Utility of Longitudinal Strain Imaging by Speckle Tracking in Predicting Obstructive Coronary Artery Disease in Patients without Regional Wall Motion Abnormality on 2D Echocardiography

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ABSTRACT

BACKGROUND

Strain imaging by speckle tracking is a well-established method to assess left ventricular function. The objective of this study was to define the utility of strain imaging in predicting obstructive coronary artery disease (CAD) in a subset of patients who do not have regional wall motion abnormality (RWMA) on routine 2D echocardiography.

METHODS

This is a prospective study. Consecutive patients with no RWMA scheduled to undergo coronary angiography (CAG) for clinical indications were included in the study. Longitudinal strain imaging by speckle tracking using automated functional imaging (AFI) was done by a single investigator prior to CAG. All angiograms were reported by a second investigator who was blinded to the strain imaging findings. Obstructive CAD was defined as ≥ 70% luminal stenosis of epicardial coronary arteries and/or ≥ 50% luminal stenosis of LMCA.

RESULTS

129 patients were enrolled over a 7 month period (mean age 56.07±10.7, males 69%, females 31%). For detecting obstructive CAD, strain imaging had a sensitivity of 97% for LAD, 90.69% for RCA, 91.6% for LCX, a negative predictive value of 81.81% for LAD, 91.3% for RCA, 92.3% for LCX, a specificity of 15.2% for LAD, 13.9% for RCA, 22.8% for LCX and a positive predictive value of 57.6% for LAD, 34.5% for RCA and 21.3% for LCX territories. Patients with obstructive CAD had a lower global strain value of -18.37 ± 4.13 as compared to -21.18 ± 3.81 in patients who did not have obstructive CAD (p value <0.01).

CONCLUSIONS

Peak longitudinal strain imaging by speckle tracking is a very sensitive (ranging from 90.69% to 97.14%) test with a high negative predictive value (ranging from 75% to 92.3%) for identifying obstructive coronary artery lesions on coronary angiography. These properties make strain imaging a good screening test to rule out significant CAD, especially when the pre-test probability is low.

KEYWORDS

Strain Echocardiography, Speckle Tracking, Coronary Angiography

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BACKGROUND

Strain imaging has come of age in the field of echocardiography and is increasingly being used in clinical practice, including in coronary artery disease (CAD). Speckle tracking is an established and reliable method for obtaining two dimensional (2D) strain measurements. Tracking the motion of naturally occurring acoustic markers is the basis of speckle tracking. Strain abnormalities may appear even before regional wall motion abnormalities (RWMA) in the ischemic cascade. Previous studies have reported 93.8% accuracy in predicting regional wall motion abnormalities in patients with ST elevation myocardial infarction (STEMI).[1] Left ventricular (LV) strain abnormalities have been reported to have a sensitivity of 79% and specificity of 79% for detection of severe coronary artery disease, even if no regional wall motion abnormalities are noted on routine 2D echocardiography.[2]

In coronary artery disease (CAD), strain imaging has been found to be useful to indirectly quantify the extent of myocardial damage and evaluation of the effectiveness of coronary revascularization. Strain abnormalities have been found to revert following revascularization. Augmentation of strain and strain rate during dobutamine stress imaging is a good indicator of myocardial viability.[3,4,5] Strain rate imaging has also been used to differentiate transmural from non-transmural infarction.[6] There are studies on regional correlation of strain with coronary angiography, which have shown a sensitivity of 68% and a specificity of 77%.[7] Normal values for strain analysis vary between studies.[8]

Though longitudinal strain imaging by speckle tracking has widespread application in clinical studies, the optimal utility of this imaging modality in the clinical evaluation of coronary artery disease is yet to be defined. Since abnormalities in strain appear before regional wall motion abnormalities, this study was designed to evaluate the performance of strain analysis in predicting obstructive lesions in coronary angiography in a subgroup of patients with suspected coronary artery disease who had no wall motion in routine two dimensional echocardiography. The aim of the study was to assess the sensitivity, specificity, positive and negative predictive value of peak longitudinal strain analysis by speckle tracking in patients who are to undergo coronary angiography (CAG) for clinical indications and have a no wall motion abnormalities in resting 2D echocardiography.

METHODS

Study Population

The study was conducted as a descriptive cross sectional study at the Department of Cardiology at Government Medical College, Trivandrum, Kerala, India, a major tertiary care teaching hospital in Kerala, India. One hundred and twenty nine consecutive patients with clinical indications for coronary angiography (symptoms suggestive of coronary artery disease/effort angina and/or positive exercise stress test, history of previous unstable angina or Non ST elevation myocardial infarction- NSTEMI) who are being taken up for elective coronary angiography without regional wall motion abnormalities in the routine 2D echocardiogram, were selected for the study. Patients who have had a prior angiogram which has shown obstructive coronary artery disease, Left Bundle Branch Block (LBBB) on baseline electrocardiogram, hypertrophic cardiomyopathy, dilated cardiomyopathy, restrictive cardiomyopathy, significant valvular heart disease, history of adriamycin chemotherapy in the past, were excluded from the study. All the selected patients underwent strain echocardiography by speckle tracking prior to coronary angiography (Figure 1). Approval for the study was obtained from the Institutional Review Board and Ethics Committee.

Echocardiography

The echocardiography machine used was Vivid E-9 manufactured by GE (General Electric) using Automated Functional Imaging (AFI) software. Conventional echocardiographic analysis was done using a 3.5 MHz Active Matrix Array probe. The same probe was used for event timing. Aortic valve opening and closure was marked out using pulse Doppler interrogation of the valve. Apical 3-chamber, apical 4-chamber and apical 2-chamber views were taken. Automatic functional imaging was used for strain analysis. Three endocardial identification points- two at the base at the mitral annulus and one at the LV apex at the end systolic period were marked out. The software then traced out the endocardial border and the myocardial layer based on these points. After confirming that the tracing was adequate and the endocardial border was adequately defined, the images were approved. The software then calculated the peak systolic longitudinal strain (PSLS) and constructed a bull's eye image of the 17 left ventricular segments. Strain imaging was done for all patients by the principal investigator prior to the coronary angiography. This investigator was blinded to the subsequent angiographic findings. All patients were subjected to strain analysis prior to angiogram by a single operator, to avoid inter-observer variability. The quality of images acquired for strain analysis was verified by two senior cardiologists. A pilot study was done in 51 patients using tissue Doppler derived strain to optimize imaging and segmental analysis.

Angiography

Angiographic findings were assessed by the second investigator who was blinded to echocardiographic findings of strain analysis. Significant coronary artery disease was defined as a ≥70% epicardial coronary artery luminal diameter stenosis and/or a ≥50% left main luminal diameter stenosis. All coronary angiograms were read and analysed by a single investigator. Lesions in the left main coronary artery (LMCA), left anterior descending (LAD) coronary artery, major diagonals, left circumflex artery (LCX), obtuse marginals, ramus intermedius (RI), right coronary artery (RCA) and lesions in the PDA and PLB were assessed. Dominance of the coronary anatomy was assessed as this is important is assigning LV segments to the RCA and the LCX. Angiography analysis was done in the Siemens Artis Zee cardiac catheterization laboratory work station.

Previous studies have used global average of the peak systolic longitudinal strain values as a continuous variable and used receiver operator curves to make cut offs for predicting coronary artery disease. Since the bull's eye picture with colour coding is available, it was possible to assess each artery separately and look at the sensitivity, specificity, positive and negative predictive values. The proximal, mid and distal divisions of each artery were individually assessed. The variability in dominance (right dominant, left dominant and co-dominant systems) posed a challenge in the analysis, and so did the presence or absence of major arterial branches. The following operational algorithms were made- (1) Dominant or co-dominant RCA included the basal infero-septal, basal inferior, mid inferior and apical inferior segments. (2) Non dominant RCA included only the basal infero-septal segments. (3) All the LAD arteries in this study were type 3 and so the mid infero-septal overlap segment was assigned to the distal LAD territory. (4) Dominant or co-dominant LCX would include the basal inferior, basal infero-lateral, mid inferior, mid infero-lateral, apical inferior and apical lateral segments. (5) The antero-lateral overlap territory could be affected by lesions in the first diagonal, first intermedio-lateral branch (early Obtuse marginal or Ramus) and so these were analysed together. (6) Significant lesions in the proximal segments would affect the peak systolic longitudinal strain of the corresponding LV segments as well as the distal LV segments. So the averaged value of the corresponding segment and all distal segments was assigned to the proximal lesion. (7) In the event of significant proximal and distal obstructive lesions in the same artery, the strain values were averaged and assigned to the proximal segment. (8) Major OM, unless a very early OM, was considered part of the distal LCX segment. (9)Early major OM was considered an intermedio-lateral branch and the antero-lateral overlap territory was assigned to it. (10) PDA and PLB lesions were assigned to RCA or LCX depending on the dominance. In a co-dominant system, depending on which vessel had the lesion, the analysis was done.

Statistical Methods

Data collection for strain and angiographic data was done using a user form created in Microsoft Access. The baseline data for patients including demographic profile and indications were taken from the cardiac catheterization registry of the institution (MySQL relational database). The data from both these sources were exported and combined in Microsoft Excel. The process of assigning segments and algorithms for calculation of average peak longitudinal strain value for each arterial segment were done using visual basic programming and nested if-then-else statements in Microsoft Excel. The final data was then imported to GNU PSPP (Open Source statistical software) to create 2 x 2 tables to determine specificity, sensitivity, positive and negative predictive values.

RESULTS

Baseline Characteristics

129 patients were included in the study, with strain imaging and coronary angiography being done in all patients. The mean age of the study population was 56.07±10.7 years (69% males and 31% females). Systemic hypertension was seen in 49.7% and diabetes mellitus in 38.8%. The most common indication for CAG was a history of NSTEMI (35.65%). Baseline characteristics of the study group are described in Table 1.

Angiographic Findings

Significant CAD by coronary angiography was seen in 50.38% of patients. Single vessel disease was seen in 18.6% of patients; two vessel disease was seen in 21.7% of patients and triple vessel disease in 8.53% of patients. Significant left main involvement was seen in 2 patients (1.55%) of the study population. 13.95% had non obstructive CAD (Table 2). One third of the patients had normal epicardial coronaries (33.33%). One patient had obstructive CAD in a small vessel (obtuse marginal) less than 2 mm size. Myocardial bridge in mid LAD was noted in one patient, and this patient did not have any other coronary lesion. The coronary anatomy of the study population is summarized in Table 2.

Strain Echocardiographic Findings

Strain imaging had a sensitivity of 97.14% for detection of obstructive lesions in LAD, 90.69% for RCA and 91.67% for LCX (Table 3). The negative predictive value was 81.81% for LAD, 75% for RCA and 92.3% for LCX. The specificity was 15.25% for LAD, 13.9% for RCA and 22.85% for LCX. Positive predictive value was 57.62% for LAD, 34.51% for RCA and 21.35% for LCX. Overall, strain imaging had very good sensitivity and negative predictive value, but very low specificity and suboptimal positive predictive value. These features would make strain imaging by speckle tracking a good test for ruling out obstructive coronary artery disease in the study population.

The sensitivity gradually decreased from 96% to 66% from proximal to distal LAD segments, while specificity gradually increased from 14% in proximal LAD to 47.9% in distal LAD. The same trend was seen in the RCA segments, the sensitivity decreased from 100% to 33.33% from proximal to distal RCA, and the specificity increased from 14.1% in proximal LAD to 86.32% in distal RCA. However for the left circumflex artery, sensitivity remained high at 80% in proximal LCX and 100% in distal LCX. Specificity in proximal LCX was 31.93% and was 39.3% in distal LCX. The antero-lateral overlap territory had the maximum variability. The sensitivity ranged from 0% in distal antero-lateral overlap territory to 100% in mid antero-lateral overlap territory. The specificity was 28.57% in proximal antero-lateral overlap territory and increased to 81.67% in distal antero-lateral overlap territory. The negative predictive value ranged from 91.3% to 100% in the LAD, LCX and RCA territories. The negative predictive value in the antero-lateral overlap territories ranged from 83% to 100%.

Continuous Variables			
Characteristic	Unit	Mean Value ± Standard Deviation	
Age	Years	56.07 ± 10.70	
Pulse rate	Beats per minute	70.88 ± 9.65	
Ejection fraction	Percentage	63.57 ± 10.29	
Categorical Variables			
Characteristic	**Subgroup**	**No.**	**%**
Gender	Male	89	69
	Female	40	31
Diabetes status	Diabetic	50	38.8
Systemic hypertension	Hypertensive	64	49.7
Smoking status	Current smoker	16	12.4
	Ex smoker	35	27.1
	Non smoker	78	60.5
Effort angina	NYHA FC I	14	10.9
	NYHA FC II	57	44.2
	NYHA FC III	16	12.4
	NYHA FC IV	1	0.8
Diastolic dysfunction	Stage 1	52	40.3
	Stage 2	5	3.9
Indication for angiography	Atypical chest pain	3	2.32
	Chronic stable angina	28	21.7
	Dyspnea on exertion	30	23.25
	NSTEMI	46	35.65
	Unstable angina	22	17.05

Table 1. Baseline Characteristics of the Patients

Vessel involvement		No.	%
Normal Coronaries		43	33.33
Non Obstructive CAD		18	13.95
Small Vessel Disease		1	0.77
Myocardial Bridge in LAD		1	0.77
Single Vessel Disease	LAD	8	
	LCX	5	
	RCA	10	
	Ramus	1	
	Total	24	18.60
Two Vessel Disease	LAD + LCX	8	
	LAD + RCA	12	
	LCX + RCA	8	
	RCA + Ramus	1	
	Total	28	21.70
Triple Vessel Disease	LAD + LCX + RCA	10	
	LAD + RCA + Ramus	1	
	Total	11	8.53
Left Main Disease	LMCA to LAD	1	
	LMCA + 2VD	1	
	Total	2	1.55

Table 2. Angiographic Profile of the Study Population

Artery	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)
LAD	97.14	15.25	57.62	81.81
RCA	90.70	13.95	34.51	75.00
LCX	91.67	22.85	21.35	92.30
Antero-Lateral Overlap Territory	72.00	27.88	19.35	80.55

Table 3. Sensitivity, Specificity, Positive and Negative Predictive Values of Strain Imaging for Different Arterial Territories

Final Angiographic Diagnosis	Mean Peak Global Strain ± S.D
Normal coronaries	-21.64 ± 4.06
Non obstructive coronary artery disease	-20.00 ± 2.93
Single vessel disease	-18.58 ± 3.62
Two vessel disease	-18.72 ± 4.43
Triple vessel disease	-16.54 ± 4.39
Significant Left main disease	-21.00 ± 2.82

Table 4. Angiographic Diagnosis and Mean Peak Longitudinal Strain Values

Patients with obstructive CAD had a lower mean peak global strain value (-18.37 ± 4.13) as compared to patients who did not have obstructive CAD (-21.18 ± 3.81); p value <0.01, independent samples T test. Patients with normal coronaries had a mean peak global strain value of -21.6, which progressively decreased as the severity of disease increased (Table 4). An aberration was noted - a patient who had LMCA with 2 vessel disease had a global strain value of -23. This patient had recurrent rest pains and had Wellens phenomenon on the ECG (deep T inversions in the anterior precordial leads), suggestive of significant proximal LAD stenosis. The pretest probability of this patient having obstructive coronary artery disease was very high. This case illustrates the importance of considering the clinical scenario while choosing and interpreting investigative modalities.

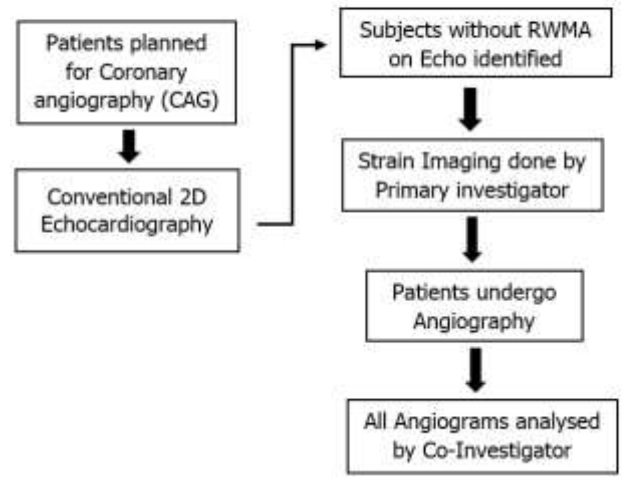

Figure 1. Flow Chart of Events During the Study

DISCUSSION

Strain imaging is a useful, yet underutilized investigative modality in the evaluation of coronary artery disease. This study was done in patients with no regional wall motion abnormalities in baseline routine resting 2D echocardiogram, to assess if strain abnormalities could predict angiographic obstructive coronary artery disease. Independent blinded investigators performed the strain analysis and the angiographic reporting, hence obliterating bias.

In this study, peak longitudinal strain value derived by speckle tracking was found to have a high sensitivity and high negative predictive value, but low specificity and low positive predictive value. This would make it an ideal test to rule out obstructive coronary artery disease in a low risk population. A high sensitivity coupled with a low positive predictive value would, however, result in a high number of false positives. Anwar et al[7] found the sensitivity, specificity, accuracy, positive predictive value and negative predictive value of strain imaging to detect significant angiographic coronary artery stenosis (defined as a luminal diameter stenosis more than 50%) to be 68.6%, 77%, 72%, 81.8%, and 62.1% respectively. The sensitivity rates for the diagnosis of LAD, LCX and RCA were 68.5%, 69.3%, and 68%, respectively. The corresponding specificity rates were 77.1%, 76%, and 78%, respectively. The accuracy rate was 72% for the diagnosis of three vessel disease.

Madhavan et al[9] found that global longitudinal strain correlates well with angiographic severity of CAD in female patients with effort angina (sensitivity of 94% and specificity of 76%). The optimum cut-off GLS score to predict significant coronary artery lesion was – 17.5.

In the current study, using global strain as a measure to predict obstructive coronary artery disease showed that the mean value of patients with normal coronaries was -21.64, which decreased to -16.54 in patients with triple vessel disease. Patients with obstructive CAD had a lower global strain value (-18.37 ± 4.13) as compared to patients who did not have obstructive CAD (-21.18 ± 3.81); p value <0.01, independent samples T test.

In segmental analysis, the sensitivity was seen to decrease from proximal to distal arterial territories and the specificity was found to increase. The reason for this observation is that when a proximal angiographic lesion was present, strain abnormalities in the corresponding and immediately distal segment were attributed to it, thus increasing the detection rate. When proximal and distal lesions coexisted, the abnormal strain value was assigned to the proximal rather than to the distal lesion. This improved the specificity in the distal arterial territories.

History of NSTEMI (Non-ST segment elevation myocardial infarction) was the most common indication for coronary angiography in the current study population, this might reflect the growing number of NSTEMI identified by high sensitivity Troponin T estimation. Atici et al studied 150 patients with NSTEMI and no RWMA and found that global and territorial longitudinal strain (GLS and TLS) were significantly different compared to a control group. In addition, as the high sensitivity troponin values increased, the GLS decreased significantly.[10] Thus, quantification of strain abnormalities can have prognostic value in acute coronary syndromes.

Our study indicates that echocardiographic strain imaging by speckle tracking is a useful adjunct to clinical evaluation and routine 2D echocardiography to predict obstructive coronary artery disease by coronary angiography. Apart from its role in risk stratification, understanding the regional strain pattern could also be one way to assess the functional impact of coronary stenosis on myocardial segmental function. In strain imaging (as is true with all cardiac investigations), accurate measurement, judicious interpretation and application of the obtained information to the clinical context of the individual patient is of paramount importance.

CONCLUSIONS

Peak longitudinal strain imaging by speckle tracking is a very sensitive (sensitivity ranging from 90.69% to 97.14%) test with a high negative predictive value (ranging from 75% to 92.3%) for identifying obstructive coronary artery lesions on coronary angiography (defined as ≥ 70% luminal stenosis of epicardial coronary arteries and/or ≥50% luminal stenosis of LMCA). These properties make strain imaging a good screening test to rule out significant coronary artery disease, especially when the pre-test probability is low. Patients with obstructive CAD had a lower global strain value (- 18.37 ± 4.13) as compared to patients who did not have obstructive CAD (-21.18 ± 3.81); p value <0.01). Strain imaging is a useful adjunct to predict CAD in appropriately selected patient subsets in clinical practice.

Appendix

- CAD - coronary artery disease
- 2D - 2 dimensional
- RWMA - regional wall motion abnormality
- STEMI - ST segment elevation myocardial infarction
- LV - left ventricle
- CAG - coronary angiogram
- LBBB - left bundle branch block
- PSLS - post systolic longitudinal strain
- LMCA - left main coronary artery
- LAD - left anterior descending
- LCX - left circumflex artery
- OM - obtuse marginal
- RI - ramus intermedius
- RCA -right coronary artery
- PDA - posterior descending artery
- PLB - posterolateral branch
- NSTEMI - non ST segment elevation myocardial infarction
- GLS - global longitudinal strain
- TLS - territorial longitudinal strain

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