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Original Article

Echocardiographic Findings in Hemodialysis Patients in a Tertiary Care Hospital

Nayab Balqees, Sajjad Hussain, Rizwan Yusuf, Mir Jalal-ud-Din*, Jahanzab Ali, Tabasum Muzaffar***, Hafsa Khalil****, Shaista Naseem****, Ayesha Sana******

Combined Military Hospital Abbottabad/National University of Medical Sciences (NUMS) Pakistan, *Woman Medical College & Hospital, Abbottabad Pakistan **Armed Cardiac Center, Lahore Pakistan, ***Combined Military Hospital/National University of Medical Sciences (NUMS) Rawalpindi Pakistan, ****Armed Forces Institute of Cardiology/National Institute of Heart Diseases (AFIC/NIHD)/National University of Medical Sciences (NUMS) Rawalpindi Pakistan

ABSTRACT

Objective: To find out the echo abnormalities in a south Asian cohort on maintenance hemodialysis in a tertiary care hospital.
Study Design: Descriptive cross-sectional study.
Place and Duration of Study: Combined Military Hospital Abbottabad, from Feb 2022 to Apr 2022.
Methodology: 57 adult patients on maintenance hemodialysis had a non-contrast transthoracic echocardiographic study recording parameters of left and right ventricular systolic and diastolic function.
Results: We had 57 patients. 71.9% (n=41) were male, and females 28.1% (n=16), diabetics 47.4 % (n=27), hypertensives 84.2% (n=48), smoking 28.1% (n=16); 15.8%(n=9) had some form of ischemic heart disease. Left ventricular hypertrophy was noted in 78.9% (n=45) of the entire patient population. 84% (n=48) of hypertensive patients had LVH. Overall, 82% (n=47) of hypertensive patients had some degree of diastolic dysfunction compared to non-hypertensive patients (p<0.0001). Diastolic dysfunction of Grades I, II, III was seen in 35.1%(n=20), 29.8%(n=17), 17.5% (n=10). Mean E/e' ratio was 24.9±15, with 40.3%(n=23) having a value ≥15. The LV systolic dysfunction noted was: Mild 26.3%(n=15), Moderate 19.3%(n=11), Severe 1.8%(n=1). For the medial mitral annular systolic velocity(s') 19.3%(n=11) had normal s', while 80.7%(n=46) had reduced s'. The mean Pulmonary artery acceleration time (PA-AT) was was <100 ms in 68.4%(n=39). The mean tricuspid plane systolic excursion (TAPSE) was < 17 mm in 19.3%(n=11) of patients indicating RV systolic dysfunction. The Minimum PASP was 16, max 64, mean 41.5±14mm Hg.
Conclusion: In our study of CKD patients on regular hemodialysis, we found high rates of LVH, DD, LV systolic dysfunction, RV systolic function, and pulmonary hypertension. This creates a case for a larger scale study of these patients in a south Asian cohort as well as institution of a screening program in CKD patients on hemodialysis.

Keywords: Chronic kidney disease, End-stage renal disease, Hemodialysis, Left ventricular hypertrophy, Mitral annular calcification, Mitral annular velocities.

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INTRODUCTION

Chronic kidney disease (CKD) is defined as abnormalities in renal function characterized by reduction in glomerular filtration rate (GFR) <60 mL/min/1.73 m^2 that have been present for >3 months and have an impact on health.[1] CKD and cardiovascular diseases (CVD) share multiple interfaces, especially in patients with diabetes mellitus (DM) and hypertension (HTN). The increased morbidity and mortality in CKD can be due to a wide range of clinical entities. The cardiovascular consequences of CKD include left ventricular hypertrophy (LVH), Left ventricular (LV) diastolic dysfunction, LV systolic dysfunction due to uremic cardiomyopathy, accelerated calcification in vessels, mitral annulus,[2] aorto-mitral curtain and the aortic valve. CKD also predisposes patients to contrast induced acute kidney injury. Of the 25% of patients who develop a cardiorenal syndrome during hospitalization for heart failure, approximately one third recover baseline renal function, one third have a residual reduction in eGFR, and the final third have progressive cardiorenal disease resulting in either death or the need for renal replacement therapy.[3] Importantly, the long-term cardiac outcomes in renal patients are worse than the general population. 50% of patients with CKD stage 4 to 5 have CVD,[4] and half of all deaths in patients with CKD 4 to 5 are due to CVD,[5] compared with 26% in controls with normal kidney function. The current gold standard for myocardial tissue characterization in health and disease is Cardiac Magnetic Resonance (CMR). The inherent risk of Nephrogenic systemic fibrosis in patients with chronic kidney diseases precludes the use of Gadolinium in these patients, leaving the field open for echocardiography for detection of cardiovascular complications and associations of CKD.

Correspondence: Dr Sajjad Hussain, Department of Medicine, Combined Military Hospital, Abbottabad, Pakistan

In this study we sought to study the echo abnormalities in CKD patients on maintenance hemodialysis.

Objective: To find out the echo abnormalities in a South Asian cohort on maintenance hemodialysis in a Tertiary Care Hospital.

METHODOLOGY

This study was conducted at Combined Military Hospital, Abbottabad from February 2022 to April 2022 by taking formal approval from ERC(Ltr#2020-012-17044)

Sample Size: The sample size was calculated using Open Epi sample size calculator by taking 26% prevelance of CKD in cardiovasular diseases[6] was n=57.

Inclusion criteria included all adult patients on maintenance hemodialysis who consent to a non-contrast echo study.

Exclusion criteria included, non consenting patients, suboptimal image quality of the echo study, patients with known congenital heart disease and valvular heart disease, active acute coronary syndrome, acute decompensated heart failure.

Transthoracic echocardiogram (TTE) was performed on all patients undergoing hemodialysis at this hospital who fulfilled the inclu-sion criteria. All TTE studies were done with ECG gating, and the measurements performed and classi-fied according to Recommendations for Cardiac Cham-ber Quantification by Echocardiography in Adults by the American Society of Echocardiography and the European Association of Cardiovascular Imaging.[6] The TTE was performed on a Vivid E9 (GE Corp, USA) echo cardiography machine using the M5S Echocar-diographic probe (4.6 MHz). Where the images were suboptimal, an attempt was made to use the 4V Echocardiographic probe (4.0 MHz) which can simul-taneously image in 2 planes and generate 3D images. All echocardiograms were performed by a Cardiologist Board certified in Echocardiography.

The imaging plane chosen for the imaging of the RV was the RV-focused apical 4 chamber view. Tissue harmonic imaging was employed to improve image quality. The image settings were chosen to provide a clear delineation between the endocardial and myocardial borders.

We measured LV volume, LVEF by Simpson's biplane summation method, and mitral inflow pattern using pulsed-wave Doppler, positioned at the mitral leaflet tips during diastole at end-expiration. These measurements included the peak early (E) and late (A) diastolic velocities and the E/A ratio. Pulse Doppler (PW) tissue imaging of mitral annular movement was acquired from the apical four-chamber view with a 2-mm sample volume was placed at the septal side of the mitral annulus. To obtain the peak systolic (s') and early diastolic (e') velocity, we measured three end-expiratory beats and averaged these values for further analysis. We used the septal e' velocity sides of the mitral annulus, to calculate the ratio of mitral inflow E velocity to e' velocity (average E/e'). Mitral annular calcification (MAC) was defined as the presence of dense echo structure located at the junction of the atrioventricular groove and the posterior or anterior mitral leaflet on the parasternal long-axis, apical four-chamber, or two-chamber view. Settings for the doppler measurements were as follows: the sweep speed was set to 100 cm/sec; the baseline and scale was shifted to optimize the entire doppler signal of interest as large as possible. All doppler studies were done in greyscale. For PW Doppler, the gain was set to ensure a clear doppler envelope without excess background noise. Sample volume was set at 4-5mm. With regard to the maximal thickness of the dense echo structure, the severity of MAC was categorized into two groups: mild to moderate (1–4 mm) and severe (>4 mm). We used color flow imaging to determine the absence or presence of mitral or aortic regurgitation. According to ASE recommendations, the severity of mitral or aortic regurgitation was graded using the following measurements: jet area, vena contracta width, pressure half-time of the regurgitant jet for aortic regurgitation severity grading and structural parameters (i.e., mitral and aortic leaflet, left atrial, and LV size). The results were averages of three measured values. When measuring the RV systolic and diastolic areas, the myocardial trabeculations were included as a part of the RV cavity. All studies were done in greyscale, where the greyscale images did not allow for adequate delineation of endomyocardial interface, we changed the greyscale setting to other colors. For measurements, the PW Doppler sample volume was placed in the center of the RVOT, about 5–10 mm proximal to the PV. Sweep speed was set at 100cm/sec. Image analysis was done with the analysis tools on the machine at the time of examination.

The list of variables studied is listed in the data collection form (Annex A). These were entered into Microsoft Excel 2019 and further exported for analysis to SPSS v23. The data was summarized using descriptive and inferential statistics. Mean and standard deviation were reported for the scale variables; and

frequencies reported for the nominal variables. Where means were compared a *p*-value less than 0.05 was deemed as significant.

RESULTS

Our study had a total of 57 patients of whom 71.9% (n=41) were male, and females 28.1% (n=16), diabetics 47.4 % (n=27), hypertensives 84.2% (n=48), smoking 28.1% (n=16); 15.8%(n=9) had some form of ischemic heart disease. Left ventricular hypertrophy (LVH) was noted in 78.9% (n=45) of the entire patient population. 84% (n=48) of hypertensive patients had LVH. Overall, 82% (n=47) of hypertensive patients had some degree of diastolic dysfunction (DD) compared to non-hypertensive patients (p<0.0001). DD of Grades I, II, III was seen in 35.1%(n=20), 29.8%(n=17), 17.5% (n=10) respectively as shown in Table-I.

Table-I: Baseline charcacteristics of patients

Variables(n=57)		n (%)
Gender	Male	41(71.9%)
	Female	16(28.1%)
DM		27(47.4%)
HTN		48(84.2%)
Smoking		16(28.1%)
IHD		9(15.8%)
Left ventricular hypertrophy (LVH)		45(78.9%)
Diastolic dysfunction	Grade-I	20(35.1 %)
	Grade-II	17(29.8%)
	Grade-III	10(17.5%)
Normal Diastolic function		5(8.8%)

8.8%(n=5) had normal diastolic function and 8.8% (n=5) The Mean E/e' ratio was 24.9±15, with 40.3% (n=23) having a value ≥15 indicating a raised Left atrial pressure (LAP). The LV systolic dysfunction was subcategorized by ejection fraction (EF) into mild, moderate, severe categories based on ejection fraction. The distribution was: Mild 26.3%(n=15), Moderate 19.3% (n=11), Severe 1.8% (n=1). 52.6% (n=30) had normal LV function as shown in the Figure-1.

The medial mitral annular systolic velocity(s') measured by PW doppler was categorized into 2 categories of "normal" and "reduced" using a cut off of 7.5 cm/sec. 19.3% (n=11) had normal s', while 80.7% (n=46) had reduced s'. The percentage of people with reduced s' values in patients with normal EF was 85.1% (n=23), while in those with reduced EF 14.9% (n=7) had reduced s' values. The mean Pulmonary artery acceleration time (PA-AT) was 94.7±23.9 ms. The mean tricuspid plane systolic excursion (TAPSE) was 20.75±5 mm. 68.4% (n=39) had a value of <100 ms, indicative of pulmonary hypertension. TAPSE was less than 17 mm in 19.3% (n=11) of patients indicating RV systolic dysfunction. The Minimum PASP was 16, max 64, mean 41.5±14 mm Hg. Other scale clinical and echo data is presented in Table-II.

Figure-1: LV Systolic Dysfunction Sub characterized by EF

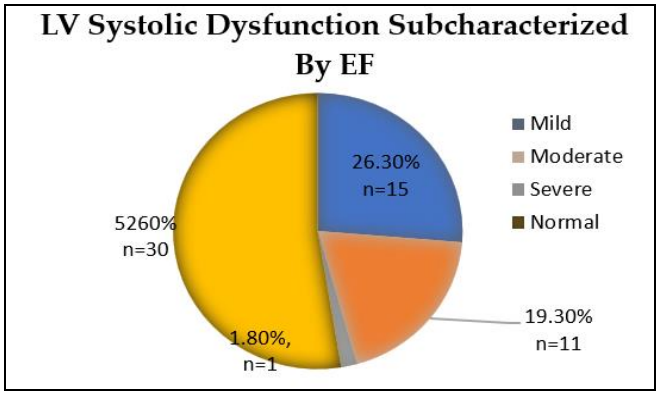

Table-II: Clinical and Echo Data

	Min	Max	Mean±SD
Age	32	75	56.67±11.24
Height (cm)	150	180	166.61±8.15
Weight (kg)	45	92	62.74±11.79
Frequency of HD (sessions/ week)	1	3	2.02±0.48
Time since last HD (hours)	0.5	2.0	1.202±0.60
LVIDd	30	62	47.96±8.72
LVIDs	20	51	36.46±8.95
IVSd	9	23	12.63±3.16
PA diameter (mm)	17	70	26.96±7.26
RV Systolic area (cm)	6	26	18.62±6.15
RV Diastolic area (cm)	13	36	27.80±7.25
FAC (%)	14	57	33.94±10.66
MV E wave (cm/sec)	36.00	162.00	96.1228±35.91
MV A wave (cm/sec)	34.00	148.00	89.9649±34.78658

In other findings 14% (n=8) patients had varying degrees of mitral annular calcification (MAC). Five patients had severe mitral regurgitation (MR), 3 had moderate and 1 patient had mild MR. The aortic valve was calcified in 8 patients. We only found one patient who had a mild pericardial effusion, without a tamponade effect.

DISCUSSION

Our study results show an overall high (82%) prevalence of some degree of diastolic dysfunction in hypertensive patients. The LV systolic function (EF) was normal in 52.6% patients, while the rest had reduced LV systolic function. The s' was reduced in 80.7% of subjects indicating a reduction in LV systolic function. The percentage of people with reduced s'

values in patients with normal EF was 85.1% meaning that there was a subtler element of LV systolic dysfunction that was below the detection range of the biplane Simpson's method. Conventional measures of systolic function may be preserved until late in CKD. Measures of myocardial deformation such as GLS have been found to be impaired early in the course of CKD (stage 2 or 3) in the absence of previous history of diabetes mellitus or cardiovascular disease.[7] As discussed above, in our we found the s' to be decreased in patients despite a preservation of EF. In one study early changes in s' in hypertensive patients with and without concomitant DD despite a normal EF.[8]

In a study of more than 20,000 patients it was seen that patients with stage 4 and 5 CKD had more severe diastolic dysfunction and reduction in ejection fraction. Furthermore, the 3-year mortality was higher in these patients compared to those in CKD stage 1 and 2. This study suggested that the current practice of cardioprotection for CKD patients should be prioritized at an early stage.[9] The different echocardiographic changes and their clinical significance in CKD patients warrant some discussion. The diastolic dysfunction in patients with CKD may be multifactorial. Changes in myocardial echotexture may have a significant role in this. While investigating the effect of hemodialysis on myocardial tissue characterization on echo using myocardial cyclic variation of integrated backscatter (CVIBS) Fijalkowski *et al.* found that fluid reduction caused by hemodialysis is associated with a reduction in myocardial water content as well and thus reduction in CVIBS and LA volume.[10] These findings are supported by cardiac MRI of similar patients. Cardiac MRI scans of patients on hemodialysis have shown a reduction in native myocardial T1 values immediately after HD indicating that there is a significant component of myocardial edema that settles after hemodialysis.[11] In another study it was shown that echocardiographic diastolic dysfunction and cardiac fibrosis are common in patients on hemodialysis with preserved ejection fraction, and are associated with an elevation in serum levels of procollagen type I C-terminal peptide (PICP) which is a marker of myocardial fibrosis. The study conclusions raised the possibility of PCIP being a future marker for detecting diastolic dysfunction in patients on hemodialysis.[12] The above data point to reversible myocardial edema as well as irreversible myocardial fibrosis as possible etiologies of diastolic dysfunction that need further evaluation. In relation to diastolic dysfunction, mitral E/e' ≥15 has been shown to accurately predict LV filling pressures or Left atrial pressure (LAP), and mortality.[13] In our study the Mean E/e' ratio was ≥15 in 40.3% indicating a raised LAP. Patients with CKD and heart failure benefit more from the combined use of transmitral doppler velocities and eGFR in determining the prognosis.[13] Left ventricular DD has also been shown to be a significant predictor of rapid decline in residual renal function and adverse cardiac out comes in in patients starting peritoneal dialysis.[14] LV mechanical dispersion and GLS were found to be predictive of arrhythmia risk and sudden cardiac death in patients on peritoneal dialysis.[15]

RV dysfunction and pulmonary hypertension is associated with increased mortality in CKD patients.[16] In our study the mean FAC was reduced (33.94%) to <35% indicating RV systolic dysfunction. Similarly, TAPSE was less than 17mm in 19.3% of patients indicating RV systolic dysfunction. 3D TTE and CMR take into account the pyramidal shape of the RV and are the ideal investigations for determining RV function and are better than TAPSE and FAC. In our study we found markers of pulmonary hypertension. The mean PASP was 41.5±14mm Hg. The normal PA-AT is > 100ms, and a value ≤100 ms reflects abnormal Pulmonary artery pressures. In our study 68.4%(n=39) had a value of <100 ms.

Mitral annular calcification, is a frequent finding in patients with CKD (36%),[17] and it is associated with inflammation (higher C-reactive protein levels) and may indicate increased cardiovascular risk.[18] In our study 14% (n=8) patients had varying degrees of mitral annular calcification (MAC). The low number may be due to a smaller sample size, and the true prevalence would be suggested by a larger sample. Valvular aortic stenosis is frequently seen in CKD patients (28%).[19,20] Calcification of the aortic valve is an independent predictor of progression to aortic stenosis in patients on hemodialysis.[21] In our study 14% (n=8) patients had aortic valve calcification.

LIMITATIONS OF STUDY

In our study we did not evaluate cardiac mechanics by the advanced technique of strain and strain rate. Using these techniques may have led to an increased detection of cardiac mechanical abnormalities.

CONCLUSION

In our study of CKD patients on regular hemodialysis, we found high rates of LVH, DD, LV systolic dysfunction, RV systolic function, and pulmonary hypertension. This creates a case for a larger scale study of these patients in a south Asian cohort as well as institution of a screening program in CKD patients on hemodialysis.

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Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

NB: Concept, design,manuscript writing, approval of the final version to be published

SH: Data analysis,manuscript writing, interpretation of data
RY: Concept, manuscript writing, approval of the final version to be published

MJD: Data analysis, manuscript writing, approval of the final version to be published

JA: Data analysis

TM: Intellectual contribution, interpretation of data, data analysis

HK: Data analysis,

SN: Intellectual contribution, Intellectual contribution, manuscript writing

AS: Data collection, manuscript writing, Concept

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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