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Original article

Correlation of mitral and aortic annular calcifications with carotid intima media thickness as a marker of extensive atherosclerosis in non-diabetic chronic kidney disease patients

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Abstract

Objective: The primary goal of the current investigation was to study the correlation of mitral and aortic annular calcifications with carotid intima media thickness as a marker of extensive atherosclerosis in non-diabetic chronic kidney disease patients. **Subjects and methods**: In this Prospective Case control study, 200 participants were included: 150 CKD stage 3. 4 and 5 for group 1. 2 and 3 respectively and 50 healthy participants of matched age and sex. Detailed history taking, Routine laboratory investigation and measurement of carotid intima-media thickness were done for all participants. **Results**: The GFR level and each of the following variables revealed a statistically significant negative relationship (p-value <0.05): age, SBP, DBP, creatinine, urea, phosphorus, PTH, LDL, TG, cholesterol, and CIMT. The calcification levels of the mitral and aortic

valves showed a statistically significant negative correlation with a p-value <0.001, but a positive correlation with the CIMT level. The GFR level sensitivity and specificity test showed a cut-off value of 53.6 and a sensitivity of 83.6 percent and a specificity of 50%, respectively.**Conclusion**: Our research showed that there was a positive link with CIMT degree but a statistically significant negative correlation with the calcification levels of the mitral and aortic valves and GFR degree. Age, BMI, PLT, GFR, phosphorus, LDL, and cholesterol levels were shown to have statistically significant predictor effects, according to the multivariate linear regression model analysis. Patients with chronic kidney disease may benefit from routine echocardiographic follow-up as a means of risk classification.

1. Introduction:

A persistent rise in cardiovascular mortality is linked to the loss of renal function and the advancement of chronic kidney disease (CKD). In reality, the majority of individuals' initial renal replacement therapy have poor cardiovascular function and size. It is the most prevalent reason for death for dialysis patients. The findings indicate that unconventional risk elements, such as uremia, disordered mineral-bone disease, inflammatory and oxidative stresses, early cardiovascular tissue damage, and more, are more important in clarifying the observed outcomes than standard risk factors like hypercholesterolemia or arterial hypertension (1)**.**

We will discuss recent developments about cardiovascular calcifications in individuals with CKD. As the condition progresses, these calcifications become more prevalent and are reliable markers of cardiovascular morbidity and death in CKD sufferers (2).

Some have suggested that cardiovascular calcification in CKD is not a meaningful target for treatment because it is simply a byproduct of vascular inflammation (3)**.**

On the other hand, degenerative calcification, such as that of the vascular

media, does not usually include inflammation. Better survival is also a result of interventions that experimentally lessen vascular calcification linked to CKD and do not always affect inflammatory processes (4).

We do admit, however, that there is currently a lack of evidence to support this in CKD patients, and that treatment interventions that impact calcification in patients typically have a wide range of side effects **(5).**

In patients receiving dialysis, cardiac valve calcification (CVC) is a crucial element in the onset of CVD and structural alterations in the heart. The incidence of CVC is rising as a result of prolonged use of calcium and phosphate binders, persistence of calcium and phosphorus problems, and an increase in dialysis frequency. According to the KDIGO guidelines, cardiac Doppler echocardiography should be used to routinely monitor and assess the hazard of CVC in individuals with CKD stages 3-5 (5).

Your carotid arteries' inner and middle layers can be measured using a carotid intima-media thickness (CIMT) test. Physicians can use this information to diagnose carotid artery disease before you have any symptoms by determining the amount of plaque accumulation in your arteries (5, 6).

The methods utilized to assess the CIMT, dietary habits, lifestyle, and ethnicity of individuals across the globe all influence the normal values of the test; in addition, the individual's gender and age range should be taken into account (7, 8).

Numerous non-invasive markers are available to evaluate arterial wall abnormalities, such as coronary artery calcification, endothelial dysfunction, and arterial wall thickness and stiffness (8, 9).

B-mode ultrasonography is a simple, safe, reliable, and affordable way to measure the CIMT. When the test is performed at several extracranial carotid locations, the predictive value of the results is enhanced (10)**.**

It is possible to quantify the CIMT from the carotid artery's near- and far-walls. It has been claimed that measuring at the far wall, where the media-adventitia interaction is typically easy to discern, is more precise (11)**.**

Increased CIMT measured by B-mode ultrasonography is regarded to be a sign of extensive atherosclerosis (12)**.** Once CIMT > 0.75 mm was linked to cardiovascular death, it was shown that CIMT was associated with cardiovascular disease (CVD). Originally, CIMT was related to both CVD and mortality in patients receiving chronic dialysis (13).

Therefore, the present research's goal was to investigate the relation between CIMT and mitral and aortic annular calcifications as a sign of severe atherosclerosis in individuals with chronic renal disease who were not diabetic.

2. Patients and Methods:

The current prospective case-control research was performed at Beni-Suef University Hospital's internal medicine and cardiology department from December 2021 to May 2022.

150 patients were chosen for this study. Furthermore, a control group of fifty healthy adults who were matched for age and sex was chosen.

They were divided into the following groups:

Group 1: 50 patients are CKD stage 3.

Group 2: 50 patients are CKD stage 4.

Group 3: 50 patients are CKD stage 5 (on hemodialysis).

Group 4: 50 Healthy persons.

CKD was classified based on KDIGO clinical practice guideline for the diagnosis (14).

2.1. Inclusion criteria:

- Patients with stage 3 chronic kidney disease (e GFR: 30 - 59)
- Patients with stage 4 chronic kidney disease (e GFR: 15- 29)
- Patients with stage 5 chronic kidney disease (e GFR: ≤ 15)

2.2. Exclusion criteria:

- Patients with acute kidney injury.
- Patients known to have rheumatic heart disease.
- Patients with age less than 18 years.
- Patients with diabetes mellitus.
- Patients who underwent prosthetic valve replacement.

2.3. All participants were subjected to:

Thorough history taking that covers factors like age, smoking status, length of hemodialysis, etiology of end-stage renal disease (ESRD), medication history, current course of treatment, and related comorbidities like diabetes mellitus, hypertension, chronic vascular disease, heart disease, and surgical history.

Body mass index (BMI), systolic and diastolic blood pressure measurements, and a comprehensive clinical examination were all carried out.

Calculation of e GFR by MDRD equation as follows:

(GFR (mL/min/1.73 m^2) = 175 × (Scr)-1.154 × (Age)-0.203 × (0.742 if female) (1.212 if African American) (conventional units) (Ann Intern Med. 2006 Aug 15;145(4):247-54).

Routine laboratory investigation include: CBC, serum calcium, serum phosphorus, kidney function tests (creatinine, urea), PTH.

Lipid profile include (serum triglycerides, total cholesterol, LDL-C,

HDL-C). Patients in all groups had trans-thoracic echocardiography (T.T.E.) with an ultrasonography device (EPIQ 7, Philips Medical Systems) operating in the left lateral position in order to detect mitral annular calcification. Every patient's echocardiogram was performed using the identical ultrasound equipment. Images were acquired from apical and parasternal long-axis perspectives.

Mitral and Aortic annular calcification are classified into 5 grades accordingly to:

A: Grade 0: No calcification (normal).

B: Grade 1: Dot of calcium on one of leaflets.

C: Grade 2: 2 dots of calcium on each leaflet or patch of calcium on one of the leaflets.

D: Grade 3: Patch of calcium on both leaflets.

E: Grade 4: Multiple patches of calcium on both leaflets.

Carotid intima-media thickness measurement: The patient was placed in a supine posture with their neck hyperextended, and the measurements were taken in a quiet environment with a consistent temperature of 22 ± 1°C after they had rested for at least ten minutes. The Vivid S5 ultrasonography device was used for the investigation, along with an 8 MHz linear array probe. Also employed was a B-mode system with great resolution. To maximize the recognition of non-obstructive plaques, the common carotid artery (CCA) was located in the transverse or longitudinal plane and examined from its origin to bifurcation from various angles.

To aid in edge identification, the focus depth (30–40 mm), frame rate (>15–25 Hz), and gain parameters were optimized. After that, image sequences (videos with at least five beats of cine-loops) were collected for offline assessment from the CCA, the location of the CCA bifurcation, and the ICA bulb longitudinal perspectives. Images were captured when the patient was in apnea and without swallowing.

Far wall CIMT was assessed during offline evaluation at the final stage of the diastole (peak R wave), choosing the best end-diastolic frame out of the loop in the centimeter at the carotid bifurcation as well as at the carotid bulb site. IMT is described as a double-line pattern seen in a longitudinal perspective on both common carotid artery (CCA) walls using 2D echo. It is formed by two parallel lines, the lumen-intima and media-adventitia interfaces, which are the leading edges of two anatomical boundaries. Each side had three CCA IMT observations, and the average IMT of these results was computed.

Ethical considerations

1. All involved parties provided written informed consent.
2. Approval of the ethical committee of Beni-Suef University was taken.
3. All study-related information was stored securely at the study sites.

Statistical analysis:

- The data was coded to allow for data change and double entry into Microsoft Excel then the Statistical Package of Social Science (SPSS) software version 22 for Windows (SPSS Inc., Chicago, IL, USA).
- Basic descriptive statistics using percentages and numbers for the qualitative findings, with arithmetic methods employed to measure central tendency and standard deviations used to gauge the dispersion of the quantitative parametric results. Each of the group's quantitative data was first subjected to a One-Sample Kolmogorov-Smirnov test to ensure normalcy, after which inferential statistic tests were chosen.
- Regarding numerical parametric data:

• Independent samples: quantitative outcomes were compared using the t-test.

• When comparing two independent groups' quantitative non-parametric data

- To contrast quantitative indicators, the one-way ANOVA test is employed.

▪ When comparing more than two independent groups, the Kruskal Wallis test is employed.

▪ The Mann-Whitney test was employed to evaluate two separate groups.

- Regarding qualitative variables

▪ The Chi square test is utilized for comparing two or more qualitative samples.

- The identification of risk factors and the relationship among quantitative dependent and independent variables are tested using multiple linear regressions.
- The "Receiver Operating Characteristic" (ROC) curve is used for evaluating a new test for sensitivity and specificity.
- Use the bivariate Sperman correlation analysis to determine whether two quantitative, non-parametric factors are related.
- The relationship between two quantitative parametric parameters is examined using the bivariate Pearson correlation analysis.
- A P-value of less than 0.05 was deemed statistically significant.

3. Results:

The table showed that, in terms of CIMT comparing the study groups, there was a statistically significant variation (p-value <0.001). There was a greater thickness in groups 2 and 3.

Table (1): Comparisons of CIMT thickness in different study groups.

Groups	CIMT	
	Mean	SD
Group 1	0.064	0.01
Group 2	0.069	0.023
Group 3	0.069	0.010
Group 4	0.056	0.008
P-value	**<0.001**	
Sig.	**HS**	

The table demonstrated a statistically significant difference in the degree of mitral valve calcification (p-value <0.001) between the study samples. Higher percentage of grade 1 valvular calcification noticed among group 3, and grade 2 and 3 valvular calcification noticed among group 2.

Table (2): Comparisons of Mitral valve calcification grades in different study groups.

Groups	Mitral valve calcification grades							
	Grade 0 (N=112)		Grade 1 (N=29)		Grade 2 (N=41)		Grade 3 (N=18)	
	No.	%	No.	%	No.	%	No.	%
Group 1	37	74%	2	4%	11	22%	0	0%
Group 2	9	18%	5	10%	**20**	40%	**16**	32%
Group 3	18	36%	**20**	40%	10	20%	2	4%
Group 4	48	96%	2	4%	0	0%	0	0%
P-value	**<0.001**							
Sig.	**HS**							

The table demonstrated a statistically significant variance in the degree of aortic valve calcification (p-value <0.001) between the research groups. Higher percentage of grade

1 of valvular calcification noticed among group 1, and higher percentage of grade 2 in group 3.

Table (3): Comparisons of Aortic valve calcification grades in different study groups.

Groups	Aortic valve calcification grades					
	Grade 0 (N=143)		Grade 1 (N=47)		Grade 2 (N=10)	
	No.	%	No.	%	No.	%
Group 1	36	72%	**14**	**28%**	0	0%
Group 2	30	60%	16	32%	4	8%
Group 3	27	54%	17	34%	**6**	12%
Group 4	50	100%	0	0%	0	0%
P-value	**<0.001**					
Sig.	**HS**					

The table illustrated that there was a statistical significant higher mean of urea and creatinine level and a lower mean of GFR among cases with valvular calcification with p-value <0.001.

Table (4): Comparisons of kidney function in different valvular calcification groups.

Variables	Valvular calcification				P-value	Sig.
	No calcification (N=110)		Calcification (N=90)			
	Mean	SD	Mean	SD		
Creatinine	1.9	2.3	**3.4**	2.5	**<0.001**	**HS**
Urea	66.7	37.9	**99.3**	52.9	**<0.001**	**HS**
GFR	67.9	46.9	**29.9**	20.9	**<0.001**	**HS**

The data showed that the calcification grades of the mitral and aortic valves had a statistically significant negative association (p-value <0.001) with the GFR level, but a positive correlation with the CIMT grade.

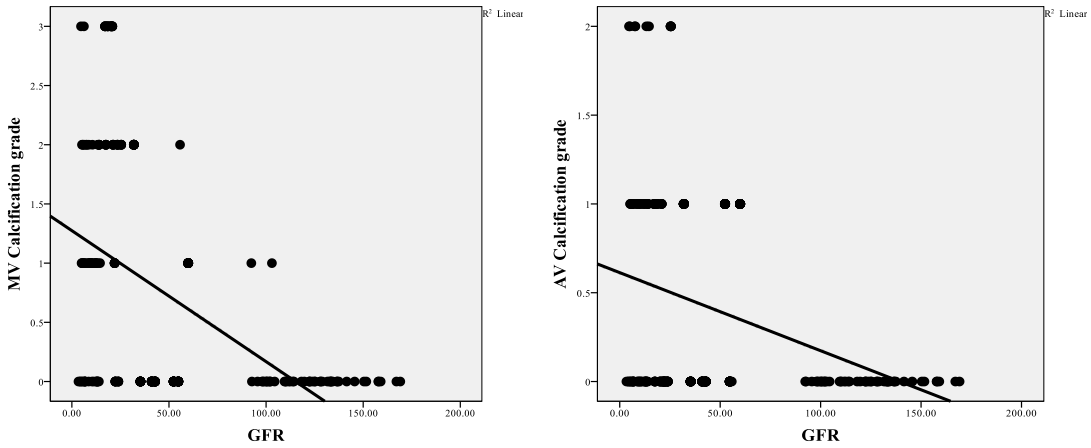

Figure (1): Correlation between GFR and Mitral valve and Aortic valve calcification grade among study group**.**

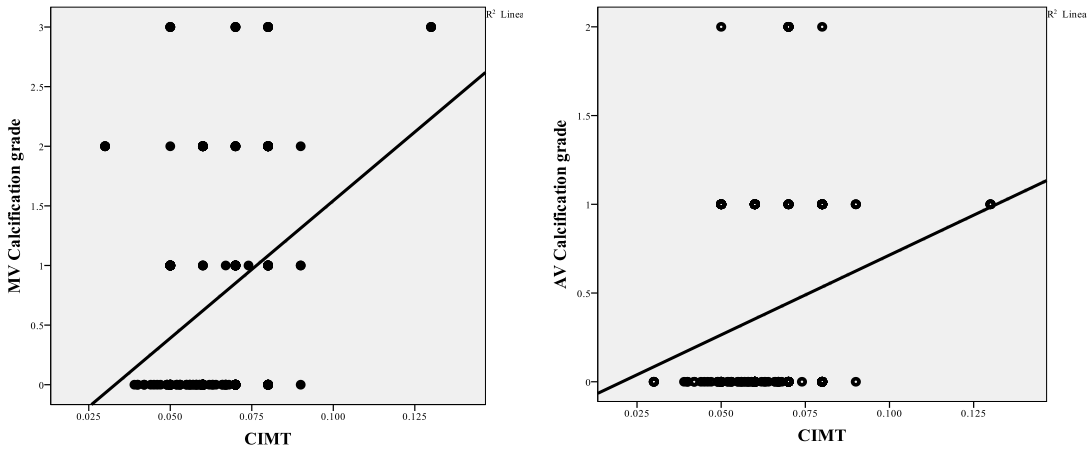

Figure (2): Correlation between CIMT and Mitral valve and Aortic valve calcification grade among study group.

Sensitivity and specificity test of GFR level illustrated a sensitivity of (83.6%) and a specificity of (50%) at cut off value (53.6).

Table (5): Sensitivity and specificity of GFR in diagnosis of valvular calcification.

Variable	Sensitivity	Specificity	AUC	Cut off point	P-value
GFR	83.6%	50%	74.3%	53.6	0.001

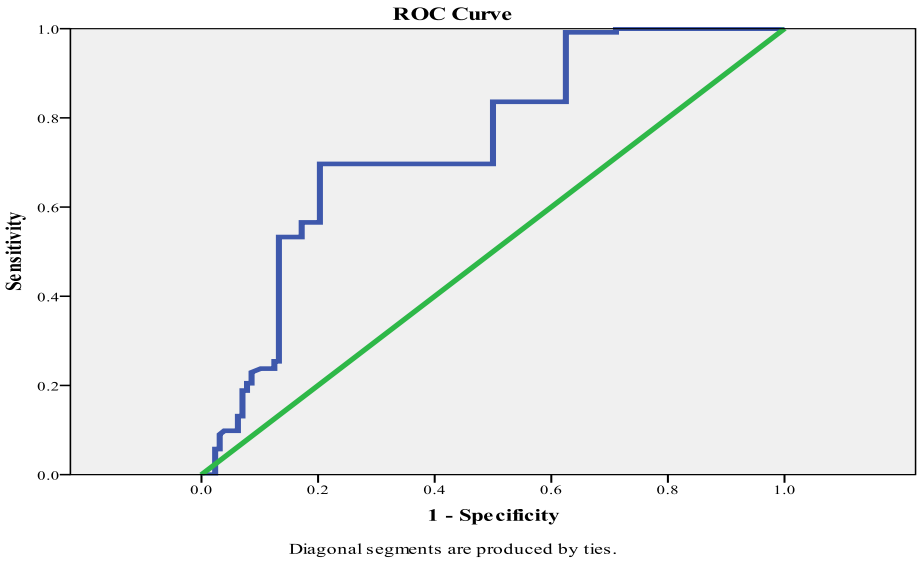

Figure (3): ROC curve for GFR in diagnosis of valvular calcification.

4. Discussion:

Around 15% of persons globally suffer from CKD, which is described as the existence of renal structural change and impairment lasting more than three months. Public health is significantly impacted by this CVD remain to be a major consequence of CKD and are accompanied by a rising probability of mortality and morbidity among individuals with CKD. There is growing evidence that vascular calcification is a primary reason of CVD in people with CKD and an important indicator of death (15).

Cardiovascular complications are more common in people with CKD than in healthy people. Non-traditional warning signs should be prioritized alongside with conventional risk factors such age, male gender, high blood pressure, high cholesterol, and obesity in order to determine the fundamental reason of accelerated atherosclerosis. On evaluating the probability of CVD in individuals with CKD, CVC should take precedence, according to the Kidney Disease Improving Global Outcome (KDIGO) Recommendations (16).

Uremic toxins might serve as a vital mediator of calcification in people with end-stage renal disease. Many researches have revealed a noteworthy incidence of CVC and the onset of stenosis in individuals undergoing renal replacement therapy. Aortic valve calcification and aortic stenosis can appear in a way dependent on GFR during the early stages of renal failure. CVC was found to be related to fatality

from cardiovascular and other causes in hemodialysis patients, yet its accuracy needed consistency. Many risk factors have been studied for CVC, encompassing common ones like age, diabetes, and hypertension as well as uncommon ones like inflammation, malnutrition, hyperphosphatemia, calcium phosphate product, and fibroblast growth factor 23. It's crucial to identify independent risk factors for CVC in people with chronic renal disease. However, there is still plenty that we don't know about the pathophysiology of CVC (17).

This study's primary goal was to investigate the correlation between carotid intima media thickness and mitral and aortic annular calcifications as a sign of severe atherosclerosis in individuals with chronic renal disease who were not diabetic.

This prospective case control study was performed at Beni-Suef University Hospital's internal medicine and cardiology department from December 2021 to May 2022. This study comprised 50 healthy participants of comparable ages and genders as a control group and 150 patients chosen from Beni-Suef University Hospital's outpatient clinic.

They were divided into the following groups:

Group 1: 50 patients are CKD stage 3.

Group 2: 50 patients are CKD stage 4.

Group 3: 50 patients are CKD stage 5 (on hemodialysis).

Group 4: 50 Healthy persons.

Regarding age, height, weight, and BMI, there was a statistically significant disparity (p-value <0.001) between the research groups. Group 2 had a lesser mean height and weight than Group 3, and Group 3 had older ages. Additionally, group 3's systolic and diastolic blood pressure levels were statistically significantly higher. A statistically significant difference was seen between the percentage of males in group 3 and the percentage of girls in group 1. However, there was no discernible variation in BMI between the groups.

While, in the study of Indrayanti et al. (2019) (18), the case group consisted of adults with CKD who had received a diagnosis within the preceding five years, while the control group composed of adults without CKD. The age range of the patients included people in their early 20s to those who were over 80. There was no obvious difference in the groups' ages. The patients' average age when the two groups were pooled was 53.96 ± 12.59

years. It was observed that the incidence of CKD increased with ageing. More men were reported in the case group (60.0%) than in the control group (53.3%). In every group, hypertension was the most common comorbidity. The patient group had a higher proportion of these comorbidities than the opposite group, as would be predicted.

Whereas, Lawal et al. (2019) (19), revealed that the age range of those involved was 23 to 65. The patients and controls had identical average ages (51.06 ± 11.09 vs. 51.65 ± 13.80; P =.906). In each group, there were 17 females and 33 males. There were no statistically significant variations in weight, height, or body mass index (BMI) between the patients and the control group. The CKD participants and the control group differed significantly in cardiovascular characteristics, including heart rate and mean arterial pressure (1.67 ± .10 vs 1.66 ± 0.09, P =.007 and 106.99 ± 18.46 vs 84.55 ± 10.73, P <.05), respectively.

However, in the study of Ghelichi-Ghojogh et al. (2022) (20), 350 CKD sufferers and 350 sex- and age-matched healthy participants made up the study. The age difference between the patients and controls was 59.6 ± 12.4 and 58.9 ± 12.2, respectively (p = 0.83). There were 208 patients (59.4%) and 200 controls (57.1%) who were male (p = 0.54).

Between 8% and 16% of the world's population has CKD, which is commonly misdiagnosed by both patients and healthcare providers and distinguished with a GFR of less than 60 mL/min/1.73 m^2 or by symptoms of kidney injury (such as hematuria or anatomic anomalies like polycystic or dysplastic kidneys) that last longer than three months. In low- and middle-income countries, CKD is more prevalent than in higher-income nations. The most common manifestations of CKD globally are diabetes and/or hypertension. Yet, Asia, sub-Saharan Africa, and many poor countries also frequently experience glomerulonephritis, infections, and environmental exposures (for example air pollution, air pollution, herbal remedies, and pesticides) (21).

The current investigation revealed that group 2 had a statistically significant greater mean of phosphate, LDL, TG, and cholesterol and a statistically significant decreased mean of HB, calcium, and HDL. Additionally, group 3 showed decreased levels of GFR and calcium as well as high levels of creatinine, urea, PTH, and other substances. Group 1 had the lowest PLT

level, with a p-value of less than 0.05. However, in terms of TLC level, there was no statistically significant variance with a p-value >0.05.

Our results were supported by study of Lawal et al. (2019) (19), indicating that, in comparison to the controls, they reported that the serum chemistry of the CKD patients showed less kidney function indices, demonstrated by lower eGFR rates (52.11 ± 18.57 vs 85.95 ± 22.30, $P < .001$) and increased serum urea and creatinine (8.70 ± 6.14 vs 3.81 ± 0.91, $P < .001$). Participants with chronic renal illness also had poorer lipid profile results when contrasted with controls.

Myocardial infarction and stroke are accompanied by a rise in the intima-media thickness (IMT) of the carotid artery in the entire population. It is acknowledged that chronic renal disease, especially in its latter phases, is an independent indicator of carotid arterial IMT. Research has demonstrated that HD patients had a greater incidence of IMT in their carotid arteries than the controls of the same age and gender. For the recognition of CVDs, noninvasive testing is crucial, especially in individuals with HD who show atherosclerotic changes. Certain hypotheses suggest that IMT in the carotid artery could be one of the long-term markers of the survival rates of HD patients. B-mode ultrasonography is one method for detecting atherosclerotic changes (22).

According to the present investigation, there was a highly significant variance in CIMT across the study groups, with a p-value of less than 0.001. There was a greater thickness in groups 2 and 3.

The present outcomes agreed with those of Lawal et al. (2019) (19). It was found that the average CIMT values for the common carotid arteries, both left and right, were considerably higher in individuals with chronic kidney disease (CKD) when compared to the control group (1.1 ± 0.38 vs 0.70 ± 0.10 and 1.1 ± 0.43 vs 1.0 ± 0.11; $P < .001$ for both sides, respectively).

Similarly, Rizikalo et al. (2021) (23), stated that, the stage 4 CKD group had significantly greater initial CIMT scores and more atherosclerotic plaques than the stage 2 CKD group demonstrated.

The current findings disagreed with those done by Zoungas et al. (2000) and Zoungas et al. (2007) (24, 25) they found that the CIMT of CKD sufferers was significantly thicker than that of controls. A few additional researchers have presented similar outcomes (26, 27).

In the study of Abbasi et al. (2016) (28), in order to measure atherosclerotic modifications, 62 HD subjects (40 of whom were males) participated in the study. The results of the ultrasonography indicated that the bifurcation point in the left (0.77 ± 0.16 mm) and right (0.78 ± 0.18 mm) carotid arteries had the greatest CIMT, while the internal carotid arteries in the left (0.66 ± 0.15 mm) and right (0.64 ± 0.14 mm) sides had the least CIMT.

Furthermore, Roumeliotis et al. (2019) (29)**,** revealed that participants with lower renal function and significantly older were found in the higher CIMT group. They were more likely to acquire progressive atherosclerosis in either carotid artery or peripheral arterial disease.

Moreover, Kumar et al. (2009) (30)**,** demonstrated that the mean CIMT score for ESRD participants was 1.0 mm, whereas the mean score for controls was 0.73 mm.

ESRD is linked to a markedly elevated danger of cardiovascular death. Cardiovascular disease is the greatest reason for death for patients on maintenance hemodialysis (MHD). Individuals receiving hemodialysis or peritoneal dialysis are ten to twenty times more likely to die from CV than healthy people. Individuals on dialysis are frequently susceptible to CVC, a condition that is associated with structural changes in the heart and the onset of cardiovascular disease. There is proof that individuals undergoing hemodialysis on an event basis have a higher incidence of CVC (57.5%), which involves aortic and mitral valve calcification (AVC and MVC). Consequently, anomalies in the metabolism of phosphate and calcium could be connected to CVC (31)**.**

Regarding the incidence of valvular calcification, there was a statistically significant variance (p-value <0.001) among the studied patients. Group 2 had a greater proportion of instances with valvular calcification. In terms of the degree of mitral valve calcification, there was a statistically significant variance (p-value <0.001) between the research groups. Group 2 showed a greater proportion of grade 2 and 3 valvular calcification, while group 3 showed a significant percentage of grade 1 calcification. Regarding the degree of aortic valve calcification, there was a statistically significant variance between research groups with a p-value of <0.001. There was a greater proportion of grade 1 valvular calcification in group 1 and grade 2 in group 3. Regarding mitral regurge incidence, there was a statistically

significant variance (p-value 0.001) between the study groups. A higher MR % was seen in group 3.

The current findings are in line with a study by Xiong et al. (2022) (32)**.** These results showed that out of the 293 individuals with ESKD, 93 (31.7%) had CVC, 68 had AVC 37 had MVC, and 12 patients had both (MVC + AVC).

Also, in the study of Bai et al. (2022) (33), echocardiography was used to qualitatively evaluate the valve calcification of 434 hemodialysis patients who were part of the research. AVC was present in 31.8% of patients and MVC in 27.2% of individuals overall on echocardiography.

In a systematic review conducted by Zhang et al. (2023) (34), in which there were 22 articles reviewed, CVC raised the risk of cardiovascular in patients with CKD. Nevertheless, the predictive potential of CVC for death was no longer significant for dialysis patients.

According to Rattazzi et al. (2013) (35), for those with ESKD, aortic calcification and stenosis are the most prevalent valvular problems. According to reports, the prevalence ranged from 6% to 13%.

In the study of Vavilis et al. (2019) (36), Over the course of a median follow-up period of 5.1 years (IQR: 3.3 to 6.1 years), 5,858 patients (0.5%) had aortic stenosis (AS) that was clinically diagnosed.

In addition, Wang et al. (2022) (37) disclosed that 2,756 CKD subjects with CVC made up the subset of the study. In all, 163 people (5.91%) had CVC.

According to the present investigation, there was a statistically significant variance (p-value <0.05) between the calcification groups with respect to the distribution of sexes and MR. Among instances with MR, there was a greater proportion of valvular calcification observed, with males making up 37.7% of the group compared to 19.5% of those without valvular calcification. Patients with valvular calcification had a statistically significant elevated mean systolic and diastolic blood pressure (p-value <0.05). Among patients with valvular calcification, there was a statistically significant lower mean GFR and a statistically significant raise in the mean amount of urea and creatinine (p-value <0.001). Among patients with valvular calcification, there was a statistically significant decreased mean of calcium and an elevated mean of PTH and phosphorus levels (p-value <0.001). Among patients with valvular calcification, there was a statistically significant raise in the average levels of triglycerides,

cholesterol, and carotid intramedia thickness (p-value <0.001).

The current results agreed with the study by Cottignoli et al. (2015) (38), who reported that hypertension is one of the known causes for CVC. Additionally, regression analysis showed that pulse pressure was a separate indicator of risk for CVC.

Furthermore, Wang et al. (2022) (37), revealed that there was a significant relationship ($p < 0.05$) observed between the frequency of CVC and serum albumin stages, age, low-density lipoprotein cholesterol, and a history of CVD.

The findings of the current investigation demonstrated a statistically significant positive relation between the concentrations of hemoglobin, PLT, calcium, and HDL and the GFR degree. Furthermore, a statistically significant negative association was observed between the GFR level and the following variables: age, urea, creatinine, phosphorus, PTH, LDL, TG, cholesterol, and CIMT. However, there was no statistically significant difference between TLC levels and BMI or GFR degree, with a p-value >0.05. The CIMT level and each of the following variables showed a statistically significant positive link (p-value <0.05): age, BMI, creatinine, urea, PTH, LDL, TG, and cholesterol. Furthermore, a statistically significant negative connection was observed with a p-value of less than 0.05 between the levels of CIMT and HDL and calcium. However, there was no statistically significant association found between the levels of phosphorus, hemoglobin, DBP, TLC, and CIMT and each of the other six parameters.

The calcification levels of both the mitral and aortic valves and GFR grade showed a statistically significant negative correlation, however there was a positive correlation with the content of CIMT. To investigate the explanatory power of various research and risk variables in predicting of CIMT, a multivariate linear regression model analysis was performed. It shown that the following variables had statistically significant predictive effects: age, BMI, PLT, GFR, phosphorus, LDL, and cholesterol levels, with p-values less than 0.05.

In the study of Roumeliotis et al. (2019) (29), peripheral atherosclerosis, reduced eGFRs, carotid artery plaque, and atherosclerosis were all more common in older adults with elevated CIMT levels. It was demonstrated that male gender (beta=−0.339, p =.005), decreased eGFR (beta = 0.353, p

=.003), and greater BMI (beta = −0.29, p =.01) all predicted higher CIMT.

Furthermore, Rizikalo et al. (2021) (23), revealed that in both CKD groups, GFR and CIMT showed a significant negative association during all follow-up periods (P < 0.001).

Also, Kuswardhani et al. (2018) (39), stated that there were shown to be relationships between CIMT and plasma higher-sensitivity C-reactive protein (R=0.279, P=0.030), calcium-phosphate product (R=-0.284, P=0.011), serum phosphate (R=-0.294, P=0.015), age (R=0.607, P<0.001) and plasma albumin (R=-0.291, P=0.016). However, age was the only variable that consistently altered the CIMT score, according to the outcomes of the multiple linear regression analysis (β=0.452, P<0.001).

Our findings demonstrated that the ROC curve could be used to measure the sensitivity and specificity of the GFR level in order to identify valvular calcification. At the cutoff value of 53.6%, the sensitivity was 83.6% and the specificity was 50%.

There were certain limitations on this investigation. The primary restriction is the very small sample size. A further limitation is that this is a single center study.

5. Conclusion and Recommendations:

In conclusion, our study showed a statistically significant negative correlation between the aortic and mitral valve calcification levels and GFR level, but a favorable correlation with the level of CIMT. Age, BMI, PLT, GFR, phosphorus, LDL, and cholesterol levels were all found to have statistically significant prognostic impacts in the multivariate linear regression model study.

Periodic follow-up echocardiography can be a useful tool for individuals with chronic renal illness to determine their risk. Multicenter prospective cohort follow-up studies with large sample sizes are necessary to confirm the validity of our findings and find out whether stopping CVC treatment will reduce the mortality risk in CKD patients.

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