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Screening for asymptomatic carotid and peripheral atherosclerosis in chronic kidney disease patients with coronary artery disease

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Abstract:

Introduction: Chronic kidney disease (CKD) affects about 10% of the worldwide population and is associated with increased morbidity and mortality. Doppler ultrasound is a simple bedside tool that can detect atherosclerosis in different vascular beds.

Aim of the study: To screen for the presence of subclinical asymptomatic carotid and peripheral atherosclerosis in patients with CKD with documented coronary atherosclerosis.

Subjects and methods: Patients with an established diagnosis of CKD and documented coronary artery disease with no history of carotid or peripheral arterial disease were recruited. Carotid and femoral arterial duplex were done to detect the presence of asymptomatic atherosclerosis.

Results: A total of 110 patients were recruited. The mean age of the patients was 59 years and they were predominantly males. Dyslipidemia and hypertension were the most common atherosclerotic risk factors exceeding 80% of the patients. About 84% of the patients had evidence of diffuse carotid atherosclerosis while 83% of them had evidence of diffuse femoral atherosclerosis. The prevalence of carotid and femoral atherosclerotic plaques was around 50%. The independent predictors of increased CCA IMT were higher body weight and elevated TG levels. The independent predictors of increased femoral IMT were the presence of hypertension, elevated levels of LDL-C and lower levels of HDL-C.

Conclusion: Asymptomatic carotid and peripheral atherosclerosis are common among patients with CKD and established CAD. The traditional atherosclerotic risk factors are important mechanistic for the development of carotid and peripheral atherosclerosis in this patient group.

Keywords: Chronic Kidney Disease; Asymptomatic Carotid Atherosclerosis; Asymptomatic Peripheral Atherosclerosis; Coronary Atherosclerosis

1. Introduction

Chronic kidney disease (CKD) is a common worldwide disease associated with increased morbidity and mortality [1]. Patients with CKD are at high risk of

cardiovascular disease [2, 3]. However, they are often underrepresented or excluded in clinical trials, causing an important knowledge gap in the epidemiology, diagnosis and management of cardiovascular disease in this critical patient group.

Arterial atherosclerosis with subsequent cerebrovascular, cardiovascular and peripheral arterial adverse outcomes is not uncommon in patients with CKD [4-6] and the incidence increases in patients with dialysis [7]. Unfortunately, this incidence remains high after kidney transplantation [8].

Multiple risk factors play an important role in explaining this relation, including the traditional atherosclerosis risk factors including diabetes mellitus, hypertension, dyslipidemia, smoking and obesity [2]. Other risk factors that occur due to renal dysfunction include inflammation, abnormal calcium-phosphorus metabolism, and accumulation of uremic toxins [9] that can lead to vascular calcification including intima arterial calcification or medial arterial calcification (MAC) [10].

Doppler ultrasound is a simple, bedside, noninvasive method for assessment of carotid and peripheral atherosclerosis. It offers excellent delineation of the intimal thickening and detection of atherosclerotic plaques and its significance [11].

Doppler ultrasound has been widely used for the detection of carotid and peripheral atherosclerosis and to correlate with the risk of coronary atherosclerosis and cardiovascular adverse outcomes [12].

The study aimed to screen for the presence of subclinical asymptomatic carotid and peripheral atherosclerosis in patients with CKD with documented coronary atherosclerosis.

2. Subjects & Methods

2.1. Study design

This was a prospective observational study that included patients with CKD admitted to the cardiology department of Kasr Alainy School of Medicine Cairo University with documented coronary artery disease between May 2021 to April 2022.

Inclusion criteria

Patients > 18 years old with an established diagnosis of CKD and documented coronary artery disease with no

history of symptomatic carotid or peripheral arterial disease.

Definitions:

- CKD: CKD was diagnosed based on the KDIGO guidelines by the history of > 3-month duration of eGFR < 60 ml/min/1.73 m2 [1, 2].
- Coronary artery disease: diagnosed by a history of coronary angiography showing atherosclerotic coronary artery disease or history of revascularization either percutaneous or surgical.
- Symptomatic carotid and peripheral atherosclerosis: history of old cerebrovascular events, or ischemic events of the lower limbs or history of revascularization either percutaneous or surgical.
- Atherosclerotic plaque was defined as focal abnormal wall thickening (intima-media thickness (IMT), > 1.5 mm) or a focal thickening of > 50% of the surrounding IMT [13]. Plaque burden was calculated as the summation of the area of all the atherosclerotic plaques detected by Doppler ultrasound [14].

2.2. Methodology

After informed consent, all patients were subjected to clinical assessment for atherosclerotic risk factors and comorbidities including the presence of diabetes mellitus, hypertension, smoking status and dyslipidemia. Also, laboratory work with special emphasis on renal functions, lipid profile and glycemic profile.

A duplex study was performed using a sector transducer 8 mHz of a Philips machine. A Carotid duplex was done to measure the intima-media thickness of the common carotid artery (CCA) and detect the presence of atherosclerotic plaques. Carotid IMT was done by measuring the posterior wall of the common carotid artery.

Peripheral arterial duplex was done at the level of the common femoral artery (CFA) bifurcation and the proximal segment of the superficial femoral artery (SFA) to measure the IMT of the posterior wall of the CFA and the SFA.

2.3. Statistics

Data was analyzed by statistical package for the social sciences (SPSS, version 26.0; SPSS Inc., Chicago, Illinois, USA). Variables were presented as mean and SD. The *P*-value of less than 0.05 was considered significant. Regression analysis was done to detect the independent predictors of carotid and peripheral atherosclerosis.

3. Results

Between May 2021 and April 2022, we recruited 110 patients fulfilling the inclusion criteria of the study. The baseline characteristics of the patients are listed in **Table 1.** The mean age of the patients was 59 years. Males were more common with mean body mass index (BMI) of 31 kg/m^2. Dyslipidemia and hypertension were the most common atherosclerotic risk factors exceeding 80% of the patients while about half of the patients were diabetics.

Table 1: Baseline characteristics.

Variables	Values
Age (years)	58.7±6.9
Gender (male)	64%
Weight (Kg)	89.4±13.6
Body mass index (Kg/m^2)	31±5.5
Diabetes mellitus	52%
Diabetes mellitus duration (Months)	145.9±89.6
Hypertension	80%
Hypertension duration (Months)	103.1±63.8
Smoking (yes)	40%
Smoking severity	830±532.5
Chronic kidney disease duration (Months)	34.5±51.8
Dyslipidemia	86.7%

Laboratory workup showed abnormal renal and lipid profile with poor control of diabetes evident by elevated levels of postprandial blood glucose and HbA1c (**Table 2**).

Table 2: Laboratory workup.

Variables	Values
Serum urea (mg/dl)	80.4±31.8
Serum creatinine (mg/dl)	2.75±0.61
eGFR (ml/min/1.73 m^2)	38.6±10.3
Total cholesterol (mg/dl)	197.3±45
LDL (mg/dl)	151.2±41.7
HDL (mg/dl)	35.9±8.1
Triglycerides (mg/dl)	146.8±63
Hemoglobin (g/dl)	11.65±2.3
Fasting blood sugar (mg/dl)	113.6±21
2h PPS (mg/dl)	210±51.4
HbA1c (%)	8.6±2.3

LDL; low-density lipoprotein cholesterol, HDL; high-density lipoprotein cholesterol, 2hPPS; 2 hours postprandial sugar, HbA1c; glycosylated hemoglobin.

Duplex examination of the carotid and femoral arteries showed increased IMT of both carotid and femoral arteries in more than 80% of the patients with a mean CCA IMT of 0.83 and a mean femoral IMT of 0.85. Also, more than 50% of them had atherosclerotic plaques that were slightly more in the carotid arteries than the femoral arteries. The mean of the total plaque burden was 0.59 (**Table 3**).

Table 3: Duplex parameters.

Variables	Values
Rt CCA IMT (cm)	0.8 ±0.16
Lt CCA IMT (cm)	0.85 ±0.15
Mean CCA IMT (cm)	0.83 ±0.13
CCA IMT > 0.7	84%
Rt CFA IMT (cm)	0.75 ±0.24
Lt CFA IMT (cm)	0.73 ±0.18
Mean FA IMT (cm)	0.85 ±0.21
FA IMT > 0.6	82.7%
Plaques	56%
CCA plaques	57.1%
CFA plaques	42.9%
Total plaque burden	0.59 ±0.22

CCA; common carotid artery, IMT; intima-media thickness, CFA; common femoral artery, FA; femoral artery.

Regarding the prevalence of asymptomatic carotid and peripheral atherosclerosis in the recruited patients, 84% of the patients had evidence of diffuse carotid atherosclerosis while 83% of them had evidence of diffuse femoral atherosclerosis. The prevalence of carotid and femoral atherosclerotic plaques was around 50%.

Univariate and multivariate regression analysis were done to detect the predictors of carotid and peripheral atherosclerosis. The independent predictors of increased CCA IMT were higher body weight and elevated TG levels (**Figure 1**). The independent predictors of increased femoral IMT were the presence of hypertension, elevated levels of LDL-C and lower levels of HDL-C (**Figure 2**). The independent predictors of the presence of carotid and peripheral atherosclerotic plaques were elevated levels of TC and TG (**Figure 3**). The independent predictors of increased carotid and peripheral plaque burden were the presence of diabetes mellitus, lower eGFR and elevated TC (**Figure 4**).

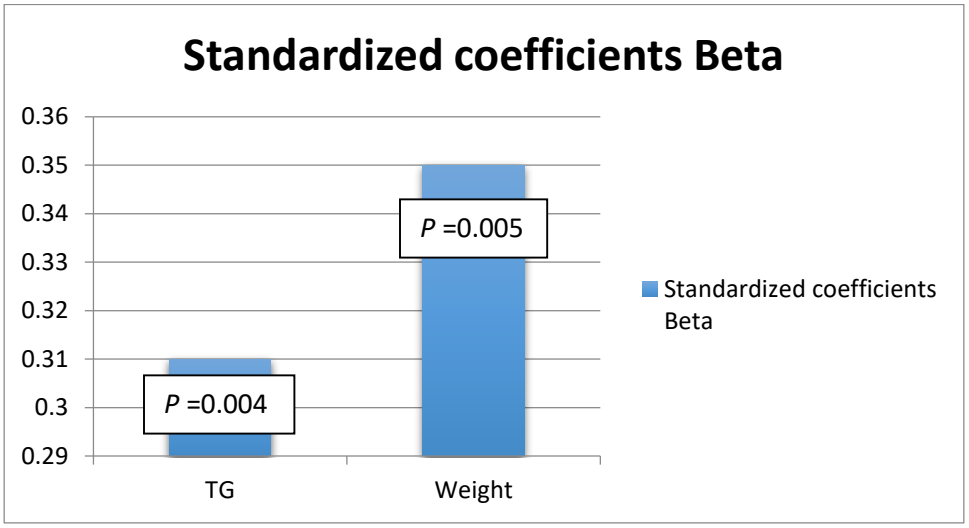

Figure 1: Independent predictors of increased carotid IMT.

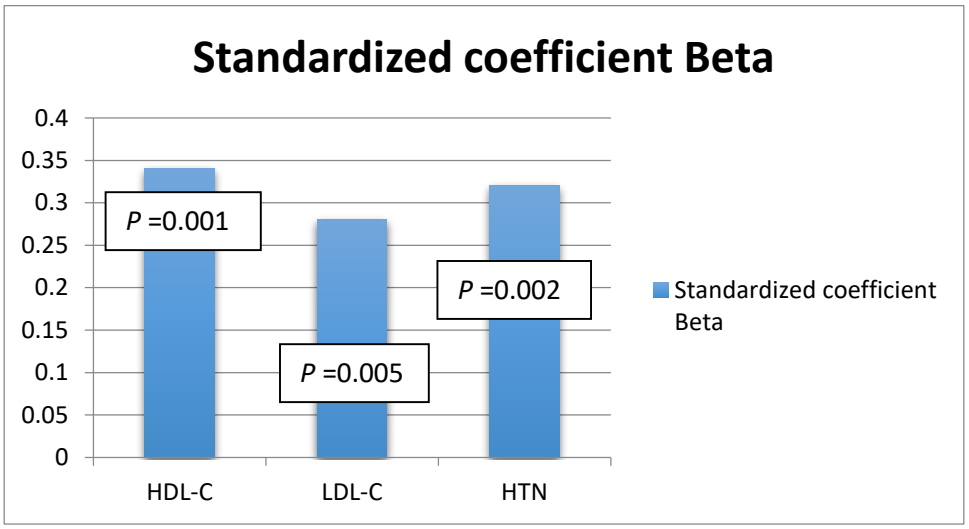

Figure 2: Independent predictors of increased femoral IMT.

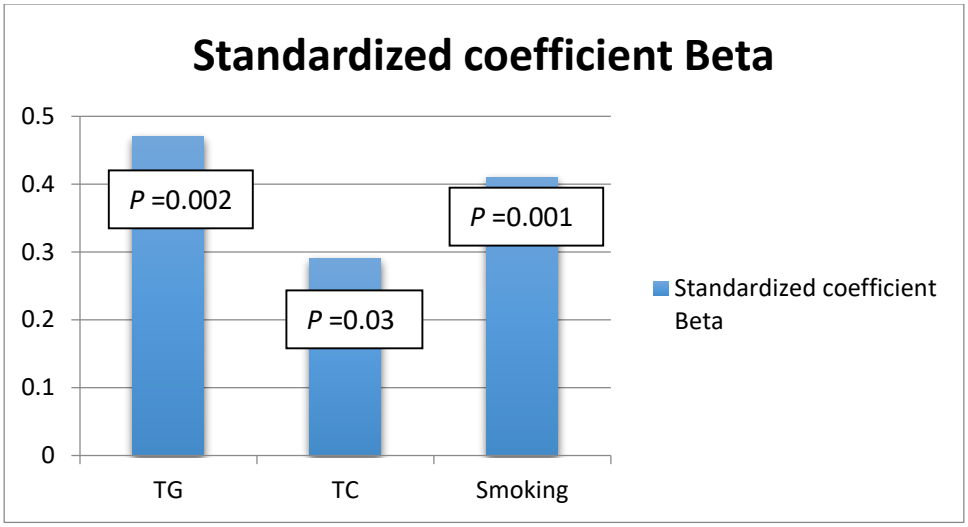

Figure (3): Independent predictors of the presence of carotid or femoral atherosclerotic plaques.

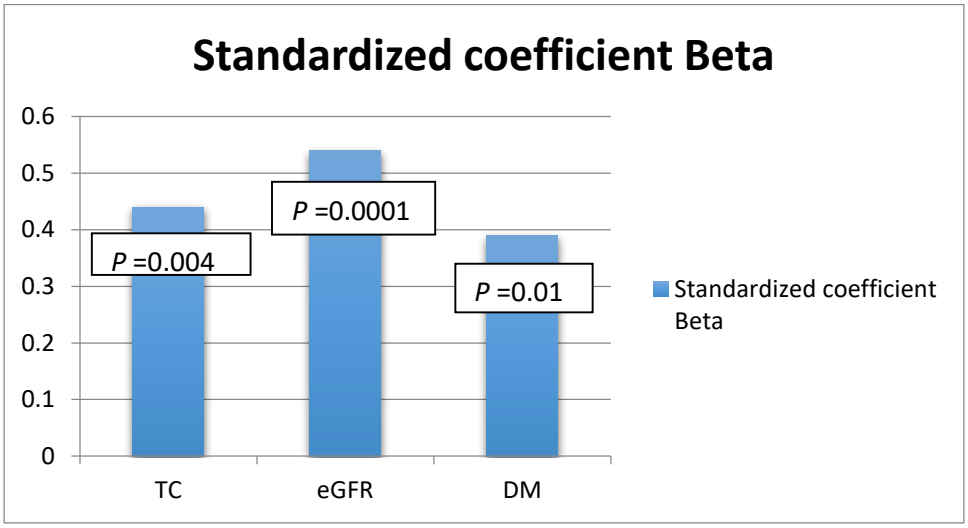

Figure 4: Independent predictors of increased plaque burden.

4. Discussion

The main findings in this study were more than 80% of the patients with CKD and documented CAD have associated asymptomatic diffuse carotid and peripheral arterial disease. Also, about half of the patients with CKD and documented CAD have carotid and femoral atherosclerotic plaques. Finally, the traditional

atherosclerotic risk factors including hypertension, diabetes mellitus, dyslipidemia and obesity are the main independent predictors of carotid and peripheral atherosclerosis in patients with CKD.

Doppler ultrasound assessment showed that 80% of the recruited patients had increased carotid and femoral IMT with mean carotid IMT of 0.83 mm and mean femoral IMT of 0.85 mm and 50% of them had carotid and femoral atherosclerotic plaques. This is consistent with the data from multiple studies showing increased carotid IMT among patients with CKD between 0.8 and 0.9 mm [16, 17]. This data confirms that a large proportion of patients with CKD and established CAD -although asymptomatic- have concomitant carotid and peripheral atherosclerosis.

Traditional atherosclerotic risk factors were prevalent among the recruited patients with over 80% of them having hypertension and dyslipidemia and about 50% having diabetes mellitus with a mean HbA1c of 8.6 among them.

This study confirms the role of the traditional atherosclerotic risk factors in the development of carotid and peripheral atherosclerosis in CKD patients as the independent predictors of the presence of diffuse atherosclerosis in the carotid arteries were obesity and elevated TG levels and in the femoral arteries were hypertension, elevated LDL-C levels and decreased HDL-C levels. The independent predictors of the presence of carotid and femoral atherosclerotic plaques were smoking and elevated TC and TG levels. Also, the independent predictors of high carotid and peripheral plaque burden were the presence of diabetes mellitus, higher levels of TC and lower levels of eGFR [15, 16].

5. Conclusion

Asymptomatic carotid and peripheral atherosclerosis are prevalent among patients with CKD and established CAD. The traditional atherosclerotic risk factors are important mechanistic for the development of carotid and peripheral atherosclerosis in this patient group.

Ethical committee approval: The study protocol was approved by the research ethical committee of the faculty of medicine, Cairo University following the guidelines of ethical considerations of the Helsinki Declaration.

Availability of data and material: The datasets used and/or analyzed during the

current study are available from the corresponding author upon reasonable request.

Competing interests: All authors declare no conflict of interest.

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AI declaration statement: Not applicable.

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