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Assessment of Left Ventricular Function by Global Longitudinal Strain in Male Patients with End Stage Renal Disease

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1. Abstract

1.1. Background: In chronic kidney disease and following end-stage renal disease (ESRD), heart failure is the most common cardiovascular illness linked with poor outcomes. However, left ventricular systolic function seems to be retained in renal patients.

1.2. Aim of the study: Assessment of subclinical left ventricular systolic failure in patients with varying degrees of renal function impairment by global longitudinal strain (GLS), and compare it with other parameters.

1.3. Patients and Methods: This case control study was done in Baghdad Teaching Hospital to analyze demographic, clinical and ultrasound data of 105 consecutive renal patients including left ventricular global longitudinal strain and mitral E peak velocity and ratio of mitral to myocardial early velocities (E/e') (50 with early stage, 55 with advance end-stage renal disease on hemodialysis). LV ejection fraction was more than 55% in all cases. To estimate the probability of a compromised GLS, we performed a multivariable logistic analysis. 60 control participants were used as controls.

1.4. Results: Patients with end stage renal disease on hemodialysis showed higher systolic pressure and a substantially higher prevalence of increased LV mass and diastolic dysfunction, global longitudinal strain associated with end stage renal disease patients on hemodialysis. At logistic regression analysis, E/e' ($p = 0.035$) was found to be an independent predictor of impaired global longitudinal strain in renal patients. E/e', systolic artery pressure, and LV mass were similarly shown to have the highest areas under the curve when using receiver operating characteristic analysis to detect a deteriorated global longitudinal strain.

1.5. Conclusion: Renal disease has been linked to early and subclinical deterioration of LV systolic function, which continues following dialysis. A higher E/e' ratio was shown to be the most effective independent predictor of abnormal GLS.

2. Introduction

Patients with end-stage renal disease (ESRD) on chronic hemodialysis (HD) have a high rate of morbidity and death, with a median survival period of 50 months after starting HD [1]. This patient group is prone to coronary heart disease (CHD), with a high prevalence of ischemic heart disease (IHD), valvular heart disease, and congestive heart failure (HF) [2]. Cardiovascular disease prevalence in ESRD, adult chronic HD patients are around 70%, and coronary artery diseases followed by heart failure are the most often reported condition. The significant fluctuation of body weight and volume during HD leads to unfavorable changes in cardiac function [3]. Therefore, evidence is increasing in adult studies that include HD in recurring sub-clinical myocardial injuries, even if the effects of the ECG, positron emissions tomography, cardiac troponin levels and varying ECHO are not obvious, even in the absence of any evident Coronary Artery or Atheroma [2]. On the other hand, there is little evidence in the juvenile age range of noninvasive studies supporting the indicated myocardial impression due to hemodialysis in the absence of atheromatous coronary artery disease [4]. Most echocardiographical research studies by conventional echocardiography in addition to tissue Doppler-derived parameters examined alterations in the systolic and diastolic cardiac functions following HD [5]. However, one of the limitations of this approach is that Doppler technology is angle-dependent.

New approaches have been proposed, including 2-dimensional speckle tracking. A major benefit of the Doppler tissue imaging approach is that it is not restricted by angle dependence and allows for systemic computing of global and segmental strains. Although, acute effects of HD have been examined in several adult trials, with contradictions results, for heart functions employing speckle echocardiography [6]. The use of the guideline is often not suitable owing to considerable co- morbidity and fragility as medical and intervention therapy [7]. In the early stages of renal insufficiency, structural changes of the myocardium dominated by hypertrophy of the left ventricular (LV) and focus remodeling are common [8]. Both comorbid diseases such as diabetes and hypertension, together with advanced renal disease, lead to LV hypertrophy and fibrosis in patients with ESRD and eventually to LV impaired with or without clinical HF [9]. In patients with renal failure, diastolic dysfunction (DD) is very common although estimating the severity of LV-impairing depends significantly on echocardiography conditions. During normal HD regimens, there will be significant fluctuations in intravascular volume, which might significantly influence the measurements utilized in the grading and evaluation of the DD [10]. GLS represents the myocardial longitudinal contraction and is verified for tagged magnetic resonance imaging (MRI) [11]. This approach can simply be measured and included in conventional echocardiography methods independently from the operator, replicable more than EF [12]. GLS has been demonstrated to be a superior predictor of cardiac events and overall mortality compared to EF in the general population and patients with heart failure. GLS has been proven to be a strong prognostic marker in individuals with cardiomyopathy and aortic stenosis following myocardial infarction and cardiac surgery in more recent days [11].

3. Subjects and Methods

This descriptive cross-sectional study was conducted at the cardiology department, echocardiography laboratory of Baghdad teaching hospital, Baghdad-Iraq, on 105 male individuals including patients with early (patients who received less than 10 sessions of dialysis), ESRD on HD and patients with advanced (patients who received more than 25 sessions of dialysis), ESRD on HD (the early and advanced: we assumed just to compare the Echo parameters among patient who just start dialysis sessions and those who received dialysis sessions for a while). The study was carried out during the period from May 2020 to February 2021. The working days were five days per week; 6 hours per day. ESRD patients with no history of major clinical events in the last 6 months were considered eligible for this study, and patients attending the tertiary care Nephrology Outpatient Unit were chosen. In addition, 60 male patients with normal renal function normotensive healthy controls were selected as a control group. The following cases were excluded from our study: Patients with angina, revascularization operations, evidence of segmental wall motion abnormalities during echocardiography, history of heart failure, aortic or mitral valve diseases, severe mitral annular calcification, hypertrophic cardiomyopathy, cardiomyopathy, stroke, peripheral artery disease and CKD. The echocardiographic studies included two-dimensional, M-mode, pulsed Doppler, and pulsed tissue Doppler imaging examinations performed using a commercially available ultrasound system (GE VIVID 9). The measurements were taken in accordance with the recommendations established by the American Society of Echocardiography.The modified Simpson's rule was used to compute LV volumes and EF from apical two- and four-chamber images. The LV mass was computed and the body surface area was indexed. The size and volume of the left atrium were also measured. The ratio of posterior wall diastolic thickness multiplied by 2 and end-diastolic diameter was used to determine relative wall thickness. As previously mentioned, midwall fractional shortening (MWFS) was computed. Tissue Doppler longitudinal velocities were measured from the 4-chamber view, with the sample volume positioned at the intersection of the LV wall (medial and lateral) and the mitral annulus. The ratio of early transmitral flow to early diastolic mitral annular velocity (E/e') was then calculated. GLS was computed by averaging the values of regional peak longitudinal strain recorded in each apical image prior to aortic valve closure, as specified in the apical long-axis view. Less negative values reflect progressive impairment in GLS and therefore in LV systolic function. In HD patients, the echocardiographic study was performed before or after dialysis session. GLS of -18% and above was considered normal, while values -16% and below was considered abnormal. Verbal communication with each participant regarding the aim of this study was conducted. Verbal consent from each participant was obtained before data collection. An ethical clearance of the study was obtained from The Ethical Committee in the Iraqi MOH, after getting the scientific approval.

4. Data Analysis

Data were analyzed using the IBM SPSS Software Package version 26. Data were shown as (mean ± SD) for continuous variables and as proportions for categorical variables. Normality of distributions was assessed using the Shapiro-Wilk test. Comparisons between continuous variables were analyzed by ANOVA. Bonferroni test was used to compare single pairs of groups. The $\chi 2$ test was used to compare categorical variables. All variables showing a p value ≤ 0.05 at univariate analysis were tested in multivariable models.

5. Results

Of the (165) male individuals who visited the echocardiography department during the study period, 105 (63.6%) patients had a diagnosis of ESRD on hemodialysis, 50 (30.3%) with Early ESRD versus 55 (33.3%) with Advance ESRD. The majority of participants aged (31-35) years (52.1%), while median age was 34 years. More than one third (40%) did not complain of known comorbidity, while (36.9%) were hypertensive and (23.1%) were diabetic (Table 1). In (Table 2) the mean and the standard deviation of the important echo parameters was EF 60.3±3.6, E/e'10±2.7

and GLS -18.3±2.8, while the other parameters were (103±23, 40±10, 42±16, 0.43±0.07, 182±58 and 19) for (LVEDV, LVESV, Left atrial volume, RWT, LV mass and LV diastolic function) respectively. (Table 3) showed that patients with renal disease (Early and Advance ESRD) were older, had higher systolic pressure, and a significantly greater prevalence of increased LV mass and diastolic dysfunction compared to controls. While according the echo parameters show that highly significant increase in the LV mass in early and advance ESRD comparted with control in addition the most important finding was the GLS was statistically significant decrease in early and advance ESRD (-17.2 and -16) in comparison with control patients (-21.2) (Table 3). Univariate and multivariate logistic regression analyses for the prediction of compromised GLS are shown in (Table 4). E/e' (p = 0.035) was independently associated with a GLS <–18%, while other variables found to be non-significant.

Table 1: Demographic characteristics of participants (N=165)

Demographic characteristics	Number	%
Age group (years)		
25-30	58	35.2
31-35	86	52.1
35-40	21	12.7
Mean ± SD age	31.725 ± 6.21	
ESRD		
No ESRD	60	36.4
Early ESRD on HD	50	30.3
Advance ESRD on HD	55	33.3
Comorbidities		
No known comorbidities	66	40
Hypertension	61	36.9
Diabetes Mellitus	38	23.1
Blood pressure (Mean±SD)		
Systolic blood pressure	137±19	
Diastolic blood pressure	78±8	

Table 2: Echo parameters of participants (N=165)

Echo Parameters	(Mean±SD)
LVEDV	103±23
LVESV	40±10
EF	60.3±3.6
Left atrial volume	42±16
RWT	0.43±0.07
LV mass	182±58
E/e'	10±2.7
GLS	-18.3±2.8

Table 3: Distribution of different variables with early and advance ESRD and control patients (n=165)

Variable	Early ESRD on HD n=50	Advance ESRD on HD n=55	Control n=60	P value
Age	34±10	31±9	28±6	<0.0001
Hypertension (%)	45(90%)	46(83.6%)	0(0%)	<0.0001
SBP	150±19	142±25	120±11	<0.0001
DBP	71±14	83±4	79±5	0.0001
LVEDV	99±19	110±24	101±26	0.053
LVESV	37±9	46±10	38±10	0.0032
EF	61±2	57±3	64±6	0.0012
Left atrial volume	35±10	49±29	45±11	0.0003
RWT	0.45±0.08	0.46±0.09	0.38±0.06	0.0001
LV mass	167±41	216±77	151±55	<0.0001
LV diastolic function	21	30	7	0.0052
E/e'	9.9±2.7	11.5±3.2	9.6±2.1	0.0005
MWFS	15.7±3.0	15.5±3.1	16.1±2.0	0.0697
GLS	–17.2±2.2	–16.0±2.1	–21.2±3.5	<0.0001

Table 4: Predictors of GLS in patients with early and advance ESRD on HD with normal ejection fraction by logistic regression analysis

Variable	Univariate OR (95% CI)	P value	Multivariate OR (95% CI)	P value
Age	1.12 (1.02–1.05)	0.069	1.11 (0.99–1.11)	0.78
Hypertension	5.08 (1.01–24.15)	0.071	5.21 (0.19–167.19)	0.51
SBP	1.02 (0.97–1.07)	0.052	1.04 (1.01–1.19)	0.62
DBP	1.01 (0.95–1.11)	0.081	1.00 (0.91–1.10)	0.61
EF	0.82 (0.76–0.99)	0.019	0.46 (0.08–2.59)	0.46
Left atrial volume	1.07 (1.01–1.15)	0.0003	1.09 (1.00–1.19)	0.2
E/e'	1.79 (1.15–2.23)	<0.0001	1.71 (1.00–2.59)	0.035

6. Discussion

Renal disease is linked with early and subclinical impairment of LV systolic function, as indicated by aberrant GLS, independent of renal function deterioration degree, according to our findings. Although all of the patients in our study had normal standard EF, individuals with early and advanced ESRD on dialysis exhibited lower negative GLS values as compared to controls. These findings are consistent with previous studies by TP Okawa et al [13], and Ravera M et al [14] who found less negative LV global longitudinal strain values in ESRD patients than in controls, whereas our results differed from a previous study by Liu Y.-W et al [15] who found better GLS values in ESRD patients on dialysis treatment than in those with ESRD who did not require dialysis yet. We have no reliable explanations for this disparity because, in both studies, volume status was similar in non-dialysis and dialysis patients, ruling out chronic fluid overload as the cause of worse GLS in the group of CKD patients not receiving extracorporeal treatment, so the variation could be due to the sample size in our study being much smaller than the other studies. In our study, reduced subclinical LV systolic function was already present in early and advanced end stage renal disease, which was the same result reported by Nicola C. Edwards et al [16] in their Subclinical Abnormalities of Left Ventricular Myocardial Deformation in Early-Stage Chronic Kidney Disease. Also, in our study, the MWFS of renal patients and controls was nearly the same. Previously, Mauro Gori et al [17] reported decreased MWFS in CKD patients with intact EF, particularly those on dialysis for end-stage renal disease. Nisha Bansal et al [18] described MWFS as gradually deteriorating. Given that GLS was aberrant in participants at all stages of renal illness, it is possible that GLS could be regarded an earlier and more accurate predictor of future systolic function impairment in the renal population than MWFS. In our research, worsening GLS was significantly linked to LV hypertrophy and an aberrant E/e' ratio, which was shown to be the most potent independent predictor of abnormal GLS. Ernesto Paoletti et al [19] found that LV hypertrophy is one of the most important predictors of adverse CV and general outcome in renal patients, whereas Paula F. Orlandi et al [20] detected that it is the strongest predictor of subsequent HF development, both in early CKD and after kidney transplantation. Interestingly, Kathrin Untersteller et al [21] stated that increased

E/e' is a reliable and early marker of diastolic dysfunction, which is often found in patients with renal disease, whereas Thomas A. Mavrakanas et al [22] reported that higher E/e' was linked with worse CV prognosis. It is possible that early subclinical systolic and diastolic dysfunction coexist in renal illness, and this reciprocal connection is most likely responsible for the high morbidity rate reported in renal patients, regardless of disease stage.

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