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Comparing of Peak Longitudinal Strain and Post Systolic Shortening in Detecting Ischemia at Rest in Stable Coronary Artery Disease: An Angiography Verified Study

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Abstract

Background: Coronary artery disease is a major public health problem. Early diagnosis and treatment of coronary artery disease is crucial. There is a need for a practical, reliable and cost-effective non-invasive imaging tool. We aimed to evaluate the rest ischemia with speckle tracking echocardiography (STE) compare to the two methods in patients who were scheduled coronary angiography according to the stress tests. Methods: We included fifty patients with stable angina pectoris who were scheduled for conventional coronary angiography after the stress tests in our study. Speckle tracking echocardiography was performed just before coronary angiography. The association of 2 parameters with coronary artery disease was investigated and compared. Results: Among 50 patients recruited for the study, 38 of them had severe CAD (>50%), whereas 12 patients had non-significant CAD. Post systolic shortening (PSS) was significantly related with CAD ($p<0.0001$). The relationship of PLS with the area at risk was found to be statistically insignificant but global longitudinal strain (GLS) was significantly lower in patients with severe CAD ($p=0.011$) Conclusion: PSS may detect coronary ischemia in patients with stable coronary artery disease and it is more sensitive and specific in patients with stable CAD. PSS is a very useful, practical and easy applicable non invasive tool for the detection of severe coronary artery disease at rest.

INTRODUCTION

Coronary artery disease(CAD) is a major public health problem. It is the leading cause of all deaths (1,2) and thus early diagnosis and treatment of CAD is of critical importance. To diagnose the CAD in patients presenting with chest pain is sometimes costly and time consuming.

Numerous clinical studies have been conducted for the early diagnosis of CAD (3-7). Currently there are various available invasive and noninvasive tests, however all of them have several limitations. Some are expensive and difficult to access, while some others have a high dose of radiation. Due to all these reasons, there is an absolute need for a reliable and cost effective non-invasive imaging method. Speckle tracking echocardiography (STE) is a new cardiac ultrasound technique that allows to assess LV function semi automatically, with a simplified operational process and high reproducibility. Furthermore, STE has been demonstrated to be superior to conventional echocardiographic methods to evaluate cardiac functions and predict cardiovascular outcomes as well (8,9). Another advantageous feature of STE is it's low intra-and inter-observer variability. Being independent from angle and index makes it more useful too and thus, with all those positive aspects it may become the optimal method for global LV systolic function evaluation (10). Peak Longitudinal strain (PLS) and post systolic shortening (PSS) have been shown to detect resting ischemia in the literature (11-15). In our study, we aimed to evaluate the rest ischemia with STE and compare it with the two methods in patients who were scheduled coronary angiography according to the stress tests .

METHODS

Study population

The study was approved by the Çanakkale Onsekiz Mart University Ethics Committee and conformed to the principles outlined in the Declaration of Helsinki. All subjects participating in the study gave informed consent. The subjects who underwent either myocardial perfusion scintigraphy or treadmill test for myocardial stress, were included in this prospective study and the ones who had positive stresss test and scheduled for coronary angiography were evaluated with STE.

All participants were initially evaluated by a standard echocardiographic examination. Patients with previous myocardial infarction, patients with acute coronary syndrome, moderate and severe valve disease, cardiomyopathy, chronic systemic or inflammatory diseases or any form of malignancy, and patients with previous thoracic surgery, were excluded from the study.

Ventricular function was assessed by STE before the angiography and it was compared with angiography results thereafter (Figure 1)

Standard echocardiography

Echocardiographic examinations were performed using a high-quality echocardiography machine (Vivid 7, GE, USA) by two cardiologists. Our echocardiography machine was additionally calibrated for international studies by an independent organization (certificate no: B14091148). Measurements of LV and LA dimensions were made in accordance with the most up to date European Society of Echocardiography recommendations (16). LVEF was measured using the modified biplane Simpson's rule. The ratio between peak early (E) and late (A) diastolic LV filling velocities and E wave deceleration time was determined by standard Doppler imaging. The timing of mitral and aortic valve opening and closing were defined by a pulsed-wave Doppler tracing of the mitral inflow and LV outflow. Lateral wall and septal tissue Doppler parameters (E' and A') were measured as well. E/E' was calculated manually. Particular attention was given to limit myocardial tissue and extracardiac structures, providing sufficient reliable data to obtain a gray-scale image.

Speckle tracking echocardiography

Apical four and two-chamber, apical long-axis and parasternal short-axis images were acquired using conventional two-dimensional gray-scale echocardiography for speckle tracking evaluation on breath hold with a stable ECG recording and further Speckle tracking evaluation was performed by the same cardiologist. Three consecutive heartbeats were recorded and averaged. The frame rate was adjusted to between 90 and 120 frames per second. Automatic function imaging method was used for the assessment. The region of interest (ROI) was manually outlined by marking the endocardial borders at the mitral annulus level and at the apex on each digital loop. The epicardial surface was generated by the software (EchoPac, version 7.0.1 GE, USA) so that the ROI was created (Figure 2). The ROI was corrected manually at the end, if needed. After manual adjustments, ROI was divided into six segments and each segment was scored automatically by the software according to the image quality. Whether the tracking quality for each segment could be considered acceptable was determined by the software. The peak systolic strain values in a 17-segment LV model were used in the presented study. End- systole was defined as aortic valve closure in the apical long-axis view. The results for all three planes were then combined in a single bulls-eye summary that provided the global longitudinal strain

Defining peak longitudinal strain and post systolic shortening

Peak longitudinal systolic strain (PLS) was measured as the maximum value of strain in systole, which was defined as the time interval between the aortic valve opening and closure. Strain values were also evaluated segmentally according to the area at risk. Values above -18 were considered significant for PLS.

PSS is described as myocardial contraction that occur after end systole or aortic valve closure. Criteria for

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pathologic PSS was, when PSS exceeds 20% of ejection time and when it takes more than 90 ms after AVC (5).

Statistical analysis

Statistical analysis was carried out with the SPPS program (version 21.0, SPSS, Chicago, İllinois, USA). All measurements were evaluated with the Kolmogorov-Smirnov test for normality. A comparison of continuous variables between the groups was performed using the Mann-Whitney U test. All continuous variables were expressed as mean ± standartd deviation values. PLS values were compared to according to presence of more than 50% stenosis least one vessel. Categorical variables were analysed using the Chi-square test. Presence of PSS in each segment were compared according to more than 50% stenosis in segment related coronary artery. We also evaluated the relation between presence of PSS of segments and presence of severe coronary artery disease of at least one vessel. Correlations between coronary artery disease severity and peak systolic strain for each coronary artery and its territory was evaluated by a Pearson correlation test where two-sided P values <0.05 were accepted as statistically significant

RESULTS

50 patients were recruited in our study. The general characteristics of the study population depicted in table 1. Echocardiographic findings of the study population were in normal range. Conventional echocardiography parameters shown in table 2. 38 patients had severe CAD (>50%) whilst 12 patients had no significant CAD. PSS was significantly related with CAD and area at risk in all echo planes. ($p<0.0001$) LV wall analysis of PSS according to the coronary occlusion was showed in Table 3. In the segmental PSS analysis, the presence of PSS in the basal anterior and mid anterior segments was found to be significantly associated with left anterior descending artery (LAD) stenosis, respectively $p<0.001$, $p<0.001$. The presence of PSS in the basal lateral wall was found to be significantly associated with circumflex (LCX) stenosis, $p=0.032$. The presence of PSS in the basal inferior wall was found to be significantly associated with right coronary artery (RCA) stenosis, $p=0.021$. Detailed segmental analysis of PSS according to the coronary artery stenosis was showed in supplementary table 1. The relationship of PLS with the area at risk was found to be statistically insignificant whereas GLS was significantly lower in patients with severe CAD ($p=0.011$). LV wall analysis of PSS according to the coronary occlusion was showed in Table 4. The presence of PSS was not associated with the coronary stenosis in segmental PLS analysis. Detailed segmental analysis of PSS according to the coronary artery stenosis was showed in supplementary table 2.

DISCUSSION

In our study we found that PSS is more sensitive and specific for coronary arterial lesion than PLS in patients with stable CAD. We also found that GLS was lower in patients with severe coronary artery disease but there was no correlation with ischemic risk area. It has been shown that in different clinical and experimental studies, that PSS is superior to conventional methods, such as wall thickening and peak longitudinal systolic strain in detecting acute coronary ischemia and coronary artery disease (4,17,18). We also tested the capability of PSS and PLS to predict coronary lesions in patients scheduled for coronary angiography as a result of a stress test and confirmed the results with coronary angiography.

It has been proven in a vast number of studies that strain is highly correlated with severity of coronary artery disease (3-10) and that PLS and PSS can detect acute coronary ischemia (4,12,15). Additionally, it is also known that PSS can be seen in around 15% of normal healthy people, particularly in basal segments. We applied the criteria from previous studies for PSS assessment to avoid false positive results (5). PSS was mostly seen in the basal and mid segments in our study too. Similarly, it has been shown that PSS is more common in basal segments (5), and contraction anomalies are seen in apical segments rather than temporal anomalies (19).

Experimental animal studies have also demonstrated that PLS and PSS are significantly reduced in coronary artery occlusion (20-22). PSS continued while systolic strain recovered rapidly after reperfusion. Even after 2 minutes of occlusion, PSS was persisting (23, 24). These findings depicted that PSS can be more sensitive

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and specific in detecting intermittent mild ischemia. Mechanism of PSS is still speculative. Some studies claimed that it is due to prolonged contraction and delayed relaxation (25) while some others suggested that fatty acid metabolism is responsible fot that, which is suppressed during ischemia (26,27). This may also be a combination of active and passive processes (28,29).

Stable CAD and low-risk unstable angina are most commonly caused by atheromatous plaques in the coronary arteries that obstruct blood flow and may lead to the silent ischemia (30). Silent ischaemia is common and prognostically important entity (31). There is also evidence that silent myocardial ischemia is seen more frequently than anginal attacks in patients with coronary artery disease (32). It has been already found that more than 70% of patients with stable angina have frequent episodes of silent ischemia (33). In different studies silent myocardial ischemia has been indicated to occur frequently even during treatment with conventional anti-anginal drugs (33, 34). Both an increase in myocardial oxygen demand and abnormalities of coronary vasomotor tone appear to play a significant role in the genesis of silent ischemia (34). For this reasons, we consider that silent ischemia is present in stable coronary artery patients and we suggest that PSS may detect serious coronary artery disease without performing stress test.

GLS was lower in patients with severe coronary artery disease, similar to previous studies (7-10). However, segmental analysis was not performed in these above mentioned studies. Unlike previous studies, we performed segmental analysis and also investigated the relationship between PLS and the area at risk as well. No relation was found between the area with severe coronary artery disease and PLS in our study. Although strain values are within normal limits, PSS was seen in ischemic segments in patients with severe coronary lesion. Similarly, a recent published study demonstrated that PLS could be a sensitive but nonspecific imaging method to determine significant CAD at rest (35). Figure 3

STUDY LIMITATIONS

The major limitation of our study was echo window quality. Good echo window is *sine qua non for an accurate* speckle tracking imaging. Despite a high quality echocardiography machine we used and experienced cardiologists, we couldn't overcome this problem completely when particularly the problem is patient related. Another limitation was that we could not exclude microvascular disease in our study. Furthermore, regrettably in some patients coronary lesion severity was evaluated visually and FFR technique was not available for all patients.

CONCLUSION

PSS may detect coronary ischemia in patients with stable CAD and it is more sensitive and specific in patients with stable CAD. STE is a great help for clinicians as it is a practical, useful, easy applicable cost effective noninvasive tool for detecting severe coronary artery disease at rest.

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Author contributions :

All authors contributed to: substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data, drafting the article or revising it critically for important intellectual content, and, final approval of the version to be published.

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Figure Legends Figure 1. Study protocol Figure 2. Contouring of left ventricle by speckle tracking echocardiography. LV=left Ventricle, LA=Left Atrium, RV=Right Ventricle,RA= Right Atrium Figure 3. A: Normal strain values and no PSS in 4ch view. B and C: Strain analysis indicates significant PSS in basal inferior and basal posterior wall. D: Normal strain values in bulls eye image. E: Coronary angiography showed that diffuse atherosclerosis and severe occlusion before the bifurcation in the RCA, RCA=Right Coronary Artery

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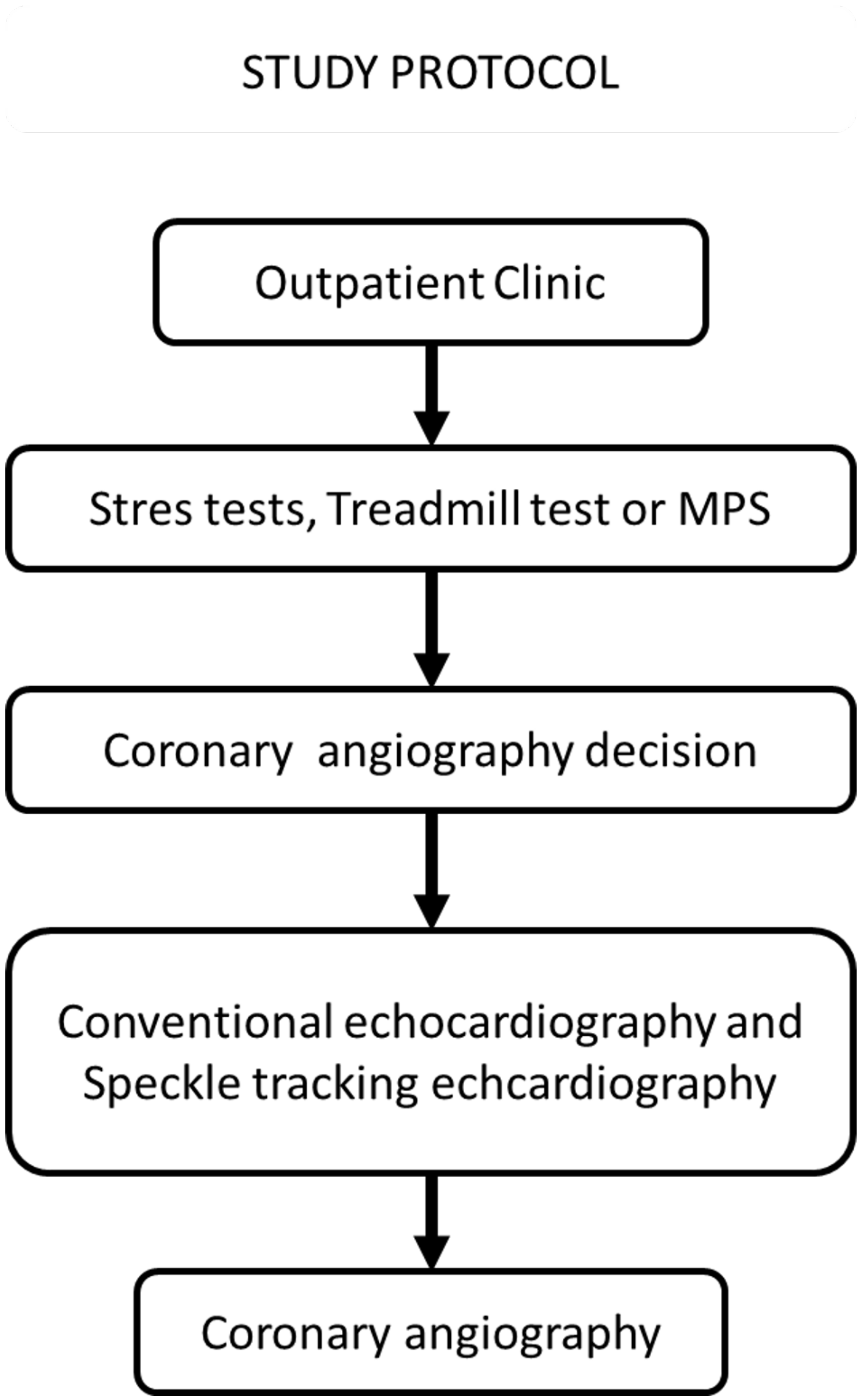

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