

Title: THE RELATIONSHIP BETWEEN FEMORAL ARTERY INTIMA-MEDIA THICKNESS AND ATHEROSCLEROSIS INPATIENTS WITH CHRONIC KIDNEY DISEASE- A ONE YEAR HOSPITAL-BASED CROSS-SECTIONAL STUDY

Type of manuscript: Original article.

Authors:

¹ Minisha A Jenifer, ² Allwin vino, ³ Assvath O C, ⁴ Nisha A Jenifer, ⁵ Jenish Babu A
.Department of Radiodiagnosis, Anaesthesia and Critical Care, Sree Mookambika Institute of Medical Sciences, Kulasekharam, Kanyakumari District, Tamil Nadu, India.

Corresponding Author: Assvath O C Department of Radiodiagnosis, Assistant Professor, Sree Mookambika Institute of Medical Sciences, Kulasekharam, Kanyakumari District, Tamil Nadu.

E-mail: mini13.jnf@gmail.com Contact Number:9976670785

Conflicts of Interest:

The authors have no conflicts of interest to declare.

Abstract:

Introduction: Cardiovascular disease, a global health concern, is exacerbated by chronic kidney disease (CKD). Atherosclerosis, a hallmark of cardiovascular disease, is understudied in relation to femoral artery intima-media thickness (IMT) in CKD patients. This study explores the association between femoral artery IMT and atherosclerosis in CKD, considering the unique pathophysiological mechanisms of CKD.

Materials and Methods: A one-year hospital-based cross-sectional study was conducted on 99 CKD patients at a tertiary care center. Femoral artery IMT was assessed using Doppler ultrasonography. Clinical data, including CKD stage, gender, comorbid conditions, and laboratory values, were collected. Statistical analyses were performed using ANOVA, correlation, regression, and chi-square tests.

Results: The study population, predominantly male (70.71%), had a mean age of 52.39 years. Raised IMT was prevalent in 69.70% of patients. CKD stage 5 was the most common (61%) among participants. Diabetes was associated with higher IMT, and a positive correlation existed between reduced estimated glomerular filtration rate (eGFR) and raised IMT. Additionally, triglyceride levels showed an association with lower eGFR values.

Conclusion: The study highlights a significant association between femoral artery IMT and atherosclerosis in CKD patients. Associations with diabetes, eGFR, and triglyceride levels emphasize the multifaceted nature of CKD's impact on atherosclerosis. These findings underscore the importance of comprehensive cardiovascular assessment in CKD patients, potentially informing risk stratification and targeted interventions. Limitations include the small sample size and lack of histopathological confirmation of atherosclerosis. Further research and interventions addressing these limitations could enhance our understanding and management of atherosclerotic complications in CKD.

KEYWORDS: Doppler ultrasonography of femoral artery, atherosclerosis in CKD, Prevalence.

INTRODUCTION:

Cardiovascular disease remains a major global health concern, with chronic kidney disease (CKD) emerging as a significant contributor to its prevalence and severity. Atherosclerosis, characterized by the thickening of arterial walls due to plaque formation is a central pathological feature of cardiovascular disease^[1,2]. The femoral artery, a critical conduit for blood flow to the lower extremities, serves as an important site for the assessment of atherosclerosis. The relationship between femoral artery intima-media thickness (IMT) and atherosclerosis in patients with CKD presents a crucial avenue for exploration, given the high burden of cardiovascular complications in the patient population^[3,4].

Chronic kidney disease, a growing public health concern worldwide, is associated with an elevated risk of cardiovascular morbidity and mortality. Peripheral artery disease (PAD), often manifesting as atherosclerosis in the lower extremities, represents a common vascular complication in CKD patients, with a prevalence estimated to be between 11% and 13% globally^[5]. While traditional cardiovascular risk factors such as hypertension, dyslipidemia, and diabetes play pivotal roles in the development of atherosclerosis, CKD itself introduces unique pathophysiological mechanisms that contribute to arterial remodelling and plaque formation^[6].

Femoral artery IMT has emerged as a non-invasive surrogate marker for atherosclerosis and cardiovascular risk assessment. This measure is obtained through ultrasonography, reflects the combined thickness of the intimal and medial layers of the arterial wall^[4]. Elevated IMT has been associated with increased cardiovascular risk and serves as an early indicator of atherosclerotic changes. However, the relationship between femoral artery IMT and atherosclerosis in the context of CKD remains understudied^[7].

The rationale for investigating the relationship between femoral artery IMT and atherosclerosis in patients with CKD is multi-faceted. First, CKD presents a unique pathological environment characterized by chronic inflammation, oxidative stress, endothelial dysfunction, and mineral imbalances, all of which can accelerate atherosclerotic processes^[8,9]. Second, given the high prevalence of PAD in CKD patients, understanding the association between femoral artery IMT and atherosclerosis could provide valuable insights into the progression and clinical implications of vascular disease in this population^[10].

Furthermore, identifying potential correlations between femoral artery IMT and other clinical parameters, such as CKD stage, gender, and comorbid conditions like diabetes, offers the potential for risk stratification and targeted interventions. This information could facilitate early identification of CKD patients at higher cardiovascular risk and guide preventive strategies aimed at reducing atherosclerotic burden and associated adverse outcomes^[3].

In this hospital-based cross-sectional study, it was aimed to add to the body of knowledge by determining the prevalence of atherosclerosis in the femoral arteries of CKD patients and exploring potential relationships between femoral artery IMT and different clinical and demographic variables. The findings from this study could shed light on the intricate interplay between CKD and atherosclerosis, ultimately informing clinical practice and guiding interventions to mitigate cardiovascular risk in this vulnerable patient population.

OBJECTIVES:

1. To assess the femoral vessel IMT in CKD subjects.
2. To calculate the estimated eGFR in CKD patients and analyse the relationship of femoral IMT in subjects with low eGFR.

MATERIALS AND METHODS:**Study Design:**

This study employed a cross-sectional design to investigate the relationship between femoral artery intima-media thickness (IMT) and atherosclerosis in patients with chronic kidney disease (CKD) over a one-year period.

Study Site:

The study was conducted at the tertiary care centre of Department of Radio Diagnosis at Sree Mookambika medical college, Kanyakumari.

Study Duration:

The study was conducted from August 2022 to July 2023.

Study Population:

The study population consisted of subjects with CKD who were undergoing ultrasound scans at the Department of Radio-diagnosis at Sree Mookambika medical college, Kanyakumari

Inclusion Criteria:

- All subjects with CKD undergoing ultrasonography at the Department of Radio-diagnosis at Sree Mookambika medical college, Kanyakumari
- CKD defined as a glomerular filtration rate (GFR) less than 60 ml per min per 1.73 m² for more than 3 months with renal insult or absence of it.

Exclusion Criteria:

- Patients with past renal transplant.
- Patients with a known history of renal malignancy.
- Patients diagnosed with hypertension or a history of smoking.
- Patients who underwent surgical/interventional treatment of femoral arteries for atherosclerotic disease.

Sample Size:

All diagnosed cases of CKD over a one-year period at Sree Mookambika medical college, Kanyakumari were included. The average number of patients with CKD referred to the department of radio-diagnosis over the past three years was around 84-96 per year, with a mean of 90. The sample size was calculated within +/- 10% of the mean, resulting in a range of 80-100. The study was carried out on 99 patients visiting the hospital's OPD/IPD for a 12-month duration.

Methodology:

Participants provided informed written consent and clinical data were collected using a pre-structured proforma. Comprehensive histories, relevant risk factors (smoking, hypertension, hyperlipidemia, obesity), and laboratory investigations (random blood sugar) were recorded. Femoral artery Doppler ultrasonography was performed using a PHILIPS – EPIC ELITE machine with a linear array transducer.

Examination Technique:

Patients were positioned supine with legs extended. Transverse scans of the left and right thigh regions were conducted, focusing on the common femoral artery (CFA) and superficial femoral artery (SFA). Intima-media thickness (IMT) measurements were taken on the transverse axis.

Data Collection Tools:

Data were recorded in a structured research proforma. Analysis was performed, and results were presented using tables, graphs, figures, and diagrams.

Statistical Analysis:

Descriptive statistics, including mean and standard deviation, were used for continuous quantitative variables. ANOVA, correlation, and regression analyses were used for comparative purposes between

groups based on qualitative characteristics. Discrete variables were represented by medians. Graphs were used to depict comparisons and convey categorical data. Chi-square or Fisher's exact test was used to evaluate relationships between results, clinical, and demographic characteristics. A significance level of $p < 0.05$ was considered important for all tests.

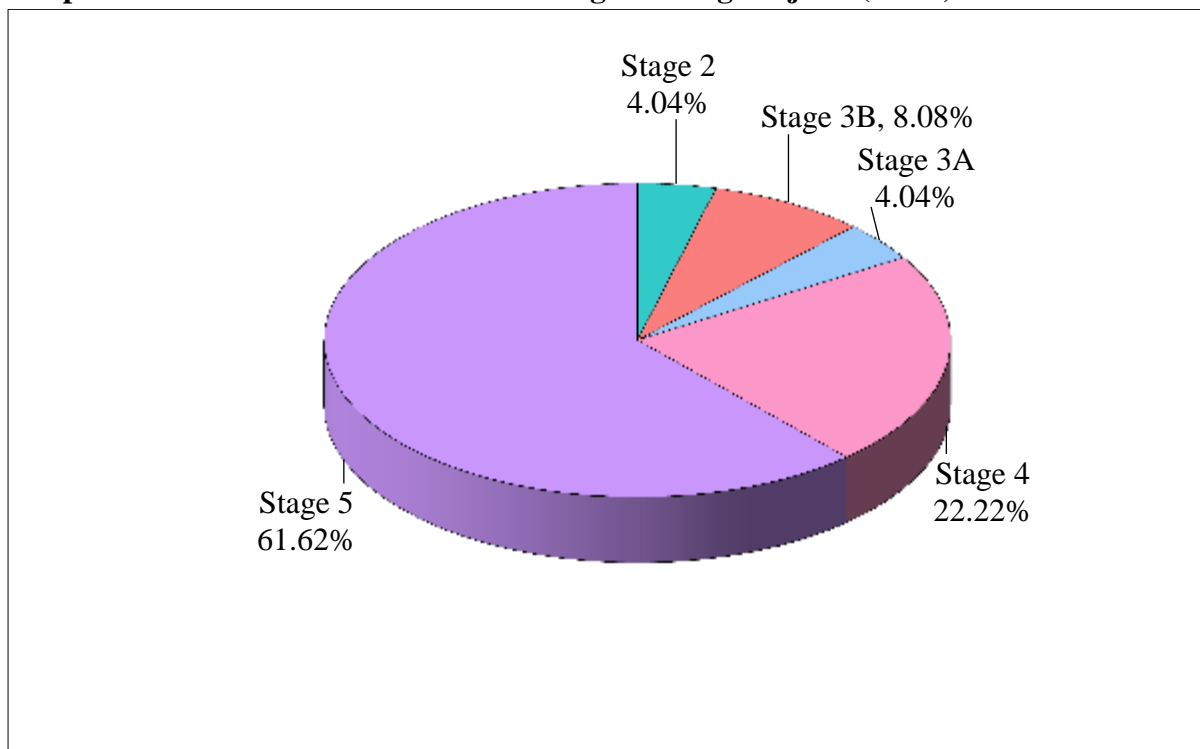
Ethical Considerations:

The study was approved by an institutional human ethics committee. Informed written consent was obtained from all participants, ensuring they understood the risks, benefits, and voluntary nature of participation. Participant confidentiality was maintained.

RESULTS:

s. no	Demographic details	Number (n=99)	Frequency (%)
1	Age groups	<=30 years	10
		31-40 years	13
		41-50 years	19
		51-60 years	26
		61- 70 years	23
		71-80 years	8
		Mean = 52.39	SD= 15.89
2	Gender	Male	70
		Female	29
3	Symptoms	Edema	46
		Urticaria	10
		Foot black discolouration	15
		Decreased urine output	28
4	HB low(gm/dl)	Yes	91
		No	8
5	On dialysis	No	83
		Yes	16

Graph 1: Distribution in terms of CKD stages among subjects (N=99).

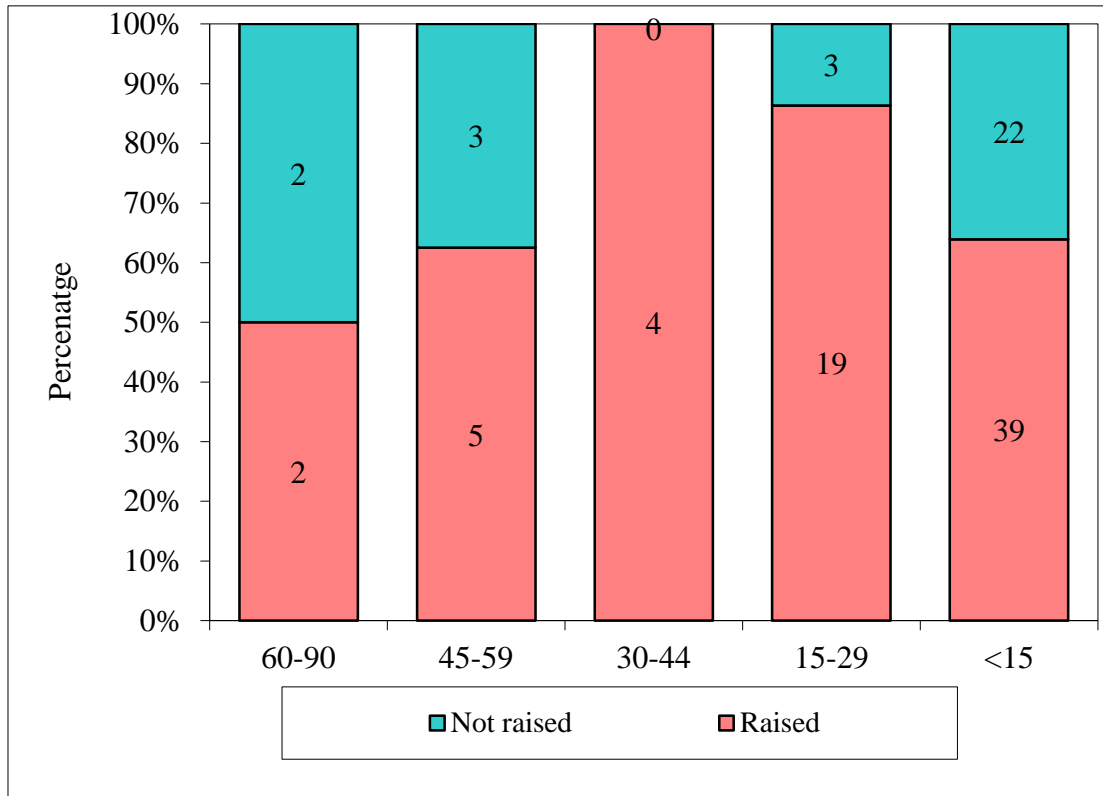


Maximum number (61) of subjects were in stage 5 . Only 4 subjects were in stage 2.

s. no	Prevalence of co-morbid conditions		Number (n=99)	Frequency (%)
1	Prevalence of diabetes	No	51	51.52
		Yes	48	48.48
2	Prevalence of raised Creatinine levels (mg/dl)	1.3-10	92	92.93
		11-21	6	6.06
		>21	1	1.01
3	Prevalence of raised Urea levels (mg/dl)	40-100	62	62.63
		101-200	34	34.34
		> 201	3	3.03
		40-100	62	62.63
4	Distribution in terms of eGFR levels (mL/min/1.73m ²)	60-90	4	4.04
		45-59	8	8.08
		30-44	4	4.04
		15-29	22	22.22
		<15	61	61.62
5	Raised triglycerides (TG) (mg/dl)	100-200	5	5.05
		201-300	43	43.43
		>301	51	51.52
6	Prevalence of raised IMT	Raised	69	69.70
		Not raised	30	30.30
7	Prevalence of femoral wall calcification	Present	36	36.36

		Absent	63	63.64
8	Prevalence of PVD among subjects	No	79	79.80
		Yes	20	20.20

Graph 2: Graphical representation of association between eGFR & IMT.



The study showed that all the patients with eGFR range 30-44 mL/min/1.73m² had raised IMT. And most of the patients (86.36%) with eGFR range 15-29 mL/min/1.73m² had raised IMT.

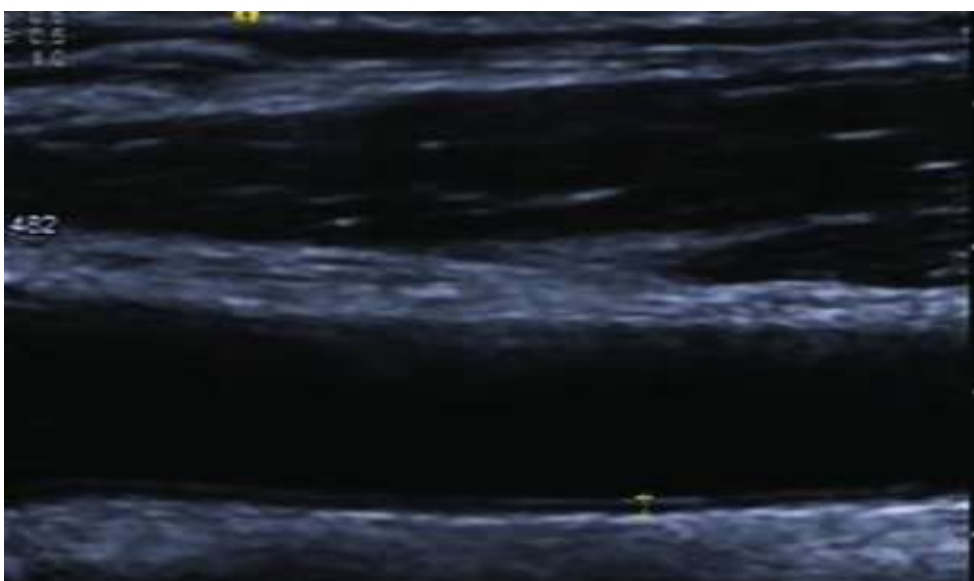


Figure 1: USG image showing normal IMT measurement even with CKD.

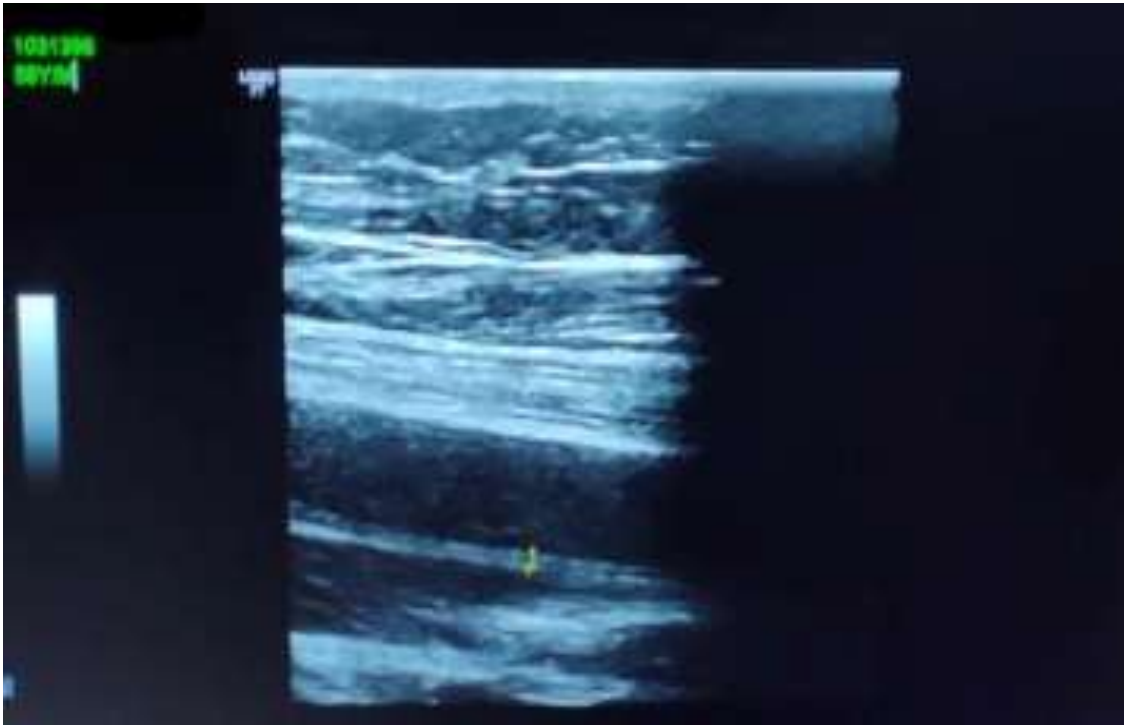


Figure 2 shows B mode USG image showing raised IMT of 1.0mm.

DISCUSSION:

Chronic renal disorder is a stand-alone threat for atherosclerosis. Colour Dopplerultrasonography is a non-invasive and cost-effective imaging modality that has a vitalfunction in assessing the severity of atherosclerotic disease in PVD in CKD patients^[1].

The presented study aims to investigate the relationship between femoral artery intima-media thickness (IMT) and atherosclerosis in patients with chronic kidney disease (CKD). The study utilizes a cohort of 99 individuals to explore the prevalence and potential associations of these parameters in CKD patients. The findings provide valuable insights into the impact of CKD on atherosclerotic disease and its implications for patient management.

Demographic and Clinical Characteristics:

The study's demographic data reveals a higher proportion of male patients with CKD compared to females. The age distribution highlights that the majority of participants fall within the 50-70 age range, with the highest prevalence in the 60-70 age group. These demographics are consistent with the expected age-related prevalence of CKD and atherosclerosis. The presence of symptoms such as edema and decreased urine output underscores the clinical significance of these conditions^[2,11].

Prevalence of Atherosclerosis and IMT:

The study employs color Doppler ultrasonography to assess IMT and atherosclerotic plaques. The prevalence of raised IMT is notably high (69.70%), indicating a strong association between CKD and atherosclerosis. This finding is supported by prior research, including studies by Nariman et al^[12], and Simova et al.^[3], which found similar associations between femoral IMT and chronic renal disorder subjects. Additionally, the observed IMT values are within the range reported in literature.

Association with Diabetes:

A noteworthy finding is the higher prevalence of raised IMT among diabetic CKD patients. This association underscores the synergistic effect of diabetes and CKD in accelerating atherosclerosis development. The study's results align with the research of Le et al.^[8], suggesting a substantial impact of diabetes on IMT thickening.

eGFR Distribution and CKD Stages:

The study utilizes estimated glomerular filtration rate (eGFR) to categorize CKD stages. The majority of patients are categorized in stage 5 CKD, which corresponds to the advanced stage of renal dysfunction. The distribution of eGFR values reflects the expected decline in kidney function in CKD patients. This categorization facilitates the examination of associations between eGFR, CKD stages, and atherosclerosis indicators^[13,14].

Association between eGFR, CKD Stages, and IMT:

The study reveals a strong positive correlation between reduced eGFR values and raised IMT. Patients with eGFR values of 15-29 mL/min/1.73m² exhibit the most significant correlation with IMT thickness. This correlation aligns with the understanding that impaired kidney function contributes to systemic inflammation and endothelial dysfunction, both of which promote atherosclerosis^[15,16].

Association with Triglyceride Levels:

A novel finding in the study is the association between reduced eGFR values and elevated triglyceride levels. This relationship underscores the intricate metabolic disturbances in CKD patients and their role in atherosclerosis development^[17,18].

Limitations:

Examination technique and small sample size are the limitations of the study. Large sample size would have helped in establishing a correlation between femoral intima-media thickness and atherosclerosis. And also in determining the cut-off values for femoral intima-media thickness in atherosclerosis in chronic kidney disease patients.

Since the ultrasound technique depends on the skill of the examiner, there is a lot of intra and inter-observer variations in assessing IMT.

Also, there were a lot of unavoidable risk factors which were not matched in the study such as age, BMI, smoking habits, and hypertension which would have also been factors in raising the intima media thickness.

Lastly, atherosclerosis was not confirmed by histopathology which is the most gold standard for confirmation of the same.

CONCLUSION:

Chronic kidney disease (CKD) is strongly associated with peripheral artery disease (PAD), with a global prevalence of 11-13%. This study contributes to our understanding of the intricate relationship between femoral artery IMT and atherosclerosis in the context of chronic kidney disease. In conclusion, the study highlights the relationship between femoral artery IMT and atherosclerosis in patients with CKD. However, the study also reveals complexities in the associations, potentially due to the multifaceted nature of CKD and its interaction with atherosclerosis. By shedding light on the prevalence of atherosclerosis and its associations with gender, diabetes, eGFR, and lipid levels, the findings underscore the importance of comprehensive cardiovascular assessment and management in CKD patients. Further research and interventions targeting these interrelated factors could hold promise for reducing the burden of atherosclerotic complications in individuals with chronic kidney disease.

REFERENCES:

1. Bikbov B, Purcell CA, Levey AS, Smith M, Abdoli A, Abebe M, et al. Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *The Lancet* 2020;395(10225):709–33.
2. Cockwell P, Fisher LA. The global burden of chronic kidney disease. *The Lancet* 2020;395(10225):662–4.
3. Simova' 'Iana. Intima-media thickness: appropriate evaluation and proper measurement [Internet]. [cited 2023 Aug 30];13(21). Available from: <https://www.escardio.org/Journals/E-Journal-of-Cardiology-Practice/Volume-13/Intima-media-thickness-Appropriate-evaluation->

- and-proper-measurement-described, <https://www.escardio.org/Journals/E-Journal-of-Cardiology-Practice/Volume-13/Intima-media-thickness-Appropriate-evaluation-and-proper-measurement-described>
4. Soneye MA, Adekanmi AJ, Obajimi MO, Aje A. Intima-media thickness of femoral arteries and carotids among an adult hypertensive Nigerian population: A case-control study to assess their use as surrogate markers of atherosclerosis. *Ann Afr Med* 2019;18(3):158–66.
 5. Shu J, Santulli G. Update on peripheral artery disease: Epidemiology and evidence-based facts. *Atherosclerosis* 2018;275:379–81.
 6. Leon BM, Maddox TM. Diabetes and cardiovascular disease: Epidemiology, biological mechanisms, treatment recommendations and future research. *World J Diabetes* 2015;6(13):1246–58.
 7. Centurión OA. Carotid Intima-Media Thickness as a Cardiovascular Risk Factor and Imaging Pathway of Atherosclerosis. *Crit Pathw Cardiol* 2016;15(4):152–60.
 8. Le TD, Nguyen NPT, Nguyen ST, Nguyen HT, Tran HTT, Nguyen THL, et al. The Association Between Femoral Artery Intima-Media Thickness and Serum Glucagon-Like Peptide-1 Levels Among Newly Diagnosed Patients with Type 2 Diabetes Mellitus. *Diabetes Metab Syndr Obes* 2020;13:3561–70.
 9. Lee K, Kong T, Park KM, Jeon Y, Cho SG, Hong K. Evaluation of the Femoral Artery IMT as a Risk Factor of Cardiovascular Disease. *Journal of Surgical Ultrasound* 2019;6:53–7.
 10. Arinze NV, Gregory A, Francis JM, Farber A, Chitalia VC. Unique aspects of peripheral artery disease in patients with chronic kidney disease. *Vasc Med* 2019;24(3):251–60.
 11. Kovesdy CP. Epidemiology of chronic kidney disease: an update 2022. *Kidney Int Suppl* (2011) 2022;12(1):7–11.
 12. Nezami N, Ghabili K, Shokouhi-Gogani B, Mirchi M, Ghojzadeh M, Safa J, et al. The Relationship between Carotid and Femoral Artery Intima-Media Thickness and Histopathologic Grade of Atherosclerosis in Patients with Chronic Kidney Disease. *Nephron* 2018;139(2):159–69.
 13. Levey AS, Coresh J, Tighiouart H, Greene T, Inker LA. Measured and estimated glomerular filtration rate: current status and future directions. *Nat Rev Nephrol* 2020;16(1):51–64.
 14. Stevens LA, Coresh J, Greene T, Levey AS. Assessing Kidney Function — Measured and Estimated Glomerular Filtration Rate. *New England Journal of Medicine* 2006;354(23):2473–83.
 15. Nankivell BJ, Nankivell LFJ, Elder GJ, Gruenewald SM. How unmeasured muscle mass affects estimated GFR and diagnostic inaccuracy. *eClinicalMedicine* [Internet] 2020 [cited 2023 Aug 30];29. Available from: [https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370\(20\)30406-5/fulltext](https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(20)30406-5/fulltext)
 16. Nezu T, Hosomi N, Aoki S, Matsumoto M. Carotid Intima-Media Thickness for Atherosclerosis. *J Atheroscler Thromb* 2016;23(1):18–31.
 17. Quinn MP, Cardwell CR, Kee F, Maxwell AP, Savage G, McCarron P, et al. The finding of reduced estimated glomerular filtration rate is associated with increased mortality in a large UK population. *Nephrol Dial Transplant* 2011;26(3):875–80.
 18. Association of Mildly Reduced Kidney Function With Cardiovascular Disease: The Framingham Heart Study | *Journal of the American Heart Association* [Internet]. [cited 2023 Aug 30]; Available from: <https://www.ahajournals.org/doi/10.1161/JAHA.120.020301>