The Egyptian Journal of Hospital Medicine (Apr. 2016) Vol. 63, Page 133- 137

Incremental Value of 2-Dimensional Longitudinal Radial and Circumferential Speckle Tracking Strain Imaging to Wall Motion Analysis for Detection of Coronary Artery Disease in Patients Undergoing Dobutamine Stress Echocardiography

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ABSTRACT

Background: DSE is considered one of the good options in clinical practice but due to some limitations new promising modalities like speckle tracking echocardiography (STE) was introduced. STE is a new imaging technique that allows evaluation of global and regional myocardial function independently from the angle of acquisition and from cardiac translational movements.

Objectives: Determine optimal cutoff values for longitudinal, radial and circumferential strains at peak DSE for detection of significant stenosis on CA. Also investigate incremental value of combining strain measurements to wall motion analysis. **Methods:** The study population comprised 100 patients (age 50 ±9 years) underwent high dose DSE, STE followed by CA. DSE and STE results were compared and added to each other and finally compared to CA result.

Results: GLS cutoff points (-16.75%) showed significantly higher accuracy when compared to GCS and GRS, with highest balanced sensitivity and specificity to predict CAD. GLS, GRS and GCS reduced the DSE false positivity by 83%, 72.2% and 66.6% respectively. STE also showed better Agreement with CA than DSE in detecting coronary territorial affection especially LAD (Kappa= 0.775).

Conclusions: STE is feasible during DSE, it helps increasing the diagnostic accuracy of DSE and decreasing its false positivity. Both global and segmental longitudinal strain can offer accurate, feasible and non invasive assessment of CAD.

Keywords: Coronary angiography (CA), Coronary artery disease (CAD), Dobutamine stress echocardiography (DSE), Global circumferential strain (GCS), Global longitudinal strain (GLS), Global radial strain (GRS), Left anterior descending (LAD), Left circumflex artery (LCX), Left ventricle (LV), Speckle tracking echocardiography (STE), Right coronary artery (RCA), Wall motion score index (WMSI)

INTRODUCTION

STE is considered one of the good options assessing the presence, localization and extent of CAD.[1] But wall motion analysis during DSE is subjective, and an expert observer is required to achieve the published levels of accuracy.[2] *S*TE is a new technique based on pure 2D grayscale ultrasound acquisition allowing calculation of segmental strains markers that can be tracked from frame to frame throughout the cardiac cycle.[3] It has been integrated into the most recent echocardiographic systems for quick, automated or manual evaluation of LV function. It is commercially available software that automatically or manually tracks myocardial motion throughout the cardiac cycle and allows rapid generation of regional myocardial strain curves that are site specific and angle independent.[4] Although the use of WMSI during DSE relies on visual assessment of myocardial radial thickening, 2D speckle tracking not only allows quantification of LV radial strain but also LV circumferential and longitudinal strains that are not visually apparent. However, the comparative diagnostic accuracies of these 3 orthogonal myocardial strains during DSE for the detection of CAD have not been previously reported.[5]

OBJECTIVES

Determine optimal cutoff values for longitudinal, radial and circumferential strains at peak DSE for detection of significant stenosis on CA. Also investigate incremental value of combining strain measurements to wall motion analysis.

received:15/12/2015
accepted:30/12/2015 DOI: 10.12816/0023839

PATIENTS AND METHODS

Study population: One hundred patients from cardiology department, Ain Shams university hospitals were recruited in this study. A full consent was taken from all patients, then all underwent full history taking, ECG, full echocardiography study, high dose DSE, 2D STE and coronary angiography (CA). Twenty patients with DSE negative testing were excluded from this study. Also, patients with heart failure, recent myocardial infarction, severe hypertension, non sinus rhythm, resting segmental wall motion abnormality (SWMA) were excluded from the study, 80 consecutive patients were identified and formed the derivation study population.

DSE: DSE was performed using a standard protocol. Dobutamine was infused through a peripheral intravenous line with a mechanical pump starting at a dose of 5 μg /kg/minthen increased at every 3-minute intervals to 10, 20, 30, 40, and 50 μg/kg/min, with intravenous atropine (up to 2 mg) given if necessary. A positive test was defined by a new wall motion abnormality in 2 adjacent segments.[1]

Image analysis: Wall motion analysis was done using 18 myocardial segment model as recommended by the American Heart Association and American Society of Echocardiography. A semi quantitative scoring system (1 = normal; 2 = hypokinesia; 3 = akinesia; 4 = dyskinesia; 5 = Aneurysm; 6 = Aneurysm and scar) was used to analyze each segment, and a global wall motion score index (WMSI) was calculated.[6]

2D STE: The 2D loops from the routine echocardiographic examination were processed offline. The end-systolic frame was first defined in the apical long-axis (3-chamber) view, where the aortic valve was directly visible. Aortic valve closure time is marked. This allows accurate timing of systole, diastole, and aortic valve closure on all views.[7]

During analysis, the endocardial border was manually traced at end systole and the region of interest width was adjusted to include the entire myocardium. The software then automatically tracked and accepted segments of good tracking quality and rejected poorly tracked segments while allowing the observer to manually override its decisions based on visual assessments of tracking quality. The global circumferential and radial strains were obtained directly from the mid-ventricular short-axis view, and longitudinal strains were determined in the apical views.[7]

Bull's eye diagram was then created from the data obtained from all myocardial segments with inter planar values interpolated. Values obtained from the 17 segment model Bull's eye were analyzed according to the following segmental strain reference values listed in table (1) to determine the presence or absence of ischemia in each segment. The territorial analysis was done as following: Antero-septal, anterior and apical segments represent LAD (Left anterior descending), Lateral and inferior segments represent LCX (Left circumflex) and Septal and posterior segments represent RCA (Right coronary artery). Two consecutive segments without coronary blood supply overlap were needed to diagnose territorial lesion.[1]

Coronary angiographic correlation: Selective coronary angiography was performed in multiple projections according to the Judkins technique in all patients. Significant coronary stenosis was defined as ≥ 50% diameter stenosis of the affected vessel using multiple planes.

STATISTICAL ANALYSIS

The collected data was revised, coded, tabulated and introduced to a PC using Statistical package for Social Science (SPSS 20). Data was presented and suitable analysis was done according to the type of data obtained for each parameter. Analytical statistics: The ROC Curve (receiver operating characteristic) provides a useful way to evaluate the sensitivity and specificity for quantitative diagnostic measures that categorize cases into one of two groups. Kappa statistics to compute the measure of agreement between two investigational methods Kappa's over 0.70 is excellent, 0.40 to 0.70 is good, and below 0.40 is poor. P value, level of significance: $P>0.05$: Non significant. $P< 0.05$: Significant. $P<0.01$: Highly significant.

RESULTS

The mean age of the study group was 55 +/- 9 years, mean blood pressure was 127.31 +/- 9.17 and 79.56 +/- 6.32 for systolic and diastolic pressures respectively. As for the cardiovascular risk; hypertension was the commonest risk factor, as 78% of the patients were hypertensive.

Echocardiographic data**:** Left ventricular internal dimensions were around normal values with a mean LVEDD of 52.8 mm and mean LVESD of 34.97mm, mean IVS thickness was 10.33mm. The mean ejection fraction was 57.69 +/- 9% ranging from 50 - 70%

Coronary angiography data: Twenty-five point five percent of the study population had normal coronary vessels, 77.5% had significantly diseased coronary vessels. The study group included 36 patients with single vessel disease, 14 patients with 2-vessel disease and 12 patients with multi vessel disease. Forty-five patients had significant LAD lesion, while 19 patients had LCX significant lesion and 36 patients had RCA significant lesion.

Dobutamine stress echocardiographic data: The eighty patients were classified into 2 groups according to CA results as follows: True positive DSE (62 patients) and false positive DSE (18 patients). According to the number of diseased vessels and territorial affection, the study group included 69 patients with single vessel disease, 10 patients with 2-vessel disease and 1 patient with multi vessel disease. Forty-seven patients had significant LAD lesion, 6 patients had LCX significant lesion and 39 patients had RCA significant lesion. The mean SWMI at peak DSE was 1.39 +/- 0.15.

Speckle tracking: 2D strain data: The average global longitudinal peak systolic strain (GLS) in the study population was -15.69 +/- 4.68%. Mean GRS was 31.23 +/- 16.74% and the mean GCS is -16.87 +/- 5.43%. There was a significant difference ($p< 0.01$) between normal and diseased groups as regard mean GLS and mean GCS but there was no significant difference ($P= 0.141$) as regard mean GRS. The study group included 38 patients with single vessel disease, 17 patients with 2-vessel disease and 5 patients with multi vessel disease. Forty patients had significant LAD lesion, while 31 patients had LCX significant lesion and 16 patients had RCA significant lesion.

Roc curves and Comparative data: With the receiver operating characteristic (ROC) curve, the cutoff point for GLS, GCS and GRS were -16.75%, -20.75% and 34% respectively. The 3 ROC curves were compared against each other, it was found that the best results were that of GLS and GCS cutoff points which showed the highest AUC (0.735 and 0.731 respectively) with the highest balanced sensitivity and specificity to predict significant CAD (Table 2). With the ROC curve, the cutoff point for LAD and non-LAD territorial strain were -15.4%, -16.9% with 77.78%, 82.93% sensitivity and 82.86%, 53.85% specificity respectively to detect significant LAD and non-LAD lesions.

Incremental value in using STE with DSE to predict significant CAD:

GLS reduced the DSE false positivity by 83%, both GRS and Bull's eye mapping (Segmental territorial analysis) reduced the DSE false positivity by 72.2 and GCS reduced the DSE false positivity by 66.6reduced the DSE false positivity by 72.2%

STE also showed better agreement with CA than DSE in detecting coronary territorial affection especially LAD (Kappa= 0.775) and in detecting number of diseased vessel with kappa= 0.579.Also, territorial strain cutoff points showed a better agreement with CA than DSE in detecting territorial lesions; LAD cutoff point showed excellent agreement with Kappa= 0.783 and Non-LAD cutoff point showed good agreement with Kappa= 0.699, while DSE showed good agreement with Kappa= 0.438 for LAD lesions and poor agreement with Kappa= 0.224 for non-LAD lesions.

DISCUSSION

This study showed a significant difference between diseased and normal patients regarding mean GLS and mean GCS ($p<0.01$) but there was no significant difference as regard GRS ($P= 0.16$). The mean GLS decreased (higher negative) from -20.05+/- 3.17% in normal patients to -14.23 +/- 4.18% in diseased patients. Also the mean GCS decreased from -20.70 +/- 5.80% in normal patients to -15.59 +/- 4.69% in diseased patients. This was in accordance with **Thor *et al.***[8] who concluded that there was a significant difference in the strain values in CAD positive (−15.7 +/- 2.9%) and CAD negative patients (-21.7 +/- 3.0%).

As for the GLS, GRs and GCS cutoff points; GLS had higher diagnostic accuracy than GRS and GCS when compared to CA result.

This was in accordance with **Arnold *et al.*[9]** in the fact that GLS cutoff point had highest diagnostic accuracy. The cut off points were little bit different from ours on ROC curve analysis, different study groups could be the explanation; the study was conducted on 102 patients; only 25 patients had significant CAD on CA versus 62 patients in our study population. Different software used or different study population also can explain the difference in strain values and the cutoff points. **Sun *et al.*[10]** evaluated a mixed Caucasian and Asian population and reported that the strain values obtained from Asians were higher than those of Caucasians**.**

As for Bull's eye mapping territorial-wise analysis; STE showed superior results over DSE in detecting LAD and RCA lesions, agreement with CA was kappa 0.775 and 0.415 respectively. Also, by using the ROC curve to predict LAD lesion, the AUC of territorial strain for LAD was 0.783, the sensitivity and specificity were 77.8%, 82.9% respectively at cut off value -15.4% while, the AUC of territorial strain for non-LAD was 0.699, the sensitivity and specificity were 82.9%, 53.8% respectively at cut off value -16.9%. Segmental analysis with 2D STE in general gave a superior result over DSE especially when assessing LAD (Anterior circulation). But still both lack sensitivity in the regions supplied by the RCA and LCX (Posterior circulation).

Hanekom et al.[11] reported the same fact that 2D STE was feasible during DSE and feasible in detecting territorial lesions; with the best sensitivity in LAD (sensitivity 77%, specificity 79%, and accuracy 78%) exceeded these findings in the LCX (71, 66, and 67%) and RCA (65, 56, and 59%). His explanation for the lower sensitivity in detecting CAD in the posterior-lateral circulation was due to problems with image quality in the inferior, lateral, and posterior walls, evidenced by a higher tracking score compared with the anterior segments.

Limitations

The study was confined to a certain population; without LV dysfunction, overt heart failure, left bundle branch block or heart failure. Also, poor quality images were excluded. So, it doesn't represent the whole population. Assessment of false negative DSE test wasn't possible in this study because the analyzed patients did not include those who were not referred for CA. Because of which we couldn't test DSE sensitivity, specificity and accuracy. Also we couldn't assess and compare STE false negativity with DSE because of the above mentioned reason.

CONCLUSIONS

STE is feasible during DSE; it helps increasing the diagnostic accuracy of DSE and decreasing its false positivity. Both global and segmental longitudinal strain can offer accurate, feasible and non invasive assessment of CAD.

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Table (1): Segmental values for Normal, Hypokinetic and Akinetic segments

	Normal	**Hypokinetic**	**Akinetic**
Basal segments	<-10.9%	-10.9 to -6.2%	*>-6.2%*
Mid segments	*<-12.6%*	-12.6 to -7.9%	*>-7.9%*
Apical segments	*<-14.1%*	-14.1 to -9.1%	>-9.1%

Table (2): Comparison between the 3 ROC curves generated to predict significant CAD

ROC curve	**Cutoff point**	**AUC**	**P value**	**Sensitivity**	**Specificity**	**Accuracy**
GLS	-16.75	0.735	0.003	77.42%	83.33%	78.75%
GCS	-20.75	0.731	0.003	93.55%	66.67%	87.5%
GRS	34	0.658	0.042	69.35%	72.22%	70%