

## DISCUSSION

Non-invasive methods for assessment of regional myocardial function are important in the diagnosis of coronary artery disease (CAD), risk stratification of patients and choice of therapeutic interventions. Resting echocardiography is usually conducted to evaluate ventricular function or to rule out other causes of cardiovascular diseases such as valvular heart disease, but is not useful in the diagnosis of CAD because wall motion abnormalities are usually absent even in patients with left main CAD or severe three-vessel CAD.<sup>(62)</sup>

Stress echocardiography (exercise or pharmacologic) is often indicated to establish the likelihood of advanced CAD; it requires expertise, is technically challenging with respect to acquisition of images and is associated with inter-operator variability and subjectivity in interpretation of regional wall motion abnormalities.<sup>(63)</sup> Moreover, in some patients, stress echocardiography may be non-conclusive because of failure to achieve the required heart rate. And in rare cases, cardiovascular complications such as myocardial infarction, severe arrhythmias and even sudden death can occur.

Measurement of strain by echocardiographic strain imaging, also known as deformation imaging, has been introduced as a quantitative means to objectively assess regional myocardial function.<sup>(64)</sup> Such measurements were first derived from velocity data by tissue Doppler imaging and have recently been obtained by the 2-D speckle tracking echocardiography (2-D STE).<sup>(65)</sup>

The aim of the present study was to evaluate the diagnostic power of longitudinal 2D strain obtained by speckle tracking echocardiography in prediction severe coronary artery disease in the resting echocardiogram.

The present study enrolled 60 patients presented to Alexandria Main University hospital for evaluation of chest pain by both echocardiography & coronary angiography. Based on the coronary angiography results, patients were grouped as high risk (group A): LT main or 3 vessel coronary artery disease, low risk group (group B): one or two vessels coronary artery disease, and. normal control group (group C).

The present study results showed that mean global peak systolic longitudinal strains (PSLSs) in patients with normal coronary angiogram was  $-21.6\%$ , this is in accordance with Yingchoncharoen et al.<sup>(66)</sup> who in a meta-analysis of 2597 subjects from 24 studies reported mean normal value of GLS =  $-19.7\%$ ; (95% CI,  $-20.4\%$  to  $-18.9\%$ ). Global PSLS was lower in the high-risk group (mean global PSLS =  $-15.33\%$ ), this is consistent with Nucifora et al.<sup>(67)</sup> who reported mean global PSLS of  $-15.8\%$  in patients with obstructive coronary artery disease. Also Zuo et al.<sup>(68)</sup> reported mean global PSLS of  $-16.65\%$  in patients with atherosclerotic lesions  $\geq 75\%$  of luminal diameter. Choi et al.<sup>(67)</sup> reported higher mean global PSLS ( $-18\%$ ) than reported in the present study this may be explained by more severe coronary lesions in the present study as 80% of patients had high stenotic lesions versus 58% in Choi study.

The present study results showed that global PSLS at rest could be used to predict high-risk CAD. The optimal cutoff point was  $-17.9\%$  with a sensitivity and specificity of 95% and 95%, respectively. This data are consistent with and add evidence to those reports that longitudinal strain at rest is a sensitive and powerful tool for detecting CAD. Zuo et al.<sup>(68)</sup> reported a GLS value  $\geq -17.75\%$  for prediction of 75% coronary stenosis. Nucifora

et al.<sup>(67)</sup> found that a GLS value  $\geq -17.4\%$  yielded high sensitivity (83%) and specificity (77%) in identifying patients with obstructive CAD, although they defined obstructive CAD as stenosis  $\geq 50\%$  and they used 64-slice multislice computed tomography angiography instead of coronary angiography as the standard of diagnosis. Choi et al.<sup>(69)</sup> reported that a PLS of  $-19.4\%$  of PLS was helpful in discriminating CAD as left main (stenosis  $\geq 50\%$ ) or three-vessel ( $\geq 70\%$ ) CAD (sensitivity = 76.3%, specificity = 71.4%), and they used the same computer algorithm (AFI) for strain calculation as done in the present analysis. The different cutoff values and different sensitivity and specificity between those reports and the present study could be due to different CAD definitions and baseline characteristics of the study patients.

There are several proposed mechanisms for impaired myocardial function in patients with CAD. Choi et al.<sup>(69)</sup> suggested that repetitive ischemic insults to the left ventricle, which occur with significant coronary stenosis, can reduce systolic longitudinal function, although resting regional wall motion remains normal. In an animal model, Reant et al.<sup>(70)</sup> studied myocardial deformation before and during dobutamine infusion. They found that both circumferential and longitudinal strain was significantly decreased at rest in the presence of flow-limiting stenosis and during dobutamine infusion in the presence of non-flow-limiting stenosis. In contrast, radial strain was significantly decreased only in the presence of severe flow-limiting stenosis and only during dobutamine infusion. The investigators suggested that 2D strain can evaluate longitudinal or circumferential abnormalities, which precede the decrease in radial deformation and wall thickening during ischemia. Because subendocardial myocardial fibers, which are mainly longitudinally oriented, are more susceptible to ischemia, it might be expected that longitudinal function is altered earlier than radial function.<sup>(71)</sup> This is very much in line with the present study findings that longitudinal strain might be impaired in patients with visually normal LV function even under resting conditions. Another hypothesis was suggested by Edvardsen et al.<sup>(72)</sup> They suggested that subclinical myocardial damage may be a marker of coronary atherosclerosis even in the absence of myocardial infarction, mainly because of small-vessel microembolization, endothelial dysfunction, or chronic ischemia. Geer et al.<sup>(73)</sup> described morphologic changes in the subendocardial myocardium that appeared to be caused by severe, chronic subendocardial ischemia in patients with unstable angina and congestive heart failure with no evidence of myocardial infarction by clinical and morphologic criteria. This could imply that deformation imaging can recognize early, subclinical myocardial dysfunction and damage.

The present study results showed that segmental PLSs were lower in the high-risk group than in the other two groups. Segmental analysis showed that reductions in PLS were more evident in the LV mid- and basal segments than in the apical segment. According to ROC curve analysis, the optimal cutoff value for combined mid- and basal PLS for the detection of high-risk CAD was  $-16.5\%$  (sensitivity = 95% and specificity = 87.5%). Similar findings have been reported by Choi et al.<sup>(69)</sup> who reported cut off value of  $-17.9\%$  (sensitivity = 78.3% and specificity = 79.3%) and Zuo et al.<sup>(68)</sup> who reported cut off value of  $-16.3\%$  (sensitivity = 66.7% and specificity = 64.7%)

The finding that both in patients and controls, PLS values in apical segments were higher compared with that of basal segments could be due to possibly incorrect estimation of longitudinal function of apical segments by 2D speckle tracking strain. This was also suggested by Choi et al.<sup>(69)</sup> and Biering-Sørensen et al.<sup>(74)</sup> who reported better diagnostic

performance of GLS for the detection of CAD when apical segments were omitted from GLS calculation. Choi et al.<sup>(69)</sup> speculated that the apex of LV has prominent rotational movement in addition to longitudinal and short-axis motion, and this might result in the incorrect estimation of longitudinal function in this segment. Moreover, inner myocardium, which is known to be most susceptible to myocardial ischemia, and which is the major component responsible for long-axis function, has a helical fiber orientation.<sup>(75)</sup> This helical structure might result in parallel alignment of longitudinal axis and inner myocardium only in the LV mid or base. Apical myocardium is rather aligned in a circular direction, which might be associated with short-axis function or rotational movement. In line with this, the present study speculates that, in the apical region, 2D speckle tracking software measures a combination of longitudinal and circumferential strain resulting in higher than expected values of PLS. Nonetheless, a recent 2D speckle tracking study investigating multilayer strain confirmed the existence of a basal-to-apical gradient in longitudinal strain in the inner and middle myocardial layers, with longitudinal strain being highest in the apex and lowest in the base.<sup>(76)</sup> While this is in line with the present study results, it is in discordance with previous studies reporting fairly constant longitudinal strain across the left ventricle.<sup>(77)</sup> The existence of longitudinal basal-to-apical strain gradient could be particularly important for establishing robust threshold values for segmental longitudinal strain.

The latent longitudinal LV systolic dysfunction despite the normal ejection fraction in coronary artery disease patients may be explained by: First, Impairment in longitudinal systolic function is known to be compensated by augmentation of circumferential deformation. As left ventricular ejection fraction (LVEF) is measured in the parasternal long axis view, it is not affected by reduction of longitudinal strain.<sup>(78)</sup> Second, in chronic ischemia, it has been demonstrated that recurrent ischemia and stunning can lead to structural changes such as fibrosis and loss of myocytes, contributing to reduction of longitudinal deformation in affected patients with normal EF. Third, limited sensitivity of ejection fraction (EF); was demonstrated by Edvardsen et al<sup>(79)</sup>, who stated that; the apparently normal systolic function in heart failure with normal ejection fraction (HFNEF) reflects limited sensitivity of EF, and assessment of regional systolic function by STE provides important diagnostic information. This was further confirmed by Sjøli et al<sup>(80)</sup>, who compared LV global strain measured by 2D STE and LVEF measured by conventional echocardiography for evaluation of LV function and infarct size in patients with ST-elevation myocardial infarction (STEMI) treated with thrombolysis. They found that LVEF is limited by observer variability and suboptimal agreement with reference methods while LV global strain seems to have several advantages over LVEF in evaluation of LV function

There are some limitations in our study. First, a relatively small numbers of patients were enrolled. Second, Two-dimensional speckle tracking echocardiography measurement has the advantage of being relatively angle independent. It is, however, like all echocardiographic methods, dependent on image quality. In the present study, all efforts were made to obtain high-quality images. Third, the patients with significant CAD had medications such as  $\beta$ -blocker, angiotensin-converting enzyme inhibitor, and angiotensin II receptor antagonist more frequently. As PLSs were known to be influenced by loading condition, these medications might have some effect on the PLS values. Fourth, it should also be noted that only symptomatic patients scheduled for coronary angiography were

included in this study and therefore, the true prevalence of regional LV dysfunction in patients with critical LAD stenosis remains unknown.

Fifth, we did not evaluate strain rate, circumferential and radial strain which could not be obtained directly from AFI software. However, as PSLS is a primary parameter that can be directly calculated via the speckle tracking method, strain might be a more relevant parameter than tissue Doppler study.

Finally, the reduction in PSLS may not be specific to severe CADs and may be present in other conditions than ischemia, such as advanced age, hypertension, diabetes mellitus and other myopathic conditions and further clinical investigations will be necessary to validate our observations.

## SUMMARY

Non-invasive methods for assessment of regional myocardial function are important in the diagnosis of coronary artery disease (CAD), risk stratification of patients and choice of therapeutic interventions. Resting echocardiography is usually conducted to evaluate ventricular function or to rule out other causes of cardiovascular diseases such as valvular heart disease, but is not useful in the diagnosis of CAD because wall motion abnormalities are usually absent even in patients with left main CAD or severe three-vessel CAD.

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Conventional 2D echocardiographic examinations were performed using a Vivid q system with a (1.7-4 MHz) transducer. Examinations included measurements of cardiac dimensions, volumes, and LV ejection fraction. Images were obtained in the apical long-axis, four-chamber, and two chamber views for the global and segmental analysis of peak systolic longitudinal strain (PSLS).

PSLS was measured successfully with good tracking quality in the 60 patients enrolled in this study.

The mean age was  $55.5 \pm 7.9$  and 28 (46.7%) of the patients were men.

No significant difference was found between the three study groups in terms of LV end diastolic and end-systolic volumes of and LV ejection fraction. Global and segmental PSLSs were lower in the high-risk group than in the other two groups. Segmental analysis showed that reductions in PSLS were more evident in the LV mid- and basal segments than in the apical segment.

Mean global PLS in patients with normal coronary angiogram was  $-21.6\%$ . Global PLS was lower in the high-risk group (mean global PLS =  $-15.33\%$ ). The optimal cutoff point to predict severe CAD was global PLS of  $-17.9\%$  with a sensitivity and specificity of  $95\%$  and  $95\%$ , respectively.

In Conclusion, Measurement of global and segmental longitudinal strain using 2D speckle tracking echocardiography is sensitive and accurate tool in the prediction of severe CAD.