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Original Article

Physiology Section

Vascular Calcification in Chronic Kidney Disease Patients- A Cross-sectional Study

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ABSTRACT

Introduction: Vascular Calcification (VC) is considered as a cardiovascular risk marker in Chronic Kidney Disease (CKD) patients. VC is a process characterised by thickening and loss of elasticity of muscular arteries walls. The three pathological forms of cardiovascular disease in CKD are cardiac geometry, atherosclerosis and arteriosclerosis of the large vessels (carotid artery or aorta).

Aim: To evaluate VC as a cardiovascular risk marker in CKD patients.

Materials and Methods: This cross-sectional study was conducted in the Nephrology Department at Sri Ramachandra Medical College and Research Institute, Chennai, Tamil Nadu, India, from November 2019-December 2020. The study included 27 CKD patients who were on maintenance haemodialysis. The participants were 20-70 years of age, and of both genders. The Intima Media Thickness (IMT) was assessed by ultrasonography. Peak Systolic Velocity (PSV) measurement was done using doppler ultrasonography. Both the measurements were done on Common Carotid Artery (CCA), and Internal Carotid Artery (ICA) on both sides of the neck. Student's t-test and Chi-square test was used in this study. Data were expressed as mean±SD. The p-value <0.05 was considered as statistically significant.

Results: Out of 27 study participants, 20 (74%) were male and females were 7 (26%), with mean age of 48 years. There was significant increase in IMT of the ICA on the right side of the neck compared to left side (p-value=0.01). Also, there was significant increase in PSV of ICA on the right side compared to left side of the neck (p-value=0.04). There were no statistically significant differences in IMT and PSV when CCA on the right side was compared to that of the left side of the neck.

Conclusion: The IMT was increased in ICA and CCA. But there was statistically significant difference only in ICA, where it was more prominent on the right side compared to left side. CKD patients on haemodialysis management could have the risk factors in the form of increased IMT predisposing them to early mortality from cardiovascular complications.

Keywords: Carotid artery, Intima media thickness, Ultrasonography

INTRODUCTION

The Chronic Kidney Disease (CKD) is being recognised as a global public health burden [1,2]. Global prevalence is estimated to be as high as 13.4% [3]. Various causes for the increasing cases of CKD are increasing aging populations, type 2 diabetes mellitus, hypertension, obesity, sedentary life style and increased intake of high calorie diet [3]. The incidence rates reported by various studies range from 26.8% to 47.2% [4]. A study done in Japanese population, showed an incidence of 33.4% [4]. In CKD patients, glomerular filtration rate is decreased, which is associated with an increase in the Cardiovascular (CV) complications [5,6]. Patients with CKD develop Vascular Calcification (VC) in major arteries such as carotid arteries, which decrease the elasticity of the involved arteries [7]. So, VC can be considered as a cardiovascular risk marker in CKD patients.

The cardiovascular complications are seen in the advanced stages of CKD, especially stage 3 onwards [8]. The Kidney Disease Improving Global Outcomes International clinical practice guideline suggests that the stages 3, 4, and 5 of CKD patients are highly prone to CV complications [9].

In patients with cardiovascular disease, there is widespread subclinical inflammation, insulin resistance and endothelial dysfunction; these factors accelerate the progression of atherosclerosis [10]. Carotid artery intima media is considered to be a surrogate marker of atherosclerosis and related to ethnicity, age, sex, and various risk factors of CVD. Black population have greater carotid artery Intima Media Thickness (IMT) than that of Asians [11]. There are few studies that aimed to obtain age and gender-specific values for IMT of internal and common carotid arteries [10]. The high prevalence of carotid atherosclerosis in CKD patients, with an otherwise low Framingham risk score, necessitates the need for screening of subclinical atherosclerosis [12].

This increased arterial stiffness causes significant changes in the heart, leading to left ventricular hypertrophy and cardiac failure. Arterial stiffness can be estimated by Carotid IMT (C-IMT) [13]. In CKD patients, Peak Systolic Velocity (PSV) is an index measured in spectral doppler ultrasound. On a doppler waveform, the peak systolic velocity corresponds to each tall "peak" in the spectrum window [14].

Carotid IMT (C-IMT) is a measurement of thickness of both the tunica intima and media of the carotid arteries and it is a surrogate marker of subclinical atherosclerosis. In non uremic and uremic population C-IMT is an index of atherosclerosis which correlates with the occurrence of coronary heart disease and stroke [15,16]. Increase in the C-IMT is associated with many cardiovascular risk factors like age, hypertension, dyslipidemia, diabetes mellitus, inflammation and smoking [17,18].

B-mode ultrasound, that measures the C-IMT in the Common Carotid Artery (CCA) and visualises the arterial walls, helps in identifying early atherosclerotic changes [19]. This is especially important in chronic renal failure patients who are on maintenance haemodialysis (HD), where the quantity of burden can be measured [20,21]. It is found to be the useful as non invasive and accurate method and it is useful in stratifying patients who are at risk for cardiovascular complications [22]. Hence, this study aimed to measure the values of IMT in common carotid and ICA bilaterally and doppler index measurements (PSV) in CKD patients on haemodialysis also, to assess if VC can be used as a predictor of cardiovascular risk in such patients.

MATERIALS AND METHODS

This cross-sectional study was conducted on the patients admitted in the Nephrology Department at Sri Ramachandra Medical College and Research Institute , Chennai, Tamil Nadu, India, from November 2019-December 2020. Institutional Ethics Committee clearance (No: IEC-NI/17/JAN/57/02) was obtained before the study was initiated.

After explaining the procedure clearly to the patient and the care takers, written informed consent was taken.

Inclusion criteria: Patients of both sexes, aged between 20-70 years, and who were CKD patients on haemodialysis were included in the study.

Exclusion criteria: Patients with coronary artery disease, cushing syndrome, obesity, history intake of drugs such as oral contraceptive pills and steroids were excluded from the study.

Procedure

Under aseptic precautions fasting blood sample was collected from the CKD patients, stored at -80°C until analysis. The IMT was assessed using B-mode ultrasonography and PSV measurement was taken using spectral doppler ultrasonography in the following arteries: bilateral CCA and ICA.

The examination of the carotid arteries was performed with a 3.5-10 MHz linear transducer and abdominal aorta by 1.5-4 MHz convex transducer. IMT is defined as the thickness of the hypoechoic layer between the two echogenic lines in the far wall of the corresponding artery- near line formed by the interface between the medial and adventitial layers of the arterial wall and the far line formed by the interface between the intimal wall layer and the blood. IMT was measured at the diastolic phase (to avoid the imaging artifacts) and in the area without any intimal plaque [23]. PSV measurement was also done in the segments without any intimal plaque or significant focal luminal stenosis. Assessment was done in the longitudinal axis of the bilateral CCA (~3 cm below the carotid bifurcation), bilateral ICA arteries (~2 cm above the carotid bifurcation) and abdominal aorta (approximately at the level of the origin of the renal arteries) [24].

STATISTICAL ANALYSIS

Statistical analysis was done using Statistical Package for the Social Sciences (SPSS) software. Student's t-test and Chi-square test was used in this study. Data were expressed as mean±SD. The p-value <0.05 was considered as statistically significant.

RESULTS

This cross-sectional study included 27 CKD patients on haemodialysis. The study participants were in the age group of 20-70 years, with mean age of 48 years. Out of 27 study participants, males were 20 (74%) and females were 7 (26%).

The CCA-IMT and ICA-IMT values were significantly higher on the right side when compared to left side. The [Table/Fig-1] shows the mean and standard deviation of IMT and PSV in ICA and CCA on both sides of the neck. The mean values of IMT in ICA 0.65±0.17 mm and 0.60±0.18 mm on the right and left sides of the neck, respectively (p-value=0.01). The mean values of IMT in CCA were 0.70 mm and 0.71 mm on the right and left sides of the neck, respectively (p-value=0.23). The PSV in ICA were 78.18±22.54 (cm/sec) and 73.66±17.66 (cm/sec) on the right and left sides, respectively (p-value=0.04). The PSV in the CCA were 71.48±20.50 (cm/sec) and 74.14±20.46 (cm/sec), respectively (p-value=0.05). The PSV ratio did not show statistically significant difference between the sides (p-value=0.06) as shown in [Table/Fig-1].

Variables		Right side of neck Mean±SD	Left side of neck Mean±SD	p-value
Intima Media Thickness (IMT) (mm)	ICA-IMT	0.65±0.17	0.60±0.18	0.01*
	CCA-IMT	0.70±0.19	0.71±0.16	0.23
Peak Systolic Velocity (PSV) (cm/sec)	CCA	71.48±20.50	74.14±20.46	0.05
	ICA	78.18±22.54	73.66±17.66	0.04*
	PSV ratio	1.12±0.27	1.03±0.25	0.06

[Table/Fig-1]: Shows comparison of intima media thickness and peak systolic velocity of common Carotid (CCA) and Internal Carotid Arteries (ICA).
CCA: Common carotid artery; ICA: Internal carotid artery; *p-value <0.05 was considered as statistically significant

[Table/Fig-2] shows the distribution of individuals having normal and increased IMT of ICA and CCA. Chi-square done showed statistically significant difference in ICA (p-value=0.02) as well as in CCA (p-value=0.01).

Intima media thickness		Normal n (%)	Abnormal n (%)	p-value
Common carotid artery	RT	14 (51.9%)	13 (48.1%)	0.01*
	LT	11 (40.7%)	16 (59.3%)	
Internal carotid artery	RT	11 (40.7%)	16 (59.3%)	0.02*
	LT	10 (37%)	17 (63%)	

[Table/Fig-2]: Distribution of individuals having normal and increased intima media thickness of normal and abnormal common Carotid (CCA) and Internal Carotid Arteries (ICA).
RT: Right side of neck; LT: Left side of neck; *p-value <0.05 was considered as statistically significant

DISCUSSION

The non invasive methods of assessing the morphological changes in the arteries play a crucial role in the assessment of cardiovascular risk in patients with CKD. The measurement of IMT by B-mode ultrasound is inexpensive and non invasive; hence it can assess the atherosclerotic changes in the arteries. This indirectly reflects the changes in the coronary arteries of heart indicating future risk of acute myocardial infarction [25]. Research studies have shown that CKD patients have significantly higher carotid arterial wall thickness in comparison to age matched controls [26].

Atherosclerosis in carotid arteries, assessed by ultrasonography in the HD patients, has been little investigated and almost exclusively in studies of cross-sectional design. The mean C-IMT values of 0.5 mm for younger age groups (between 20-30 years) and of 0.9 mm for older participants (between 60 and 70 years) have been reported [5,23]. The normal C-IMT, as evaluated by B-mode ultrasound imaging, was 0.74±0.14 mm and C-IMT at or above 1 mm and is associated with atherosclerosis. This has contributed to significant increase in CVD risk in any age group [27-29]. In the present study, 50% of the participants had higher IMT values that were more than 0.74 mm in both internal and common carotid arteries. The IMT of internal and common carotid arteries in this study were found to be similar to the findings by Kumar KS et al., [30]. According to Nakayama M et al., calcification found in the carotid arteries was an independent cardiovascular event in End-Stage Renal Disease (ESRD) [31].

Tanaka M et al., in 1003 patients aged ≥50 years, found a decline in renal function in patients with CKD as assessed by estimated Glomerular Filtration Rate (eGFR). He stated that with decreasing eGFR VC and atherosclerotic changes become more prominent [32].

This is similar to another study that found IMT to be significantly higher in HD patients, than in age and gender matched control subjects. IMT in CKD patients was between 0.9-1.0 mm, whereas, in controls it was between 0.5-0.6 mm. IMT of carotid arteries was increased in CKD patients with increased age, progression of stage of CKD and proteinuria as well as presence of associated hypertension or dyslipidemia [18]. Paul J et al., also concluded that C-IMT is a surrogate marker for atherosclerosis in patients with chronic renal failure on HD [33].

In the present study, IMT was higher on the right side in ICA, while in CCA, IMT was higher on the left side. Another study also indicated that the frequency of atherosclerotic plaques is far larger in dialysis patients in comparison with healthy subjects [12]. A study by Savage T et al., documented that calcified plaques are common in dialysis patients [34]. In the present study, the extent of VC was not done since the sample size was small. The study by Sarraf S et al., concluded that CKD patients have significantly more carotid arterial wall thickness in comparison to age matched controls and this does not differ according to different stages of CKD [35].

The peak systolic velocity measurement gives additional information about the changes in the arterial walls in patients with CKD. In the present study, PSV, ICA/CCA ratio Doppler measurements in left and right CCAs and ICAs showed that the values within the normal

range. Salk I et al., found that PSVs in HD groups were significantly higher than that of the normal group [36].

Limitation(s)

The major limitation is the small sample size. Hence, stratifying the sample according to age, gender or stage of CKD was not possible. Apparently healthy individuals were not included to calculate normal IMT and PSV.

CONCLUSION(S)

Carotid artery IMT in CKD patient is considered as a cardiovascular risk marker for VC. Intima media thickness and peak systolic velocity were significantly increased on the right ICA. No such significant changes were seen in the CCA. Carotid IMT indicates the risk for cardiovascular complications in patients with CKD. Thus, screening the patients for cardiovascular complications especially in the last stages of CKD patients reduces morbidity and mortality.

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