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Assessment of LV Function by Global Longitudinal Strain in Patients with Chronic Kidney Disease

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Abstract: ***Background: Patients with chronic kidney disease (CKD) exhibit an increased risk of cardiovascular morbidity and mortality, with heart failure (HF) hospitalization being one of the most frequent cardiovascular events. Chronic pressure and volume overload as well as non-haemodynamic factors, such as oxidative stress and inappropriate rennin-angiotensin-aldosterone system activation, lead to the development of left ventricular (LV) systolic and diastolic dysfunction. Left ventricular ejection fraction (LVEF), calculated from two-dimensional echocardiography, is the most frequently used parameter to define LV systolic function, However, LVEF has been shown rather insensitive to the detection of LV systolic dysfunction, particularly in patients with CKD. Left ventricular global longitudinal strain (GLS), assessed with two-dimensional speckle tracking echocardiography, may provide more detailed information on LV systolic function.***

Keywords: Chronic kidney disease, left ventricular ejection fraction, global longitudinal strain

1. Introduction

Cardiovascular (CV) disease still remains the most important cause of morbidity and mortality in patients with renal disease [1]. Heart failure (HF) is the most prevalent CV disease observed in renal patients, either in early chronic kidney disease (CKD) or in end-stage renal disease (ESRD), and is associated with poor outcome [2, 3]. In CKD patients, conventional echocardiography is not sensitive in detecting early deterioration of cardiac function [4]. A novel imaging modality, speckle-tracking echocardiography with myocardial deformation (strain) analysis, is a semi-automated method for operator-independent quantification of myocardial systolic function.

Nevertheless, left ventricular (LV) systolic function as estimated according to conventional methods is preserved in a great proportion of patients with early CKD and in dialysis patients [5-7]. Thus, more accurate assessment of systolic function may significantly improve the detection of early subclinical LV systolic dysfunction in patients with renal disease, who are reportedly at increased risk of future HF or other major CV events.

Global longitudinal strain (GLS), which is the negative ratio of the maximal change in LV longitudinal length in systole to the original length as assessed by speckle tracking echocardiography, proved to be superior to standard LV ejection fraction (EF) in predicting cardiac events and all-cause mortality in the general population [7-8]. Abnormal GLS was independently associated with both all-cause and CV mortality also in patients with CKD and those undergoing hemodialysis (HD) [8-10].

This study evaluate LV function by speckle tracking echocardiography in subjects with different degrees of renal dysfunction, with the aim of ascertaining the role of renal impairment in early LV systolic dysfunction of subjects with normal standard EF.

Two-dimensional speckle-strain.

LV volumes and EF were calculated from apical two-and four-chamber views using the modified Simpson's rule. Speckled tracking echocardiography was performed on three consecutive cardiac cycles of two-dimensional LV images from the three standard apical views.

The endocardial borders were traced in the end-systolic frame of the two-dimensional (2D) images from the three apical views. Speckles were tracked frame-by-frame throughout the LV wall during the cardiac cycle and basal, mid and apical regions of interest were created. Segments that failed to track were manually adjusted by the operator. GLS was calculated as the mean strain of all 18 segments. Impaired GLS was defined as greater than −16% (a less negative value reflects a more impaired GLS) [11-13].

Objective

a) To characterize the relationship of GLS and estimated glomerular filtration rate (eGFR),
b) To evaluate the association of traditional and renal-specific CV risk factors with GLS

2. Methodology

An observational study, the study population will consist of patients with chronic kidney disease (CKD) and preserved left ventricular (LV) ejection fraction (EF). CKD will be defined as an estimated glomerular filtration rate (eGFR) of less than 60 mL/min/1.73 m2 for at least 3 months. LV systolic function will be assessed by global longitudinal strain (GLS) using two-dimensional speckle-tracking

echocardiography. GLS is a measure of the longitudinal contraction of the myocardium and can detect subtle changes in LV function

Sample Size:
100 patients with chronic kidney disease with or without hemodialysis

Inclusion Criteria
- Age ≥ 18 years
- Diagnosis of CKD with eGFR < 90 mL/min/1.73 m2
- Preserved LVEF (≥ 50%)

Exclusion Criteria
- History of coronary artery disease, heart failure, valvular heart disease, cardiomyopathy, arrhythmia or pacemaker implantation
- Acute kidney injury, dialysis or kidney transplantation
- Severe comorbidities such as cancer, liver cirrhosis, chronic obstructive pulmonary disease or autoimmune disease
- Poor echocardiographic image quality or contraindications to echocardiography

Statistical analysis
The data collected were entered into Microsoft excel 2019 and the master chart was created. The qualitative variable was expressed using frequency and percentage and the quantitative variable using mean and standard deviation. To compare the distribution of qualitative variables between the cases and controls, chi square test was used. To compare the mean between the CrCl groups, independent samples t test was used. To find out the correlation between creatinine clearance and GLS%, Pearson correlation coefficient test was applied. A P value of less than 0.05 was considered to be statistically significant.

3. Results

The mean age among the participants with CrCl< 60 was 50.04 ± 7.68 years and among those with CrCl> 60, the mean was 49.62 ± 5.65 years. The mean age was found to be similar between the two CrCl groups with P value of more than 0.05.66% were male in the CrCl< 60 group and in the CrCl>60 it was 72%. The distribution of sex was found to be similar between the groups with P value of more than 0.05. Among the participants in the CrCl< 60 group, 62% were diabetics and in the CrCl>60 group, the proportion was 58%. The proportion of hypertensives was 86% and 80% for those in the groups CrCl<60 and CrCl>60, respectively.24% had dyslipidaemia in the CrCl<60 and 18% had dyslipidaemia in CrCl>60 group. The proportion of diabetics, SHTN and dyslipidaemia was similar between CrCl< 60 and CrCl>60 groups with P value of more than 0.05, respectively. The mean CrCl in the CrCl< 60 group was 39.64 ± 1.40 ml/min/1.73m^2 and for the CrCl>60 group the mean was 70.40 ± 5.27 ml/min/1.73m^2. The mean was significantly lower in the former group than in the latter. All participants in the CrCl<60 group had undergone haemodialysis while none had undergone haemodialysis in the CrCl>60 group (Table 1).

The mean GLS% among those in the CrCl<60 was-15.95 ± 2.11% and in the CrCl>60 it was-18.45 ± 2.01%. The mean GLS% was more in the CrCl<60 group than in the CrCl>60 group with P value of less than 0.05 (Fig 1). The mean ejection fraction was 62.36 ± 4.82 % and 62.94 ± 4.40% among those with CrCl<60 and CrCl>60 groups, respectively. The mean ejection fraction was found to be similar between CrCl>60 and CrCl<60. The mean haemoglobin value was 9.93 ± 1.18 in the CrCl<60 group and the mean was 10.33 ± 0.88 in the CrCl>60 group. The mean RBS was 139.58±41.27 mg/dl in the CrCl< 60 group and 138.96 ± 39.21 mg/dl in the CrCl>60 group. The mean haemoglobin and mean RBS were similar between CrCl<60 and CrCl>60 groups with P value of more than 0.05 (Table 2).

Table 1: Baseline characteristics among the study groups

Variable		Clcr< 60 (n=50)	Clcr>60 (n=50)	P value
Age (in years)		50.04 ± 7.68	49.62 ± 5.65	0.756
Sex	Male	33 (66)	36 (72)	0.517
	Female	17 (34)	14 (28)	
Diabetes	Yes	31 (62)	29 (58)	0.683
	No	19 (38)	21 (42)	
SHTN	Yes	43 (86)	40 (80)	Aa
	No	7 (14)	10 (20)	
Dyslipidaemia	Yes	12 (24)	9 (18)	0.461
	No	38 (76)	41 (82)	
Clcr (ml/min/1.73m^2)		39.64 ± 10.41	70.40±5.27	0.001
Haemodialysis	Yes	50 (100)	0	0.001
	No	0	50 (100)	

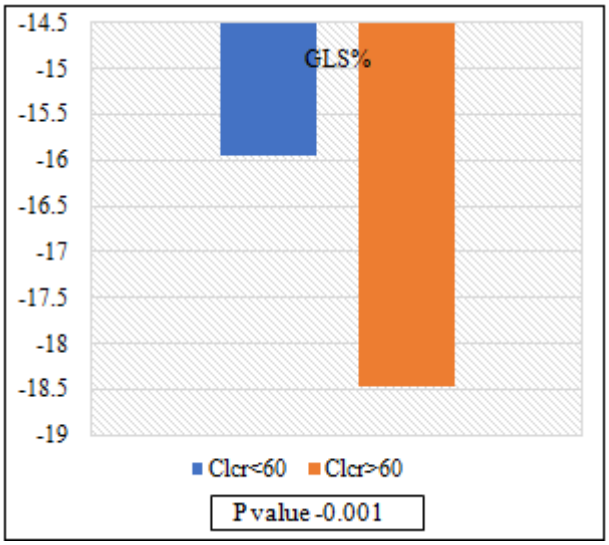

Figure 1: Comparison of GLS between Clcr<60 and Clcr>60.

Table 2: Other parameters compared between Clcr<60 and Clcr>60.

Variable	Clcr< 60 (n=50)	Clcr>60 (n=50)	P value
Ejection fraction (%)	62.36 ± 4.82	62.94±4.40	0.532
Haemoglobin (gm%)	9.93 ± 1.18	10.33 ± 0.88	0.056
RBS (mg/dl)	139.58 ± 41.27	138.96 ± 39.21	0.939

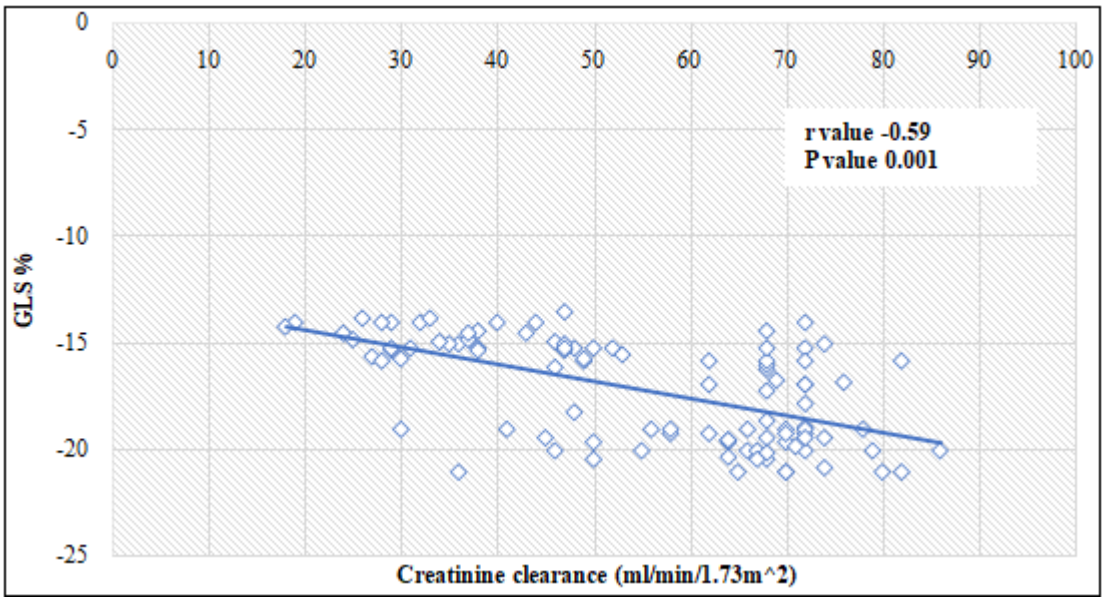

Figure 2: Correlation between Creatinine clearance and GLS% among the participants.

4. Discussion

This study evaluates the use of left ventricular global longitudinal strain (GLS) as a marker of left ventricular (LV) systolic function in chronic kidney disease (CKD) patients with preserved ejection fraction (EF). An important finding of our study is that renal disease is associated with early and subclinical impairment of LV systolic function, as expressed by abnormal GLS, regardless of the degree of renal function worsening. In our sample, although each patient had normal standard EF, less negative GLS values were demonstrated in both CKD and dialysis patients.

The rationale for using GLS as a measure of LV systolic function is based on several advantages over conventional echocardiographic parameters such as LV EF. GLS reflects the longitudinal contraction of the myocardium, which is mainly determined by the subendocardial fibers that are more susceptible to ischemia, fibrosis and hypertrophy than the subepicardial fibers [13]. Therefore, GLS can detect subtle changes in myocardial contractility and viability that may precede an overt impairment of LV EF. Moreover, GLS is less influenced by loading conditions, image quality and angle dependency than LV EF, and has higher reproducibility and feasibility [14].

Previous studies have shown that GLS is a sensitive and reliable marker of LV systolic function in various cardiac conditions, such as ischemic heart disease, valvular heart disease, cardiomyopathies and heart failure. GLS has also been shown to have prognostic value in these conditions, as it can predict adverse outcomes such as mortality, hospitalization, myocardial infarction, stroke and heart failure [15, 16].

However, there is limited evidence on the prognostic value of GLS in CKD patients with preserved EF. Only a few studies have investigated the predictive role of GLS for cardiovascular events or mortality in this population [15, 16]. These studies have reported conflicting results, possibly due to differences in study design, sample size, follow-up duration and outcome definition. Therefore, more studies are needed to confirm whether GLS can provide incremental prognostic information over conventional echocardiographic parameters in CKD patients with preserved EF.

CKD has been previously shown to be independently associated with lower values of LV GLS in patients with HF and preserved LVEF. The underlying mechanisms of decreased LV function in CKD patients are complex and not thoroughly understood. There are several contributing factors of LV dysfunction in CKD/ESRD patients, such as hypertension, diabetes mellitus, LV hypertrophy, LV remodeling, coronary artery disease, drop in capillary density, cardiac fibrosis, increased oxidative stress, apoptosis, and inadequate dialysis.

The study also has some limitations that should be acknowledged. First, the study will use a convenience sample of CKD patients from one tertiary care center, which may limit the generalizability of the findings to other settings or populations. Second, the study will use eGFR as a surrogate marker of renal function instead of measured GFR. Third, the study will not include patients with end-stage renal disease on dialysis who may have different patterns of LV systolic function and prognosis than non-dialysis CKD patients.

5. Conclusion

GLS is known to detect subtle cardiac changes such as myocardial hypertrophy and fibrosis and therefore may be a more sensitive discriminator. The results of this observational study should prompt future longitudinal investigations into the possible pathological mechanisms of impaired strain in CKD. The reliability and feasibility of strain assessment using 2D speckle tracking echocardiography should also encourage future application of this technique in clinical trials. Further studies are required to determine the impact of various interventions on GLS. For now, GLS is emerging as a promising tool for LV function assessment and monitoring in CKD and also improve the risk stratification and management of CKD patients with preserved EF, and potentially identify those

who may benefit from early intervention to prevent further cardiac deterioration and adverse outcomes.

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