Kaohsiung Journal of Medical Sciences (2013) 29, 374–378

Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: http://www.kjms-online.com

ORIGINAL ARTICLE

Evaluation of left ventricular mechanical dyssynchrony in chronic heart failure patients by two-dimensional speckle tracking imaging

Feng-Xia Jiang, Rui-Qiang Guo*, Jin-Ling Chen

Department of Ultrasound, Renmin Hospital of Wuhan University, Wuhan, China

Received 16 May 2012; accepted 29 August 2012
Available online 16 January 2013

KEYWORDS
Heart failure;
Left ventricular dyssynchrony;
Speckle tracking

Abstract The purpose of this study was to evaluate left ventricular mechanical dyssynchrony (LVMD) in chronic heart failure (CHF) patients using two-dimensional speckle tracking imaging (2D-STI), and also to compare the usefulness of three patterns of myocardial deformation in mechanical dyssynchrony assessment. Furthermore, the relationships between left ventricular ejection fraction (LVEF), QRS duration (QRSd), and LVMD were explored. In total, 78 patients and 60 healthy individuals (group 3) were enrolled. The patients were classified into two subgroups: LVEF $\leq$ 35% (group 1), 35% $<$ LVEF $<$ 50% (group 2). All participants underwent two-dimensional echocardiography, and dyssynchrony indices derived from 2D-STI were calculated. According to statistical principles, the cut-off value of LVMD was defined as mean $\pm$ 1.645 SD of the normal population. Dyssynchrony rates were calculated in CHF subgroups and compared within each subgroup, respectively. Compared with group 3, all indices in group 1 were remarkably higher ($p < 0.05$), and some of the indices in group 2 were significantly higher ($p < 0.05$). A significant difference of dyssynchrony rate was noted within both group 1 and group 2 ($\chi^2 = 25.55$, $p < 0.05$ vs. $\chi^2 = 23.88$, $p < 0.05$), and the highest value was derived from the longitudinal index in both subgroups. LVEF was related to all three forms of strain/strain rate ($p < 0.05$), whereas no relationship existed between QRSd and dyssynchrony indices ($p > 0.05$). CHF patients have different extents of LVMD. Longitudinal deformation shows the best detectability of dyssynchrony motion. Left ventricular systolic function was closely related to mechanical dyssynchrony, whereas QRSd showed no significant correlation.

Introduction

Cardiac mechanical dyssynchrony is prevalent in chronic heart failure (CHF) patients. In recent years, these patients

* Corresponding author. Department of Ultrasound, Renmin Hospital of Wuhan University, Jiefang Road 238#, Wuchang District, Wuhan 430060, China.
E-mail address: meredith.j2010@hotmail.com (R.-Q. Guo).

http://dx.doi.org/10.1016/j.kjms.2012.11.005

despite optimal pharmacological therapy have been suggested to have cardiac resynchronization therapy (CRT) [1]. The principle of CRT is to revert asynchronous mechanical events, leading to myocardial systolic efficiency increase and clinical improvement. However, it was reported that approximately 30% of patients did not respond to CRT [2]. Studies showed that the absence of left ventricular mechanical dyssynchrony (LVMD) preoperation was partly responsible for nonresponse [3]. Therefore, an accurate assessment of LVMD plays a crucial role in ameliorating CRT outcomes.

In recent years, several echocardiographic techniques have been adopted to quantify LVMD, including tissue Doppler imaging (TDI), real-time three-dimensional echocardiography (RT-3DE), and two-dimensional speckle tracking imaging (2D-STI). TDI is limited by angle dependence, and RT-3DE restricts at low frame rates. However, 2D-STI has overcome these disadvantages. This technique reflects myocardial deformation in three directions: radial thickening, circumferential shortening, and longitudinal shortening [4].

Therefore, using 2D-STI, the purpose of this study was to evaluate LVMD in CHF patients referring to normal healthy people, and then to compare the usefulness of three patterns of myocardial deformation in mechanical dyssynchrony assessment. Furthermore, the relationships between left ventricular ejection fraction (LVEF), QRS duration (QRSd), and LVMD were explored.

Materials and methods

Study population

A total of 78 systolic heart failure patients were enrolled in this study. Etiology of CHF included idiopathic dilated cardiomyopathy ($n = 41$) and ischemic cardiomyopathy ($n = 37$). Selection criteria were as follows: sinus rhythm in standard 12-lead electrocardiography (ECG), QRSd $\geq$ 120 milliseconds, and New York Heart Association (NYHA) cardiac function class II—IV. Exclusion criteria were as follows: frequent premature systolic, valvular heart disease, and congenital heart disease. All patients underwent standard echocardiographic examination, and LVEF was measured by the biplane Simpson method [5]. Patients were classified into two subgroups: (1) LVEF $\leq$ 35% ($n = 38$, group 1) and (2) 35% $<$ LVEF $<$ 50% ($n = 40$, group 2). A total of 60 healthy individuals with similar age and gender comprised the control group (group 3). The study was carried out according to the Helsinki Declaration and approved by the ethics committee of our institution. All participants gave oral and written informed consent.

Echocardiographic examination

Standard echocardiography examinations were performed by a commercially available system (iE33, Philips Medical System, Bothell, WA, USA) using a 1—5 MHz transducer. After connecting the ECG, M-mode and two-dimensional images were acquired with the participants in the left lateral decubitus position. All images were obtained during breath holding and stored in three consecutive cardiac cycles. Gain, depth, and focal range were adjusted to ensure optimal left ventricular border display and high frame rate ($>$110 fps). Left ventricular end-diastolic diameters (LVEDDs) were measured by M-mode echocardiography. Left ventricular end-systolic volumes (LVESVs) and end-diastolic volumes (LVEDVs) were measured from the apical two- and four-chamber views.

2D-STI and dyssynchrony indices

Post-processing was performed using Qlab software (Version 6.0, Philips Medical Systems). For speckle tracking analysis, standard two-dimensional images were recorded in apical two-, three-, and four-chamber views as well as the parasternal short-axis views of basal level and mid level. First, three points, at the cardiac apex and the two sides of mitral valve, were marked on the endocardium cavity interface in apical views; and a center point of the endocardium cavity was marked in short-axis views. After that, the whole left ventricular myocardium was identified as the region of interest automatically. According to the 17-segment model, both basal and mid-ventricular level consist of six segments, as well as the apex consisting of four segments and an apical cap [6]. Different colors were used to code 17 segments. Manual modification of the region of interest was feasible to ensure accurate tracking of all myocardium regions. Finally, the so-called speckles, which were acoustic markers distributed across the myocardium equally, were tracked throughout the whole cardiac cycle. Information about three patterns of deformation was displayed into 17 segmental time-strain and time-strain rate curves.

A total of 12 segments of basal level and mid level in both apical and short-axis views were selected. The time interval from Q-wave of the ECG to peak systolic strain/strain rate was measured for each segment. For each type of deformation analysis, two dyssynchrony indices were obtained: standard deviation (SD) of time to peak systolic strain/strain rate in 12 segments (Ts-12SD) and the maximal time delay between peak systolic strain/strain rate of 2 segments in 12 segments (Ts-12Dif).

Statistical analysis

Statistical computations were performed with SPSS version 17.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean $\pm$ SD, and one-way analysis of variance (ANOVA) was used to compare multiple groups. Categorical data were presented as percentages, and compared using χ^2 test. Pearson correlation was performed to assess the relationship between LVEF, QRSd, and dyssynchrony indices. A total of 30 participants were randomly selected to test inter- and intraobserver variabilities for Tsls-12SD, Tsrs-12SD, and Tscs-12SD. A coefficient of variation (CV), defined as the SD/mean ratio of each parameter, was used for this assessment. A p value $<$ 0.05 was considered statistically significant.

Results

Demographic data and echocardiographic characteristics of all participants are summarized in Table 1. The three

Table 1 Demographic data and echocardiographic characteristics.

Indices	Group 1 ($n = 38$)	Group 2 ($n = 40$)	Control (Group 3) ($n = 60$)
Age (y)	57.15 ± 12.09	54.58 ± 12.50	54.91 ± 11.11
Gender (M/F)	21/17	23/17	32/28
Heart rate (beats/min)	77.19 ± 17.89	75.00 ± 16.27	74.00 ± 16.70
LVESV (mL)	$129.34 \pm 47.01^{*,\#}$	$66.25 \pm 24.66^{*}$	23.95 ± 9.19
LVEDV (mL)	$184.82 \pm 59.11^{*,\#}$	$122.19 \pm 34.69^{*}$	57.07 ± 17.21
LVEDD (mm)	$69.38 \pm 6.69^{*}$	$61.67 \pm 7.50^{*}$	47.76 ± 5.88
LVEF (%)	$29.58 \pm 6.02^{*,\#}$	$46.97 \pm 6.33^{*}$	58.08 ± 6.74

LVEDD = left ventricular end-diastolic diameter; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume; *compared with controls, $p < 0.01$; #compared with group 2, $p < 0.05$.

groups were similar in age, gender, and heart rate ($p > 0.05$). LVESV, LVEDV, and LVEDD in CHF patients (Groups 1 and 2) were remarkably higher than those in the control group ($p < 0.01$). The values of LVESV and LVEDV in Group 1 were significantly higher than those in Group 2 ($p < 0.05$). LVEF values in CHF patients were remarkably lower than those in the control group ($p < 0.01$). Group 1 patients had a significantly lower LVEF than patients in Group 2 ($p < 0.05$). No differences were found in QRSd between Group 1 and Group 2 (134.45 ± 31.43 milliseconds vs. 126.1 ± 32.64 milliseconds, $p > 0.05$).

Dyssynchrony indices of the three groups are listed in Table 2. Compared with group 3, all indices in Group 1 were remarkably higher ($p < 0.05$), and some of the indices (Tsls-12SD, Tsls-12Dif, Tslsr-12SD, Tslsr-12-Dif, and Tsrs-12SD) in Group 2 were significantly higher ($p < 0.05$). Reproducibility for Tsls-12SD was better than Tsrs-12SD and Tscs-12SD in both inter- and intraobserver assessments (Table 3). Interobserver variability was higher for each index than intraobserver variability.

Correlation analysis was performed between LVEF and dyssynchrony indices in CHF patients (Table 4). LVEF was related to all three forms of strain/strain rate ($p < 0.05$), and the highest value was observed for longitudinal index ($r = -0.525$, $p < 0.01$). No relationship existed between QRSd and dyssynchrony indices ($p > 0.05$).

According to the statistical principles for setting the normal reference range, the cut-off value of LVMD was defined as mean $\pm$ 1.645 SD of the normal population. In this study, a cut-off value was calculated for each index, and dyssynchrony rates were obtained in two CHF subgroups, respectively. Comparison of dyssynchrony rates was performed within each subgroup. Results revealed that significant differences were noted within both Group 1 and Group 2 ($\chi^2 = 25.55$, $p < 0.05$ vs. $\chi^2 = 23.88$, $p < 0.05$), and that the highest detection rate was derived from the longitudinal index in both subgroups (Table 5).

Discussion

2D-STI is based on tracking characteristic speckle patterns at a high frame rate and providing myocardial deformation data, recorded as strain and strain rate, in a whole heart cycle [7]. Previous investigators have used this technology to evaluate LVMD and predict CRT response [8–10]. However, the present study employed different indices. CHF patients usually showed left ventricular remolding, which means cardiac chamber enlargement and cardiac apex roundout. These special changes make it difficult to completely include apex and apical cap in echocardiographic images. For the correctness of the results, this

Table 2 Dyssynchrony indices of three groups.

Indices	Group 1	Group 2	Control (Group 3)
Tsls-12SD (ms)	$108.67 \pm 50.09^{*}$	$89.01 \pm 49.11^{*}$	43.37 ± 27.63
Tslsr-12SD (ms)	$102.01 \pm 29.23^{*}$	$84.99 \pm 29.02^{*}$	61.37 ± 27.32
Tsrs-12SD (ms)	$123.88 \pm 35.05^{*}$	$116.42 \pm 42.89^{*}$	93.50 ± 36.88
Tsrsr-12SD (ms)	$102.89 \pm 48.15^{*}$	85.47 ± 27.78	77.89 ± 28.16
Tscs-12SD (ms)	$75.07 \pm 42.14^{*}$	45.66 ± 29.00	33.69 ± 27.77
Tscsr-12SD (ms)	$68.77 \pm 34.05^{*}$	57.64 ± 25.78	47.25 ± 17.36
Tsls-12Dif (ms)	$284.20 \pm 135.34^{*}$	$255.07 \pm 154.97^{*}$	134.12 ± 90.35
Tslsr-12Dif (ms)	$288.73 \pm 85.22^{*}$	$264.92 \pm 100.96^{*}$	185.35 ± 88.95
Tsrs-12Dif (ms)	$327.04 \pm 93.06^{*}$	285.84 ± 109.14	240.89 ± 75.18
Tsrsr-12Dif (ms)	$287.02 \pm 103.43^{*}$	238.55 ± 80.17	219.61 ± 72.24
Tscs-12Dif (ms)	$222.72 \pm 116.80^{*}$	140.62 ± 92.31	102.97 ± 85.77
Tscsr-12Dif (ms)	$210.95 \pm 117.48^{*}$	181.99 ± 70.15	146.72 ± 60.75

cs = circumferential strain; csr = circumferential strain rate; ls = longitudinal strain; lsr = longitudinal strain rate; rs = radial strain; rsr = radial strain rate; Ts-12Dif = the maximal time delay between peak systolic strain/strain rate of two segments in 12 segments; Ts-12SD = the standard deviation of time to peak systolic strain/strain rate in 12 segments; *Compared with controls, $p < 0.05$.

Table 3 Reproducibility measures for Tsls-12SD, Tsrs-12SD, and Tscs-12SD.

Echocardiographic measure	Intraobserver (CV, %)	Interobserver (CV, %)
Tsls-12SD (ms)	9.7	14.1
Tsrs-12SD (ms)	23.1	36.9
Tscs-12SD (ms)	15.5	24.6

Abbreviations as in Table 2.

study selected the remaining 12 segments in the left ventricle, eliminating unstable factors.

In this study, a comparison of dyssynchrony indices was performed between healthy controls and CHF patients. The results showed that all indices in group 1 were higher than those in group 3, whereas some indices in group 2 were higher than those in group 3. This implied that CHF patients had different degrees of LVMD. Moreover, there was a significantly negative linear correlation between LVEF and all indices in CHF subgroups, which implied that systolic function deteriorated as mechanical dyssynchrony motion worsened. A possible explanation may be as follows: dyssynchrony contraction in the left ventricle usually occurs in heart failure patients. The early-stimulated region contracts at low chamber pressure and fails to contribute to effective ejection. The late-stimulated region starts contraction while the former enters relaxation. Conflicting wall motion leads to ineffective blood circulation in the left ventricular chamber. As a result, global systolic efficiency decreases and stroke volume reduces.

Preimplantation left ventricular dyssynchrony is considered to be an essential condition for a beneficial response to CRT. The current recommendation for CRT candidates mainly focuses on QRSd [1]. However, a wide QRS complex may not be synonymous with substantial LVMD. As a result, the relationship between electrical dyssynchrony and mechanical dyssynchrony has become an issue in research. Bleeker et al. discussed the relationship between QRSd and LVMD in patients with end-stage heart failure, and defined LVMD as an electromechanical delay on TDI $\geq$ 60 milli seconds between the septum and lateral wall [11]. They found that severe dyssynchrony was observed in 27% of patients with narrow QRS complex, 60% with intermediate QRSd, and 70% with wide QRS complex. Furthermore, no relationships were found between QRSd and septal-to-lateral delay. Andrikopoulos et al. evaluated the correlation of mechanical dyssynchrony with QRSd as measured by three methods [12]. The results revealed that 60.4%, 69.4%, and 73.5% of the studied patients had QRS $\geq$ 120 milliseconds, respectively, based on three different measurements. Moreover, interventricular but not intraventricular delay was correlated with QRSd. In the present study, no significant correlations were observed between QRSd and 2D-STI dyssynchrony indices. Our findings are in accordance with the results above.

Table 4 Relationships between LVEF and dyssynchrony indices in CHF patients.

Indices	r	p
Tsls-12SD	−0.525	0.001
Tslsr-12SD	−0.422	0.001
Tsrs-12SD	−0.373	0.005
Tsrsr-12SD	−0.272	0.043
Tscs-12SD	−0.382	0.004
Tscsr-12SD	−0.324	0.017
Tsls-12Dif	−0.445	0.001
Tslsr-12Dif	−0.360	0.007
Tsrs-12Dif	−0.318	0.018
Tsrsr-12Dif	−0.329	0.014
Tscs-12Dif	−0.364	0.007
Tscsr-12Dif	−0.276	0.043

Abbreviations as in Table 2.

Table 5 Comparison of dyssynchrony rates within each CHF subgroup.

Indices	Group 1	Group 2
Tsls-12SD	66.7%	53.3%
Tslsr-12SD	41.2%	26.7%
Tsrs-12SD	25.0%	12.5%
Tsrsr-12SD	12.5%	6.3%
Tscs-12SD	50.0%	18.8%
Tscsr-12SD	25.0%	25.0%
Tsls-12Dif	61.1%	53.3%
Tslsr-12Dif	41.2%	33.3%
Tsrs-12Dif	25.0%	12.5%
Tsrsr-12Dif	18.8%	6.3%
Tscs-12Dif	50.0%	18.8%
Tscsr-12Dif	18.8%	18.8%
χ^2	25.55	23.88
p	0.008	0.013

Abbreviations as in Table 2.

At present, there is no gold standard to assess LVMD and the results for the different echocardiographic methods are inconclusive. Referring to the healthy population, this study calculated statistically based cut-off values for each 2D-STI dyssynchrony index and a comparison of dyssynchrony rates within each CHF subgroup was made, respectively. The results indicated that dyssynchrony rates showed statistically significant differences within each subgroup, and the detection rate of longitudinal indices proved to be the highest among all rates, which demonstrated that longitudinal indices were better indicators for LVMD than radial indices or circumferential indices. The purpose of intraventricular mechanical analysis is to guide the CRT procedure effectively. In the past, the clinical value of three patterns of myocardial deformation in predicting CRT response was compared in some studies [13,14]. However, the parameters in these studies included a small range of left ventricular segments and failed to reflect cardiac motion comprehensively. The 12-segment indices in this study excluded unstable segments and included the remaining segments in the left ventricle, which theoretically gave better expression to cardiac motion. These findings still need to be replicated in a large-scale study.

In conclusion, 2D-STI is capable of identifying intraventricular mechanical dyssynchrony. CHF patients have

different extents of LVMD. Left ventricular systolic function was closely related to mechanical dyssynchrony, whereas QRSd showed no significant correlation. Referring to the normal population, longitudinal indices showed better detectability of dyssynchrony motion than radial indices or circumferential indices.

References

[1] Epstein AE, DiMarco JP, Ellenbogen KA, Estes 3rd NA, Freedman RA, Gettes LS, et al. ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices): developed in collaboration with the American Association for Thoracic Surgery and Society of Thoracic Surgeons. Circulation 2008;117:e350—408.

[2] Yu CM, Fung WH, Lin H, Zhang Q, Sanderson JE, Lau CP, et al. Predictors of left ventricular reverse remodeling after cardiac resynchronization therapy for heart failure secondary to idiopathic dilated or ischemic cardiomyopathy. Am J Cardiol 2003;91:684—8.

[3] Bax JJ, Bleeker GB, Marwick TH, Molhoek SG, Boersma E, Steendijk P, et al. Left ventricular dyssynchrony predicts response and prognosis after cardiac resynchronization therapy. J Am Coll Cardiol 2004;44:1834—40.

[4] Kawagishi T. Speckle tracking for assessment of cardiac motion and dyssynchrony. Echocardiography 2008;25:1167—71.

[5] Schiller NB, Shah PM, Crawford M, DeMaria A, Devereux R, Feigenbaum H, et al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. J Am Soc Echocardiogr 1989;2:358—67.

[6] Cerqueira MD, Weissman NJ, Dilsizian V, Jacobs AK, Kaul S, Laskey WK, et al. Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart: a statement for healthcare professionals from the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association. Circulation 2002;105:539—42.

[7] Bohs LN, Trahey GE. A novel method for angle independent ultrasonic imaging of blood flow and tissue motion. IEEE Trans Biomed Eng 1991;38:280—6.

[8] Becker M, Kramann R, Franke A, Breithardt OA, Heussen N, Knackstedt C, et al. Impact of left ventricular lead position in cardiac resynchronization therapy on left ventricular remodelling. A circumferential strain analysis based on 2D echocardiography. Eur Heart J 2007;28:1211—20.

[9] Lim P, Buakhamsri A, Popovic ZB, Greenberg NL, Patel D, Thomas JD, et al. Longitudinal strain delay index by speckle tracking imaging: a new marker of response to cardiac resynchronization therapy. Circulation 2008;118:1130—7.

[10] Suffoletto MS, Dohi K, Cannesson M, Saba S, Gorcsan 3rd J. Novel speckle-tracking radial strain from routine black-and-white echocardiographic images to quantify dyssynchrony and predict response to cardiac resynchronization therapy. Circulation 2006;113:960—8.

[11] Bleeker GB, Schalij MJ, Molhoek SG, Verwey HF, Holman ER, Boersma E, et al. Relationship between QRS duration and left ventricular dyssynchrony in patients with end-stage heart failure. J Cardiovasc Electrophysiol 2004;15:544—9.

[12] Andrikopoulos GK, Tzeis S, Kolb C, Sakellariou D, Avramides D, Alexopoulos EC, et al. Correlation of mechanical dyssynchrony with QRS duration measured by signal-averaged electrocardiography. Ann Noninvasive Electrocardiol 2009;14:234—41.

[13] Tanaka H, Nesser HJ, Buck T, Oyenuga O, Jánosi RA, Winter S, et al. Dyssynchrony by speckle-tracking echocardiography and response to cardiac resynchronization therapy: results of the Speckle Tracking and Resynchronization (STAR) study. Eur Heart J 2010;31:1690—700.

[14] Delgado V, Ypenburg C, van Bommel RJ, Tops LF, Mollema SA, Marsan NA, et al. Assessment of left ventricular dyssynchrony by speckle tracking strain imaging comparison between longitudinal, circumferential, and radial strain in cardiac resynchronization therapy. J Am Coll Cardiol 2008;51:1944—52.