Impact of chronic kidney disease on the extent and severity of coronary plaque burden in general population: evaluation by Coronary CT angiography

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Article

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Abstract

Background Previous studies have reported an association between chronic kidney disease (CKD) and coronary artery calcification. However, data on the quantitative assessment of coronary plaques in patients with CKD without overt coronary events are limited. The current study aimed to examine the association of CKD with the composition and burden of coronary atherosclerotic plaques in the general population.

Methods The authors studied 1747 subjects who underwent coronary computed tomographic angiography as part of health checkup. Atherosclerotic plaque burden was measured by atheroma burden obstructive score (ABOS), segment involvement score (SIS), and segment stenosis score (SSS). Based on the number of segments with plaques, the extent of coronary artery disease (CAD) was categorized as non-extensive (SIS ≤4 or SSS <7) or extensive (SIS >4 or SSS ≥7).

Results In all participants, calcified plaques were more frequently detected than mixed or non-calcified plaques. Regarding the grade of luminal stenosis, obstructive plaques (> 50% stenosis) were more frequently observed in the CKD group than in the non-CKD group. Individuals with CKD had significantly higher ABOS, SIS, and SSS than those without CKD. After adjusting for traditional risk factors, CKD was independently associated with obstructive mixed plaques (odds ratio [OR]: 1.937, P=0.012) and extensive CAD (SIS >4 [OR: 1.645; P=0.043]; SSS ≥7 [OR: 1.660; P=0.045]). Subgroup analyses revealed no significant heterogeneity between CKD and obstructive mixed plaques in each subgroup. However, a more prominent association between CKD and the risk of extensive CAD was observed in subjects aged <65 years.

Conclusions Renal dysfunction was independently associated with obstructive mixed plaque pattern and increased atherosclerotic plaque burden. Our findings support that CKD is a major risk factor for the development of obstructive and extensive CAD.

Clinical Perspective

What is new?

- Chronic kidney disease was independently associated with obstructive mixed plaque pattern, suggesting an association between impaired renal function and the feature of plaque vulnerability in coronary arteries.
- Subjects with chronic kidney disease had a higher coronary plaque burden and an increased risk of extensive coronary artery disease.

What are the clinical implications?

- More aggressive efforts to decrease the progression of mixed plaques and reduce the total plaque burden are important in subjects with chronic kidney disease to prevent future cardiovascular events.

Introduction

Chronic kidney disease (CKD), defined as dysfunction of the glomerular filtration apparatus, is an independent risk factor for the development of coronary artery disease (CAD).[1] The risk increases as renal function declines. Even patients with mildly reduced renal function [estimated glomerular filtration rate (eGFR) 60–90 ml/min/1.73 m^2] are at an increased risk of obstructive CAD.[2] A lower level of kidney function is associated with a marked increase in the probability of atherosclerotic cardiovascular disease over 5 years.[3] Furthermore, CKD is associated with increased risks of death, cardiovascular events, and hospitalization in a large, community-based population.[4] However, atypical presentation of cardiac ischemia in patients with CKD often leads to delay in diagnosis and treatment.[5]

Coronary computed tomographic angiography (CCTA) has been playing a significant role in the assessment of coronary artery stenosis. CCTA can be used to noninvasively assess the presence and burden of atherosclerotic plaque, including plaque composition and plaque volume.[6] Prospective multicenter studies have demonstrated the diagnostic accuracy of CCTA, with a sensitivity between 85% and 99% and a specificity between 64% and 92%, in patients with suspected but unconfirmed CAD.[7–11] Patients with a comparable plaque burden carried similar risks of downstream major cardiovascular events regardless of whether they had non-obstructive or obstructive CAD.[12] Several studies have reported associations between CKD and coronary artery calcification (CAC). The Chronic Renal Insufficiency Cohort (CRIC) Study investigators found a graded relationship between CKD severity and CAC score, independent of conventional risk factors for atherosclerosis.[13] In addition, non-obstructive calcified plaque is the most common imaging feature in patients with CKD.[14] The identification of non-obstructive plaque is an important advantage of CCTA that is overlooked by ischemia-based imaging assessments and should prompt the consideration of preventive medical therapies. Nevertheless, data on the quantitative assessment of coronary plaques in patients with CKD without overt coronary events are limited. Based on the accuracy of plaque burden assessments on CCTA and their association with cardiovascular events, the current study aimed to examine the association of CKD with the presence and burden of coronary atherosclerotic plaques in the general population.

Methods

Study population

This study was a cross-sectional observational study. Subjects who underwent CCTA using 256-slice multidetector computed tomography as part of a general routine health examination at a single medical center in Taipei, Taiwan, between January 2014 and July 2017, were surveyed. Before enrollment, the medical history of each participant was reviewed in detail to obtain data on smoking status and risk factors for atherosclerosis such as age, hypertension, type 2 diabetes, pre-existing renal dysfunction, and other comorbidities. Hypertension was defined as elevated office blood pressure (systolic blood pressure ≥ 140 or diastolic blood pressure ≥ 90 mmHg) or regular use of antihypertensive medications. Type 2

diabetes was defined as fasting glucose ≥ 126 mg/dL or glycosylated hemoglobin (HbA1c) level ≥ 6.5% or use of hypoglycemic agents. CKD was defined as an eGFR < 60 mL/min/1.73 m^2. The modified glomerular filtration rate estimating equations for Chinese patients were used to calculate eGFR.[15] Subjects with a prior history of CAD were excluded. All participants gave written informed consent. This study complied with the principles of the Declaration of Helsinki, and the study protocol was approved by the Institutional Review Board of Taipei Veterans General Hospital.

CCTA imaging protocol and analysis

CCTA was performed with a multiple detector computed tomography scanner (Definition Flash, Siemens Healthineers, Erlangen, Germany). Before each CCTA process, beta-blockers or calcium channel blockers were given to subjects with an initial heart rate > 80 beats per minute. CCTA was performed using retrospective gated helical scanning with the parameters set at 64 × 0.5 mm–128 × 0.625 mm collimation, 270–350 ms gantry rotation time, and 80–135 kV based on body size. After injecting 50–100 mL of iodinated contrast medium (Iopamiro 370, Bracco Imaging SpA, Milan, Italy; Ultravist 370, Bayer Pharma AG, Berlin, Germany) at a rate of 4.5–5.0 mL per second followed by 50 mL of normal saline at a rate of 5.5 mL per second based on the individual's body size and renal function, the bolus-tracking method was used for imaging. The workstation automatically selected the best phase of image. If the image quality was suboptimal, a phase with the best possible image quality was manually reconstructed by certified CCTA technician. All images were transferred to an external workstation (EBW, Amsterdam, Netherlands) for analysis. Detailed plaque morphology and the degree of coronary luminal stenosis were assessed based on previous guidelines.[16] In this study, coronary arteries were divided into 4 branches, including the left main (LM), left anterior descending (LAD), left circumflex (LCX), and right coronary (RCA) arteries, and into 16 segments according to a modified standard of the American Heart Association.[17] The extent of stenosis caused by plaques was classified as obstructive and nonobstructive based on a threshold of 50% luminal narrowing. Plaques were visually classified as calcified (plaques with higher CT attenuation than the contrast-enhanced lumen, Fig. 1A), non-calcified (plaques with lower CT attenuation than the contrast-enhanced lumen without any calcification, Fig. 1B), and mixed (calcified and noncalcified elements in a single plaque, Fig. 1C).

The extent and severity of coronary atherosclerotic burden were measured by several CCTA scores,[18,19] including CAC score, atheroma burden obstructive score (ABOS), segment involvement score (SIS), and segment stenosis score (SSS). The CAC score was calculated using the Agatston method and graded as follows: 0, 1–99, 100–399, and ≥ 400. The ABOS was defined as the number of plaques with > 50% stenosis in the entire coronary artery tree. To measure the overall coronary artery plaque distribution, the SIS was calculated as the total number of coronary artery segments that exhibited plaques, regardless of the degree of luminal stenosis within each segment (minimum = 0; maximum = 16). The SSS was used as a measure of the overall extent of coronary artery plaques. To determine the SSS, each individual coronary segment was graded as having no to severe plaques (scores ranging from 0 to 3 points) based on the extent of obstruction of the coronary luminal diameter. Then, the extent scores from all 16 individual segments were summed to yield a total score that ranged from 0 to 48. Based on previously

published studies,[20–22] the extent of CAD was categorized as non-extensive (SIS ≤ 4 or SSS < 7) or extensive (SIS > 4 or SSS ≥ 7).

Laboratory measurements

Before undergoing CCTA procedure, blood samples were collected from the participants after an overnight fast of at least 8 hours. Serum levels of blood urea nitrogen, creatinine, aspartate aminotransferase, alanine aminotransferase, uric acid, glucose, HbA1c, and lipid profiles including total cholesterol, triglycerides, high- and low-density lipoprotein cholesterol (HDL-C and LDL-C, respectively) were measured using a TBA-c16000 automatic analyzer (Toshiba Medical Systems, Tochigi, Japan).

Statistical analysis

Data were expressed as mean and standard deviation (SD) for numerical variables and as number (percentage) for categorical variables. Comparisons of continuous variables between groups were performed by Student's *t*-test. Subgroup comparisons of categorical variables were assessed using a Chi-square or Fisher's exact test. To determine the association of CKD with coronary plaque composition and extent and severity of atherosclerotic plaque burden, a multivariate logistic regression analysis was performed after considering variables, including age, sex, body mass index (BMI), smoking status, and history of hypertension, diabetes, and hyperlipidemia. Subgroup analyses were undertaken to investigate the consistency of the impact of CKD on coronary plaque composition and plaque burden among subjects aged ≥ 65 years, sex, smoking status, BMI ≥ 27, and the presence of hypertension, diabetes, and hyperlipidemia. Data were analyzed using SPSS software (version 17.0, SPSS Inc, Chicago, IL, USA). A 2-sided *P* value of < 0.05 indicated statistical significance.

Results

Patient characteristics

One-thousand eight-hundred fifty-three subjects were initially surveyed. After excluding 85 individuals with a prior history of CAD, 17 without data regarding renal function, and 4 with poor image quality, 1747 subjects (mean age: 58.06 ± 9.73 years; 1243 men and 504 women) were enrolled in our study. The study flowchart is shown in Fig. 2. One-hundred and five (6.0%) subjects were classified as having CKD based on their eGFR level, and 1642 (94.0%) were not. The baseline characteristics of the study participants are shown in Table 1. No significant differences were noted between individuals with and without CKD with respect to age, smoking status, BMI, systolic and diastolic blood pressure, and serum triglycerides levels. However, subjects with CKD comprised more men; had a significantly higher prevalence of hypertension, diabetes, and hyperlipidemia; and were more likely to present with higher levels of serum fasting glucose, HbA1c, and uric acid than those without CKD. Furthermore, CKD subjects had significantly lower serum lipid profiles, including total cholesterol, HDL-C, and LDL-C levels.

Table 1
Baseline characteristics of patients with and without CKD

	With CKD	Without CKD	
	(n = 105)	(n = 1642)	P-value
Age (years)	65.9 ± 10.5	57.6 ± 9.5	0.227
Male	89 (84.8)	1154 (70.3)	0.001
Current smoker	33 (31.4)	527 (32.1)	0.887
Hypertension	63 (60.0)	517 (31.5)	< 0.001
Diabetes mellitus	28 (26.7)	203 (12.4)	< 0.001
Hyperlipidemia	36 (34.3)	341 (20.8)	0.001
Body mass index (kg/m^2)	25.4 ± 3.4	25.0 ± 3.4	0.687
Systolic BP (mmHg)	130.2 ± 18.5	123.9 ± 16.9	0.227
Diastolic BP (mmHg)	78.6 ± 11.1	78.3 ± 10.4	0.935
Lipid profiles (mg/dL)			
Triglycerides	157.4 ± 75.8	139.8 ± 91.6	0.739
Total cholesterol	198.1 ± 43.8	204.7 ± 38.1	0.012
High-density lipoprotein	41.9 ± 10.4	47.5 ± 13.0	0.001
Low-density lipoprotein	123.8 ± 39.2	127.5 ± 33.9	0.008
Fasting glucose (mg/dL)	107.1 ± 47.1	98.7 ± 24.2	< 0.001
HbA1c (%)	6.2 ± 0.9	5.8 ± 0.8	0.006
Uric acid (mg/dL)	7.6 ± 2.1	6.5 ± 1.5	0.001
Creatinine (mg/dL)	1.5 ± 1.3	0.9 ± 0.2	< 0.001
eGFR (ml/min/1.73m^2)	50.4 ± 9.9	84.1 ± 12.4	< 0.001
Values are mean ± SD or number (%).			
CKD: chronic kidney disease; BP: blood pressure; HbA1c: hemoglobin A1c; eGFR: estimated glomerular filtration rate.			

Impact of CKD on coronary artery plaque morphology and plaque burden

Table 2 shows the atherosclerotic plaque patterns and severity in the coronary arteries. The total CAC score significantly increased with decreasing renal function. The mean CAC score was 124 in subjects

without CKD and 292 in those with CKD (P < 0.001). The most commonly diseased coronary vessel was the LAD artery, followed by the RCA, LCX, and LM arteries. Coronary plaques were detected in over half of the participants, and the presence of coronary plaques correlated with the severity of renal function (57.7% vs. 77.1%, P < 0.001). Among all participants, calcified plaques were more frequently detected than mixed or non-calcified plaques. Calcified, non-calcified, and mixed plaques were more commonly observed in subjects with CKD than in those without CKD. Regarding the grade of luminal stenosis, obstructive plaques were also more frequently observed in the CKD group than in the non-CKD group. The proportion of obstructive mixed plaques was higher than that of other constituents of the obstructive-plaque type, especially in CKD subjects. Compared with individuals without CKD, those with CKD had significantly higher ABOS, SIS, and SSS, as shown in Fig. 3.

Table 2
Characteristics of coronary artery calcium score and atherosclerotic plaque morphology stratified by CKD

	With CKD	**Without CKD**	
	(n = 105)	(n = 1642)	P-value
Total calcium score	292.29 ± 460.46	124.08 ± 328.06	< 0.001
Left main	23.80 ± 52.93	5.49 ± 25.25	< 0.001
LAD	125.75 ± 197.95	51.33 ± 123.27	< 0.001
LCX	42.51 ± 93.66	18.46 ± 67.12	< 0.001
RCA	100.24 ± 227.28	49.01 ± 176.23	0.002
Overall plaque	81 (77.1)	948 (57.7)	< 0.001
Calcified plaque	53 (50.5)	531 (32.3)	< 0.001
Non-calcified plaque	25 (23.8)	254 (15.5)	0.024
Mixed plaque	46 (43.8)	459 (28.0)	0.001
Obstructive (> 50% stenosis) calcified plaque	13 (12.4)	94 (5.7)	0.006
Obstructive (> 50% stenosis) non-calcified plaque	7 (6.7)	43 (2.6)	0.027
Obstructive (> 50% stenosis) mixed plaque	28 (26.7)	149 (9.1)	< 0.001
Values are mean ± SD or number (%).			
CKD: chronic kidney disease; LAD: left anterior descending artery; LCX: left circumflex artery; RCA: right coronary artery; CAD: coronary artery disease.			

Independent correlates of obstructive mixed plaques and extensive CAD

The results of multiple logistic regression model for the association of CKD with coronary artery plaque pattern, extent, and severity are presented in Table 3. After adjusting for age, sex, hypertension, diabetes, hyperlipidemia, smoking, and BMI, CKD was independently associated with obstructive mixed plaques (odds ratio [OR]: 1.937, P = 0.012) and extensive CAD (SIS > 4 [OR: 1.645; P = 0.043]; SSS ≥ 7 [OR: 1.660; P = 0.045]). Subgroup analyses stratified by age, sex, BMI, the presence of hypertension, diabetes or hyperlipidemia, and smoking status demonstrated no significant heterogeneity between CKD and obstructive mixed plaques in each subgroup. (Fig. 4A). However, a more prominent association between CKD and an increased risk of extensive CAD was observed in subjects aged < 65 years than in those aged ≥ 65 years (P for interaction < 0.05), as shown in Figs. 4B and 4C.

Table 3
Multivariate regression analysis of the association of CKD with coronary artery plaque pattern, extent, and severity

Dependent Variables	Odds ratio (95% CI)	P-value
Presence of any plaque	1.126 (0.655—1.938)	0.667
Presence of calcified plaque	1.245 (0.807—1.921)	0.322
Presence of non-calcified plaque	1.402 (0.850—2.311)	0.186
Presence of mixed plaque	1.104 (0.703—1.734)	0.667
Presence of obstructive (> 50% stenosis) calcified plaque	1.168 (0.604—2.257)	0.645
Presence of obstructive (> 50% stenosis) non-calcified plaque	1.730 (0.715—4.186)	0.224
Presence of obstructive (> 50% stenosis) mixed plaque	1.937 (1.157—3.244)	0.012
Segment involvement score > 4	1.645 (1.015—2.667)	0.043
Segment stenosis score ≥ 7	1.660 (1.011—2.727)	0.045
Adjusted for age, sex, BMI, smoking status, the presence of hypertension, diabetes, and hyperlipidemia.		
CKD: chronic kidney disease.		

Discussion

The present study demonstrated a correlation between renal dysfunction and the characteristics of coronary atherosclerotic plaques detected by CCTA. Subjects with CKD had a higher coronary plaque burden and an increased risk of extensive CAD. In addition, CKD was independently associated with obstructive mixed plaque pattern after adjusting for traditional cardiovascular risk factors, suggesting an association between impaired renal function and the feature of plaque vulnerability in coronary arteries. In subgroup analysis, CKD retained its positive association with obstructive mixed plaques, with no significant heterogeneity between the subgroups. However, the effect of renal dysfunction on the extent and severity of CAD was more prominent in the younger population.

CCTA has emerged as a promising non-invasive alternative to invasive coronary angiography for the diagnosis of CAD which provides additional information regarding atherosclerotic plaque composition. Based on the relative amounts of calcified and non-calcified components, plaques are typically classified into 1 of 3 categories: calcified, non-calcified, or partially calcified (mixed) plaques. Kawai *et al.* demonstrated that calcified plaques were more frequently observed in CKD patients than in non-CKD patients. Compared with calcified plaques, the number of high-risk plaques (low-attenuation plaque and/or positive remodeling) did not increase despite progression of renal insufficiency.[23] In addition, Joosen *et al.* also demonstrated that patients with mild or moderate CKD had significantly higher proportions of calcified plaques, while no significant differences regarding the presence of mixed and non-calcified plaques were observed compared with patients with normal renal function.[24] However, a previously published study revealed that the prevalence of any plaque and mixed plaques was positively correlated with CKD after adjusting for traditional risk factors.[25] Therefore, the impact of CKD on coronary plaque composition still remains controversial. The current study demonstrated that nonobstructive calcified plaques were the most common imaging feature in patients with CKD. After adjusting for conventional risk factors, the presence of CKD was significantly associated with obstructive mixed plaques. Although one small study demonstrated that CKD patients with type 2 diabetes mellitus had more obstructive mixed plaques,[14] the associations between CKD and obstructive mixed plaques were similar in all subgroups in the present study.

Results of the ACCURACY trial which was designed to determine the relationship between coronary plaque composition as detected by CCTA and lumen diameter stenosis as quantified by invasive coronary angiography demonstrated a strong association between the presence of mixed plaque composition and obstructive CAD at a per-segment and per-patient level assessment.[26] Hou *et al*. investigated the prognostic value of CCTA features for future outcomes and found that the probability of 3-year major adverse cardiac events was 5.5% for calcified plaque, 22.7% for non-calcified plaque and 37.7% for mixed plaque,[27] indicating that mixed plaques are associated with the worst prognosis. From the CONFIRM registry, the optimal CCTA parameter for the prediction of mortality was the number of proximal segments with mixed or calcified plaques.[28] In addition, the CAFÉ-PIE study also revealed that the presence of remodeled and mixed atherosclerotic plaques on CCTA predicts major adverse cardiac events.[29] To the best of our knowledge, the present study is the first to demonstrate an independent association between CKD and the presence of obstructive mixed plaques. This implies that impaired renal function is accompanied by a higher risk of vulnerable plaques and obstructive stenosis, suggesting the predictive role of CKD in the development of cardiovascular events. Our findings did support that CKD is an independent risk factor for CAD as well as more severe coronary heart disease, such as acute coronary syndrome.

CCTA not only allows the accurate detection of coronary atherosclerotic plaques but also enables quantitative analysis of plaque vessel area, lumen area, and plaque burden. Min *et al.* proposed a scoring system (SIS and SSS) to quantify the coronary plaque burden in 2007. The SIS, which is the total number of segments with plaque, and the SSS obtained by grading the stenosis severity of each segment with

plaque were both significantly associated with 2-year all-cause mortality (SIS: risk-adjusted HR: 1.16; 95% CI: 1.05–1.28, and SSS: risk-adjusted HR: 1.52; 95% CI: 1.09–2.14).[18] Similarly, results from the CONFIRM registry also showed SIS to be an independent predictor of major adverse cardiac events (HR: 1.22; 95% CI: 1.03–1.44).[28] Thereafter, several other studies also demonstrated that CCTA was able to predict clinical outcomes on the basis of atherosclerotic plaque burden evaluated using the SIS and SSS.[30–32] In addition, Bittencourt *et al.* demonstrated that patients with extensive CAD (SIS > 4) have a higher rate of cardiovascular death or myocardial infarction than those with non-extensive disease (SIS ≤ 4), thus also emphasizing the importance of quantifying plaque burden.[21] Recent studies even revealed that total coronary atherosclerotic plaque burden, not stenosis per se, is the predominant predictor of risk for cardiovascular events, and plaque burden adds incremental prognostic value over CCTA obstructive stenosis and single photon emission computed tomography (SPECT) ischemia.[12,33] However, data regarding the association between CKD and coronary plaque burden are limited. Roy *et al.* reported that mild and moderate pre-dialysis CKD are independent risk factors for atherosclerotic plaque burden evaluated with total plaque score, SIS, and SSS.[34] Consistent with the previous study, our data revealed that subjects with CKD had significantly higher ABOS, SIS, and SSS than those without CKD. Moreover, this study is the first to correlate CKD with extensive CAD (SIS > 4 or SSS ≥ 7). We found CKD to be independently associated with CAD extent and severity. This relationship remained consistent in most of the subgroups. With advancing age, this association seemed to be attenuated because of other potent coronary atherosclerosis risk factors. More aggressive efforts to decrease the progression of mixed plaques and reduce the total plaque burden are important in CKD subjects to prevent future cardiovascular events.

This study had some limitations that should be considered. First, our study was a cross-sectional design study that we could not identify the causal relationship between CKD and coronary plaque formation. Second, the present study did not collect all the information on medication use for data analysis. Thus, we could not entirely rule out the potential effects of drugs (such as statins) on coronary plaque composition and progression, if there were any. Finally, it was a single-center retrospective study that did not include outcome data. The relationship between coronary plaque burden and adverse cardiac events could not be investigated in the current study.

In conclusion, CCTA not only permits the accurate evaluation of coronary plaque morphology but also enables the quantitative analysis of plaque distribution and plaque burden. Impaired renal function is associated with obstructive mixed plaques and increased atherosclerotic plaque burden. Our findings support that CKD is a major risk factor for the development of obstructive and extensive CAD.

Declarations

Data availability

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

References

1. Sarnak MJ, Levey AS, Schoolwerth AC, Coresh J, Culleton B, Hamm LL, McCullough PA, Kasiske BL, Kelepouris E, Klag MJ, Parfrey P, Pfeffer M, Raij L, Spinosa DJ, Wilson PW. Kidney disease as a risk factor for development of cardiovascular disease: a statement from the American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. Circulation 2003; 108:2154–2169.
2. Yahalom G, Kivity S, Segev S, Sidi Y, Kurnik D. Estimated glomerular filtration rate in a population with normal to mildly reduced renal function as predictor of cardiovascular disease. Eur J Prev Cardiol. 2014; 21:941–948.
3. Manjunath G, Tighiouart H, Ibrahim H, Macleod B, Salem DN, Griffith JL, Coresh J, Levey AS, Sarnak MJ. Level of kidney function as a risk factor for atherosclerotic cardiovascular outcomes in the community. J Am Coll Cardiol. 2003; 41: 47–55.
4. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med 2004; 351: 1296–1305.
5. Sosnov J, Lessard D, Goldberg RJ, Yarzebski J, Gore JM. Differential symptoms of acute myocardial infarction in patients with kidney disease: a community-wide perspective. Am J Kidney Dis 2006; 47:378–384.
6. Daghem M, Bing R, Fayad ZA, Dweck MR. Noninvasive imaging to assess atherosclerotic plaque composition and disease activity: coronary and carotid applications. JACC Cardiovasc Imaging. 2020; 13(4):1055–1068.
7. Budoff MJ, Dowe D, Jollis JG, Gitter M, Sutherland J, Halamert E, Scherer M, Bellinger R, Martin A, Benton R, Delago A, Min JK. Diagnostic performance of 64-multidetector row coronary computed tomographic angiography for evaluation of coronary artery stenosis in individuals without known coronary artery disease: results from the prospective multicenter ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) trial. J Am Coll Cardiol. 2008; 52(21):1724–1732.
8. Meijboom WB, Meijs MF, Schuijf JD, Cramer MJ, Mollet NR, van Mieghem CA, Nieman K, van Werkhoven JM, Pundziute G, Weustink AC, de Vos AM, Pugliese F, Rensing B, Jukema JW, Bax JJ, Prokop M, Doevendans PA, Hunink MG, Krestin GP, de Feyter PJ. Diagnostic accuracy of 64-slice computed tomography coronary angiography: a prospective, multicenter, multivendor study. J Am Coll Cardiol. 2008; 52(25):2135–2144.
9. Arbab-Zadeh A, Miller JM, Rochitte CE, Dewey M, Niinuma H, Gottlieb I, Paul N, Clouse ME, Shapiro EP, Hoe J, Lardo AC, Bush DE, de Roos A, Cox C, Brinker J, Lima JA. Diagnostic accuracy of computed tomography coronary angiography according to pre-test probability of coronary artery disease and severity of coronary arterial calcification. The CORE-64 (Coronary Artery Evaluation Using 64- Row Multidetector Computed Tomography Angiography) International Multicenter Study. J Am Coll Cardiol. 2012; 59(4):379–387.

10. Neglia D, Rovai D, Caselli C, Pietila M, Teresinska A, Aguadé-Bruix S, Pizzi MN, Todiere G, Gimelli A, Schroeder S, Drosch T, Poddighe R, Casolo G, Anagnostopoulos C, Pugliese F, Rouzet F, Le Guludec D, Cappelli F, Valente S, Gensini GF, Zawaideh C, Capitanio S, Sambuceti G, Marsico F, Perrone Filardi P, Fernández-Golfín C, Rincón LM, Graner FP, de Graaf MA, Fiechter M, Stehli J, Gaemperli O, Reyes E, Nkomo S, Mäki M, Lorenzoni V, Turchetti G, Carpeggiani C, Marinelli M, Puzzuoli S, Mangione M, Marcheschi P, Mariani F, Giannessi D, Nekolla S, Lombardi M, Sicari R, Scholte AJ, Zamorano JL, Kaufmann PA, Underwood SR, Knuuti J; EVINCI Study Investigators. Detection of significant coronary artery disease by noninvasive anatomical and functional imaging. Circ Cardiovasc Imaging. 2015; 8(3):e002179.
11. Linde JJ, Kelbæk H, Hansen TF, Sigvardsen PE, Torp-Pedersen C, Bech J, Heitmann M, Nielsen OW, Høfsten D, Kühl JT, Raymond IE, Kristiansen OP, Svendsen IH, Vall-Lamora MHD, Kragelund C, de Knegt M, Hove JD, Jørgensen T, Fornitz GG, Steffensen R, Jurlander B, Abdulla J, Lyngbæk S, Elming H, Therkelsen SK, Jørgensen E, Kløvgaard L, Bang LE, Hansen PR, Helqvist S, Galatius S, Pedersen F, Abildgaard U, Clemmensen P, Saunamäki K, Holmvang L, Engstrøm T, Gislason G, Køber LV, Kofoed KF. Coronary CT angiography in patients with non-ST-segment elevation acute coronary syndrome. J Am Coll Cardiol. 2020; 75:453–463.
12. Mortensen MB, Dzaye O, Steffensen FH, Bøtker HE, Jensen JM, Rønnow Sand NP, Kragholm KH, Sørensen HT, Leipsic J, Maeng M, Blaha MJ, Nørgaard BL. Impact of Plaque Burden Versus Stenosis on Ischemic Events in Patients With Coronary Atherosclerosis. J Am Coll Cardiol. 2020; 76:2803–2813.
13. Budoff MJ, Rader DJ, Reilly MP, Mohler ER 3rd, Lash J, Yang W, Rosen L, Glenn M, Teal V, Feldman HI; CRIC Study Investigators. Relationship of estimated GFR and coronary artery calcification in the CRIC (Chronic Renal Insufficiency Cohort) Study. Am J Kidney Dis. 2011; 58(4):519–526.
14. Deng W, Peng L, Yu J, Shuai T, Chen Z, Li Z. Characteristics of coronary artery atherosclerotic plaques in chronic kidney disease: evaluation with coronary CT angiography. Clin Radiol. 2019; 74(9):731.e1–731.e9.
15. Ma YC, Zuo L, Chen JH, Luo Q, Yu XQ, Li Y, Xu JS, Huang SM, Wang LN, Huang W, Wang M, Xu GB, Wang HY. Modified glomerular filtration rate estimating equation for Chinese patients with chronic kidney disease. J Am Soc Nephrol 2006; 17:2937–2944.
16. Abbara S, Blanke P, Maroules CD, Cheezum M, Choi AD, Han BK, Marwan M, Naoum C, Norgaard BL, Rubinshtein R, Schoenhagen P, Villines T, Leipsic J. SCCT guidelines for the performance and acquisition of coronary computed tomographic angiography: a report of the society of Cardiovascular Computed Tomography Guidelines Committee: Endorsed by the North American Society for Cardiovascular Imaging (NASCI). J Cardiovasc Comput Tomogr. 2016;10(6):435–449.
17. Austen WG, Edwards JE, Frye RL, Gensini GG, Gott VL, Griffith LS, McGoon DC, Murphy ML, Roe BB. A Reporting System on Patients Evaluated for Coronary Artery Disease. Report of the *Ad Hoc* Committee for Grading of Coronary Artery Disease, Council on Cardiovascular Surgery, American Heart Association. Circulation (1975) 51(4 Suppl):5–40.

18. Min JK, Shaw LJ, Devereux RB, Okin PM, Weinsaft JW, Russo DJ, Lippolis NJ, Berman DS, Callister TQ. Prognostic value of multidetector coronary computed tomographic angiography for prediction of all-cause mortality. J Am Coll Cardiol. 2007; 50: 1161–1170.
19. Hadamitzky M, Hein F, Meyer T, Bischoff B, Martinoff S, Schömig A, Hausleiter J. Prognostic value of coronary computed tomographic angiography in diabetic patients without known coronary artery disease. Diabetes Care. 2010; 33(6):1358–1363.
20. Lin FY, Shaw LJ, Dunning AM, Labounty TM, Choi JH, Weinsaft JW, Koduru S, Gomez MJ, Delago AJ, Callister TQ, Berman DS, Min JK. Mortality risk in symptomatic patients with nonobstructive coronary artery disease: a prospective 2-center study of 2,583 patients undergoing 64-detector row coronary computed tomographic angiography. J Am Coll Cardiol. 2011; 58:510–519.
21. Bittencourt MS, Hulten E, Ghoshhajra B, O'Leary D, Christman MP, Montana P, Truong QA, Steigner M, Murthy VL, Rybicki FJ, Nasir K, Gowdak LH, Hainer J, Brady TJ, Di Carli MF, Hoffmann U, Abbara S, Blankstein R. Prognostic value of nonobstructive and obstructive coronary artery disease detected by coronary computed tomography angiography to identify cardiovascular events. Circ Cardiovasc Imaging. 2014; 7:282–291.
22. Jiang Y, Pang T, Shi R, Qian WL, Yan WF, Li Y, Yang ZG. Effect of Smoking on Coronary Artery Plaques in Type 2 Diabetes Mellitus: Evaluation With Coronary Computed Tomography Angiography. Front Endocrinol (Lausanne). 2021; 12:750–773.
23. Kawai H, Sarai M, Motoyama S, Harigaya H, Ito H, Sanda Y, Biswas S, Anno H, Ishii J, Murohara T, Ozaki Y. Coronary plaque characteristics in patients with mild chronic kidney disease. Analysis by 320-row area detector computed tomography. Circ J. 2012; 76(6):1436–1441.
24. Joosen IA, Schiphof F, Versteylen MO, Laufer EM, Winkens MH, Nelemans PJ, Kooman JP, Hofstra L, Wildberger JE, Leiner T. Relation between mild to moderate chronic kidney disease and coronary artery disease determined with coronary CT angiography. PLoS One. 2012; 7(10):e47267.
25. Wang C, Cheng G, Duanmu Y, Zhu Y, Xu L. Correlation of coronary plaque characteristics and obstructive stenosis with chronic kidney disease by coronary CT angiography. Cardiovasc Diagn Ther. 2015; 5(6):435–443.
26. Min JK, Edwardes M, Lin FY, Labounty T, Weinsaft JW, Choi JH, Delago A, Shaw LJ, Berman DS, Budoff MJ. Relationship of coronary artery plaque composition to coronary artery stenosis severity: results from the prospective multicenter ACCURACY trial. Atherosclerosis. 2011; 219(2):573–578.
27. Hou ZH, Lu B, Gao Y, Jiang SL, Wang Y, Li W, Budoff MJ. Prognostic value of coronary CT angiography and calcium score for major adverse cardiac events in outpatients. JACC Cardiovasc Imaging. 2012;5(10):990–999.
28. Hadamitzky M, Achenbach S, Al-Mallah M, Berman D, Budoff M, Cademartiri F, Callister T, Chang HJ, Cheng V, Chinnaiyan K, Chow BJ, Cury R, Delago A, Dunning A, Feuchtner G, Gomez M, Kaufmann P, Kim YJ, Leipsic J, Lin FY, Maffei E, Min JK, Raff G, Shaw LJ, Villines TC, Hausleiter J; CONFIRM Investigators. Optimized prognostic score for coronary computed tomographic angiography: results

from the CONFIRM registry (COronary CT Angiography EvaluatioN For Clinical Outcomes: An InteRnational Multicenter Registry). J Am Coll Cardiol 2013; 62:468–476.

29. Guaricci AI, Pontone G, Brunetti ND, De Rosa F, Montrone D, Guglielmo M, Mushtaq S, Fusini L, Maffei E, Cademartiri F, Macarini L, Andreini D, Di Biase M, Bartorelli AL, Pepi M. The presence of remodeled and mixed atherosclerotic plaques at coronary CT angiography predicts major cardiac adverse events - The CAFÉ-PIE Study. Int J Cardiol. 2016; 215:325–331.
30. Hadamitzky M, Täubert S, Deseive S, Byrne RA, Martinoff S, Schömig A, Hausleiter J. Prognostic value of coronary computed tomography angiography during 5 years of follow-up in patients with suspected coronary artery disease. Eur Heart J. 2013; 34(42):3277–3285.
31. Dougoud S, Fuchs TA, Stehli J, Clerc OF, Buechel RR, Herzog BA, Leschka S, Alkadhi H, Kaufmann PA, Gaemperli O. Prognostic value of coronary CT angiography on long-term follow-up of 6.9 years. Int J Cardiovasc Imaging 2014; 30:969–976.
32. Tesche C, Plank F, De Cecco CN, Duguay TM, Albrecht MH, Varga-Szemes A, Bayer RR Nd, Yang J, Jacks IL, Gramer BM, Ebersberger U, Hoffmann E, Chiaramida SA, Feuchtner G, Schoepf UJ. Prognostic implications of coronary CT angiography-derived quantitative markers for the prediction of major adverse cardiac events. J Cardiovasc Comput Tomogr. 2016; 10(6):458–465.
33. Ahmed AI, Han Y, Al Rifai M, Alnabelsi T, Nabi F, Chang SM, Chamsi-Pasha MA, Nasir K, Mahmarian JJ, Cainzos-Achirica M, Al-Mallah MH. Added prognostic value of plaque burden to computed tomography angiography and myocardial perfusion imaging. Atherosclerosis. 2021; 334:9–16.
34. Roy SK, Cespedes A, Li D, Choi TY, Budoff MJ. Chronic kidney disease is associated with increased coronary artery atherosclerosis as revealed by multidetector computed tomographic angiography. Tex Heart Inst J. 2012; 39(6):811–816.

Figures

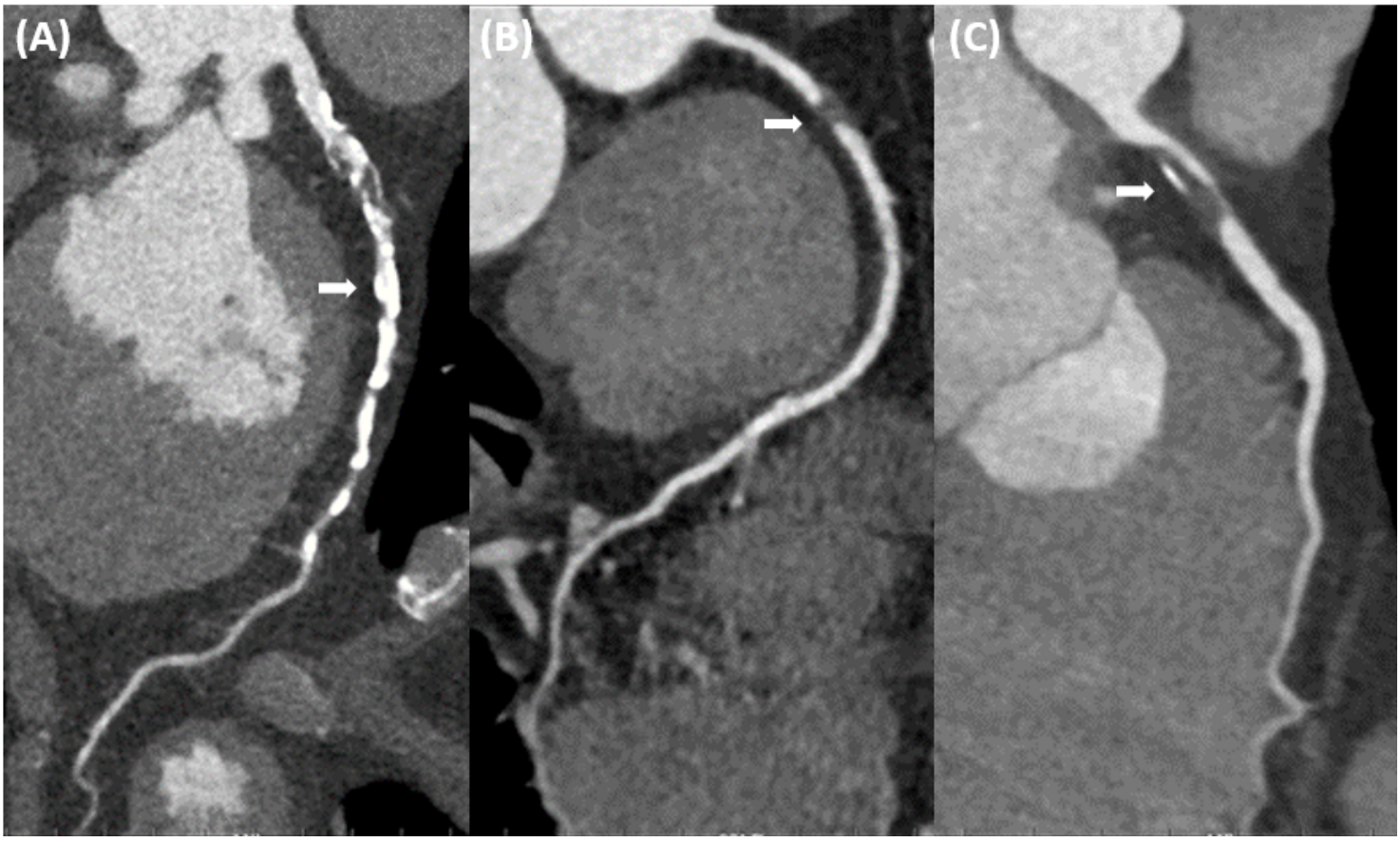

Figure 1

Representative images of obstructive (>50% stenosis) calcified (A), non-calcified (B) and mixed (C) plaques as detected by coronary CT angiography.

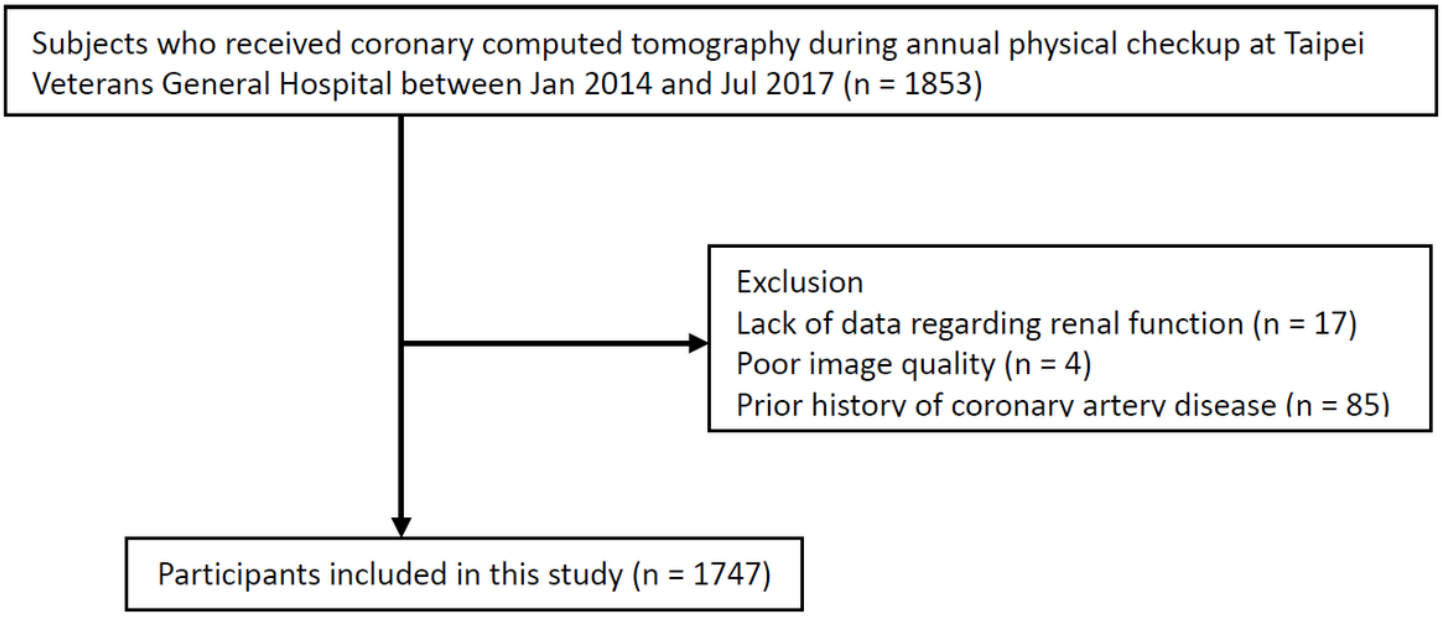

Figure 2

Flowchart of the selection of study population.

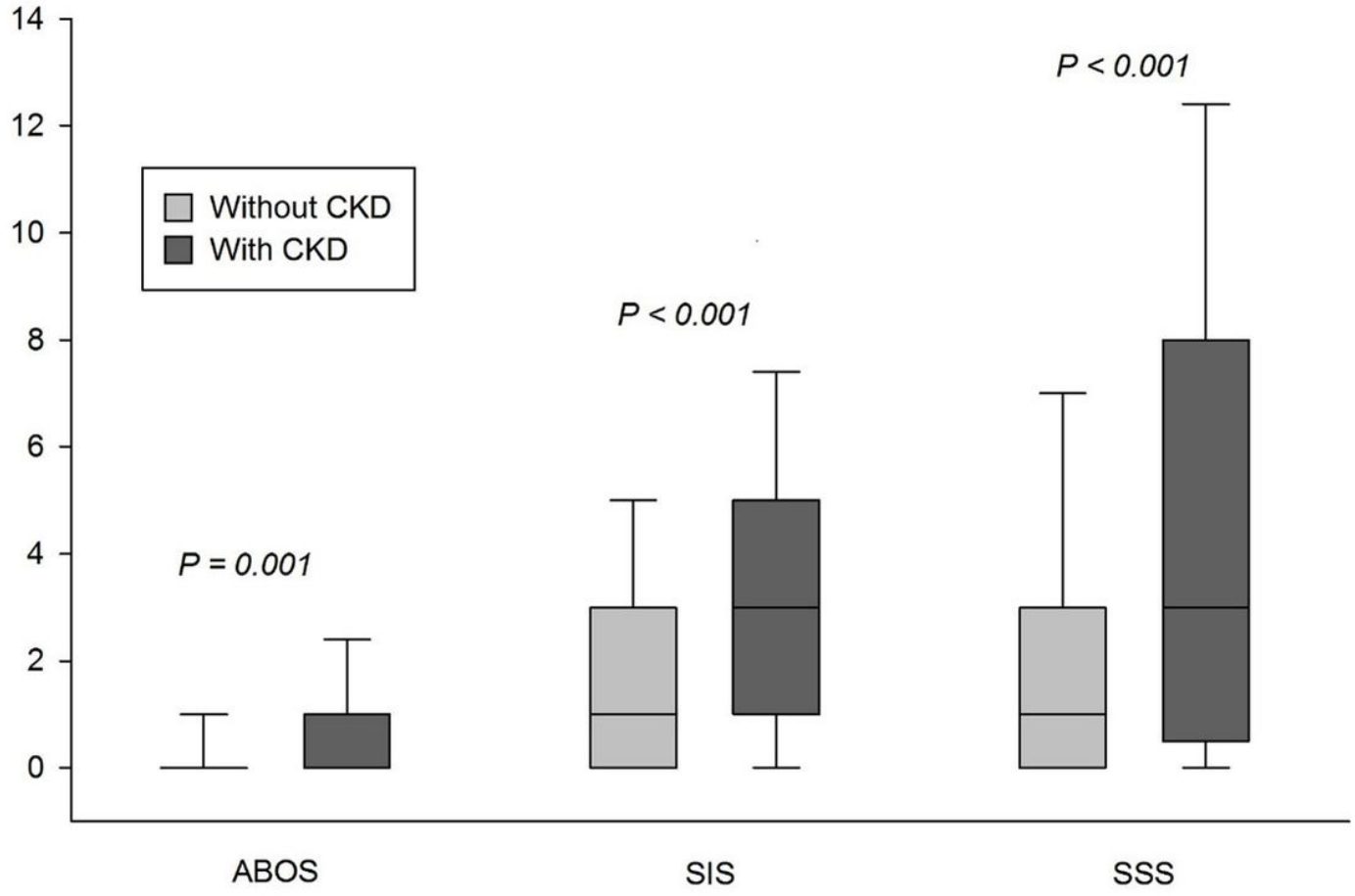

Figure 3

Association of coronary atherosclerotic plaque burden and severity of renal function. CKD = chronic kidney disease; ABOS = atheroma burden obstructive score; SIS = segment involvement score; SSS = segment stenosis score.

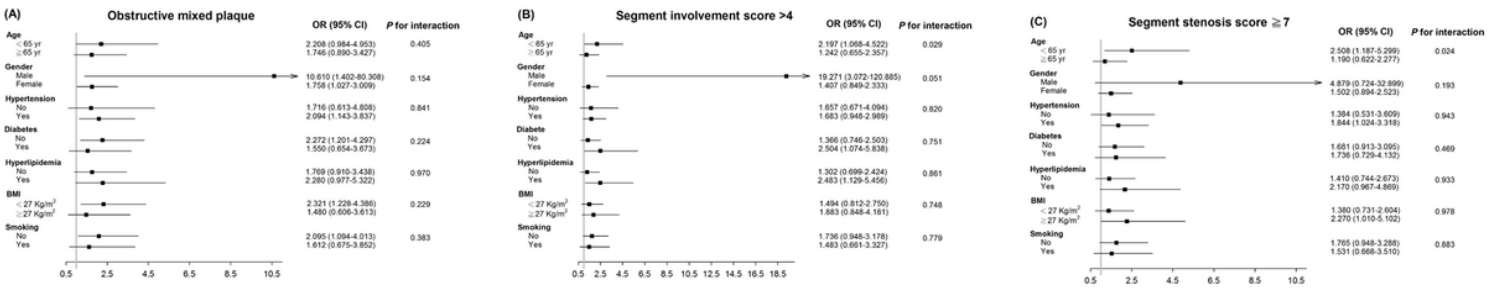

Figure 4

Subgroup analyses for the impact of CKD on obstructive mixed plaques (A) and extensive CAD [segment involvement score >4 (B); segment stenosis score ≥7 (C)].