Original Research Article

Echocardiographic assessment of systolic time intervals in hemodialysis patients with normal ejection fraction

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International Archives of Integrated Medicine, Vol. 6, Issue 4, April, 2019.

Available online at http://iaimjournal.com/
ISSN: 2394-0026 (P) **ISSN: 2394-0034 (O)**
Received on: 13-03-2019 **Accepted on:** 19-03-2019
Source of support: Nil **Conflict of interest:** None declared.
How to cite this article: R. Karthikeyan, V. Ramkumar. Echocardiographic assessment of systolic time intervals in hemodialysis patients with normal ejection fraction. IAIM, 2019; 6(4): 42-48.

Abstract

Background: Chronic Kidney Disease (CKD) and Cardiovascular Disease (CVD) have been inextricably linked since the earliest days of hemodialysis. Several statistics accrued since that time attests to the impact of cardiovascular disease in renal patients. Approximately one-half of all deaths in end-stage renal disease patients are attributable to cardiovascular disease, a proportion that is remarkably similar throughout the world.

The aim of the study: To Evaluate latent systolic dysfunction and its relation with diastolic dysfunction in hemodialysis patients with normal ejection fraction, using Doppler-derived systolic time intervals.

Materials and methods: This retrospective study was conducted in the Department of General Medicine, Government Mohan Kumaramangalam Medical College, Salem in 2017. Patients with systolicand diastolic blood pressures above 140 and 90 mmHg were grouped as hypertensive. According to this classification, 44% of patients were hypertensive. The control group comprised of healthy normotensive persons with no cardiovascular complaints, normal electrocardiogram (ECG) and normal blood chemistries.

Results: In our study, 90% of patients with systolic dysfunction had normal IVRT and 84.4% of patients with diastolic dysfunction had normal STI index. However, as in the previous study, the impaired STI index, and prolonged IVRT are independent of the presence of hypertension or left ventricular hypertrophy and IVRT was more sensitive than E/A ratio to diagnose diastolic dysfunction.

Conclusion: The most common features of uremic cardiomyopathy namely left ventricular hypertrophy, diastolic dysfunction and systolic dysfunction were present in 40%, 24%, and 40% of our hemodialysis patients respectively. The diastolic dysfunction and latent systolic dysfunction (STI>0.4) were randomly distributed. Impaired STI index and prolonged Isovolumetric relaxation time are independent of the presence of hypertension or left ventricular hypertrophy.

Key words

Chronic Kidney Disease, Coronary Artery Disease, Echocardiogram Fractional shortening, Ejection Fraction.

Introduction

Chronic Kidney Disease (CKD) and Cardiovascular Disease (CVD) have been inextricably linked since the earliest days of hemodialysis. Several statistics accrued since that time attests to the impact of cardiovascular disease in renal patients [1]. Approximately one-half of all deaths in end-stage renal disease patients are attributable to cardiovascular disease, a proportion that is remarkably similar throughout the world [2]. Several factors are thought to contribute to this high burden of cardiac disease in chronic kidney disease patients. First, the prevalence of many traditional risk factors for cardiovascular disease such as diabetes, hypertension is higher among CKD patients than in the general population. Second, several metabolic and hemodynamic disturbances that occur and progress in relation to declining renal function may modify cardiovascular risk [3]. There is growing evidence that uremia-related risk factors (Anemia, hyper cholesterolemia, hyper homocysteinemia, divalent ion abnormalities, oxidative stress) contribute to the excess burden of cardiovascular disease in chronic kidney disease patients [4]. The frequency of fatal and non-fatal cardiovascular events is increased even in the earliest stages of chronic kidney disease [5]. It appears that uremia acts to amplify the incidence of fatal ischemic heart disease by aconstant factor irrespective of the baseline incidence in the general population. Ischemic heart disease may be atherosclerotic or nonatherosclerotic in origin [6]. Congestive heart failure results from ischemic heart disease, cardiomyopathy or both. The manifestations of uremic cardiomyopathy include concentric left ventricular hypertrophy, eccentric left ventricular hypertrophy, Systolic dysfunction, and diastolic dysfunction [7]. Risk factors for cardiac disease in uremia include age, diabetes-mellitus, hypertension, anemia, volume overload, hyperparathyroidism, dyslipidemia and perhaps uremia itself. Although studies have traditionally focused on the dialysis population it has become evident that risk factors for cardiovascular disease and their initial consequences to the heart already are present during the pre-dialysis phase and persist despite significant amelioration in the transplantation phase [8]. The annual incidence of myocardial infarction or angina requiring hospitalization among hemodialysis patients is 8% and that of heart failure requiring hospitalization or treatment with ultrafiltration is 10% [9]. Systolic dysfunction disorders that are predictive of congestive heart failure can be detectable even before the overt decline in left ventricular ejection fraction from the Doppler-derived STI indices. Appropriate medical treatment or adequate ultrafiltration of patients at high risk (Prolonged STI index) for developing congestive heart failure, will decrease the death rate resulting from congestive heart failure [10].

Materials and methods

This retrospective study was conducted in the Department of General Medicine, Government Mohan Kumaramangalam Medical College, Salem in 2017. The study population included 25 hemodialysis patients (21 male, 4 female, mean age 36 years) and 25 healthy controls (15 Male, 10 female, mean age 37$\pm$10 years). Patients who were on dialysis longer than three months were

included in this study. Eighteen patients were dialysed thrice weekly and the remaining seven patients received dialysis twice weekly. Patients with systolic and diastolic blood pressures above 140 and 90 mmm Hg were grouped as hypertensive. According to this classification 44% of patients were hypertensive. The control group comprised of healthy normotensive persons with no cardiovascular complaints, normal electrocardiogram (ECG) and normal blood chemistries.

Inclusion and exclusion criteria

Hemodialysispatients who were on dialysis longer than three months were included in the present study (mean time on dialysis 20+ 6 months) Patients with - Diabetes mellitus, Acute ischemic syndromes or previous myocardial infarction, Cardiac arrhythmias, Valvular heart diseases, Patients using Angiotensin-converting enzyme inhibitors were excluded.

Echocardiographic analysis

An echocardiographic examination was carried out by using a VINGMED CFM 725 echocardiographic system and a 2.5 MHZ phase-array transducer. Cardiac rhythm was recorded during the examination. Hemodialysis patients were examined using Doppler echocardiography the day after hemodialysis. The means of three consecutive measurements of the Doppler echocardiographicparameters on a good quality recording was taken for each parameter. Measured parameters were mitral early filling (E wave) Peak velocity (PV), mitral late filling (A wave) peak velocity, the ratio of E wave PV to A wave PV, mitral deceleration slope and deceleration time. The isovolumetric relaxation time (IVRT) and isovolumetric contraction time were measured (IVCT). The interval from the end of aortic flow or aortic valve closure to the beginning of mitral flow or mitral valve opening was taken as the isovolumetric relaxation time. The interval from the end of mitral valve closure to the beginning of aortic flow or aortic valve opening was taken as the isovolumetric contraction time (IVCT). The presenceof abnormal left ventricular filling, distensibility and diastolic stiffness or in other words diastolic dysfunction was diagnosed according to thecriteria ofworking group.

Statistical analysis

The statistical analysis was carried out with the use of a statistical package for social sciences (SPSS) for windows ver 5.0 Numerical variables were given as mean+SD. Non-numerical parameters were given as frequency and percentage. Group analysis was performed with the use of an unpaired students' t-test. 'P' values< 0.05 were accepted as significant.

Results

Left ventricular hypertrophy was present in 40% of the hemodialysis patients (**Table – 1**). Left ventricular wall thickness, left ventricular diastolic and systolic internal diameters, aortic root, left atrial dimensions and left ventricular mass index were increased in hemodialysis patients compared with controls. There was no difference in the left ventricular ejection fraction (EF 74.08Vs 73.72% P= not significant) and fractional shortening (FS 34.92 Vs 35.64%, P= not significant) between hemodialysis patients and controls.

In the assessment of systolic time intervals, both the pre-ejection period (PEP) and systolic time interval index (STI index) were significantly higher in hemodialysis patients compared with controls. (PEP 69.20M sec Vs 69.20 msec P= 0.000) (STI index 0.3252 Vs 0.2716 P=0.000). The difference in left ventricular ejection time between hemodialysis patients and controls was not statistically significant (LVET 217.60 msec Vs 231.84 msec P= 0.224). Prolonged STI index (>0.4) was present in 40% of hemodialysis patients. In our controlled study, 44% of hemodialysis patients had hypertension and left ventricular hypertrophy. Hemodialysis patients were compared according to the presence or absence of hypertension, to assess whether the differences observed in STI parameters will be sustained across these subgroups. The PEP and STI indexes were similar between patients with

or without Hypertension. The STI index (0.3579 in normotensive group Vs 0.2716 in control group P=0.045 statistically significant) was still higher inthe normotensive hemodialysis group compared withcontrols suggests the prolonged systolicparameters are independent of the presence of hypertension or left ventricular hypertrophy. In the assessment of the diastolic function the isovolumetricrelaxation time (IVRT) was prolonged>100 msec in six patients 92.4%), deceleration time >220 msec in eleven patients (44%) and an E/A ratio of less than one in two patients (8%). Two among the 11 patients with prolonged deceleration time also had prolonged IVRT>100 msec and E/A ratio less than one. Overall 48% of patients had diastolic dysfunction. When hemodialysis patients without hypertension were compared with controls, the IVRT was still significantly prolonged. However, the E/A ratio change did not reach statistical significance (**Table – 2**).

Table – 1: Comparison of m mode parameters of hemodialysis patients to controls.

Parameters	HD Patients	Controls	P value
LVEDD mm	50.80	41.92	0.001
IVS mm	11.12	8.04	0.000
LVPW mm	10.80	7.80	0.000
ARD mm	27.60	23.04	0.000
LAD mm	33.92	23.56	0.000
EF%	74.08	73.72	NS
FS%	34.92	35.64	NS

Table – 2: Comparison of Doppler parameters between HD patients and controls.

Parameters	HD Patients	Controls	P value
PEP msec	69.20	69.20	0.000
LVET msec	217.60	231.84	0.224
STI index	0.3252	0.2716	0.000
E/A ratio	1.630	1.400	0.000
Deceleration Slope msec	194.00	180.00	0.000
IVRT msec	84.80	72.28	0.000
A wave PV msec	0.682	0.624	0.000

Discussion

The most common features of uremic cardiomyopathy namely left ventricular hypertrophy, diastolic dysfunction and systolic dysfunction were present in 40%, 24%, and 40% of our hemodialysis patients respectively [11]. The diastolic dysfunction and latent systolic dysfunction (STI>0.4) were randomly distributed. 90% of patients with systolic dysfunction had normal IVRT [12]. Impaired STI index and prolonged IVRT are independentof the presence of hypertension or left ventricular hypertrophy. 90% of patients with systolic dysfunction had normal IVRT. 84.4% of patients withdiastolic dysfunction (IVRT >100 msec) had normal STI index [13]. Combined systolic and diastolic dysfunctions were present in 12% of our hemodialysis patients. IVRT is more sensitive than E/A ratio in the diagnosis of diastolic dysfunction in our hemodialysis patients [14]. In the recent HEMO study, the most common cause of death in dialysed patients was ischemic heart disease (20.4%) followed by cardiac rhythm disorder (10.4%), cerebrovascular disease (8.6%) and infections (7.7%). The prospective Canadian study reported an incidence of approximately 10% per year for both ischemic heart disease and cardiac failure significantly higher than the values seen in the

general population [15]. The features of uremic cardiomyopathy like Left ventricular hypertrophy, diastolic dysfunction, and systolic dysfunction were detected in 40%, 24% and 40% of our hemodialysis patients [16]. These rates were comparable to those reported in previous studies. In non-renal patients, hypertension and left ventricular hypertrophy are closely related, but this relationship is less marked in patients with renal failure. LV hypertrophy develops in uremic animals despite normalization of blood pressure by administration of angiotensin converting enzyme inhibitors, alpha and betablockers or diuretics [17]. LV hypertrophy progresses with time on dialysis even when patients kept normotensive. LVH tend to be associated with hypertension, anemia, high arteriovenous fistula flow and poor control of volume overload. At an early stage,the systolic function is usually normal or even increased but evidence of diastolic dysfunction can be found even in asymptomatic patients [18]. LVH is not an innocent finding, it is an independent predictor of death in dialysis patients. Several studies have shown that hypoalbuminemia is a powerful predictor of poor outcome in patients with ESRD. Hypoalbuminemia is associated with LV dilatation and predisposes to cardiac failure. The mechanisms underlying this association are unknown [19]. Hypoalbuminemia is associated with a hypercoagulable state and therefore may predispose to myocardial infarction and ischemic cardiomyopathy. Congestive heart failure may result from systolic dysfunction or diastolic dysfunction, the latter occurring because of left ventricular concentric or eccentric hypertrophy. Ischemic heart disease is an additional independent predictor. Among patients with diastolic dysfunction, congestive heart failure results from impaired ventricular relaxation. This leads to an exaggerated increase in left ventricular end-diastolic pressure for a given increase in end-diastolic volume [20]. As a result, a smallexcess of salt and water can rapidly lead to a large increase in left ventricular end-diastolic pressure, culminating in pulmonary edema. In dilated cardiomyopathy, cardiac output is maintained at the expense of an increase in both end-diastolic fiberlength and end-diastolic volume [21]. Congestive heart failure carries a poor prognosis. Actual survival at 2 years is not more than 33% as compared to 80% in patients without heart failure. Previous studies reported 61% diastolic dysfunction in 61% of 86 patients, with nearly 48% of patients with diastolic dysfunction having an STI index within normal limits and the remaining 52% of patients with systolic dysfunction having a normal IVRT [22]. In comparison with this study, we observed, 24% of our patients had diastolic dysfunction and 40% had systolic dysfunction. These rates were definitely less than to those reported in the previous study. This may be related to the small sample size of our study. We also observed combined systolic and diastolicdysfunction in only 12% of our patients which is again very low compared to the previous study in which 30% of patients had combined systolic and diastolic dysfunction [23]. Our study markedly differs from the previous one where only half of the patients with systolic or diastolic dysfunction had normal IVRT or STI index [24]. But in our study, 90% of patients with systolic dysfunction had normal IVRT and 84.4% of patients with diastolic dysfunction had normal STI index. However, as in the previous study, the impaired STI index, and prolonged IVRT are independent of the presence of hypertension or left ventricular hypertrophy and IVRT is more sensitive than E/A ratio to diagnose diastolic dysfunction [25]. In our study, we have observed that in hemodialysis patients, latent systolic or diastolic dysfunction may coexist or be present alone, and can be diagnosed using non-invasive Doppler study even before the overt decline in the left ventricular ejection fraction [26].

Conclusion

The most common features of uremic cardiomyopathy namely left ventricular hypertrophy, diastolic dysfunction and systolic dysfunction were present in 40%, 24%, and 40% of our hemodialysis patients respectively. The diastolic dysfunction and latent systolic

dysfunction (STI >0.4) were randomly distributed. Impaired STI index and prolonged Isovolumetric relaxation time are independent of the presence of hypertension or left ventricular hypertrophy.

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