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THREE-DIMENSIONAL SPECKLE TRACKING ECHOCARDIOGRAPHY FOR EVALUATION OF LEFT ATRIAL FUNCTION IN CORONARY ARTERY DISEASE PATIENTS WITH PRESERVED LEFT VENTRICLE EJECTION FRACTION

By

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ABSTRACT

Background: The left atrium (LA) is much more than simply a conduit for left ventricular (LV) filling, and its size and remodeling are recognized as a predictor of poor outcomes in multiple disease states. LA function is a surrogate marker of LV diastolic dysfunction.

Objective: To assess left atrial function in coronary artery disease patients with preserved left ventricle ejection fraction, with and without left atrial expansion by three dimensional speckle tracking echocardiograghy.

Patient and methods: Fifty patients with chronic coronary syndrome were divided according to left atrial dilation into two groups high risk group where left atrial dilation was more than 4cm (8 males and 8 females) and low risk group where left atrial dilation was less than 4 cm (18 males and 16 females) in addition to 20 healthy individual as control group (7 males and 13 females) who presented to the Cardiology Department at Al-Hussain University Hospital and Al-Azhar Islamic Center for elective coronary angiography from May 2019 to June 2020.

Results: There was a statistically significant increase in control group in comparison to low risk and high risk. The LA peak ventricular systolic area strain (ASs %) in patients group was significantly lower than in the control group, whereas in the low risk group was significantly higher than in the high risk group. The LA peak pre-atrial contraction area strain (ASa %) in patients group was significantly lower than in the control group, whereas in the low risk group was significantly higher than in the high risk group.

Conclusion: Three-dimensional speckle tracking echocardiography represented a non-invasive, relatively simple and reproducible technique to assess left atrial myocardial function in patients with chronic coronary syndrome.

Keywords: Coronary heart disease, Chronic coronary syndromes, Left atrium, 3D-STE.

INTRODUCTION

Coronary heart disease (CAD) has the dynamic nature results in various clinical presentations, which can be conveniently categorized as either acute coronary syndromes (ACS) or chronic coronary syndromes (CCS). Those risks for future cardiovascular events, e.g. death or

myocardial infarction (MI), and the risk may change over time *(Knuuti et al., 2019)*.

The left atrium (LA) is much more than simply a conduit for left ventricular (LV) filling, and its size and remodeling are recognized as a predictor of poor outcomes in multiple disease states. LA dilation has been associated with increased risk of atrial fibrillation (AF), ischemic stroke, mortality after acute myocardial infarction, and heart failure with both reduced and preserved LV systolic function *(Yoshida et al., 2011)*.

Assessment of LA function has been performed by measuring LA size or volume with two-dimensional (2D) echocardiography and Doppler echocardiographic measurements. A method known as strain imaging is used for the quantitative assessment of myocardial deformation. Three dimensional speckle tracking imaging has overcome the problems that faces two-dimensional (2D) echocardiography and Doppler echocardiographic measurements by Area of strain that is the most sensitive parameter of LA function *(Kleijn et al., 2011)*.

Speckle tracking echocardiography (STE) is a non–Doppler-based method for the objective quantification of myocardial deformation from standard bi-dimensional data sets *(Cameli et al., 2011)*, and it allows to obtain the quantification of longitudinal myocardial LA deformation dynamics *(Muranaka et al., 2010)*.

However, 2D imaging has several limitations. First, full LA segmental data are obtained from multiple planes in different cardiac cycles. Because of this non-simultaneous data acquisition, myocardial function may be altered beat by beat during unstable cardiac conditions. Second, the whole heart moves through the 2D plane of interest. Therefore, the 2D plane of interest disappears through a cardiac cycle, which is well known as the ‘through-plane’ or ‘out-of plane phenomenon’. 3D full-volume data acquisitions have the potential to overcome the limitation of plane-dependency of 2D imaging *(Feigenbaum et al., 2012)*.

In three dimensional speckle tracking (3D-STE), area of strain is the most sensitive parameter of LA function, Area strain is a combination of longitudinal and circumferential deformations and is calculated by the rate of change in endocardial surface area from its original size *(Kleijn et al., 2011)*.

This study was designed to assess left atrial function in coronary artery disease patients with preserved left ventricle ejection fraction with and without left atrial expansion by three dimensional speckle tracking echocardiograghy.

PATIENTS AND METHODS

Fifty patients with chronic coronary syndrome were divided according to left atrial dilatation into two groups: High risk group where left atrial dilation were more than 4cm (8 males and 8 females) and low risk group where left atrial dilatation less than 4 cm (18 males and 16 females) in addition to 20 healthy individual as control group (7 males and 13 females) who presented to the Cardiology Department at Al-Hussain University Hospital, Al-Azhar Islamic Center for

elective coronary angiography from May 2019 to June 2020.

Inclusion criteria: Patients more than 40 years old diagnosed as chronic coronary artery disease according to coronary angiography and have positive findings.

Exclusion criteria: All patients with history of congestive heart failure, moderate or severe valvular disease, congenital heart disease, conduction abnormalities, ongoing arrhythmia, pacemaker and acute coronary syndrome.

Each patient was subjected to the following after giving an informed consent:

i. **History was taken including:** (1) Age and gender. (2) Smoking recognized as a life time history of >100 cigarettes in their entire life and had continued smoking in the last 6 months was considered a positive smoking history. (3) Diabetic patients were recognized as having DM if they had history of DM on admission. (4) Dyslipidemia was defined by total cholesterol ≥220 mg/dl. (5) Hypertension was defined as systolic/diastolic blood pressure ≥140/90 mmHg or patients had a history of hypertension. (6) Previous PCI procedures and previous CABG. (7) Anemic patients defined if haemoglobin level less than 14 gm⁄dl in males and less than 12 gm⁄dl in females. (8) Patient defined as renal impairment of creatinine clearance less than70 ml ⁄min. (9) Other co-morbid conditions, such as peripheral vascular disease.

ii. **A full clinical examination:** Including vital signs, BMI and cardiac examination.

iii. **Electrocardiography:** A 12-lead surface electrocardiography (ECG) was done for each patient on admission. The electrocardiograms were recorded at a paper with speed of 25 mm/s and an amplification of 10 mm/mv.

iv. **Laboratory investigations:** Serum glycated haemoglobin (HbA1c) was measured. Serum creatinine was measured. The creatinine clearance was calculated. Admission complete blood count was measured. Lipid profile including, high density lipoprotein (HDL), low density lipoprotein (LDL), total cholesterol (TC) and triglycerides (TG) were measured.

Echocardiography was performed which included conventional M-mode, and 2-D transthoracic echocardiographic examination and Doppler study using standard parasternal and apical views to assess left ventricular diastolic function via transmitral mitral inflow velocities, left atrial volumes and left ventricular chamber dimensions, volume and function.

For 3D-STE analysis, we obtained apical full-volume acquisition to visualize the entire left atrium in a volumetric image as apyramidal volume. Each 3D data set was displayed in a five-plane view: (A) an apical four chamber view, (B) a second apical view orthogonal to plane A, and (C) three short-axis planes, including plane C1 in the basal potion, plane C2 in the mid left atrium, and plane C3 at the roof portion of the left atrium

plane, one marker is set at the roof of the left atrium, and the other two are set at the edges of the mitral annulus. The software then detects the LA endocardium using a semi-automated contour-tracing algorithm, and the user sets LA wall thickness to the smallest possible value. The software divides the left atrium into 16 segments. After the markers have been selected, the system performs wall motion–tracking analysis through the entire cardiac cycle and enables the calculation of maximal LA volume. The following parameters were measured: LA peak ventricular systolic area strain (ASs) and LA peak pre–atrial contraction area strain (ASa).

Statistical analysis:

Results of the present study were statistically analyzed using SPSS 25 (IBM, USA). Data were represented as median (interquartile range) or number and percentage. Numerical data were compared using one-way ANOVA followed by post hoc test, while categorical data were compared using Fisher exact test or Chi-square test as appropriate. ROC curve was used to evaluate the performance of different tests differentiate between certain groups. The level of significance at P value < 0.050 was significant.

RESULTS

Fifty patients with chronic coronary syndrome were divided into two groups: high risk (mean age 57.75±7.66 years, 8 males and 8 females) and low risk (mean age 55.26± 6.19 years, 18 males and 16 females) and 20 healthy individual as control group (mean age 56.70± 4.54 years, 7 males and 13 females). There was no statistically significant difference in demographic data regarding studied group **(Table 1)**.

Table (1): Comparison between high risk, low risk & control group as regards demographic data

Parameters \ Groups		Control (No.=20)		High risk (No.=16)		Low risk (No.=34)		Chi square test/ One way ANOVA
		No	%	No	%	No	%	P value
Sex, n (%)	Female	13	65.0%	8	50.0%	16	47.1%	0.429
	Male	7	35.0%	8	50.0%	18	52.9%	
Age(years)	Mean ±SD	56.70	4.54	57.75	7.66	55.26	6.19	0.386

There was a statistically significant increase in high risk in comparison to low risk with left ventricular end-diastolic volume (LVEDV). The left ventricular end systolic volume (LVESV), left ventricular ejection fraction (LVEF)%, left anterior descending (LAD), maximum left atrial volume (LAV max.), minimum left atrial volume (LAV min.) and E/A, but there was a statistically significant increase in low with left atrial volumes (LAV) ejection fraction (EF)%, E and A **(Table 2)**.

Table (2): Comparison between high risk, low risk & control group as regards echocardiographic changes

Groups / Parameters	Control (No.=20)		High risk (No.=16)		Low risk (No.=34)		One way ANOVA
	Mean	SD	Mean	SD	Mean	SD	P value
LVEDV(ml)	82.70	12.68	115.69	1.54	109.82	2.96	<0.001
LVESV(ml)	31.91	7.09	51.51	1.50	44.59	3.27	<0.001
LVEF (%)	55.44	0.73	60.70	2.92	58.92	2.08	<0.001
LAD (cm)	2.97	0.30	4.33	0.11	3.35	0.48	<0.001
LAV max. (ml)	18.70	3.06	26.39	1.04	20.30	2.03	<0.001
LAV min. (ml)	9.99	2.16	16.60	1.35	10.07	1.80	<0.001
LAV EF (%)	47.00	2.97	37.25	2.62	50.15	4.65	<0.001
E (c/s)	68.85	12.14	41.81	2.51	67.32	9.92	<0.001
A (c/s)	69.13	5.24	44.50	24.12	80.03	23.16	<0.001
E/A	99.25	20.47	133.50	10.48	87.09	12.41	<0.001

Post hoc test			
	Control VS low risk	Control VS high risk	High risk VS low risk
LVEDV	0.001	0.001	0.008
LVESV	0.001	0.001	0.001
LVEF%	0.005	0.001	0.001
LAD	0.001	0.001	0.001
LAV max.	0.013	0.001	0.001
LAV min.	0.871	0.001	0.871
LAV EF%	0.005	0.001	0.005
E	0.573	0.001	0.001
A	0.058	0.001	0.001
E/A	0.005	0.001	0.001

LVEDV = Left ventricle end diastolic volume; LVESV=Left ventricle end systolic volume; LVEF% = LV ejection fraction; LAD = Left atrial dimension; LAV max. = Maximum left atrial volume; LAV min. = Minimum left atrial volume; LAEF = Left atrial emptying fraction; E=Early diastolic velocity; A =Late diastolic velocity.

There was a statistically significant increase in control group in comparison to low risk and high risk with 3D speckle tracking **(Table 3)**.

Table (3): Comparison between high risk, low risk & control group as regards 3D speckle tracking

Groups / Parameters	Control (No.=20)		High risk (No.=16)		Low risk (No.=34)		One way ANOVA	
	Mean	SD	Mean	SD	Mean	SD	f	P value
ASs(%)	78.50	9.65	28.69	10.90	61.82	6.04	158.918	<0.001
Asa(%)	40.70	6.42	14.50	4.75	31.06	3.96	126.065	<0.001

Post hoc test			
	Control VS low risk	Control VS high risk	High risk VS low risk
ASs	0.001	0.001	0.001
ASa	0.001	0.001	0.001

LA peak pre–atrial contraction area strain. ASa = ASs = LA peak ventricular systolic area strain;

ASs has positive correlations with Asa, CRCL, LVEF%, LAV EF%, E and A but has negative correlations with CR, HbA1C, LVEDV, LVESV, LAD, LAV max., LAV min, E/A and Coronary score. Also, ASa has positive correlations with ASa, CRCL, LVEF%, LAV EF%, E and A, but has negative correlations with CR, HbA1C, LVEDV, LVESV, LAD, LAV max., LAV min, E/A and coronary score in case group **(Table 4)**.

Table (4): Correlation between 3D speckle tracking among studied parameters in case group

Tracking / Parameters	ASs		ASa	
	r	P value	r	P value
ASa	0.989	0.001	--	--
Age	-0.137	0.341	-0.170	0.237
Height	0.121	0.402	0.119	0.412
Weight	0.036	0.803	0.030	0.838
BMI	-0.045	0.758	-0.042	0.772
HB	-0.138	0.341	-0.160	0.267
CR	-0.343	0.015	-0.371	0.008
CRCL	0.382	0.006	0.402	0.004
LDL	-0.095	0.512	-0.076	0.601
TG	-0.139	0.336	-0.092	0.523
HDL	0.012	0.934	0.015	0.918
HbA1C	-0.463	0.001	-0.483	0.001
LVEDV	-0.987	0.001	-0.978	0.001
LVESV	-0.988	0.001	-0.980	0.001
LVEF%	0.821	0.001	0.842	0.001
LAD	-0.994	0.001	-0.984	0.001
LAV max.	-0.992	0.001	-0.984	0.001
LAV min.	-0.994	0.001	-0.987	0.001
LAV EF%	0.940	0.001	0.914	0.001
E	0.995	0.001	0.985	0.001
A	0.896	0.001	0.886	0.001
E/A	-0.996	0.001	-0.991	0.001
GS	-0.704	0.001	-0.730	0.001
SS	-0.663	0.001	-0.691	0.001

ASa= LA peak pre–atrial contraction area strain; ASs = LA peak ventricular systolic area strain; BMI: Body mass index; HB=Hemoglobin in blood; CR=Creatinine; CRCL: Creatinine Clearance; LDL-C = low-density lipoprotein cholesterol; TG= triglycerides; HDL-C= high density lipoprotein cholesterol; HbA1c = glycated haemoglobin; LVEDV = Left ventricle end diastolic volume; LVESV=Left ventricle end systolic volume; LVEF = LV ejection fraction; LAD = Left atrial dimension; LAV max. = Maximum left atrial volume; LAV min. = Minimum left atrial volume; LAEF = Left atrial emptying fraction; E=Early diastolic velocity; A =Late diastolic velocity; GS = Ginsini Score; SS = SYNTAX Score.

DISCUSSION

This study was conducted aiming to assess the left atrial function in coronary artery disease patients with preserved left ventricle ejection fraction with and without left atrial expansion by three dimensional speckle tracking echocardiograghy.

The current study revealed that no statistically significant differences were

found among the study groups (high risk, low risk and controls) as regards age, sex. This balance in the baseline characteristics provides the basis for comparison between the study groups as it helps to minimize bias *(Sedgwick, 2014)*.

The current study revealed that no statistically significant differences were found between the high risk and low risk study groups as regards past history of ischemic heart disease or family history. This balance in the baseline characteristics helps to minimize bias when comparing between the study groups *(Sedgwick, 2014)*.

The current study revealed that no statistically significant differences were found between the high risk and low risk study groups as regards ECG findings. This absence of significant ECG changes with different atrial volume might be explained by the finding that none of the commonly used ECG left or right atrial enlargement criteria provided high accuracy for detecting anatomic left or right atrial enlargement and that high sensitivity was achieved only with lower specificity and vice versa. Furthermore, hypertension may affect P wave characteristics on ECG independently of atrial size *(Tsao et al., 2012)*.

The current study revealed that no statistically significant differences were found among the study groups (high risk, low risk and controls) as regards the mean results of some of the performed laboratory investigations namely: hemoglobin level, creatinine level, creatinine clearance and triglycerides level. Meanwhile, statistically significant differences were found among the three groups as regards LDL and HDL levels (with the significant differences being found when control group was compared versus either high risk or low risk groups) as well as in HbA1C level (with the significant differences being found when control group was compared versus either high risk or low risk groups as well as when comparing high risk group versus low risk group) *(Rayyan et al., 2012)*.

Statistically significant differences were found among the three groups as regards all studied echocardiographic findings which were found with pairwise comparisons in case of LVEDV, LVESV, LVEF%, LAD, LAV max., LAV EF%, A and E/A. On the other hand, the statistically significant difference in case of LAV min. was found only between the control and high risk group and in case of E between the high risk group and either the controls or low risk group. Statistically significant differences also were found among the three groups as regards 3D speckle tracking findings which were found with pairwise comparisons in case of ASs and ASa with their mean values being lowest in the high risk group. There were statistically significant differences between the high and low risk groups as regards the coronary score with higher GS and SS mean values being found in the high risk group *(Elmedany et al., 2017)*.

No statistically significant correlations were found between either age, height, weight, body mass index (BMI), hemoglobin level, LDL level, HDL level, TG level on one hand and either ASs or ASa on the other hand . Meanwhile, a strong positive correlation was found between ASs and ASa as well as between LVEF%, LAV EF%, E and A on one hand and ASs and ASa on the other hand.

Furthermore, a moderate positive correlation was found between CRCL and both ASs and ASa. Moderate negative correlation was found between CR, HBA1C SS and GS on one hand and ASs and ASa on the other hand. A strong negative correlation was found between LVEDV, LVESV, LAD, LAV max., LAV min. and E/A on one hand and ASs and ASa on the other hand *(Halilbašić et al., 2014)*.

CONCLUSION

Three-dimensional speckle tracking echocardiography represented a non-invasive, relatively simple and reproducible technique to assess left atrial myocardial function in patients with chronic coronary syndrome. The reservoir and conduit function of the left atrium were impaired in these patients compared with controls, LA peak ventricular systolic area strain and LA peak pre-atrial contraction area strain were significantly positive correlated with both left atrium 2D Doppler echocardiographic parameters and LV contractile function and could be suggested as a better indicator to evaluate LA function as a preferred parameter of Speckle tracking echocardiography.

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إستخدام التتبع النقطي ثلاثي الأبعاد لتقييم وظيفة الأذين الأيسر في مرضى قصور الشريان التاجي الذين ليس لديهم إعتلال بوظيفة القلب

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خلفية البحث: الأذين الأيسر هو أكثر بكثير من مجرد قناة لتعبئة البطين الأيسر، ويتم التعرف على حجمه وإعادة تصميمه كمنبئ للنتائج السيئة في حالات الأمراض المتعددة حيث أن وظيفته تعتبر كمؤشر على الخلل الانبساطي للبطين الايسر وتمدده نتيجة لقصور الشريان التاجي مرتبط بزيادة خطورة فشل عضلة القلب مع الاحتفاظ بوظيفة البطين الأيسر الانقباضية.

الهدف من البحث: تقييم وظيفة الاذين الايسر باستخدام الموجات الصوتية على القلب بالتتبع النقطي ثلاثي الابعاد في المرضى الذين يعانون من متلازمة الشريان التاجي المزمن مقارنة مع الاصحاء.

المرضي وطرق البحث: شمل هذا البحث 50 مريضا يعانون من متلازمة الشريان التاجي المزمنة مقسمة حسب اتساع الأذين الأيسر إلى مجموعتين أحدهما عالية الخطورة حيث اتساع الأذين أكثر من 4 سم (8 ذكور و 8 إناث) والاخرى منخفضة الخطورة حيث اتساع الأذين أقل من 4 سم (18 ذكور و 16 إناث) بالإضافة إلى 20 فردًا سليمًا كمجموعة ضابطه (7 ذكور و 13 إناث) الذين قدموا إلى قسم أمراض القلب في مستشفى الحسين الجامعي ومركز الأزهر الإسلامي حيث تم تصوير الأوعية التاجية الاختيارية وذلك فى الفترة من شهر مايو 2019 الى شهر يونيو 2020.

نتـــائج البحـــث: كانـــت هنـــاك زيـــادة ذات دلالـــة إحصـــائية فـــي المجموعـــة الضـــابطه مقارنـــة بمنخفضـــة الخطـــورة وعاليـــة الخطـــورة وكانـــت مســـاحة منطقـــة الاذيـــن الايســـر أثنـــاء ذروة الانقبـــاض البطينـــي (٪) فـــي مجموعـــة المرضـــى أقـــل بكثيـــر ممـــا كانـــت عليـــه فـــي المجموعـــة الضـــابطه بينمـــا كانـــت فـــي المجموعـــة منخفضـــة الخطـــورة أعلـــى بكثيـــر منهـــا فـــي المجموعـــة عاليـــة الخطـــورة وكانـــت مســـاحة منطقـــة الاذيـــن الايســـر قبـــل ذروة انقباضـــه (٪) فـــي مجموعـــة المرضـــى أقـــل بكثيـــر ممـــا كانـــت عليـــه فـــي المجموعـــة الضـــابطه بينمـــا كانـــت فـــي المجموعـــة منخفضة الخطورة أعلى بكثير منها في المجموعة عالية الخطورة.

الاســـتنتاج : يوصـــي بتقيـــيم وظيفـــة الأذيـــن الأيســـر فـــي المرضـــي الـــذين يعـــانون مـــن قصـــور مـــزمن فـــي الشـــريان التـــاجي مـــع عـــدم الاخـــتلال بوظيفـــة القلـــب باســـتخدام موجـــات القلـــب الصـــوتية ذو التتبـــع النقطـــي ثلاثـــي الأبعـــاد بســـهولة ويسر.

الكلمـــات الدالـــة: التتبـــع النقطـــى ثلاثـــى الابعـــاد، الأذيـــن الأيســـر، قصـــور الشـــريان التاجى، إعتلال وظيفة القلب.