

## Left Ventricular Remodeling at Dilated Cardiomyopathy: Haemodynamic Data and Functional Status

Nato Katamadze, Manana Kiknadze

Department of Internal Medicine of General Medicine Faculty, Tbilisi State Medical University, Georgia

### ABSTRACT

Has been carried out the investigation of structural-functional condition of left ventricular during Dilative Cardiomyopathy at early and progressive stages of disease. The present study demonstrate that left ventricular systolic function is correlated with severe impairment of dilated cardiomyopathy, according to the clinical stage. Left ventricular diastolic filling abnormalities are found, reflecting abnormal relaxation in early dilated cardiomyopathy. Our results indicate that progressive impairment of left ventricular systolic function is reciprocally related to the development of diastolic filling abnormalities. Structural changes of left ventricle appeared to be the determinant in its functional transformation, that is, in remodeling of left ventricle.

**KEYWORDS:** dilative cardiomyopathy, heart failure, left ventricular function, left ventricular remodeling, ejection fraction

**H**eart Failure (HF) continues to be a major source of death and disability, and concepts and understanding of the disorder continue to evolve [1]. Cardiac structure has long been recognized to be the primary determinant of HF, and the cardiac weight of 500g or the Left Ventricular (LV) weight of 200g were suggested as "critical" for the natural history of the disease [2]. Progressive left ventricular enlargement, distortion and hypertrophy over time (i.e. remodeling) have been shown to be directly related to future deterioration in ventricular performance and a less favorable clinical course in these patients [3]. Whereas each of these various components of the remodeling process may contribute importantly to the overall development and progression of HF, it is extremely unlikely that any single aspect of the remodeling process itself will satisfactorily explain the progressive cardiac decompensation that occurs as HF advances. A combinatorial functional-structural approach seems to be the next step in the understanding and explanation of HF [4].

**Goals of Study:** The evaluation of structural-functional condition of LV in patients affected with chronic cardiac failure on the background of early and progressive stages of Dilative CardioMyopathy (DCM).

### MATERIALS AND METHODS

In the study have been involved 112 patients with DCM, among them: males - 92 (82%), females - 20 (18%); of average age  $51,94 \pm 16,62$ ; with idiopathic DCM 50 (45%) and with ischemic DCM 62 (55%). HF corresponded to D-stage of classification of American Association of Cardiologists/American Board of Cardiologists (2001), i.e. structural cardiopathy with clinical manifestation of HF. Patients with DCM have been divided in 2 groups: I group- patients with early stage of DCM without clinical manifestation, with Ejection Fraction (EF%) of LV more than 40 %, II group - the patients with progressive stage of DCM and clinical symptoms at HF, with EF of LV less than 40 %. The Diagnose of DCM is made by WHO/ISFC (1996) criteria. In the study have not been involved: the oncological patients, the patients with liver, kidney, thyroid gland and lung diseases, as well as the patients consuming more than 60gr alcohol every day. Control group consisted of 20 practically healthy persons.

By the apparatus Vid med-CM700 (Sonotron\*, Norvegen) the routine Echocardiography has been performed. In a

two-dimensional regime have been defined the End-Diastolic (EDV) and End-Systolic (ESV) volumes of LV (ml), Index of End-Diastolic (IEDV) and End-Systolic (IESV) volume of LV ( $\text{ml}/\text{m}^2$ ), EF LV (%), Index of LV Myocardium Mass (IMM,  $\text{g}/\text{m}^2$ ). The End-Diastolic (EDS) and End-Systolic (ESS) sizes of LV (mm), the Interventricular Septum Thickness (IST, mm) and Relative Thickness of Posterior Wall (RTPW) of LV were measured in M-regime. RTPW of LV was measured by the formula:  $\text{RTPW} = 2 \times \text{TPW} / \text{EDS}$ .

The systolic Myocardial Stress (MS,  $\text{din}/\text{cm}^2$ ) calculation has been performed by the formula:  $\text{MS} = \text{TA} \times \text{ESS} / 4 \times \text{TPW} \times (1 + \text{TPW} / \text{ESS})$ , where TA - is the systolic TA. We had also determined the indexes connecting the systolic function and geometry of LV:  $\text{MS} / \text{IESV}$ ,  $\text{EF} / \text{MS}$ .

Diastolic features of LV were studied using transmitral diastolic flow. Have been evaluated maximal speed of transmitral diastolic flow at early filling of LV (E), max. speed of transmitral diastolic flow at late filling of LV (A) and correlation of max speeds of flow during early and late filling of LV (E/A).

Statistical elaboration of obtained results has been carried out by using the packet applied program "Statistica" - 5.0. for Windows. All the data have been presented as a (average)  $\pm s$  (standard deviation). The reliability of difference between the obtained data has been evaluated by using t- Student statistics. The difference  $p < 0,05$  has been considered as a statistically confidence value. The parallel correlative analysis was also conducted (Person coefficient of correlation; If  $t \geq t_{\text{crit}}$  then the hypothesis  $H_0$  is turned down and the correlation between the parameters is considered as a confidence).

### RESULTS AND DISCUSSION

The reliable changes of indexes have been observed in both groups comparing with the control group (Tab.1). The obtained data indicate to the obvious increase volumes of LV and significant decrease of EF in II group patients (EDVLV -  $200,6 \pm 63,32$ , ESVLV -  $114,4 \pm 53,52$ , EF -  $27,84 \pm 7,47$ ) comparing with those I group patients (EDVLV -  $154 \pm 41,47$ ,  $P < 0,01^{**}$ ; ESVLV -  $74,42 \pm 23,99$ ,  $P < 0,001^{***}$ ; EF -  $49,89 \pm 4,77$ ,  $P < 0,001^{***}$ ).

The above-mentioned data showed that the decrease of EF of LV at DCM first of all is attributed by changing LV geometry. During the continuous reduction of Relative

Thickness of Posterior Wall of LV (from  $0,38\pm 0,09$  to  $0,33\pm 0,07$ ,  $P<0,01^{**}$ ), the significant increase of volumes has been observed. In parallel with significant increase of MS (from  $149,1\pm 7,34$  to  $173,7\pm 4,64$ ,  $P<0,001^{***}$ ) the

progress in disturbance of geometrical indexes of LV remodeling (dilatation of heart cavity and myocardium mass enhancement) is revealed, which is considered as the process progressing factor.

Haemodynamic indexes	Control group (n=20)	I Group (n=19)	II Group (n=93)
EDV LV, ml	129,5±5,15	154±41,47°	200,6±63,32°*
ESV LV, ml	55,3±4,02	74,42±23,99°	114,4±53,52°*
IEDV LV, ml/m <sup>2</sup>	73,6±4,4	79,32±20,05°	105,2±31,83°*
IESV LV, ml/m <sup>2</sup>	31,4±2,5	39,21±12,03°	59,69±27,7°*
RTPW	0,41±0,06	0,38±0,09	0,33±0,07°*
EF (%)	62,2±3,9	49,89±4,77°	27,84±7,47°*
IMM LV, g/m <sup>2</sup>	118±9,4	142,1±29,47°	172,6±43,44°*
MS, din/cm <sup>2</sup>	99,6±18,84	149,1±7,34°	173,7±4,64°*
MS/IESV	7,2±1,93	4,32±0,43°	3,61±0,2°*
EF/MS	0,44±0,04	0,35±0,02°	0,17±0,01°*
<i>Doppler echocardiographic Data</i>			
E, cm/s	80±5	66±14°	80±24*
A, cm/s	65±4	79±19°	60±22*
E/A	1,29±0,07	0,8±0,4°	1,5±0,7*

Note: ° - The confidence in comparison with the data of control group ( $P<0,05^{\circ}$  - confidence of low degree,  $P<0,01^{\circ}$  - confidence of moderate degree,  $P<0,01^{\circ}$  - high confidence).

\* - The confidence of differences between the groups data ( $P<0,05^*$  - confidence of low degree),  $P<0,01^{**}$  - the confidence of average degree,  $P<0,01^{***}$  - high confidence)

**Tab.1** Structural-functional index of LV in Patients with DCM.

	I group (n=19)			II group (n=93)		
	IESV	EF	IMM	IESV	EF	IMM
IEDV	0,63***	-0,17	0,68****	0,89****	-0,45*	0,68****
IESV		0,07	0,44*		-0,43*	0,59**
EF			-0,24			-0,25

Note: \* -  $P=0,008$ , \*\* -  $P=0,006$ , \*\*\* -  $P=0,002$ , \*\*\*\* -  $P=0,001$

**Tab.2** Correlative data of haemodynamic parameters of LV.

	IEDV LV	IESV LV	EF
E/A	0,34	0,58* $P=0,008$	-0,59** $P=0,006$

Note: \* -  $P=0,008$ , \*\* -  $P=0,006$

**Tab.3** Correlation between E/A and haemodynamic parameters of LV.

The EF/MC value, reflecting the equality of LV systolic function, has been decreasing in accordance with progressing of HF ( $0,35 \pm 0,02$  in I group at  $0,17 \pm 0,01$  in II group,  $P < 0,001^{***}$ ). The correlation MC/IESV, reflecting participation of LV cavity dilatation in compensation of myocardium loading, was also significantly decreased ( $4,32 \pm 0,43$  in I group at  $3,61 \pm 0,2$  in II group,  $P < 0,001^{***}$ ) in accordance with progress of LV systolic dysfunction.

During the study of obtained parameters of LV diastolic function has been revealed - the decrease of ratio E/A ( $0,8 \pm 0,4$ ,  $P < 0,001^{000}$ ) in patients with EF > 40% and increase of E/A ratio ( $1,5 \pm 0,7$ ,  $P > 0,05$ ) in patients with EF < 40% comparing with those of analogical data in control group. The intergroup differences were also confidence ( $P < 0,001^{***}$ ). At early stage of DCM have been observed the disturbance of myocardium relaxation. During the disease progress was observed the significant engagement of filling speed (from  $66 \pm 14$  to  $80 \pm 24$ ,  $P < 0,001^{***}$ ) in the early diastole (E) and the decrease (from  $79 \pm 19$  to  $60 \pm 22$ ,  $P < 0,001^{***}$ ) in late diastole (A); witch means that, transmitral flow takes a pseudo normal form (II type of diastolic dysfunction of LV develops).

The Analysis of data given in Tab.2 shows direct and high quality correlation between indexed volumes of LV and IMM and negative correlation between indexed volumes of LV and EF. In addition the direct significant correlation between the above-mentioned changes and progress of disease have been revealed. Have been also observed (Table #3) the close correlation between E/A and the following structural-functional indexes of LV: IEDV LV ( $r = 0,34$ ), IESV LV ( $r = 0,58$ ,  $P = 0,008$ ), EF ( $r = -0,59$ ,  $P = 0,006$ ).

Analyzing the obtained results as a whole (Tab.1, 2, 3), it was clear that the reduction of systolic feature of myocardium leads to the enhancement of dilatation role of LV cavity in compensation of pumping function of heart at continuous reduction of Relative Thickness of Posterior Wall LV. All these indicate the heart remodeling progress in accordance with the type of eccentric hypertrophy of LV (II type of LV remodeling).

The obtained data certify that the disturbance of systolic and diastolic functions of LV are correlated. Worsening of LV diastolic function is accompanied with increase of intraventricular end-diastolic pressure, that leads to the extension (widening) of LV cavity and decrease of EF. EF reduction indicates the unfull ejection of blood from the ventricular cavity and is associated with increase of end-systolic volume of LV. As a result possibility to contain the new blood flow is reduced, that in its side demands the increased atrial work (5,6). All the above-mentioned leads to the LV diastolic dysfunction progress. So, between the progresses of LV systolic dysfunction and rising of LV diastolic dysfunction there exists reason-result correlation.

### CONCLUSIONS

The present study demonstrate that left ventricular systolic function is correlated with severe impairment of dilated cardiomyopathy, according to the clinical stage. Left ventricular diastolic filling abnormalities are found, reflecting abnormal relaxation in early dilated cardiomyopathy. The combinatorial approach to the syndrome that incorporates antiremodeling strategies along with existing heart failure strategies could repression of heart failure is assessed and may also open up new opportunities for unique pharmacological intervention.

### REFERENCES:

1. Packer M. / The neurohormonal hypothesis: a theory to explain the mechanism of disease progression in heart failure. // J Am Coll Cardiol 1992;20:248-54.
2. Cohn JN./Structural basis for heart failure: ventricular remodeling and its pharmacological inhibition.// Circulation 1995;91:2504-7.
3. Florea VG, Mareyev VY, Samko AN, Orlova IA, Coats AJS, Belenkov YN./ Left ventricular remodelling: common process in patients with different primary myocardial disorders. //Int J Cardiol. 1999;68:281-7.
4. Mann DL./Mechanisms and models in heart failure. A combinatorial approach. //Circulation 1999;100:999-1008.
5. Mariell Jessup M.D., Susan Brozena M.D./ Chronic Heart Failure: Present and Perspective // New England Journal of Medicine 2003;348:2007-18.
6. Grossman W. / Defining diastolic dysfunction. // Circulation 2000; 101:2020-2021.

## **Ремоделирование левого желудочка при дилатационной кардиомиопатии: гемодинамические параметры и функциональное состояние**

*Нато Катамадзе, Манана Кикнадзе*

Кафедра внутренней медицины лечебного факультета, Тбилисский государственный медицинский университет, Грузия

### **Р Е З Ю М Е**

Проведено исследование структурно-функционального состояния левого желудочка (ЛЖ) при дилатационной кардиомиопатии. Выявлена корреляционная связь между систолической функцией ЛЖ и прогрессированием заболевания. Диастолическая дисфункция ЛЖ представлена нарушением релаксации на раннем этапе и псевдонормализацией трансмитрального потока на прогрессирующей стадии заболевания. Систолическая дисфункция ЛЖ двухсторонне связана с нарушением диастолического наполнения желудочка. Структурные изменения предшествуют функциональному ремоделированию ЛЖ.

**Ключевые слова:** дилатационная кардиомиопатия, сердечная недостаточность, функция левого желудочка, ремоделирование левого желудочка, фракция выброса левого желудочка