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## **LEFT VENTRICULAR DYSFUNCTION IN PATIENTS OF HEMODIALYSIS OF RURAL MEDICAL COLLEGE OF SUBHIMALYAN REGION OF INDIA**

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### **ABSTRACT**

This study was done for the assessment of left ventricular diastolic function in patients on hemodialysis (HD) and the correlation of this function with the duration of HD. This prospective study included 104 patients (54 females and 50 males) with chronic renal failure (CRF), treated with HD, and 100 healthy subjects (54 females and 46 males) with no history of cardiovascular disease and with normal renal function, who constituted the control group. The groups were matched for age and sex. All study patients and control subjects underwent detailed history taking and physical examination. They also underwent electrocardiogram, echocardiography and biochemical and hematological blood analyses. Significant differences were noted between the two groups in the two-dimensional and M-mode echocardiography findings concerning aortic root dimension, transverse diameter of the left atrium, thickness of the inter-ventricular septum, thickness of the left ventricular posterior wall, left ventricular diastolic diameter, left ventricular systolic diameter, shortening fraction, ejection fraction as well as findings from the pulse Doppler study, including E wave, A wave, E/A ratio, deceleration time of E wave (DT-E), acceleration time of E wave (AT-E), tricuspid E and A waves ( $E_{tr}$  and  $A_{tr}$ ) and  $E_{tr}/A_{tr}$  ratio. There were significant changes in HD patients without arterial hypertension as well in the control group subjects. Our study suggests that the left ventricular and left atrial dimensions as well as the left ventricular wall thickness are augmented in patients with CRF treated with HD compared with the control group. Additionally, the left ventricular diastolic function is also reduced in these patients. These differences were also noted in patients with CRF without arterial hypertension. Left ventricular diastolic dysfunction had no correlation with the duration of HD.

## INTRODUCTION

In dialysis patients, cardiovascular disease (CVD) is the predominant cause of mortality. An increased risk of cardiovascular morbidity and mortality is also seen in earlier stages of chronic kidney disease (CKD). Multiple risk factors may contribute to the development of CVD, such as sodium and fluid retention, hypertension, anaemia, inflammation and hyperparathyroidism. In CKD patients, left ventricular hypertrophy (LVH) is a common finding and it is associated with an increased CVD-related mortality [2]. The prevalence and severity of LVH increases in parallel with the severity of CKD [3]. Initially, LVH is a physiological response to pressure and volume overload. However, sustained overload in combination with CKD-associated factors such as anaemia and hyperparathyroidism may result in maladaptive LVH characterized by structural changes in the myocardium, such as collagen accumulation, fibrosis and calcification, resulting in systolic and diastolic dysfunction [4,5]. Myocardial function in CKD patients has been studied extensively using conventional echocardiography. This method evaluates hydrodynamic responses and therefore it is load dependent, which is a disadvantage in CKD patients in whom fluid status may vary considerably. In addition, conventional echocardiography only allows semi-quantitative and partially subjective measurements. Furthermore, it has been shown to be too insensitive to distinguish between physiological and pathological LVH and to demonstrate diastolic dysfunction in patients with LVH [6] and normal ejection fraction [7].

Nearly half the deaths in patients with terminal renal disease treated with hemodialysis (HD) is due to cardiovascular complications<sup>1,2</sup>. Arterial hypertension is present in 60-90% of the patients with renal failure before starting HD treatment. Congestive heart failure as a cause of mortality occurs in approximately 20-30% of the cases<sup>2,3,4</sup>. Echocardiography showed that hypertrophic cardiomyopathy was dominant in most of these patients,<sup>5,6</sup> while decreased left ventricular function was found less frequently<sup>7</sup>. The most frequent cause of left ventricular systolic dysfunction is coronary artery disease<sup>5,6,7</sup>. However, some patients on HD have decreased systolic function without coronary disease<sup>8</sup>. Pathophysiologic changes and prognosis of these patients still remains unclear. Diastolic dysfunction is responsible for approximately 30% of the patients with heart failure.

## AIM OF STUDY

The aim of this prospective study was the assessment of left ventricular diastolic function in patients on HD and the correlation of this finding with the duration of HD.

## METHODS

This study was undertaken in the Departments of medicine Dr RPGMC Tanda at Kangra, from January 2011 until dec 2014. The study was performed on 104 patients (54 females and 50 males) with chronic renal failure (CRF) treated with HD and 100 healthy subjects (54 females and 46 males) without any history of cardiovascular disease or renal dysfunction, who constituted the control group. The groups were matched for age and sex. All patients in the case and in the control groups underwent detailed history and physical examination as well as electrocardiography (ECG), echocardiography and biochemical and hematological, blood analyses and *Echocardiography*.

The echocardiography machine used for this study was the Phillips machine with 3.5 MHz probes. Echocardiography scan was performed using the standard parasternal view (longitudinal and transversal axis) and apical views (two and four rooms) in the left decubitus position. On the echocardiography scan, the following standard measurements were taken on two-dimensional echocardiogram and M-mode: aortic dimension (Ao), diameter of left atrium (LA), thickness of interventricular septum (IVS), thickness of left ventricular posterior wall (LVPW), left ventricular systolic diameter (LVsD), shortening fraction (SF) and ejection fraction (EF). Assessment of the left ventricular diastolic function was made by a pulse Doppler study. The valuation of this function was made by the conventional method, by transmitral pulse Doppler and measuring the inflow speed of blood at the mitral valve level. The sample volume was set at the mitral valve leaflets level. The following transmitral inflow patterns were recorded: early diastolic wave (E), atrial activity wave (A), ratio between these parameters (E/A), deceleration time (DT-E) and acceleration time (AT-E). The tricuspid inflow patterns were recorded as well: early diastolic wave ( $E_{tr}$ ), atrial activity wave ( $A_{tr}$ ) and ratio between these parameters ( $E_{tr}/A_{tr}$ ).

American Society of Echocardiography guidelines were applied for registering all 2-D and conventional Doppler variables. Analyses were performed off-line using Echopac

6.3.4. The average of three consecutive heartbeats was used. Standard echocardiographic 2-D and M-mode measurements included left ventricular end-diastolic and end-systolic dimensions, end-diastolic and systolic wall thickness of interventricular septum and left ventricular posterior wall. Ejection fraction was calculated by Simpson and complemented by subjective visual estimation and the atrio-ventricular plane displacement method. LV mass was calculated according to the modified Penn formula. LV hypertrophy was defined as the left ventricular mass index (LVMI)  $>50 \text{ g/m}^2$  in men and  $>47 \text{ g/m}^2$  in women. The relative wall thickness (RWT)  $[(\text{IVS} + \text{PWT})/\text{LV end-diastolic diameter}]$  was calculated as an index of the LV geometric pattern (concentric LVH,  $\text{RWT} \geq 0.45$ ; eccentric LVH,  $\text{RWT} < 0.45$ ). Diastolic function was assessed by determining the velocities of early (E) and late (A) diastolic transmitral flow, the ratio E-to-A (E/A) and pulmonary vein flow velocities. In addition, isovolumetric relaxation time (IVRT), deceleration time of E wave (Edec) and velocity propagation (VP) were measured.

### STATISTICAL ANALYSIS

Data are presented as mean  $\pm$  SD. Paired Student's t-test was used to evaluate the variations between the continuous variables. Fisher's exact test was used to compare variables between the groups. Values  $r$  of Pearson's correlation coefficient were calculated for pairs of continuous variables.  $P \leq 0.05$  was considered to be statistically

### RESULTS

There were significant differences in hemoglobin, red cell count, leukocyte count, cholesterol and triglyceride levels between the patients on HD and in the control group, while the difference in the blood glucose level was not significant Table 1. Two-dimensional and M-mode echocardiographic findings showed significant differences between the two groups in the following parameters: aortic diameter (Ao), transverse left atrial diameter, interventricular septum thickness, LVPW, LVdD, LVsD, SF and EF. Also, pulsed Doppler findings such as E wave, A wave, E/A ratio, deceleration time of E wave (DT-E), acceleration time of E wave (AT-E), tricuspid E and A waves ( $E_{tr}$  and  $A_{tr}$ ) and  $E_{tr}/A_{tr}$  ratio showed significant changes of the 104 HD patients, 58 had arterial hypertension and 46 had normal blood pressure before HD treatment. We compared the

findings on two-dimensional and M-mode echocardiography as well as pulse Doppler in patients with and without hypertension as well as in subjects from the control group. The findings are depicted in Table 1, Table 2 and Table 3. Left ventricular diastolic function had no significant correlation with duration of HD.

**Table 1 Comparison of laboratory findings in Hemodialysis patients and controls**

Laboratory values	Hemodialysis patients	Control group	P-value
Hematocrit (%)	0.311 ± 0.597	0.395 ± 0.395.163	<0.001
Red cells ( $\times 10^{12}$ )	3.22 ± 0.57	4.585 ± 0.45	<0.001
Hemoglobin (g/L)	101.24 ± 21.79	138.9 ± 5.37	<0.001
Leukocyte count ( $\times 10^3$ )	8.04 ± 1.95	5.81 ± 0.82	<0.001
Serum cholesterol (mmol/L)	4.285 ± 0.185	3.056 ± 1.026	<0.001
Serum triglyceride (mmol/L)	1.93 ± 0.917	1.09 ± 0.235	<0.001
Blood glucose (mmol/L)	5.61 ± 2.31	5.48 ± 0.41	0.723

**Table 2 Comparison of echocardiographic finding in HD patients and control patients**

Echocardiography findings	Hemodialysis patients	Control group	P-value
LV diastolic diameter (cm)	5.16 ± 0.75	4.91 ± 0.52	0.0788
LV systolic diameter (cm)	3.50 ± 0.90	3.01 ± 0.38	0.0064
Shortening fraction (%)	32.88 ± 8.42	36.40 ± 5.76	0.0296
Ejecting fraction (%)	60.29 ± 12.79	65.53 ± 7.11	0.0244
Interventricular septum (cm)	1.17 ± 0.12	0.83 ± 0.40	<0.001
LV posterior wall (cm)	1.03 ± 0.23	0.86 ± 0.16	<0.001
Left atria (cm)	3.82 ± 0.57	3.49 ± 0.36	0.0026
Aorta (cm)	3.36 ± 0.395	3.09 ± 0.34	0.012

Table 3. Comparison of the pulse Doppler findings in the hemodialysis patients and subjects from the control group.

Echocardiography findings	Hemodialysis patients	Control group	P-value
E (cm/s)	57.63 ± 17.02	83.64 ± 13.57	<0.001
A (cm/s)	80.76 ± 19.74	65.93 ± 13.46	<0.001
E/A	0.75 ± 0.30	1.32 ± 0.37	<0.001
DT-E	181.56 ± 60.59	150.75 ± 30.08	0.0047
AT-E	67.41 ± 31.82	69.25 ± 16.39	0.741
E <sub>tr</sub> (cm/s)	50.43 ± 10.42	64.48 ± 15.32	<0.001
A <sub>tr</sub> (cm/s)	58.68 ± 21.11	53.44 ± 15.71	0.204
E <sub>tr</sub> /A <sub>tr</sub>	0.92 ± 0.24	1.26 ± 0.31	<0.001

E: early diastolic wave, A: atrial activity wave, E/A: ratio between these parameters, DT-E: deceleration time, AT-E: acceleration time, E<sub>tr</sub>: early diastolic wave, A<sub>tr</sub>: atrial activity wave, E<sub>tr</sub>/A<sub>tr</sub>: ratio between these parameters.

## DISCUSSION

Cardiovascular complications are commonly seen in patients with CRF, especially in those on HD<sup>1,2,3</sup>. The most common cardiovascular complications seen in these patients are AHT, IHD, AMI, disturbances of the heart rhythm, etc.<sup>1,2,3,4</sup>. Cardiovascular mortality in these patients is very high. Echocardiography helps in detection of left ventricular hypertrophy and decrease in systolic function in these patients<sup>4,5,6,7</sup>. Most of the previous studies showed decreased left ventricular diastolic function<sup>7,8,9,10,11,12,13,14</sup>. Our study had assessed right ventricular diastolic function in these patients also. We found reduced right ventricular diastolic function also, which may be explained by the presence of left ventricular overload as well as increased pressure on the right heart. Furthermore, our study is the first to explore the left and right ventricular diastolic function in HD patients without AHT. We found that the left and right ventricular diastolic function is affected in these patients.

## CONCLUSION

In conclusion, in patients with CRF treated with HD, the dimensions of the left ventricle, left atrium and left ventricular posterior wall thickness are augmented in comparison with subjects from the control group. Furthermore, the left and right ventricular diastolic function in these patients is reduced. These changes are also present in CRF patients without AHT. Left ventricular diastolic function has no significant correlation with the duration of HD.

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