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A prospective study of estimated glomerular filtration rate and proteinuria as predictors of left ventricular mass index in patients of chronic kidney disease

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Abstract

Background: Chronic kidney disease (CKD) has emerged as one of the most prominent causes of death and suffering in the 21st century. Due in part to the rise in risk factors, such as obesity and diabetes mellitus, the number of patients affected by CKD has also been increasing, affecting an estimated 843.6 million individuals worldwide in 2017.

Materials and methods: A comprehensive study analyzed 92 chronic kidney disease patients over 18 months. The study compared proteinuria, creatinine clearance, and serum creatinine levels with left ventricular mass.

Results: The decline in the estimated glomerular filtration rate and the increased protein excretion had a significant impact on the left ventricular mass index ($p < 0.01$). Patients with a normal left ventricular mass index had a mean GFR of 55 ml/min and a mean proteinuria of 2.2 g. In contrast, patients with an abnormal left ventricular mass index exhibited a mean GFR of 17.9 ml/min and a mean proteinuria of 8.5 g.

Conclusion: Cardiovascular events are the leading cause of illness and death, responsible for 40 – 50% of deaths among CKD patients. Therefore, early intervention to prevent extensive proteinuria and gradual decline in glomerular filtration rate through medication and dialysis could enhance the cardiovascular well-being of CKD patients.

Keywords: Estimated Glomerular Filtration Rate; Proteinuria; Left Ventricular Mass Index; Chronic Kidney Disease

1. Introduction

Chronic kidney disease (CKD) has become a leading cause of mortality and morbidity in the 21st century. Contributing to this trend are factors such as the increasing prevalence of risk factors like obesity and diabetes mellitus, leading to a rise in the number of individuals affected by CKD, which was estimated at 843.6 million worldwide in 2017[1]. Kidney Disease Outcomes Quality Initiative (KDOQI) definitively states that to confirm chronicity and chronic kidney disease (CKD), patients must undergo testing on three occasions over three months, with at least two of the three test results consistently showing positive findings[2].

The true incidence and prevalence of chronic kidney disease (CKD) are challenging to determine due to the asymptomatic nature of early to moderate CKD. The prevalence of CKD is estimated to be approximately 10% to 14% in the general population[3]. Similarly, albuminuria (microalbuminuria or A2) and GFR less than 60 ml/min/1.73 mt^2 have a prevalence of 7% and 3% to 5%, respectively[3]. As kidney function declines, cardiovascular disease (CVD) continues to be the primary cause of death. Patients with CKD face a significantly higher risk of cardiovascular events, with cardiovascular mortality representing approximately 40% to 50% of all deaths in patients with advanced CKD (stage 4) and end-stage kidney disease (stage 5), compared to 26% in individuals with normal kidney function[4,5]. The traditional risk factors for cardiovascular disease (CVD) include age, sex, hypertension, diabetes mellitus, and smoking.

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However, non-traditional risk factors such as anemia, proteinuria, volume overload, hyperparathyroidism, uremic toxins, hyperhomocysteinemia, and malnutrition have also been identified as causes of CVD in patients with end-stage renal disease.

Kidney dysfunction, whether indicated by reduced estimated glomerular filtration rate (eGFR) or albuminuria, serves as a marker of hypertensive target organ damage. It is also independently linked to increased mortality and a higher risk of cardiovascular events[6].

The existing longitudinal data are limited, but they suggest a bidirectional relationship between kidney dysfunction and left ventricular (LV) mass. There is evidence that a higher baseline LV mass index (LVMI) is linked to a lower estimated glomerular filtration rate (eGFR) and that LV hypertrophy (LVH) is associated with a rapid decline in eGFR[7]. More recently, studies in individuals without advanced kidney disease showed that lower baseline eGFR and rapid decrease in eGFR predicted higher future LVMI[8]. Furthermore, baseline albuminuria and change in albuminuria predict LVH regression and greater left ventricular mass (LVM)[9]. The combined influence of dynamic changes in both eGFR and albuminuria on LVM has not been previously documented. Additionally, the impact of the interaction between LVMI and eGFR decline rate on predicting renal outcomes in CKD patients is still uncertain.

The present study aims to examine the potential association between the combination of LVMI and eGFR decline rate, along with proteinuria, and the composite outcome of disease progression to maintenance dialysis or death in individuals with CKD.

Objectives of study

To assess the left ventricular mass index in CKD patients who receive conservative medical treatment, to determine the glomerular filtration rate of CKD patients using 24-hour creatinine clearance and the Cockcroft Gault formula, and to measure the amount of proteinuria using urine spot PCR and 24-hour quantification. Also, to investigate whether there is a significant relationship between the amount of proteinuria and glomerular filtration rate concerning the left ventricular mass index.

2. Materials and methods

A case study with detailed descriptions was conducted on 92 patients with chronic kidney disease who were admitted to the medicine ward or attended the medicine Outpatient department of Al-Ameen Medical College Hospital, Vijayapur, over 18 months from September 2022 to March 2024. The study excluded CKD patients under 18 years of age, those with a history of smoking and alcohol consumption, obesity, athletic training, undergoing maintenance hemodialysis treatment, with arterio-venous fistula or post renal transplant status, as well as those with aortic stenosis and hypertrophic obstructive cardiomyopathy.

The data was gathered using a specific form to meet the study objectives. A comprehensive history, physical examination, and general assessment, including vital signs, cardiac, respiratory, abdominal, and central nervous system assessments, were performed. Each patient's clinical information was recorded, and necessary tests were conducted. Blood and urine samples were obtained upon admission and in the outpatient department for calculating the urine spot protein to creatinine ratio and renal function. The 24-hour urine sample was examined for quantifying proteinuria and creatinine clearance. The left ventricular mass was determined using 2D echocardiography, and the Devereux formula was utilized to calculate the left ventricular mass index[10].

2.1. Statistical Analysis

The data obtained was entered into a Microsoft Excel sheet, and statistical analysis was performed using SPSS software(Version 20). Descriptive analysis was performed using Mean ±SD, frequency, percentages, and diagrams. Independent t-test or Mann-Whitney U test was used to find the significant difference between quantitative variables. Correlation between continuous variables was found by using Pearson's/Spearman's correlation. The association between Categorical variables was compared using the Chi-square test. $p<0.05$ was considered statistically significant.

2.2. Definitions used in the study

2.2.1. Serum creatinine value

- 0.7 to 1.3 mg/dL for men
- 0.6 to 1.1 mg/dL for women

2.2.2. Urine creatinine value:

Urine creatinine (24-hour sample) values can range from 500 to 2000mg/day. Results depend greatly on age and amount of lean body mass.

2.2.3. Creatinine clearance formula:

$$\frac{[\text{Urine creatinine (mg/dL)}] \times [24 - \text{Hour Urine Volume(mL/day)}/1440\ (\text{min/day})]}{[\text{Serum Creatinine (mg/dL)}]}$$

2.2.4. Cockcroft Gault formula

$$\frac{(140 - \text{Age}) \times \text{Mass (in kilograms)} \times [0.85 \text{ if female}]}{72 \times \text{Serum Creatinine (in mg/dL)}}$$

2.2.5. Modified Devereux Formula

Left ventricular mass was calculated using the American Society of echocardiography formula modified by Devereux.

$$\text{LV Mass: } 0.8\ (1.04\ ([\text{LVIDD} + \text{PWTD} + \text{IVSTD}]^3 - [\text{LVIDD}]^3)) + 0.6$$

LVIDD = Left Ventricular Internal Diameter in Diastole
PWTD = Posterior Wall Thickness in Diastole
IVSTD = Interventricular Septum Thickness in Diastole

2.2.6. Body surface area

The DuBois and DuBois formula:

$$\text{BSA } (m^2) = 0.20247 \times \text{Height } (m)^{0.725} \times \text{Weight } (kg)^{0.425}$$

2.2.7. Left ventricular mass index

$$\frac{\text{Left ventricular mass (g)}}{\text{Body surface area (m2)}}$$

Left ventricular hypertrophy was defined in absolute terms as LVMI >134g/m^2 in men and >110 g/m^2 in women

3. Results

Table 1 Distribution Of Age With LVMI

Age	LVMI		Total	Chi value	p-value
	Normal	Abnormal			
18-29	4 8.3%	3 6.8%	7 7.6%	2.043	0.84
30-39	6 12.5%	6 13.6%	12 13.0%		
40-49	13 27.1%	7 15.9%	20 21.7%		
50-59	8 16.7%	10 22.7%	18 19.6%		
60-69	10 20.8%	11 25.0%	21 22.8%		

70-79	7 14.6%	7 15.9%	14 15.2%		
TOTAL	48 100.0%	44 100.0%	92 100.0%		

Table 1 shows the distribution of the patients in each group beginning from 18-79 yrs.

Table 2 Distribution of Gender With LVMI

Gender	LVMI		Total	Chi value	P value
	Normal	Abnormal			
Male	41 85.4%	18 40.9%	59 64.1%	3.897	0.06
Female	7 14.6%	26 59.1%	33 35.9%		
Total	48 100.0%	44 100.0%	92 100.0%		

Table 2 shows the distribution of males and females in the study group about normal and abnormal ventricular mass.

Table 3 Serum Creatinine, estimated GFR By CCG And MDRD With LVMI

Parameters	Range (LVMI)	Mean	Std. Deviation	Mean diff	t value	p-value
Serum Creatinine	Normal	2.196	1.0747	-3.8883	-12.170	<0.001***
	Abnormal	6.084	1.9085			
Estimated GFR By CCG	Normal	55.58	24.505	37.606	9.699	<0.001***
	Abnormal	17.98	8.125			
Estimated GFR By MDRD	Normal	54.38	22.942	37.284	10.055	<0.001***
	Abnormal	17.09	9.241			

Inference: Mean ±SD of s.creatinine in normal and abnormal LVMI groups was 2.196±1.0747 and 6.084±1.095 respectively. Results were found to be highly significant in comparing serum creatinine in normal and abnormal LVMI groups. The mean ±SD of estimated GFR by CCG in normal and abnormal LVMI group was 55.58±24.505 and 17.98±8.125 respectively. Results were found to be highly significant in comparing creatinine clearance by CCG in the normal and abnormal LVMI groups. The mean ±SD of estimated GFR by MDRD in normal and abnormal LVMI group was 54.38±22.942 and 17.09±9.241 respectively. Results were found to be highly significant in comparing creatinine clearance by MDRD in the normal and abnormal LVMI groups.

Table 4 Distribution Of 24 Hr Proteinuria With LVMI

24-hour proteinuria	LVMI	N	Mean	Std. deviation	p-value
	Normal	48	2234.78	1446.10	<0.001
	Abnormal	44	8533.33	3211.520	

Table 4 shows there was a statistically significant difference in the variable proteinuria when compared in the two groups of normal and abnormal/ increased left ventricular mass.

Table 5 Distribution Of Urine Spot Protein Creatinine Ratio With LVMI

Urine spot PCR	LVMI	N	Mean	Std. deviation	P value
	Normal	48	2.2254	1.3675	<0.001
	Abnormal	44	10.11	5.0776	

In the above table, a statistically significant p-value of less than 0.001 was obtained between the two groups about urine spot PCR.

4. Discussion

4.1. Age and LVMI

In the present study, the age distribution is shown (Table 1) Among the total 48(100%) in normal LVMI, a maximum of 13(27.1%) were from the age of 40-49 years and a minimum of 4 (8.3%) were from age of 18-29 years. Among the total 44(100%) increased LVMI. The p-value between the groups for the variable age was not statistically significant (p = 0.84). In a study conducted by Lawrence P. McMahon and colleagues[11]. it was discovered that age played a role in the initial development of LV hypertrophy. The impact of age on the advancement of the disease was linked to both an elevation in large vessel rigidity and a correlated decrease in glomerular filtration rate.

4.2. Gender and LVMI

In the present study, the gender distribution is shown (Table 2) Among the total 48(100%) in normal LVMI, a maximum of 41(85.4%) were male and a minimum of 7 (14.6%) were females. Among the total 44(100%) in increased LVMI, a maximum of 26(59.1%) were female, and a minimum of 18 (40.9%) were males. The p-value was not statistically significant between the two groups (p = 0.06).In a study conducted by Robert N. Foley et al[12], it was observed that males exhibited higher left ventricular mass compared to the female study population. One potential explanation for this finding is that the higher body mass index in males contributed to the increased left ventricular mass.

4.3. Glomerular Filtration Rate And LVMI

In our study, we identified a statistically significant correlation between declining GFR (Stage 4/5) and increased left ventricular thickness in patients with chronic kidney disease. The average glomerular filtration rate in the normal group ranged from 58 to 64 ml/min, while in the group with increased left ventricular mass, the mean GFR value was 17 ml/min, demonstrating a highly significant statistical correlation between the two groups (p = <0.001). Thus, we found a strong negative correlation between glomerular filtration rate and left ventricular hypertrophy, with declining GFR being an important and independent predictor of increased left ventricular mass index. According to a study conducted by Daniel E Jesuorobo et al[13], it was found that the glomerular filtration rate had a negative correlation with the left ventricular mass index. Additionally, it was identified as the most influential predictor of LVMI in patients with CKD, explaining 24.1% of the variance in LVMI.

4.4. Serum Creatinine Value And LVMI.

Our study revealed a notable variance in serum creatinine levels between the two groups. The average serum creatinine level was 1.873 in the normal left ventricle group and 6.515 in the group with increased left ventricular mass. This disparity was statistically significant (p = <0.001), suggesting that serum creatinine level is an independent predictor of the risk of left ventricular hypertrophy in patients with chronic kidney disease. In a study conducted by Harnett J. D. et al [14] it was found that high serum creatinine was identified as one of the primary factors associated with left ventricular hypertrophy (LVH) in individuals with chronic kidney disease.

4.5. Proteinuria And LVMI

Regarding 24-hour proteinuria excretion (Table 4) In our study, the mean proteinuria in the normal group was 2234 mg, and in the abnormal group was 8533 mg. The observed difference yielded a highly significant p-value of less than 0.001, indicating a strong correlation. This positive correlation demonstrated a statistically significant relationship. Additionally, Emily P. McQuarrie et al's study[15] also reported a notable correlation of 24-hour proteinuria with left ventricular hypertrophy in chronic kidney disease.

In the present study, the mean urine spot PCR value (Table 5) for the normal group was 2.2, whereas, for the increased left ventricular mass group, it averaged 10.1. This exhibited a highly significant statistical correlation, with a p-value of less than 0.001. Furthermore, a study by Emily P. McQuarrie et al[15], revealed a significant and independent association between proteinuria and left ventricular mass index in patients with chronic kidney disease.

Limitations

The study did not account for other variables that contribute to left ventricular hypertrophy in chronic kidney patients, such as anemia, volume overload, and increased systolic and diastolic blood pressure. It specifically focused on chronic kidney disease patients managed conservatively, which means the impact of hemodialysis on left ventricular thickness was not explored. Additionally, it's worth noting that measurements of left ventricular thickness via 2D echocardiography are susceptible to variations between different observers.

5. Conclusion

The global economic impact of chronic kidney disease (CKD) is substantial, with cardiovascular events being the primary cause of illness and death, affecting 40–50% of CKD patients. This study examined the risk factors linked to increased left ventricular wall thickness and discovered that the rate of decline in estimated glomerular filtration rate (eGFR) and the level of proteinuria are significantly associated with left ventricular mass index. Therefore, early intervention to address severe proteinuria and the progressive decline in eGFR through medication and dialysis could enhance cardiovascular health in CKD patients.

Compliance with ethical standards

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Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

Statement of ethical approval

The study was approved by the Institutional Ethical Committee.

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