comparable between the two groups. Tissue Doppler measures were comparable between the two groups except E'/A' ratio of the anterior wall which was significantly lower in patients with significant coronary artery obstruction. S'-wave dispersion was significantly higher in patients with significant coronary artery obstruction (p <0.00001). Sensitivity of S'-wave dispersion ≥35 % in predicting significant coronary obstruction was 63.6 %, specificity was 83.7 %, and overall accuracy was 70.8 %. Conclusion: S'-wave dispersion may be a good predictor of angiographically significant coronary artery obstruction.***

Keywords: Tissue Doppler imaging; Mitral annular velocities; S'-wave dispersion; Coronary artery disease; Coronary angiography

1. Introduction

Coronary artery disease (CAD) is a paramount cause of death. In the year 2001, the Global Burden of Disease study [1] estimated that there were about 65 million deaths worldwide; among them more than 12 million deaths were due to cardiovascular diseases. This extraordinary burden of disease necessitates early diagnosis and treatment.

Non-invasive imaging tests as stress echocardiography and radionuclide imaging are important and useful tools in everyday practice for early detection, evaluation, and risk stratification of CAD [2]. Global and regional left ventricular (LV) systolic function is an important marker of CAD in echocardiographic studies, which is usually assessed using two-dimensional echocardiography [3].

In 1989, the technique of tissue Doppler imaging (TDI) emerged as a unique, easily performed, and reproducible modality for assessing systolic and diastolic LV performance [4-6]. Using TDI, we can visualize and measure the low systolic and diastolic velocities generated by myocardial movements [7].

In trials for using TDI in the diagnosis of CAD, some investigators have used the technique for measuring diastolic function; while others have used it to measure resting or post-stress velocities of various myocardial segments [7].

Using the pulsed wave Doppler, the myocardium generates the following measures: S'-wave (systolic wave), E'-wave (early diastolic wave), and A'-wave (late diastolic wave). Other measures like E'/A' (the ratio of early and late diastolic tissue velocity as measured by TDI), and E/E' (the ratio of early diastolic transmitral flow velocity and early diastolic tissue velocity), may also be taken for evaluating LV diastolic function [8].

However, the cutoff values for maximum systolic velocity and diastolic velocities which may detect CAD are, as yet, unclear [7]. Also associated diseases, like diabetes mellitus [9] or hypertension [10] have an adverse effect on global systolic and diastolic functions of the LV which may make the use of TDI derived velocities for diagnosis of CAD more difficult.

So, we aimed to study the value of the S'-wave dispersion of TDI derived mitral annular velocities for the prediction of angiographically significant coronary artery stenosis.

2. Patients and Methods

This study had been carried out in the Cardiology Department, Zagazig University Hospitals. We included 120 patients (74 males and 46 females) with symptoms suggesting CAD in whom coronary angiography was indicated according to the 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the diagnosis and management of patients with stable ischemic heart disease [11].

Patients were excluded from the study if they had one or more of the following:

- Previous myocardial infarction (MI).

- Atrial fibrillation (AF).
- Significant valvular heart disease (more than mild stenosis or regurgitation).
- Congestive heart failure (CHF).

The study protocol had been approved by the Institutional Review Board of our institution of Zagazig University. After giving an informed written consent, we did the following to all patients:

1) Full history taking and thorough clinical examination.
2) Complete 12-leads electrocardiography:
3) Echocardiography: Echocardiographic and Doppler studies were performed for all patients using VIVID E9 machine (GE Health Medical, Horten, Norway) with 2.5 MHz transducer. The studies were performed by two expert operators unaware of the patients' clinical data and of each other measures. The following measures were taken:
   - Two-dimensional guided M-mode measurements of left ventricular end-diastolic dimension (LVEDD), left ventricular end-systolic dimension (LVESD), ejection fraction (EF) and fraction of shortening (FS) [12].
   - Doppler derived MV flow velocity waves; E-wave, A-wave, and E/A ratio [12].
   - Tissue-Doppler imaging (TDI): myocardial velocities of MV annulus were measured to all subjects at apical 4-chamber and apical 2-chamber views. We measured the velocities at the septal, lateral, anterior, and inferior walls of mitral valve annulus. Three velocities were taken for every wall, S'-wave for systole, and two waves for diastole; E'-wave at early filling phase, and A'-wave for atrial contraction phase [13]. S'-wave dispersion was calculated for every patient according to the following formula:

$$\text{S'-wave dispersion} = (\text{Maximum S'} - \text{Minimum S'})/\text{Maximum S' \%}$$

4) Coronary angiography: Coronary angiography was done to all patients. The coronary artery narrowing was visually estimated by an expert angiographer and expressed as percentage of luminal diameter stenosis. Lesions with ≥ 70% narrowing in major epicardial artery or ≥ 50 % narrowing in the left main coronary artery were considered significant angiographic stenosis [14].

According to the presence or absence of significant coronary artery (CA) obstruction, patients were classified into two groups:

Group I: Patients with significant CA obstruction (77 patients).
Group II: Patients without significant CA obstruction (43 patients).

All data were analyzed using the SPSS package program (Version 20.0; Armonk, NY, USA: IBM Corp.). Differences among the study groups were analyzed by student's t-test and χ^2-test. The correlations among different variables were investigated by Pearson correlation analysis. A p value < 0.05 was regarded as being statistically significant.

In order to assess the intraobserver variability, we repeated the measures for 25 patients within 5 days from the first measure and under the same basal conditions. The intraobserver and interobserver variability were calculated by dividing the difference between the two sets of measurements, by the mean of the two observations.

3. Results

As shown in Table 1, there was no significant difference between the study groups concerning age, sex, diabetes, hypertension, or smoking. As regard conventional echocardiographic data, there was no significant difference between the study groups concerning LVEDD, LVESD, EF, FS, MV E-wave, MV A-wave, and E/A ratio.

Results of tissue Doppler velocities of MV annulus are shown in table 2. Patients with significant CAD had a significantly lower E'/A' ratio of the anterior wall than patients without significant CAD (p = 0.023). As regard other TDI velocities of the septal wall, there was no significant difference between the two groups concerning S'-wave, E'-wave, or A'-wave. There was no significant difference between the two groups concerning S'-wave, E'-wave, A'-wave, or E'/A' ratio of the septal, lateral or inferior walls.

Patients with significant CAD had a significantly higher S'-wave dispersion than patients without significant CAD (p <0.00001). There were more patients with S'-wave dispersion ≥ 35 % among patients with significant CAD (p <0.00001).

In order to analyze the cutoff point of S'-wave dispersion for prediction of angiographically significant CAD, the receiver operating characteristic (ROC) curve was made. As shown in figure 1, for S'-wave dispersion ≥ 35 %, area under the ROC-curve was 0.821.

As shown in table 3, sensitivity of S'-wave dispersion ≥ 35 % in predicting significant CAD was 63.6 %, specificity was 83.7 %, positive predictive value was 87.5 %, negative predictive value was 56.3 %, overall accuracy was 70.8 %, Kappa was 0.341, p = 0.0014.

Inter- and intraobserver variability for different echocardiographic parameters ranged from 2.2 to 7.9 %. For the S'-wave dispersion, inter- and intraobserver variability were 7.1±3.2 % and 5.3±1.8 % respectively.

4. Discussion

In our study, S'-wave dispersion was significantly higher in patients with significant CAD, and there were significantly more patients with S'-wave dispersion ≥ 35 % among patients with significant CAD. Sensitivity of S'-wave dispersion ≥ 35 % in predicting significant CAD was 63.6 %, specificity was 83.7 %, positive predictive value was 87.5 %, negative predictive value was 56.3 %, and overall accuracy was 70.8 %.

Echocardiography is an important noninvasive tool in diagnosis and evaluation of patients with known or

suspected CAD [14]. Visual detection of segmental all motion abnormality is the basic method in diagnosis of CAD by echocardiography [15]. However, detection of wall motion abnormalities, based only on visual assessment has many limitations being a qualitative method and totally subjective method that depends to a great extent on operator experience and the quality of the images [16].

Tissue Doppler imaging has been introduced for quantification of regional and global, systolic and also diastolic LV functions. During ischemic events, the longitudinal endocardial fibers are the first being affected; then velocity changes can be detected from the apical approach. In addition to systolic velocity S', diastolic velocity E' and E'/A' ratio were found to be correlating with wall motion abnormalities [17].

Derumeaux and his colleagues [18] have found a strong correlation between myocardial systolic velocity and regional myocardial blood flow in animal models of myocardial ischemia.

Similar results were found in humans as Katz and his colleagues [19] have found that decreased maximum systolic velocity was a highly sensitive and specific figure for detection of abnormal segmental myocardial motion and was able to diminish the variability in the visual interpretation of wall motion abnormalities assessed during dobutamine stress echocardiography.

Although the great value that TDI can add to the echocardiographic detection of myocardial ischemia either at rest or during stress, it still has some limitations. One important limitation is the lack of clear, well-defined, cutoff values for maximum systolic velocity and diastolic velocities which may detect CAD [7]. This may occur because most researches depends on measuring the systolic and diastolic velocities of the examined segments which is dependent on the global LV systolic and diastolic function which in turn may be affected by other systemic diseases like diabetes mellitus [9] or hypertension [10].

Despite these limitations, the American Society of Echocardiography/ European Association of Echocardiography guidelines recommended the use of TDI in diagnosis and evaluation of CAD patients [20].

So, the aim of our study was to test the validity of S'-wave dispersion in detecting angiographically significant coronary obstruction.

In a study by Sun et al [21], they found that E/E' at rest was a good indicator of significant CAD detection. They found that a cutoff point of E/E' > 8.34 was able to detect CAD with an accuracy of 85.8 %, sensitivity 77.4 % and specificity 100 %.

However, Badran et al [22] found that increment of S'-wave less than 2.5 cm/s during dobutamine stress had 88 % sensitivity and 90 % specificity in detecting CAD, while increment of E'-wave less than 2.5 cm/s had 88 % sensitivity and 87 % specificity.

Most of the studies on TDI were done on relatively small number of patients and showed significant heterogeneity of their measured velocities in normal or abnormal segments. This heterogeneity was observed in the meta-analyses of maximum early and late diastolic velocity (pre-stress); and maximum systolic velocity and late diastolic velocity (post-stress). This heterogeneity could be the result of subtle differences in patient populations, segments in which TDI velocities were measured, models of the echocardiography machines used in the assessments, or type of tissue Doppler used (spectral Doppler, which measures the instantaneous velocity, versus color Doppler which measures the modal velocity) [7].

In our study we assumed that measuring a new different parameter of regional systolic function like "S'-wave dispersion", which has not been tested before to our knowledge, may be able to detect the regional impairment of LV systolic function caused by CAD and to some extent ameliorate the effect of other systemic diseases on global LV systolic function.

So, our results showed that S'-wave dispersion is a relatively good predictor of significant coronary obstruction and may help with other TDI parameters and conventional echocardiography in non-invasive detection of patients with CAD.

5. Conclusion

S'-wave dispersion may be a useful predictor of angiographically significant coronary artery obstruction. S'-wave dispersion ≥ 35 % can detect significant CAD with 63.6 % sensitivity, 83.7 % specificity, 87.5 % positive predictive value, 56.3 % negative predictive value, and 70.8 % overall accuracy.

Further studies on larger number of patients and on other patients' categories are recommended.

6. Study Limitations

In addition to the relatively small number of patients and being a single center study, the major limitation of our study is that it did not include many patients' categories like those with previous MI, those with AF and those with CHF. We did not include these categories because of the effect of MI on LV regional systolic and diastolic functions beyond the presence of flow limiting coronary obstruction and the variability of TDI velocities with AF.

7. Disclosures

The authors declare that there is no conflict of interest.

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Table 1: Population characteristics, risk factors, and echocardiographic data

	Significant CAD (n = 77)	No Significant CAD (n = 43)	p
Age (ys)	53.6±7.8	55.8±9.3	> 0.05
Sex Male Female	 48 (62.3 %) 29 (37.7 %)	 26 (60.5 %) 17 (39.5 %)	> 0.05
Diabetes	25 (32.5 %)	13 (30.2 %)	> 0.05
Hypertension	31 (40.3 %)	16 (37.2 %)	> 0.05
Smoking	24 (31.2 %)	13 (30.2 %)	> 0.05
LVEDD (mm)	50.3±4.78	49.2±5.63	> 0.05
LVESD (mm)	33.4±3.12	32.1±3.44	> 0.05
FS (%)	33.6±4.51	34.8±4.12	> 0.05
EF (%)	63.6±5.31	65.1±5.2	> 0.05
MV E-wave (cm/s)	83.2±16.3	87.8±13.8	> 0.05
MV A-wave (cm/s)	77.5±14.7	79.3±12.6	> 0.05
E/A ratio	1.07±0.232	1.11±0.341	> 0.05

Table 2: Tissue Doppler measurements

		Significant CAD (n = 77)	No Significant CAD (n = 43)	p
Septal:	S' (cm/s)	9.5±5.83	10.6±2.87	> 0.05
	E' (cm/s)	7.7±4.93	8.6±3.11	> 0.05
	A' (cm/s)	8±5.23	8.4±4.21	> 0.05
	E'/A'	0.96±0.433	1.02±0.398	> 0.05
Lateral:	S' (cm/s)	10.4±6.21	11.2±3.3	> 0.05
	E' (cm/s)	8.3±5.42	8.7±4.87	> 0.05
	A' (cm/s)	8.5±6.31	8.4±4.63	> 0.05
	E'/A'	0.98±0.531	1.04±0.477	> 0.05
Anterior:	S' (cm/s)	9.1±5.4	10.7±4.25	> 0.05
	E' (cm/s)	8.1±4.62	9±3.86	> 0.05
	A' (cm/s)	8.6±5.32	8.1±3.96	> 0.05
	E'/A'	0.94±0.422	1.11±0.365	0.023
Inferior:	S' (cm/s)	9.8±6.2	11.3±4.16	> 0.05
	E' (cm/s)	8.5±3.56	9.1±4.13	> 0.05
	A' (cm/s)	8.9±3.43	8.6±4.76	> 0.05
	E'/A'	0.95±0.462	1.06±0.48	> 0.05
S'-wave dispersion (%)		39.2±4.87	29.1±5.93	<0.00001
S'-wave dispersion ≥ 35 %		49 (63.6 %)	7 (16.3 %)	<0.00001

Table 3: Validity of S'-wave dispersion in prediction of significant coronary artery obstruction

	Significant CAD	No Significant CAD	Total
S'-wave dispersion ≥ 35 %	49	7	56
S'-wave dispersion < 35 %	28	36	64
Total	77	43	120

Sensitivity	Specificity	PPP	NPV	Overall accuracy	Kappa	p
63.60%	83.70%	87.50%	56.30%	70.80%	0.341	0.0014

PPV = positive predictive value, NPV = negative predictive value.

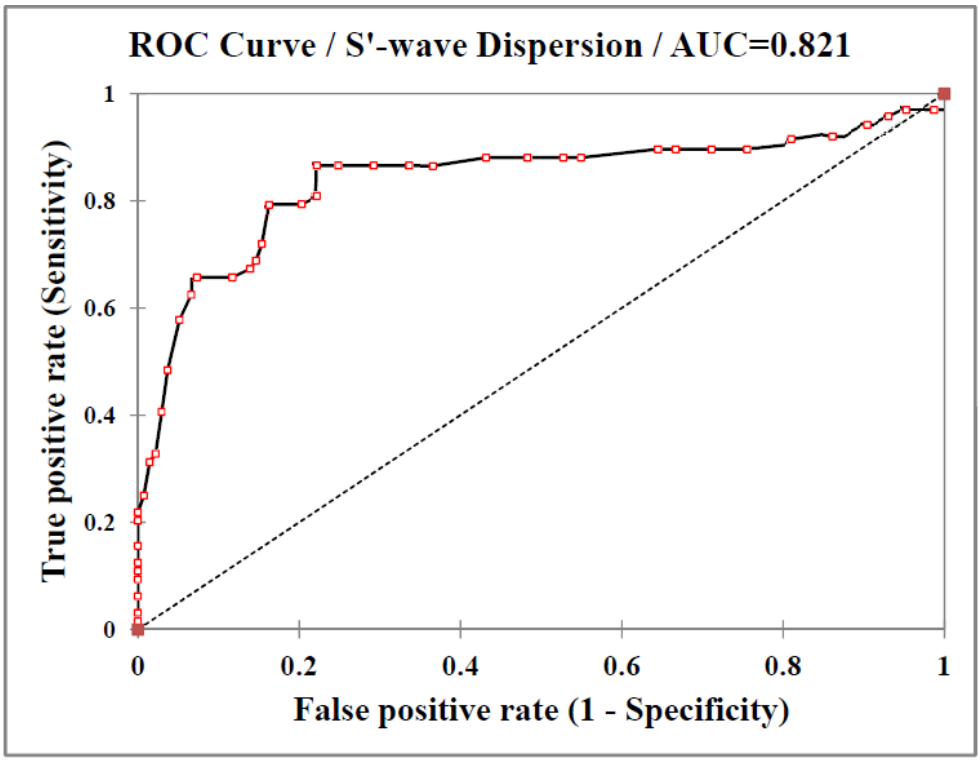

Figure 1: ROC curve for S'-wave dispersion ≥ 35 % with significant coronary artery stenosis.