IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 16, Issue 10 Ver. VI (Oct. 2017), PP 70-74
www.iosrjournals.org

Evaluation of Cardiac Function & Dyssynchrony in Patients Undergoing Cardiac Resynchronization Therapy Using Speckle Tracking Technique

*Affan Ezzat Hasan[1],Fahad Abbas Abdul Rahman[2],Ghazi Farhan Haji[3], Ghassan Mohammed Mahmoud [4]
[1,2,3](Department of Physiology, college of Medicine / Baghdad University, Iraq)
[4](Cardiology Unit, Baghdad Teaching Hospital, Medical City, Iraq)
Corresponding Author: *Affan Ezzat Hasan*

Abstract *: Since approval of Food & drug administration (FDA) on Cardiac resynchronization therapy (CRT) in 2001, CRT become one of the mainstay in treatment of patients with heart failure and left bundle branch Block (LBBB). Hence ; specific echocardiographic parameters is mandatory to identify patients who did respond and those who didn't respond to CRT and to extent of linking baseline Dyssynchrony parameters & risk factors history of Ischemic Heart Disease & diabetes with their response.*

The aim of this study is to identify the role of Longitudinal strain & Dyssynchrony parameters in three months follow up of patients with CRT.

Study Population: *eighteen patients with symptomatic Heart Failure with symptomatic Heart failure & New York Heart Association functional classification (NYHA) class II or IV symptoms, all patients included in this Study were with Sinus rhythm, prolonged QRS >120 milliseconds & their Left ventricular EF < 35%. All patients treated with CRT in Cardiology Unit, Baghdad Teaching Hospital, Medical City, Baghdad-Iraq.*

Method: *in this Before & After study, different methods for Evaluation of ventricular synchrony were used, Both Convectional Echocardiography for Dyssynchrony parameters, ejection fraction (%) & Longitudinal Stain Imaging using Speckle tracking were made to all patients at Baseline and three months after implantation of CRT.*

Results: *at three months, all patients show significant improvement in EF% from* 26.02(2.8) to *36.94(8.32) (p0.014), SPWMD from (206*.27±47.30) to (37.89±7.56) (p0.023), IVMD from (48.33±17.04) to (25.77±7.00) (p 0.002), while GLS show non-significant change (p0.16).

Conclusion, *conventional synchrony parameter not enough to predict cardiac future remodeling, Longitudinal Strain is useful tool to identify early cardiac remodeling before being clinically significant.*

Keywords: *Global Longitudinal Strain, Dyssynchrony, Cardiac resynchronization therapy, Left ventricular Function*

Date of Submission: 04 -10-2017 Date of acceptance: 14-10-2017

I. Introduction

Assessment of cardiac Function Using strain or Myocardial Deformation imaging considered one of promising advancement in echocardiography, where strain represent the percentage of deformity between two defined regions along with extent of shortening in myocardial Muscle [1]. Speckle Tracking Technique, depend on specific coherent speckles in the myocardial tissue to identify the regions that are passively moving from those contracting actively [2]. Global longitudinal strain gives information on Sub-endocardial fibers band, decrease in GLS function as measured by Strain, may be attributed to many factors including Diabetes, Hypertension, renal insufficiency, valvular Heart Diseases, infiltrative cardiomyopathies & hypertrophic cardiomyopathies [3]. Evaluation of cardiac synchrony & myocardial deformation using speckle tracking technique depend on assessment of time to reach peak strain or maximum contraction across different cardiac Regions. Predicting outcomes& Identifying patient who will benefit from Cardiac resynchronization therapy depend on the level of synchrony identify by regional timing & the contractile function reflected by myocardial peak strain [4-6].

Favorable Hemodynamic benefits from Cardiac resynchronization therapy, first time were observed in one case in mid-1990, and from that time observational studies start evaluating the Acute hemodynamic effect & cardiac performance measure of CRT [7].then in 2001, when Food & drugs administration (FDA)approve first CRT device, New Era of heart failure management was started [8],Evidence based medicine of CRT devices

where ensured by the update of the American College of Cardiology/American Heart Association (ACC/AHA) heart failure guideline in 2005 , where CRT strongly supported with Class I indication for the heart failure patients management[9]. These guideline recommendations were updated as well in 2013 along with defining the manifestation of change in ventricular conduction as ventricular Dyssynchrony [10]. definition of Ventricular Dyssynchrony depend on the duration of QRS of more than 120ms using electrocardiogram. this mean, that up to one-third of patients with heart failure (systolic) have ventricular Dyssynchrony, adding to inadequate blood ejected by failing heart, Dyssynchrony in heart failure patients linked to increased mortality [11]. The Responders rate for CRT appear to be approximately 75% & 25% are considered as non-responders, these rates similar to responders & non-Responders rate for drugs therapies in Heart failure. different factors may contribute in determining response to CRT, including sub-optimal timing of Atrioventricular & VV, suboptimal left ventricular lead placement, progression of heart Failure & ventricular Scar [12]. The Responders rate for CRT appear to be approximately 75% & 25% are considered as non-responders, these rates similar to responders & non-Responders rate for drugs therapies in Heart failure. different factors may contribute in determining response to CRT, including sub-optimal timing of Atrioventricular & VV, suboptimal left ventricular lead placement, progression of heart Failure & ventricular Scar [12].

II. Material & Methods

The study involved Eighteen (18) subjects with Heart Failure-typical LBBB with mean age of 64.84±6.94, all of them were admitted to the cardiology Unit in Baghdad Teaching Hospital, Medical City, Baghdad-Iraq, due to conventional indication for cardiac resynchronization therapy. Patients recruited in the study suffered from heart failure with functional classification of New York Heart Association (NYHA), class III or IV symptoms. All patients were with a prolonged QRS duration ≥120ms but sinus rhythm, <35% of left ventricular ejection and were on maximally tolerated medical therapy. All patients were evaluated before and after implantation of cardiac resynchronization therapy through physical examination, electrocardiography, echocardiography by both speckle tracking technique and conventional method. echocardiography was performed in all patients by a single operator using a Philips Machine , Model CX50 Compact X-treme System echocardiography machine with a probe model S5-1 [1-5MHZ] for measurements of standard 2D imaging, color flow mapping, continuous wave (CW) and pulsed wave (PW) Doppler and tissue Doppler imaging (TDI) .Convectional echocardiography was performed, according to recommendations of American society of echocardiography in 2005[13].Left ventricular function were assessed by using biplane Simpson's rule.

Interventricular mechanical delay or Dyssynchrony (IVMD) which is the difference in the time of left ventricular contraction to right ventricular contraction, measured by calculating the difference between left ventricle out flow tract and right ventricular out flow tract by both continues wave & pulsed wave Doppler image of Aortic and pulmonary flow. IVMD of > 40ms defined as high value[14]. Intraventricular Dyssynchrony, refer to the difference in the time of contraction between septum to posterior wall, M-Mode with septal to posterior wall motion delay(SPWMD) were used to asses' intraventricular motion delay, values of more than 130ms was considered as high. Two dimensional speckle tracking were used for measurement of longitudinal strain by dividing the left ventricle into 6 regions and system automatically calculate the longitudinal strain. Statistical analysis made by using Microsoft Excel for data entry then all data were analyzed using statistical Package for the Social Sciences (SPSS) v.22 (sample T test, Independent T test, Chi Square & Pearson correlation were used) .data presented in both Mean & Standard deviations with P value of <0.05 considered as statistically significant.

III. Results

Study result show that fourteen patients (78%) show significant improvement in echocardiographic parameter and defined as CRT responders, whereas four Patients (22%) show no signification improvement in echocardiographic parameters and defined as Non- Responders. Baseline characteristics for both group are illustrated in table 1.it is very clear there is no significant difference between two group in baseline characteristics except for history of ischemic heart disease and diabetes where significantly lower in Responders group (p 0.015, p0.0002 respectively) and this may be due to diabetes increase both ischemic and non-ischemic cardiomyopathy

Baseline Characteristics	**Responder**	**Non Responder**	***P* Value ***
Age ,years	65.21(7.5)	63.50(5.1)	NS
Male/Female	8/6	3/1	NS
Weight ,Kg	85.28(13.30)	82.00(8.9)	NS
Height ,meter	1.72(.048)	1.68(0.067)	NS
BMI ,kg/m^2	28.57(3.35)	29.3(5.51)	NS

Hypertension	85%	100%	NS
Diabetes Mellitus	14%	75%	0.015
Dyslipidemia	71%	100%	NS
IHD	14%	100%	0.0002
HF	50%	75%	NS

Table 1: Baseline characteristics for Responders & Non- responders, all values are in means (standard Deviation) , P<0.05 considered as Statistical significant , BMI= Body Mass Index, IHD= Ischemic Heart disease, HF= Heart Failure

Main echocardiographic outcome before and after 3 months of CRT implantation are shown in table 2, responder group of patients, the ejection fraction significantly improved (26.77 ±3.72 to 43.14± 5.72) with p0.0001, global longitudinal function not significantly increase in responders' patients (8.63±1.16) to (8.93±1.78), Interventricular Mechanical Delay evaluation after months show significantly improved in responder's patients (49.67±17.63) to (25.92 ± 756) p 0.002. Septal to posterior wall motion delay evaluation after 3 months, were also improved among responders group from (216±48.84) to (36.92±8.07) p <0.001.

In non-responder's patients, Dyssynchrony evaluation after 3 months show no significant improvement in Ejection fraction (25.75 ±1.25) to (28.17±2.38) p0.414, global longitudinal strain decrease but not statistical significant after 3 months (8.77±2.9) to (7.55±1.70) p 0.161. Septal to posterior wall motion delay also show ±significant improvement after 3 months (170.75±13.37) to 79.50±310) p 0.114, interestingly the interventricular Mechanical delay improved in the non-responder's patients)43.90±16.26) to 19.50±13.47) p0.029.

Variable	**Responder (78%)**		**P value***	**Non – Responder (22%)**		**P value***
	Before Pacemaker Implantation	**3 Months after Pacemaker Implantation**		**Before Pacemaker Implantation**	**3 Months after Pacemaker Implantation**	
EF ,%	26.77(3.72)	43.14(5.72)	p<0.001	25.75(1.25)	28.17(2.38)	0.414
GLS ,%	8.36(1.16)	8.93(1.78)	P0.058	8.77(2.94)	7.55(1.70)	0.161
IVMD ,ms	49.67(17.63)	25.92(7.56)	0.002	43.90(16.26)	19.50(13.47)	0.029
SPWMD ,ms	216.42(48.84)	36.92(8.07)	p<0.001	170.75(13.37)	79.50(3.10)	0.114

Table 2 : echocardiographic parameters before & 3 months after CRT ,all values are in Mean (standard Deviation) , P<0.05 considered statistically significant , EF% = ejection fraction ,GLS = Global Longitudinal strain , IVMD = interventricular Mechanical Delay , SPWMD = septal to posterior wall motion delay

IV. Dsicussion

Quantification and characterization of myocardial deformity can be easily recognized by recently developed Speckle-tracking echocardiography (STE) technique & this confirmed by massive increase in the number of publications on STE in the last decade.[15] This study involves Eighteen (18) patients who were treated with Cardiac Resynchronization Therapy (CRT). Baseline demographics demonstrate a high proportion of patients with underlying Hypertension (88%), diabetes mellitus (27%), Dyslipidemia (77%), & ischemic heart disease (33%) as the cause of heart failure. Baseline characteristics of the Subjects recruited into this study are comparable to previous studies of heart failure patients receiving Cardiac Resynchronization therapy. Baseline mean left ventricular ejection fraction of 26.5% are consistent with severe left ventricular systolic dysfunction, and compare similarly, with the degree of left ventricular dilatation and dysfunction seen in studies by Yu et al.[16] And the CARE-HF study[17] (median ejection fraction 25%).

In terms of echocardiographic response, varying degrees of reverse remodeling have been reported following CRT. Yu et al report improvement in ejection fraction increased from 25.9% to 33.9%[16], values comparable to the results reported in this study (26.55 % To 39.8%). In Bax et al. show less improvement in Left ventricular ejection fraction from 23% to 28%, the more modest remodeling perhaps reflecting the higher volumes and more severe left ventricular dysfunction present before CRT in this cohort of Subjects[18]. Overall the results of CRT in the current study appear to be representative of the effects of CRT in previously reported studiesWhen comparing responders to non-responders in our Study, echocardiographic responders demonstrated significant increases in ejection fraction, however global longitudinal strain showed no change in either.

Parameters of inter-ventricular Dyssynchrony have also been shown to have some role in the prediction of response to CRT. Wiesbauer et al reported that Inter-ventricular mechanical delay were able to predict response to CRT at cut-off values of 60ms [19]. Although the values were significantly different between responders and non-responders, In This Study Inter-ventricular mechanical delay was not significantly different between responders (49.67 ±17.6) and non-responders (43.90±16.2) with (P= 0.56). Several studies have reported on the utility of speckle tracking strain parameters for the prediction of response to CRT, however; prediction of response to CRT remains unclear. Results from the current study are consistent with the reports of

Knebel et al & Miyazaki et al, in that no significant differences between responders and non-responders were found in the baseline speckle tracking parameters of Dyssynchrony measured[20][21].

Zhang et al. demonstrated that ischemic etiology of heart failure was associated with a higher rate of death and hospitalization than non-ischemic etiology following CRT[22]. Analysis of data from the CARE-HF study also demonstrated a lesser degree of reverse remodeling in Subjects with ischemic compared to non-ischemic etiology.[23] In our study, the result comparable to these studies, there is significant difference as (14 %) of Responders patients have history of ischemic heart disease compared to (100%) of Non-Responders Subjects have history of ischemic heart disease (P=0.0002).

Whether ischemic etiology really affected the benefits of CRT is not known. In one study, it has been reported that the poor outcomes of Ischemic Cardiomyopathy Subjects were directly related to the large scar burden and fewer viable cardio myocytes.[24] Hence, the apparent lower usefulness of CRT in the Ischemic cardio myopathy subgroup might be related to the disease itself rather than the lower efficacy of CRT treatment. In our study, a more favorable outcome was noticed in the Non-Ischemic Cardiomyopathy subgroup.
Patients with Diabetes mellitus & Heart Failure show worse prognosis due to multiple etiology for heart failure in Diabetic Patients like dyslipidemia with atherosclerosis & hypertension; previous studies shows that diabetic patient usually more sickening than non-diabetic patients with significant high prevalence of atrial fibrillation, left ventricular enlargement, renal impairment & high systolic pulmonary pressure ,all these finding may be related to altered myofirillar proteins, that is frequently observed in patients with diabetes[25]. benefits & outcomes of CRT with magnitude of remodeling might be diminished with accumulation of interstitial fibrotic tissue in relation to diabetes [26].efficiency of CRT may be altered by cardiac abnormalities & systemic changes made by Diabetes, the impact of diabetes on the patients with diabetes and heart failure first time presented in small study by Kies et al, , this study showed that on follow up after 6 months , response & survival were similar between both diabetic and non-diabetic patients.[27] these results confirmed by CARE-HF study [17],however , other studies show difference between diabetic and non-diabetic patient in left ventricular ejection fraction recovery (p=0.057) .

Moreover, other studies showed that diabetic patient especially those treated with insulin and treated with CRT, have worse prognosis compared to non-diabetic patients. [17], [27] and this may be due to higher prevalence of ischemic etiology of Heart failure in those patients leading to less effect of CRT on remodeling of left ventricle in those patients resulting in poor echocardiographic changes [28] In this study the result of diabetic and non-diabetic patients were comparable these results with 14% of responders were non-diabetic vs 75% of non-responders were diabetics (p0.015)

V. Conclusion

Different Dyssynchrony parameter should be used to predict response to CRT, yet Echocardiography is gold standard, global longitudinal strain may be useful toll to identify myocardial deformity before being clinical significant. The authors recommend to include more patients and for longer duration to have more significant results.

Acknowledgements

The Authors acknowledge there is no conflict of interest

References

[1] Bers DM:, "Calcium cycling and signaling in cardiac myocytes," Annu Rev Physiol, no. 70, p. 23, 2008.
[2] W. Mądry and M. A. Karolczak, "Physiological basis in the assessment of myocardial mechanics using speckle-tracking echocardiography 2D. Part I," J. Ultrason., vol. 16, no. 65, pp. 135–144, Jun. 2016.
[3] et al: Pirat B, Khoury DS, Hartley CJ, "A novel feature-tracking echocardiographic method for the quantitation of regional myocardial function: Validation in an animal model of ischemia-reperfusion," J Am Coll Cardiol, no. 51, p. 651, 2008.
[4] et al: Tatsumi K, Tanaka H, Yamawaki K, "Utility of comprehensive assessment of strain dyssynchrony index by speckle tracking imaging for predicting response to cardiac resynchronization therapy," Am J Cardiol, no. 107, p. 439, 2011.
[5] et al: Knappe D, Pouleur AC, Shah AM, "Dyssynchrony, contractile function, and response to cardiac resynchronization therapy. Multicenter Automatic Defibrillator Implantation Trial—Cardiac Resynchronization Therapy Investigators," Circ Hear. Fail, no. 4, p. 433, 2011.
[6] et al Delgado V, van Bommel RJ, Bertini M, ": Relative merits of left ventricular dyssynchrony, left ventricular lead position, and myocardial scar to predict long-term survival of ischemic heart failure patients undergoing cardiac resynchronization therapy.," Circulation, no. 123, p. 70, 2011.
[7] K. Vernooy, C. J. M. van Deursen, M. Strik, and F. W. Prinzen, "Strategies to improve cardiac resynchronization therapy," Nat Rev Cardiol, vol. 11, no. 8, pp. 481–493, Aug. 2014.
[8] M. Moynahan, O. P. Faris, and B. M. Lewis, "Cardiac Resynchronization Devices," J. Am. Coll. Cardiol., vol. 46, no. 12, pp. 2325–2328, 2005.
[9] S. A. Hunt et al., "ACC/AHA 2005 Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult," Circulation, vol. 112, no. 12, p. e154 LP-e235, Sep. 2005.
[10] C. W. Yancy et al., "2013 ACCF/AHA Guideline for the Management of Heart Failure," J. Am. Coll. Cardiol., vol. 62, no. 16, pp. e147–e239, 2013.

[11] A. Cheng, R. H. Helm, and T. P. Abraham, "Pathophysiological mechanisms underlying ventricular dyssynchrony," EP Eur., vol. 11, no. suppl_5, pp. v10–v14, Nov. 2009.

[12] Braunwald's, Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine, 10th ed. Philadelphia, Pa: Saunders Elsevier;, 2015.

[13] B. I. Sileikiene R, Vaskelyte J, Mizariene V, Jurkevicius J, ". Speckle tracking derived left and right atrial, left and right ventricular strain, strain rate after atrioventricular node slow pathway radiofrequency ablation. 2011;3:57–62.," Electron Electr Eng, vol. 3, no. 3, pp. 57–62, 2011.

[14] A. D. Waggoner, D. A. Agler, and D. B. Adams, "Cardiac Resynchronization Therapy and the Emerging Role of Echocardiography (Part 1): Indications and Results from Current Studies," J. Am. Soc. Echocardiogr., vol. 20, no. 1, pp. 70–75, Sep. 2017.

[15] M. Bansal and R. R. Kasliwal, "How do I do it? Speckle-tracking echocardiography," Indian Heart J., vol. 65, no. 1, pp. 117–123, Jan. 2013.

[16] C. Yu et al., "Tissue Doppler velocity is superior to displacement and strain mapping in predicting left ventricular reverse remodelling response after cardiac resynchronisation therapy," Heart, vol. 92, no. 10, pp. 1452–1456, Oct. 2006.

[17] U. C. Hoppe, N. Freemantle, J. G. F. Cleland, M. Marijianowski, and E. Erdmann, "Effect of Cardiac Resynchronization on Morbidity and Mortality of Diabetic Patients With Severe Heart Failure," Diabetes Care, vol. 30, no. 3, p. 722 LP-724, Feb. 2007.

[18] J. J. Bax et al., "Left ventricular dyssynchrony predicts response and prognosis after cardiac resynchronization therapy," J. Am. Coll. Cardiol., vol. 44, no. 9, pp. 1834–1840, 2004.

[19] F. Wiesbauer et al., "Echo Doppler parameters predict response to cardiac resynchronization therapy," Eur. J. Clin. Invest., vol. 39, no. 1, pp. 1–10, Jan. 2009.

[20] F. Knebel et al., "Circumferential 2D-strain imaging for the prediction of long term response to cardiac resynchronization therapy," Cardiovasc. Ultrasound, vol. 6, p. 28, Jun. 2008.

[21] C. Miyazaki et al., "Dyssynchrony Indices To Predict Response to Cardiac Resynchronization Therapy<span hwp:id="article-title-22" class="sub-article-title">Cl," Circ. Hear. Fail., vol. 3, no. 5, p. 565 LP-573, Sep. 2010.

[22] Q. Zhang et al., "Difference in long-term clinical outcome after cardiac resynchronisation therapy between ischaemic and non-ischaemic aetiologies of heart failure," Heart, vol. 95, no. 2, p. 113 LP-118, Dec. 2008.

[23] S. Ghio et al., "Long-term left ventricular reverse remodelling with cardiac resynchronization therapy: results from the CARE-HF trial," Eur. J. Heart Fail., vol. 11, no. 5, pp. 480–488, May 2009.

[24] E. C. Adelstein et al., "Impact of scar burden by single-photon emission computed tomography myocardial perfusion imaging on patient outcomes following cardiac resynchronization therapy," Eur. Heart J., vol. 32, no. 1, pp. 93–103, Jan. 2011.

[25] C. Fantoni et al., "Long-term outcome in diabetic heart failure patients treated with cardiac resynchronization therapy," Eur. J. Heart Fail., vol. 10, no. 3, pp. 298–307, Mar. 2008.

[26] J. Asbun and F. J. Villarreal, "The Pathogenesis of Myocardial Fibrosis in the Setting of Diabetic Cardiomyopathy," J. Am. Coll. Cardiol., vol. 47, no. 4, pp. 693–700, 2006.

[27] P. Kiès et al., "Comparison of Effectiveness of Cardiac Resynchronization Therapy in Patients With Versus Without Diabetes Mellitus," Am. J. Cardiol., vol. 96, no. 1, pp. 108–111, Sep. 2017.

[28] O. I. I. Soliman et al., "The ischemic etiology of heart failure in diabetics limits reverse left ventricular remodeling after cardiac resynchronization therapy," J. Diabetes Complications, vol. 23, no. 5, pp. 365–370, Sep. 2017.

*Affan Ezzat Hasan. "Evaluation of Cardiac Function & Dyssynchrony in Patients Undergoing Cardiac Resynchronization Therapy Using Speckle Tracking Technique." IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) , vol. 16, no. 10, 2017, pp. 70–74.