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Incidence of Ventricular Arrhythmias in Association with Left Ventricular Dyssynchrony in Chronic Ischemic Patients

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Abstract

Background: Intra ventricular mechanical dyssynchrony may play an important role in ventricular arrhythmogenesis in chronic ischemic patients.

Aim of the Study: To detect the prevalence of ventricular arrhythmia in chronic ischemic patients in association with left ventricular dyssynchrony assessed by left ventricular longitudinal strain.

Methods: The study included 50 patients with ischemic heart disease confirmed by coronary angiography. Speckle tracking echocardiography was performed. Patients were divided into 2 groups according to presence or absence of left ventricular mechanical dyssynchrony, considering difference in time to peak ≥130ms by longitudinal strain between any two opposing segment at basal and mid level in LV 12 segments positive for mechanical dyssynchrony. Every patient in both groups underwent 24 hours holter monitoring for detection of ventricular arrhythmia.

Results: The study results showed that there were 45 males and 5 females. Mean age ±SD was 51.00±7.06 years. Mean heart rate was 76.92±13.29 beat/minute. Patients were divided into 2 groups. Group I included 40 patients with left ventricular dyssynchrony and mean time to peak SD was 102.5±34.16m sec and Group II included 10 patients without left ventricular dyssynchrony and mean time to peak SD was 82.3±45.1msec. 24 hours ECG Holter monitoring data showed that there was higher incidence of ventricular runs in Group I with positive dyssynchrony patients (47.5%) than those in Group II with negative dyssynchrony patients (20%).

Conclusion: Left ventricular dyssynchrony assessed by left ventricular longitudinal strain could be a predictor for increased risk of ventricular arrhythmia.

Key Words: *Ventricular arrhythmia – Left ventricular dyssynchrony – Longitudinal strain – Speckle tracking echocardiography.*

Introduction

CORONARY Artery Disease (CAD) is a leading cause of death worldwide. Most of patients die due to Congestive Heart Failure (CHF) or Sudden Cardiac Death (SCD) which occurs due to ventricular arrhythmia [1]. Left Ventricular Ejection Fraction (LVEF) was considered an important factor for risk stratification of SCD [2,3], but it is discovered that it is not sensitive enough as studies shown that most of patients with SCD had preserved EF and not identified for ICD implantation [4,5].

Cardiac dyssynchrony means disturbance of ordered sequence of cardiac contraction and relaxation leading to mechanical and electrical heterogeneity which may lead to development of ventricular arrhythmia and SCD [6-9]. Speckle tracking echocardiography is relatively a new technique for assessment of left ventricular strain and left ventricular dyssynchrony. Therefore, the aim of our study was to detect the incidence of ventricular arrhythmia in chronic ischemic patients in association with left ventricular dyssynchrony assessed by left ventricular longitudinal strain.

Patients and Methods

The study was conducted at the Cardiology Department, Al-Azhar University Hospitals, and National Heart Institute during the period between February 2016 and February 2017. The study included 50 patients with stable ischemic heart disease and sinus rhythm. Informed consent was given by all patients for participation in the study. Exclusion criteria from the study included patients with Acute Coronary Syndrome (ACS), acute heart failure, significant valvular lesion, Chronic Obstructive Pulmonary Disease (COPD) and significant arrhythmia that may interfere with study analysis (e.g: AF). Patient with abnormal kidney function and patients with poor echo window were also excluded from the study.

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Coronary angiography:

Every patient had coronary angiography to confirm presence of ischemic heart disease. CAD was considered significant if ≥70% stenosis.

Echocardiography and 2 dimensional (2-D) speckle tracking study:

All patients were examined in left lateral position using machine (XMATRIX iE 33 Philips) and trasnsducer (Probe 5-1) Standard two dimensional and Doppler echocardiography were performed, apical four, three and two chamber views were obtained by both grey scale and 2D speckle tracking technique and digitalized for offline analysis. Visual assessment of the regional LV systolic function was performed using the 12 segment model and 5 score index at time of examination. Calculation of Ejection Fraction (EF) was performed by 2-D modified Simpson method. Calculation of global longitudinal strain from apical four, three and two chambers STE views. Each wall was divided into 3 segments: Apical, mid and basal. Longitudinal dyssynchrony was defined as maximum opposing wall delay in time to peak strain among the three apical views from basal and mid-level using cut off ≥130ms and is considered as significant dyssynchrony [10]. Patients were divided into two groups according to presence or absence of LV dyssynchrony. Group I included 40 patients with dyssynchrony, and Group II included 10 patients without dyssynchrony Figs. (1,2).

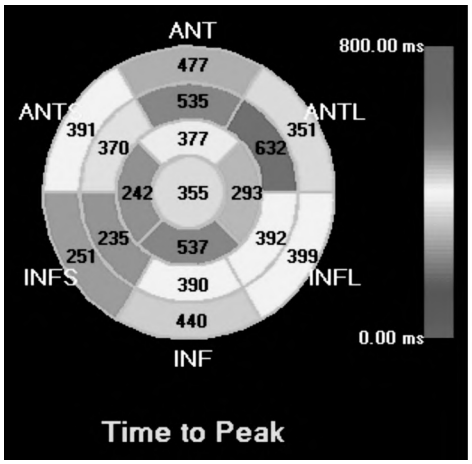

Fig. (1): Patient with LV dyssynchrony by left ventricle longitudinal strain. Difference in time to peak betw een 2 opposing segments ≥130ms.

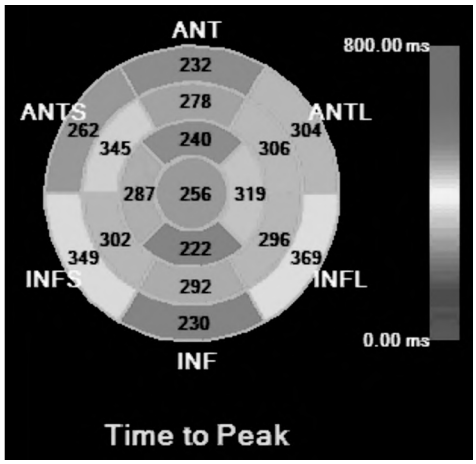

Fig. (2): A patient without LV dyssynchrony by left ventricle longitudinal strain.

Holter monitoring:

24 hour of Holter monitoring was performed for every patients within 1 to 3 days from echocardiography provided that patient clinical condition and medications remained unchanged, looking for ventricular arrhythmia.

Statistical analysis:

Data were collected, coded and entered to the Statistical Package for Social Science (IBM SPSS) Version 20. Qualitative data were presented as number and percentages while quantitative data were presented as mean, Standard Deviations (±SD) and ranges when parametric and median with interquartile range with non parametric data. The comparison between the two groups with qualitative data were done by using Chi-square test and/or Fisher exact test was used instead of Chi-square test when the expected count in any cell was found less than 5.

The comparison between the two groups regarding quantitative data with parametric distribution was done by using Independent *t*-test and also data with non parametric distribution was done by using Mann-Whitney test.

The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as that $p<0.05$: and $p<0.01$: Highly significant.

Results

Study included 50 patients with chronic ischemic heart disease. Patients were divided into two groups, Group I with left ventricular dyssynchrony and Group II without dyssynchrony assessed by left ventricle longitudinal strain.

Demographic data:

Group I included 40 patients, 36 males (90%) 4 females (10%). The mean of age ±SD was

51.65±7.6 years. Group II included 10 patients, 9 males (90%) 1 female (10%). The mean of age ±SD was 48.40±3.27 years (Table 1).

Table (1): Demographic characteristics of patients in both groups.

	Group I N=40	Group II N=10	Chi-square test χ^2/t^*	*p*-value
Age (yrs):				
Mean ± SD	51.65±7.61	48.40±3.27	–1.312*	0.196
Range	33-65	43-51		
Sex:				
Females	4 (10.0%)	1 (10.0%)	0.000	1.000
Males	36 (90.0%)	9 (90.0)%		

±SD: Standard Deviation.

Group I included 24 hypertensive patients (60%), 20 diabetics (50%) and 17 dyslipidemic (42.5%). Group II included 3 hypertensive patients (30%). 4 diabetics (40%) and 6 dyslipidemic (60%) (Table 2).

Table (2): Risk factors of both groups of patients.

	Group I N=40	Group II N=10	Chi-square test χ^2/t^*	*p*-value
HTN:				
No	16 (40.0%)	7 (70.0%)	2.899	0.089
Yes	24 (60.0%)	3 (30.0%)		
Dyslipidemia:				
No	23 (57.5%)	4 (40%)	0.986	0.321
Yes	17 (42.5%)	6 (60%)		
Smoking:				
No	19 (47.5%)	6 (60%)	0.500	0.480
Yes	21 (52.5%)	4 (40%)		
DM:				
No	20 (50.0%)	6 (60%)	0.321	0.571
Yes	20 (50.0%)	4 (40%)		
FH:				
No	18 (45.0%)	5 (50%)	0.081	0.777
Yes	22 (55.0%)	5 (50%)		

HTN : Hypertension.
DM : Diabetes Mellitus.
FH : Family History.

Coronary angiography data:

Group I included 33 patients (82.5%) with LAD lesion, 20 patients (50%) with LCX lesion and 22 patients (55%) with RCA lesion. There was more prevalent LAD lesion and the presence of LV dyssynchrony, while in Group II there was 4 patients (40%) with LAD lesion, 6 patients (60%) with LCX lesion and 5 patients (50%) with RCA lesion, (Table 3).

Table (3): Distribution of CAD in both groups.

Coronary artery affected	Group I N=40	Group II N=10	Chi-square test χ^2/t^*	*p*-value
• Left anterior descending	33 (82.5%)	4 (40%)	7.510	0.006
• Left circumflex artery	20 (50.0%)	6 (60.0%)	0.321	0.571
• Right coronary artery	22 (55.0%)	5 (50.0%)	0.081	0.777

Relation between number of CAD lesions and prevalence of ventricular arrhythmia in both groups:

In Group I patients with LV dyssynchrony, the prevalence of ventricular arrhythmia was progressively related to the number of CAD. In patients with 3 vessels disease significant ventricular arrhythmia was found in 9 patients out of 14 patients (64%), and that is much higher than that patients with 2 vessels disease 3 out of 6 (50%) higher than that patients with single vessel disease 7 out of 20 (35%) (Table 4).

Table (4): Relation between number of CAD lesions and prevalence of ventricular arrhythmia in both groups.

	1 vessel disease	2 vessels disease	3 vessels disease
Group I N=40:			
Positive VT runs	7	3	9
Group II N=10:			
Positive VT runs	1	0	1

Conventional echocardiography and speckle tracking data:

In Group I the mean Ejection Fraction (EF) was 49.65±9.55%. Resting Wall Motion Abnormality (RWMA) was detected in 30 patients (75%). The mean ± SD of GLS was –17. The mean of Time to peak SD was 102.5±34.16ms (Table 5).

Group II showed that EF was mean was 49.90± 11.22%. RWMA detected in 6 patients (60%). The GLS median was 17.5. The time to peak SD mean was 82.3±45.1ms (Table 5).

There was no statistical significant difference between both groups as regards echocardiographic and speckle tracking data (Table 5).

Twenty-four Holter ECG data:

Group I showed that mean QTc according to Bazett"s formula was 439.7±39.25ms. Ventricular runs were detected in 19 patients (47.5%). Ventricular bigeminy was detected in 6 patients (15%).

Ventricular trigiminy was detected in4 patients (10%). R on T ectopics were detected in 2 patients (5%).

Table (5): Difference between both groups as regarding echocardiographic parameters.

	Group I N=40	Group II N=10	Chi-square test χ^2/t^*	*p*-value
EF:				
Mean ± SD	49.65±9.55	49.90±11.22	0.072*	0.943
Range	30–65	30-60		
RWMA:				
No	10 (25.0%)	4 (40%)	0.893	0.345
Yes	30 (75.0%)	6 (60%)		
GLS:				
Median (IQR)	–17 (–19- –15)	–17.5 (–18- –14)	0.714*	0.729
Range	–27- –3	–20- –5		
Time to peak SD (ms):				
Mean ± SD	102.5±34.16	82.3±45.1	0.063 *	0.063
Range	44-170	42-162		

EF : Ejection Fraction.
RWMA : Resting Wall Motion Abnormality.
GLS : Global Longitudinal Strain.
±SD : Standard Deviation.

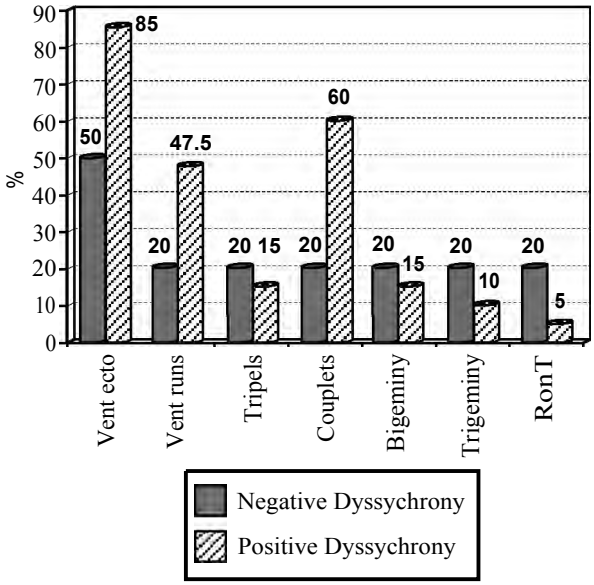

Fig. (3): Incidence of different types of ventricular arrhythmia in both groups.

Vent. ecto.: Ventricular ectopics.
vent. runs: Ventricular runs.

Group II showed that mean QTc interval was 426.93±19.72ms. Ventricular runs were detected in 2 patients (20%). Ventricular bigiminy was detected in 2 patients (20%) ventricular trigiminy was detected in 2 patients (20%). R on T ectopics were detected in 2 patients (20%) Graph (1) (Table 6).

Table (6): Twenty four hour Holter ECG obtained data in both groups.

	Group I No.=40	Group II No.=10	Chi-square test χ^2/t^*	*p*-value
QTc int (ms) (Bazzet 'sformula):				
Mean ± SD	439.70±39.25	426.93±19.72	1.469*	0.148
Range	382-497	380-459		
Total:				
Mean ± SD	109876.40±20646.41	106433.05±14253.15	0.622*	0.537
Range	76562-145351	777638-135174		
Ventricular ectopic:				
Negative	6 (15.0%)	5 (50%)	5.711	0.017
Positive	34 (85.0%)	5 (50%)		
Ventricular runs:				
Negative	21 (52.5%)	8 (80%)	2.484	0.115
Positive	19 (47.5%)	2 (20%)		
Triplets:				
Negative	34 (85.0%)	8 (80%)	0.149	0.700
Positive	6 (15.0%)	2 (20%)		
Couplets:				
Negative	16 (40.0%)	8 (80%)	5.128	0.024
Positive	24 (60.0%)	2 (20%)		
Bigeminy:				
Negative	34 (85.0%)	8 (80%)	0.149	0.700
Positive	6 (15.0%)	2 (20%)		
Trigeminy:				
Negative	36 (90.0%)	8 (80.0%)	0.758	0.384
Positive	4 (10.0%)	2 (20.0%)		
R on T ectopic:				
Negative	38 (95.0%)	8 (80.0%)	2.446	0.118
Positive	2 (5.0%)	2 (20.0%)		

SD: Standard Deviation.

Our data shows that there was significant statistical difference between both groups as regards to frequency of both premature ventricular contractions and ventricular couplets (Table 6).

Our data shows that there was a trend for higher prevalence of ventricular runs in Group I than Group II, (47.5%) versus (20%) respectively (Table 6).

Discussion

This study evaluated the prevalence of ventricular arrhythmias in patients with chronic ischemic heart disease, and showed increased risk of ventricular arrhythmia in association with LV dyssynchrony.

The study showed that the presence of significant lesion in left anterior descending artery was associated with increased incidence of left ventricular dyssynchrony.

We found that there was statistically significant difference between both groups as regards to the frequency of both ventricular ectopics and ventricular couplets.

The study demonstrated that there was a trend for higher incidence of ventricular runs in Group I with left ventricular dyssynchrony (19 patients 47.5%) than Group II with negative dyssynchrony (2 patients 20%).

There was no statistical significant difference in both groups regarding ejection fraction. This result agreed with the study conducted by Haugaa et al., [11] on 85 post myocardial infarction patients. They found that EF did not differ between patients with and without ventricular arrhythmias occurring during follow-up.

Our results agreed with the study conducted by Leong et al., [12]. On the relationship between left ventricular dyssynchrony and the risk of ventricular arrhythmia post MI. Their study included a total of 206 patients with prior MI. Speckle-tracking echocardiography for assessment of dyssynchrony by global longitudinal strain and Implantable Cardioverter Defibrillator (ICD) implantation which was retrospectively evaluated. Patients were followed-up for the occurrence of Ventricular Tachycardia (VT) for about 24 months. In total, 75 (36.5%) individuals experienced runs of VT They concluded that LV dyssynchrony is a good factor for prediction of occurrence of VT after MI.

Haugaa et al., [11] conducted a study which included 85 post myocardial infarction patients, 44 meeting primary and 41 meeting secondary ICD prevention criteria. After about 2 years of follow-up, 47 patients had no ventricular arrhythmia and 38 (44.7%) patients had recorded arrhythmias requiring appropriate ICD therapy. Longitudinal strain was measured by speckle tracking echocardiography. They found that mechanical dyssynchrony was greater in ICD patients with recorded ventricular arrhythmias compared with those patients without ventricular arrhythmia.

Bader et al., [13] had a study on heart failure patients and reported that left ventricular dyssynchrony was a prognostic marker of ventricular arrhythmia by tissue Doppler technique.

Tayal et al., [14] had a study on mechanical dyssynchrony by tissue Doppler and whether left ventricular dyssynchrony was associated with higher risk of ventricular arrhythmias after Cardiac Resynchronization Therapy (CRT) or not. Their study included 151 CRT-D patients that were prospectively included. They demonstrated that persistent and new mechanical dyssynchrony after CRT-D was associated with subsequent ventricular arrhythmia. In another study conducted by Cho et al., [15], they demonstrated that mechanical dyssynchrony was a powerful predictor of mortality or cardiac events in heart failure patients with normal and wide QRS complex.

Relation between left ventricular dyssynchrony and ventricular arrhythmia in non ischemic dilated cardiomyopathy was studied by Haugaa et al., [16]. 94 patients with non ischemic dilated cardiomyopathy were prospectively included. By speckle-tracking strain echocardiography, mechanical dyssynchrony was assessed by global longitudinal strain. After a median of 22 months of follow-up, patients with arrhythmic events had increased mechanical dyssynchrony. They concluded that mechanical dyssynchrony is a promising marker for prediction arrhythmic events in patients with dilated cardiomyopathy independently of LVEF, and may help in the risk stratification of patients with DCM not fulfilling current implantable cardioverter-defibrillator indications. In addition Kosiuk et al., [17] had a study on 20 patients with non ischemic cardiomyopathy. They demonstrated that left ventricle mechanical dyssynchrony which is defined as standard deviation of time to peak among the 16 segment of left ventricle by global longitudinal strain was higher in patients with ventricular arrhythmia detected by Holter than in patients that did not have ventricular arrhythmia.

Study limitations:

- Small number of patients in our study. We could not reach statistical significance in spite of the trends to increase incidence of ventricular arrhythmia in Group I with left ventricular dyssynchrony.
- Radial strain were not evaluated at all in assessment of LV dyssynchrony.
- Using holter which can detect arrhythmia only for short duration.

Recommendations:

- More efforts must be done in another study with much larger number of patients before documenting the usefulness of assessment of left ventricular dyssynchrony by left ventricular longitudinal strain as a parameter for predicting ventricular arrhythmia in chronic ischemic patients.
- Using tools that can detect arrhythmia for longer duration such as Loop recorder as Holter detect arrhythmias for short duration.
- The prevalence of ventricular arrhythmia in patients with left ventricular dyssynchrony pre and post CRT in relation to left ventricular longitudinal and radial strain needs to be evaluated.

Conclusion:

Left ventricular dyssynchrony assessed by left ventricular longitudinal strain could be a predictor for increased risk of ventricular arrhythmia.

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دراسة معدل إختلال الضربات البطينية فى مرضى قصور الشرايين التاجية المزمن ذوى الخلل اللاتناغمى الإنقباضى للبطين اليسر

يعتبر قصور الشرايين التاجية للقلب من الأسباب الرئيسية للوفاة عالميا ومعظم المرضى يتوفون نتيجة ضعف عضلة القلب أو نتيجة إضطرابات القلب البطينية مثل ما يحدث فى التسارع البطينى والإرتجاف البطينى.

من المحتمل أن اللاتناغم الإنقباضى فى البطين الأيسر قد يكون له دور فى زيادة معدل حدوث هذه الإختلالات البطينية.

ولقد تم عمل هذه الدراسة فى مستشفيات جامعة الأزهر ومعهد القلب القومى فى الفترة بين فبراير ٢٠١٦ وفبراير ٢٠١٧ لدراسة معدل إختلال الضربات البطينية فى مرضى قصور الشرايين التاجية المزمن ذوى الخلل اللاتناغمى الإنقباضى للبطين الأيسر.

حيث تم عمل دراسة على خمسين مريض من أصحاب القصور المزمن فى الشرايين التاجية تم تشخيصهم بالقسطرة التشخيصية على الشرايين التاجية للقلب ثم عمل موجات فوق صوتية على القلب لهم بواسطة التتبع النقطى بالموجات الصوتية ثنائية الأبعاد وحساب معدل الإجهاد الطولى للبطين الأيسر من خلال المناظر القمية الثلاثة ثم تم تقسيم الخمسين مريضا لمجموعتين المجموعة الأولى من أصحاب الخلل اللاتناغم الإنقباضى فى البطين الأيسر وتتكون من أربعين مريض أما المجموعة الثانية تتكون من عشرة مرضى لا يعانون من هذا الخلل ثم تم عمل دراسة بواسطة جهاز الهولتر لمدة ٢٤ ساعة فى المجموعتين لبيان معدل حدوث الإختلال فى الضربات البطينية وبيان مدى علاقته بالخلل اللاتناغم الإنقباضى فى البطين الأيسر.

ولقد أظهرت النتائج إصابة ٤٧.٥٪ من مرضى المجموعة الأولى بإضطرابات التسارع البطينى للقلب وإصابة ٢٠٪ من مرضى المجموعة الثانية بتلك الإضطربات مما يعنى زيادة معدل حدوث الإضطرابات البطينية فى مرضى قصور الشرايين التاجية المزمن ذوى الخلل اللاتناغمى الإنقباضى للبطين الأيسر.