Left Ventricle Functional Geometry in Cardiac Pathology

Tatiana Chumarnaya[1,2], Olga Solovyova[1,2], Yulia Alueva[3], Sergey P. Mikhailov[3], Valentina V. Kochmasheva[3], Vladimir S. Markhasin[1,2]

[1]Institute of Immunology and Physiology of Russian Academy of Sciences, Yekaterinburg, Russian Federation
[2]Ural Federal University, Yekaterinburg, Russian Federation
[3]Yekaterinburg Regional Clinical Hospital # 1, Yekaterinburg, Russian Federation

Left ventricular functional geometry (LV FG) refers to the dynamical change in the ventricular shape during contraction and relaxation. It has been shown that LV FG significantly contributes to the regulation of contractility and cardiac pump function in health and disease. The aim of our work is to evaluate the LV FG in patients with common myocardial diseases. Here we have evaluated a control group of healthy people, patients with ischemic heart disease (IHD) with preserved ejection fraction (EF); patients with dilated cardiomyopathy (DCM) before and after cardiac resynchronization therapy (CRT). We used classical 2D apical four-chamber position in ultrasound video loop to evaluate the spatio-temporal heterogeneity of LV regional wall motion and dynamics of shape indexes (sphericity, conicity, shape-power index).

We have shown that the LV FG characteristics in DCM patients significantly differed from the control and disturbances were more pronounced than that in IHD patients. It was shown a tendency in the recovery of the LV FG characteristics towards the control values along with an increase in the ejection fraction. The relative change in the sphericity index from diastole to systole, and both the end-systolic sphericity and shape-power indexes demonstrated a high diagnostic accuracy in determining CRT responding patients.

1. Introduction

This study is focused on the functional geometry (FG) of human left ventricle (LV) in cardiac pathology. FG is a coordinated dynamical change in the geometry and functional state of LV during contraction and relaxation. Spatial and temporal patterns of the changes in the LV configuration during the cardiac cycle play a role in the LV mechanical function [1]. Alterations of the patterns appear to be essential for the diagnostics, prognosis and treatment strategy of the heart pathology [2].

To the date the role of mechanical heterogeneity of LV wall motion in its pumping function remains unclear. The quantitative characteristics of changing in the LV shape during contraction has to be determined in the normal heart. This data can be used then as the reference to compare with such parameters under disease. The aim of this paper is to identify LV FG parameters in the patients with ischemic heart disease and dilated cardiomyopathy.

2. Methods

2.1. Population

The following groups of patients were evaluated: a control group of healthy people (n=24), patients with ischemic heart disease with preserved EF (IHD, n=52); patients with dilated cardiomyopathy (DCM, n=25) before and after cardiac resynchronization therapy (CRT). Ultrasound diagnostic machine Philips IE 33 was used for echocardiography.

2.2. Indexes of heterogeneity

LV images in classical 2D apical four-chamber position were recorded during the entire cardiac cycle simultaneously with ECG recording. All echocardiographic images were digitized and analyzed off-line with using custom made software [3]. The endocardial LV contours were delineated by QLab Philips in each frame.

Ventricular EF was derived from 2D end-diastolic and end-systolic images, using a modified Simpson's rule approach. We used also a 2D estimate of the EF that is the fractional difference between the end-diastolic and end-systolic LV image areas.

Regional left ventricle wall motion was assessed with using radial method. Every contoured image (frame by frame) was overlapped by aligning their centers of mass (or center moments) with the end-diastolic one, that was

used as the origin for radii drown to the digitized points of the contours. Total end-diastolic area was divided into 20 radial sectors of equal area (Fig. 1A).

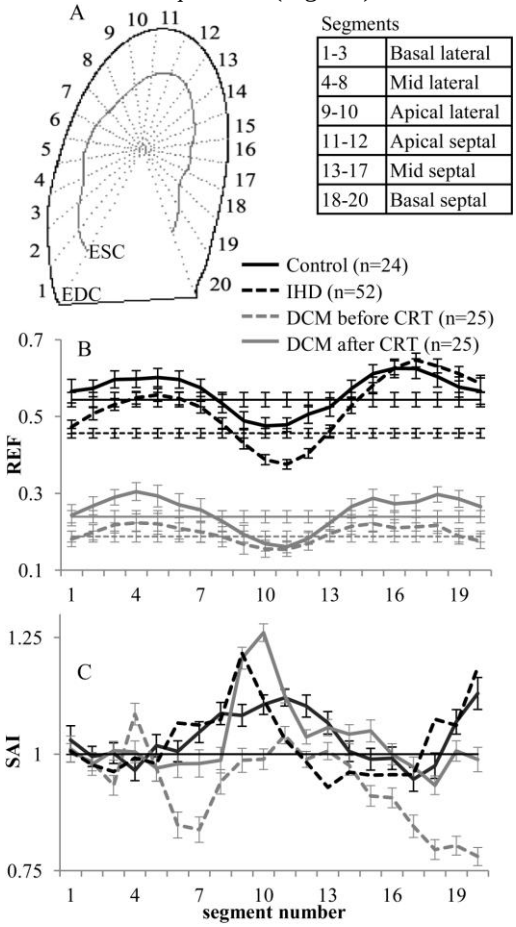

Figure 1. Panel A: Radial method. EDC and ESC is end-diastolic and end-systolic contour respectively. The dependences of the average REF (panel B, thick lines) and SAI (panel C) on the LV sector position along the LV contour are shown. Thin lines show the mean values of the 2D estimate of EF in the groups.

The time dependent changes in the sector area during the cardiac cycle were calculated. Maximal relative decrease in the sector area during the cardiac cycle against the end-diastolic area was evaluated for each sector and used as a two-dimensional estimate of the regional ejection fraction (REF). The ratio between the time required for approaching the REF and the time required for the global end-systole was used as systolic asynchrony index (SAI) of the regional movement. Coefficients of variation for the REF and SAI in a patient were used as the measures of spatial and temporal heterogeneity in the regional contraction.

2.3. Functional geometry indexes

To describe LV FG geometry we used several shape indexes. First of all we used conventional sphericity index (SI) [4] and Gibson index (GI) [5] which characterize a degree of shape circularity. We also used an apical conicity index (ACI) suggested earlier by DiDonato and co-authors [6] which shows the degree of conical shape of the apical zone. ACI was calculated as the ratio between the curvature radius of the circular approximating apical zone of the LV contour to the half of the short axis. The lesser ACI means the more conical (narrow) shape of the apical zone. Also we applied Fourier analyses suggested by Kaas and co-authors [7]. The contour is converted in polar coordinates and approximated with Fourier series. This approximation is then used to calculate Fourier shape-power index that equal to the ratio of the sum of squared coefficients of the Fourier series normalized to the first (zero-degree) coefficient, showing the complexity of the LV shape as compared to the circle.

2.4. Statistical analysis

Statistical analysis of data and group comparison was performed by “Statistica 6.1” and “SPSS 22.0” software packages. All calculated indexes were expressed as means ± std. error of the entire group of subjects. The means were compared with an unpaired, two tailed Student's t-test. Statistically significant difference between groups was since the p-value was lesser than 0.05, at the 95.0% confidence level. We used ROC analysis for evaluation of diagnostic tests and area under ROC-curve (AUC) as a measure of accuracy. If a characteristic had AUC>0.7, cut-off was determined as the balance between sensitivity and specificity.

3. Results

3.1. Healthy people

In our previous study we characterized the spatio-temporal heterogeneity of LV regional movements in healthy adult subjects [3]. The regular nonlinear dependence of the REF mean value on the LV segment position (segment number) along the LV contour in a clockwise direction is shown in Fig. 1B (black solid line). The maximal and minimal values of REF were significantly different ($p<0.05$) not only between each other, but each of them differed from the 2D-estimate of the EF (2DEF = 55±2%). The dependence of SAI mean values on the segment number also demonstrated several local extremes, and resembled the REF dependence but only in mirror representation (Fig. 1C, solid black line).

We suggest that the coefficient of variation in individual REFs (CV REF), and the coefficient of variation in SAIs (CV SAI) may characterize spatial and

temporal heterogeneity in subject LV wall motion (table 1). In the control group, the mean CV REF was 13 ± 1%, and CV SAI was 12 ± 1%. We found a negative correlation (r=-0.56, p<0.01) between the CV REF and the EF (Fig. 2).

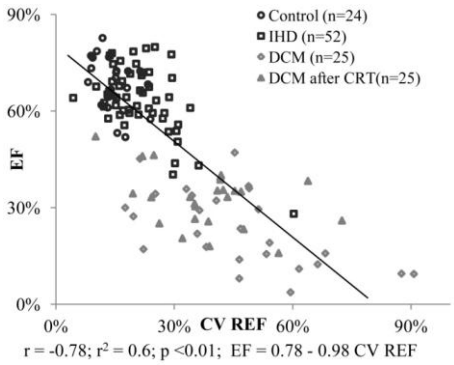

Figure 2. Correlation between heterogeneity of individual regional wall motion (assessed by variability in the regional area change) and ejection fraction. Line shows linear regression for the pooled data from control and patients.

Conventional SI decreases from diastole to systole in the control group, reflecting LV reshaping to become more narrow in longitudinal axe during systole. GI also reflects how close is the LV contour to the circle, and it accounts not only the main linear dimensions of LV, but the whole endocardial contour. Similarly with the SI, GI decreases during the systole and increases back in diastole. As SI, GI is statistically higher at the end diastole than at the end systole. The decrease from diastole to systole in either of SI or GI reflects a higher amount of LV transverse shortening versus longitudinal one in control group (34±2% vs 27±2% respectively). ACI increases from diastole to systole, i.e. apical zone sharpness increases. The FSPI significantly increases from diastole to systole. This points to a complication of LV form in systole apart from the circle (fig. 3, table 1).

3.2. Ischemic heart disease

Although the average EF was not significantly lower in IHD patients as compared to the control group (65±2% vs 70±2%), a characteristic decrease in the apical regional function in the IHD patients was found (38±2% vs 48±2%, p<0.01; AUC=0.73; cut off = 45%, sensitivity and specificity = 72%, fig. 1B, black dotted line). An increase in CV REF (AUC=0.78, cut off=17%, sensitivity and specificity = 70%) and CV SAI (AUC=0.78, cut off=15%, sensitivity and specificity = 70%) was found as compared to the control group (see Table 1). Also a strong negative correlation (r=-0.57, p<0.01) between CV REF and EF was shown (fig. 2). Dynamics of the SI, GI and ACI was not significantly differed from the control group during the cardiac cycle (fig.3, table 1). FSPI in IHD patients was statistically higher (indicating LV shape more far from spherical) throughout the contractile cycle (fig. 3, table1).

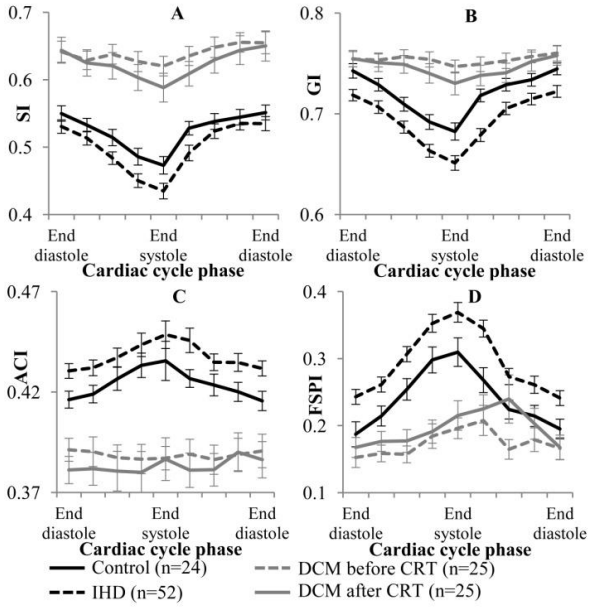

Figure 3. Dynamical changes in SI (panel A), GI (panel B), ACI (B panel), FSPI (panel D) during the cardiac cycle in the control group, in the IHD patients and DCM patients before and after CRT.

3.3. Dilated cardiomyopathy

The average EF and REF for all segments were significantly lower in DCM patients as compared to the control group and IHD patients (EF before CRT - 20±%; after CRT - 26±%). In DCM patients before CRT, the pattern of segmental distribution of REF was qualitatively destroyed as compared to the control group and IHD patients. After CRT, there was shown a qualitative change in the pattern of segmental distribution of REF toward normal one. Before CRT both CV REF (AUC=0.97, cut off =23%, sensitivity and specificity = 89%) and CV SAI (AUC=0.98, cut off =16% sensitivity and specificity=93%) were significantly higher as compared to the control group and IHD patients, and there was a tendency of a decrease in the values after CRT (see table 1). A strong negative correlation between CV REF and EF was shown (fig. 2). All LV form indexes in DCM patients before CRT showed more spherical shape in end diastole in comparison to the control group and IHD patients and the indexes almost did not change during cardiac cycle (fig. 3, table 1). Although LV form indexes did not completely recovered after CRT, there appeared a tendency of the dynamic changes in the indexes during cardiac cycle (fig. 3, table 1).

Table 1. Clinical and LV FG characteristics of the groups

Variable	Controls (n=24)	IHD (n=52)	DCM (n=25)	DCM after CRT (n=25)
Age, year	31±9	50±6	63±7	63±7
Pulse, bpm	68±2	69±2	77±4	79±2
QRS , ms	90±8	98±4	163±3*	141±2$^{*\&}$
EDV, ml	109±6	110±4	234±16*	203±17$^{*\&}$
ESV, ml	36±3$^{\#}$	38±4$^{\#}$	197±13$^{\#*}$	146±17$^{\#*\&}$
EF,%	70±2	65±4	25±2*	33±2$^{*\&}$
CV REF, %	13±1	22±1*	46± 3*	38 ± 3*
CV SAI, %	12±1	18±1*	37± 2*	25± 2$^{*\&}$
SI ED	0.55±0.0	0.54±0.0	0.64±0.0*	0.64±0.0*
SI ES	0.47±0.0$^{\#}$	0.43±0.0$^{\#}$	0.62±0.0$^{\#*}$	0.59±0.0$^{\#*}$
Δ SI, %	15±2	18±2	3±1*	9 ± 0.9$^{*\&}$
GI ED	0.74±0.0	0.72±0.0	0.75±0.0	0.75±0.0
GI ES	0.68±0.0$^{\#}$	0.65±0.0$^{\#}$	0.75±0.0*	0.73±0.0$^{\#*}$
Δ GI, %	8±0.1	9±0.1	1±0.01*	3±0.1$^{*\&}$
ACI ED	0.41±0.0	0.43±0.0	0.39±0.0*	0.38±0.0
ACI ES	0.44±0.0$^{\#}$	0.45±0.0$^{\#}$	0.39±0.0*	0.39±0.0
Δ ACI, %	4±0.5	4±0.5	0±0.2*	2±0.2
FSPI ED	0.19±0.0	0.24±0.0	0.15±0.0*	0.17±0.0
FSPI ES	0.32±0.0$^{\#}$	0.37±0.0$^{\#}$	0.19±0.0*	0.22±0.0$^{\#*}$
Δ FSPI, %	39±3	34±3	17±6*	19±6*

EDV and ESV - end diastolic and end systolic volume
$^{\#}$ $p<0.05$ ED versus ES
* $p<0.05$ versus controls
$^{\&}$ $p<0.05$ DCM before versus after CRT

We divided DCM patients into two sub-groups: the CRT responders (n=15) and nonresponders (n=10). A positive response to CRT was defined as improved quality of life and functional state (New York Heart Association class, exercise capacity) and a reduction in LV end systolic volume of >15%. Two shape indexes were showed to be significant in discrimination between responders and nonresponders: an increase in the end-systolic SI (AUC=0.73; cut off =0.59, sensitivity and specificity = 75%) and a decrease in the end-systolic FPSI (AUC=0.77; cut off =0.18, sensitivity and specificity = 73%). A decrease in the relative change in the SI during systole (AUC=0.85; cut off =9%, sensitivity and specificity = 74%) was determined as the most informative to predict CRT responders.

4. Conclusion

The data we obtained show that the LV FG characteristics in DCM patients significantly differed from the control and the disturbances were more pronounced than in IHD patients. Both CV REF and CV SAI gave good diagnostic accuracy for discriminating between norm and IHD patients, and also between norm and DCM patients.

FSPI in IHD patients was statistically higher throughout the contractile cycle compared to control with rather high diagnostic accuracy.

There was shown a tendency in the recovery of the characteristics of the LV FG towards control values along with an increase in EF. An increase in the end-systolic SI above 0.59, a reduction of the end-systolic FSPI below 0.18, and especially a reduction of the relative change in the SI during systole below 3.5% appeared to have rather high diagnostic accuracy in separating responders from nonresponders with the specificity and sensitivity above 70%.

Acknowledgements

Supported by RFBR grant 14-01-3115114(results on control and IHD groups) and RSF grant 14-35-00005 (results on DCM patients).

References

[1] Markhasin V.S., Solovyova O., Chumarnaya T.V., Sukhareva S.V. Problem of heterogeneity of myocardial. Russian Journal of Physiology 2009; 95(9): 919-943.
[2] Passino C., Barison A., Vergaro G., Gabutti A., Borrelli C., Emdin M., Clerico A. Markers of fibrosis, inflammation, and remodeling pathways in heart failure. Clinica Chimica Acta. 2015;443: 29–38.
[3] Chumarnaya T.V., Solovyova O., Sukhareva S.V., Vargina T.A., Markhasin V.S. Spatio-temporal heterogeneity of human left ventricle contractions in norm and in ischemic heart disease. Russian Journal of Physiology 2008;94(11):1217-1239.
[4] Anderson B. The normal examination and echocardiographic measurements. Second edition. MGA Graphics. Australia. 2007.
[5] Gibson DG, Brown DJ: Continuous assessment of left ventricular shape in man. Br Heart J 1975;37:904-910
[6] Di Donato M, P. Dabic. Left ventricular geometry in normal and post-anterior myocardial infarction patients: sphericity index and 'new' conicity index comparisons. Eur J Cardiothorac Surg 2006; 29 Suppl 1: 225-30.
[7] Kass DA, TA. Traill. Abnormalities of dynamic ventricular shape change in patients with aortic and mitral valvular regurgitation: assessment by Fourier shape analysis and global geometric indexes. Circ Res 1988; 62(1):127-38.

Address for correspondence.

Tatiana Chumarnaya, PhD
Institute of Immunology and Physiology UB RAS,
Pervomayskaya 106, Yekaterinburg 620049, Russia.
E-mail: t.chumarnaya@iip.uran.ru.