Nonculprit Coronary Plaque Characteristics of Chronic Kidney Disease

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Background—Chronic kidney disease (CKD) promotes the development of atherosclerosis and increases the risk of cardiovascular disease. The aim of the present study was to compare the coronary plaque characteristics of patients with and without CKD using optical coherence tomography.

Methods and Results—We identified 463 nonculprit plaques from 287 patients from the Massachusetts General Hospital (MGH) optical coherence tomography registry. CKD was defined as estimated glomerular filtration rate <60 mL/min per 1.73 m^2. A total of 402 plaques (250 patients) were in the non-CKD group and 61 plaques (37 patients) were in the CKD group. Compared with non-CKD plaques, plaques with CKD had a larger lipid index (mean lipid arc×lipid length, 1248.4±782.8 mm° [non-CKD] versus 1716.1±1116.2 mm° [CKD]; *P*=0.003). Fibrous cap thickness was not significantly different between the groups. Calcification (34.8% [non-CKD] versus 50.8% [CKD]; *P*=0.041), cholesterol crystals (11.2% [non-CKD] versus 23.0% [CKD]; *P*=0.048), and plaque disruption (5.5% [non-CKD] versus 13.1% [CKD]; *P*=0.049) were more frequently observed in the CKD group. In the multivariate linear regression model, a lower estimated glomerular filtration rate and diabetes mellitus were independent risk factors for a larger lipid index.

Conclusions—Compared with non-CKD patients, the patients with CKD had a larger lipid index with a higher prevalence of calcium, cholesterol crystals, and plaque disruption. The multivariate linear regression model demonstrated that a lower estimated glomerular filtration rate was an independent risk factor for a larger lipid index.

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Key Words: cholesterol crystal ■ chronic kidney disease ■ optical coherence tomography ■ plaque

The impact of chronic kidney disease (CKD) on cardiovascular and all-cause mortality has been well established.[1–3] It has been reported that renal function deterioration increases the risk of not only the new onset of acute coronary syndrome (ACS)[1–3] but also the major adverse clinical events during and after percutaneous coronary intervention.[4,5] Although the underlying pathophysiology is probably related to plaque type, the plaque characteristics of CKD patients have not been clearly identified. Pathology studies have demonstrated that coronary atherosclerosis and calcification were more frequent and advanced in patients with CKD compared with non-CKD patients.[6,7] A subgroup analysis of the Providing Regional Observation to Study Predictors of Events in the Coronary Tree (PROSPECT) study showed that CKD patients had a larger plaque burden, a greater necrotic core, and dense calcium in their nonculprit lesions.[8] The underlying mechanism for poor outcomes and high recurrent ischemic events in CKD patients has not been fully elucidated. In vivo coronary plaque characteristics in CKD patients may help us to understand the underlying pathophysiology. Optical coherence tomography (OCT) is a high-resolution intravascular imaging modality that allows a detailed assessment of coronary plaque morphology. The aim of the present study was to characterize the nonculprit plaques in patients with kidney disease.

Clinical Perspective on p 456

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Methods

Study Population

The MGH OCT Registry is an ongoing multicenter registry of patients who have had OCT imaging during their coronary catheterization and includes subjects from 20 sites across 6 countries.[9,10] Between August 2010 and September 2011, 912 subjects were enrolled in the registry. Among these, 53 subjects (5.8%) were excluded because of poor image quality. Plaques were identified when the diameter stenosis was >30% by OCT as compared with the reference vessel. We did not identify any native coronary artery plaques in 485 subjects (390 subjects had only poststent images, and 95 subjects had only stent restenosis lesion imaging). An additional 5 subjects were excluded because they were already on hemodialysis. On the basis of angiograms, any plaque treated by percutaneous coronary intervention was defined as a culprit plaque and was excluded. All culprit lesions were identified by the operators using a combination of ECG findings, left ventricular wall motion abnormalities, scintigraphic defects, and angiographic lesion morphology. Eighty-two subjects were excluded because of the acquired OCT images only containing the culprit plaque. Therefore, the final analysis included the remaining 287 subjects with 463 nonculprit plaques (Figure 1).

The exact location of the OCT catheter identified as the OCT pullback was recorded simultaneously with contrast injection. Coregistration of plaques on both OCT images and angiograms was performed using fiduciary landmarks such as side branches or implanted stents. All plaques were divided into coronary artery surgery segment groups for plaque identification. Plaque analysis was performed in each segment. Each plaque was separated at least 5 mm from the edge of another plaque or from an implanted stent edge as seen on the longitudinal OCT pullback. Any plaque continuous to an implanted stent was excluded. The estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease equation: eGFR (mL/min per 1.73 m^2)=$175\times(S_{cr})^{-1.154}\times(\text{age})^{-0.203}\times 0.742$ (if female)$\times 1.210$ (if black), and CKD was defined as an eGFR <60 mL/min per 1.73 m^2.[11] The registry was approved by each site's institutional review board, and all patients provided informed consent.

Acquisition of OCT Images

Images were acquired using a commercially available frequency domain (C7-XR OCT Intravascular Imaging System, St. Jude Medical, St. Paul, MN) or time domain (M2/M3 Cardiology Imaging System, LightLab Imaging, Inc, Westford, MA) OCT system. The intracoronary OCT imaging technique has been described previously.[10] In brief, in the frequency domain OCT system, a 2.7F OCT imaging catheter (Dragonfly, LightLab Imaging, Inc) is advanced distal to the lesion, and automated pullback is initiated in concordance with blood clearance by the injection of contrast media or Dextran. In the time domain OCT system, an occlusion balloon (Helios, LightLab Imaging, Inc) is inflated proximal to the lesion at 0.4 to 0.6 atm during image acquisition. The imaging wire is automatically pulled back from a distal to a proximal position at a rate of 1.0 to 3.0 mm/s, and saline is continuously infused from the tip of the occlusion balloon. The frequency domain OCT system was used in 22.6% of non-CKD patients and 29.5% of CKD patients (P=0.258). All images were deidentified and digitally stored.

OCT Data Analysis

Plaques were classified into 2 categories: (1) fibrous (homogeneous, high backscattering region) or (2) lipid (low-signal region with diffuse border).[12–14] When lipid was present in ≥90° in any of the cross-sectional images within the plaque, it was considered to be a lipid-rich plaque.[14–17] In lipid-rich plaques, the lipid arc was measured on the cross-sectional view at 1-mm intervals over the entire length, and the values were averaged. Lipid length was also measured on a longitudinal view. Lipid index was defined as the mean lipid arc multiplied by lipid length.[10] The fibrous cap thickness of a lipid-rich plaque was measured 3 times at its thinnest part, and the average value was calculated (Figure 2).[10] Thin-cap fibroatheroma was defined as a lipid-rich plaque with fibrous cap thickness ≤65 μm at the thinnest part on a cross-sectional image.[18] Calcification was also recorded when an area showed a signal-poor or heterogeneous region with a sharply delineated border (Figure 3A).[12,18] Macrophage accumulations were defined as signal-rich, distinct, or confluent punctuate regions that exceeded the intensity of background speckle noise (Figure 3B).[18–20] Cholesterol crystals were defined as thin, linear regions of high intensity within the plaque (Figure 3C).[18] Microchannels were defined as signal-poor voids that were sharply delineated in multiple contiguous frames (Figure 3D).[12,18,21] Plaque disruption was identified by the presence of fibrous cap discontinuity with a clear cavity formation inside the plaque.[12,14] Intracoronary thrombus was defined as a mass (diameter ≥250 μm) attached to the luminal surface or floating within the lumen, including red (red blood cell–rich) thrombus, which showed high backscattering with high attenuation (resembling blood) (Figure 3E), and white (platelet-rich) thrombus, which

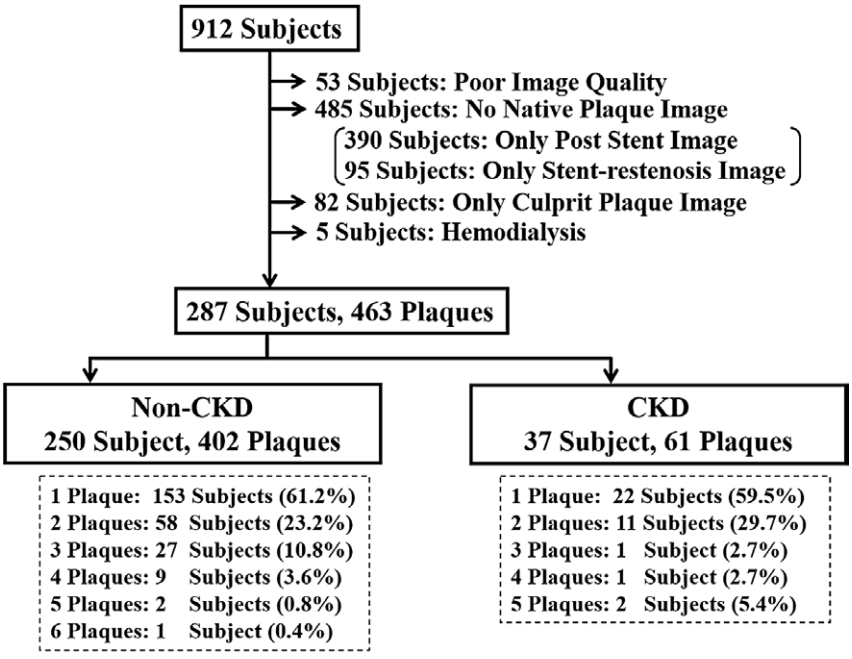

Figure 1. The patient count breakdown outline. CKD indicates chronic kidney disease.

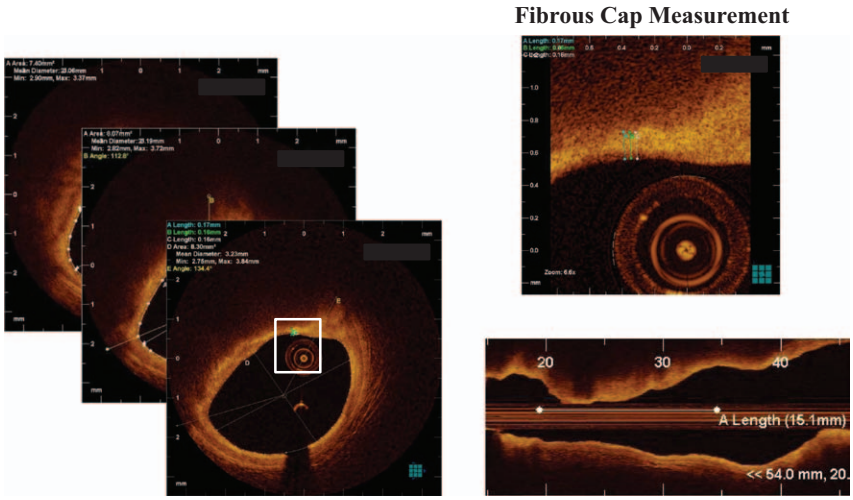

Figure 2. Optical coherence tomography measurement. In lipid-rich plaques, the lipid arc was measured at 1-mm intervals over the entire length, and the values were averaged. Lipid length was also measured on a longitudinal view. Lipid index was defined as the mean lipid arc multiplied by lipid length. The fibrous cap thickness of a lipid-rich plaque was measured 3 times at its thinnest part, and the average value was calculated.

Lipid Index = Mean Lipid Arc × Lipid Length

showed less backscattering, was homogeneous and had low attenuation (Figure 3F).[12,14,18,22] Calcification, macrophage accumulations, cholesterol crystals, microchannels, plaque disruption, and thrombus were recorded only for their presence. The OCT data were analyzed using proprietary software (LightLab Imaging, Inc) at an independent MGH OCT core laboratory by 2 experienced investigators who were blinded to the angiographic and clinical findings. When there was discordance between the investigators, a consensus reading was obtained from a third independent reviewer. The intraclass correlation coefficients for interobserver and intraobserver reliabilities of the lipid arc were 0.892 and 0.934, respectively. The estimated interobserver and intraobserver κ coefficients for cholesterol crystals were 0.810 and 0.933, respectively.

Clinical Follow-up

In the MGH OCT Registry, subjects are followed up at 6 months and then annually thereafter for 5 years. When a clinical event is identified, detailed data are collected at the study site and entered into the database. Clinical events include death resulting from any cause, myocardial infarction, any form of revascularization, ischemic cerebrovascular events, and any bleeding complications.

Statistical Analysis

All statistical analyses were performed by an independent statistician at a core laboratory. Categorical variables are presented as counts and proportions, and the comparisons were performed using a χ^2 test or Fisher exact test, depending on the data. The continuous variables are presented as mean±SD, and if necessary, median and 25th to 75th percentile are also presented. In the present study, 39 (15.6%) subjects had ≥3 plaques. The generalized estimating equations was used to take into count the within-subject correlation for the analysis of multiple plaques within a single patient. The mean values of the continuous measurements between the 2 groups were compared using generalized estimating equations with identity link and exchangeable correlation. For comparisons of between-group differences in the rates of dichotomous plaque characteristics, the analysis was performed using generalized estimating equations with logit link and exchangeable correlation structure. Univariate and multivariate linear regression models, including all patients and plaques, were fit to assess the relationship between lipid index and other factors for which the inference was carried out using generalized estimating equations with identity link and exchangeable correlation structure. Intraobserver and interobserver reliabilities were estimated by means of a κ coefficient for binary outcomes and an

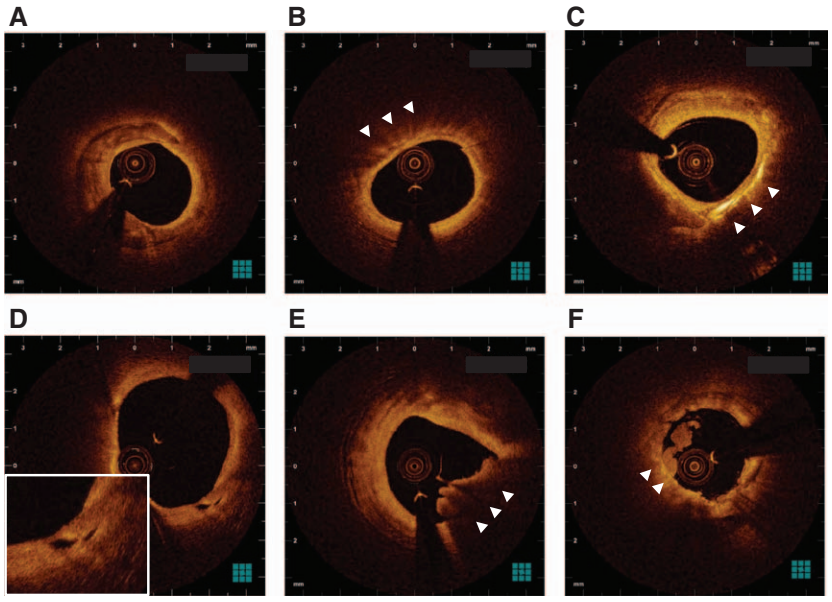

Figure 3. Representative optical coherence tomography images. **A**, Calcification is an area with low backscatter signal and a sharp border. **B**, Macrophage accumulations are observed as bright spots with high signal variances (arrows). **C**, Cholesterol crystals were defined as thin, linear regions of high intensity within the plaque (arrows). **D**, Microchannels are observed as black holes within a plaque. **E**, Red (red blood cell-rich) thrombus is highly backscattering with high attenuation (arrows). **F**, White (platelet-rich) thrombus is less backscattering and homogeneous with low signal attenuation (arrows).

Table 1. Baseline Patient Demographics

	Non-CKD (n=250)	CKD (n=37)	*P* Value
Men	197 (78.8)	24 (64.9)	0.092
Age, y	58.7±11.0	67.4±8.6	<0.001*
ACS	66 (26.4)	10 (27.0)	0.999
Hypertension	151 (60.4)	28 (75.7)	0.101
Hyperlipidemia	194 (77.6)	27 (73.0)	0.534
Smoking	64 (25.6)	4 (10.8)	0.061
Diabetes mellitus	101 (40.4)	19 (51.4)	0.216
HbA_{1c}, %†	7.5±1.4	8.0±1.8	0.216
Hb, g/dL	14.1±1.3	12.5±2.1	<0.001*
LDL-C, mg/dL	90.5±39.3	84.2±29.0	0.351
HDL-C, mg/dL	43.3±11.8	43.4±12.0	0.963
Triglycerides, mg/dL	153.4±115.6	177.0±162.6	0.277
Cre, mg/dL	0.89±0.15	1.86±2.51	0.025*
eGFR, mL/min per $1.73m^2$	85.4±17.7	48.2±12.8	<0.001*
Statin	182 (72.8)	28 (75.7)	0.843
ACE-I/ARB	98 (39.2)	23 (62.2)	0.012*
β-Blocker	112 (44.8)	20 (54.1)	0.296
LVEF, %	61.7±9.2	58.9±11.3	0.114
Imaged CASS segments	4.2±1.9	3.9±1.9	0.398

Data are presented as mean±SD or n (%). ACE-I indicates angiotensin-converting enzyme inhibitor; ACS, acute coronary syndrome; ARB, angiotensin II receptor blocker; CASS, coronary artery surgery segment; CKD, chronic kidney disease; Cre, creatinine; eGFR, estimated glomerular filtration rate; HbA_{1c}, glycohemoglobin A_{1c}; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; and LVEF, left ventricular ejection fraction.

*P<0.05; †HbA_{1c} level was calculated only in patients with diabetes mellitus.

intraclass correlation coefficient for continuous measurements. There were no type 1 error rate controls for multiple statistical comparisons because of the exploratory nature of the analyses, and a value of P<0.05 from 2-sided test was considered to be statistically significant. All analyses were performed using IBM SPSS software version 19.0 (SPSS Inc, Chicago, IL).

Results

Baseline Patient Demographics

Table 1 shows baseline patient demographics. The non-CKD group consisted of 250 subjects and the CKD group of 37 subjects. The CKD group was older, had a lower level of hemoglobin, and had a higher use of angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker.

Baseline Plaque Characteristics

A total of 463 nonculprit plaques were detected in 287 subjects: 402 plaques in the non-CKD group (1.6 plaques per patient) and 61 plaques in the CKD group (1.6 plaques per patient). The distribution of plaques in the 3 coronary arteries is shown in Table 2: 35.2% of plaques were located in the right coronary artery, 42.1% in the left anterior descending artery, and 22.7% in the left circumflex. This distribution did not differ between the groups. Although the reference diameter and area were not significantly different, the minimum area was smaller and the percentage diameter stenosis was greater in CKD patients than in non-CKD patients.

Table 2. Baseline Angiographic Findings

	Non-CKD (n=402)	CKD (n=61)	*P* Value
Plaque location, n (%)			0.763
RCA	142 (35.3)	21 (34.4)	
CASS 1	25 (6.2)	3 (4.9)	
CASS 2	58 (14.4)	8 (13.1)	
CASS 3	59 (14.7)	10 (16.4)	
LAD	165 (41.0)	30 (49.2)	
CASS 12	45 (11.2)	6 (9.8)	
CASS 13	86 (21.4)	15 (24.6)	
CASS 14	34 (8.5)	9 (14.6)	
LCX	95 (23.6)	10 (16.4)	
CASS 18	49 (12.2)	5 (8.2)	
CASS 19	46 (11.4)	5 (8.2)	
OCT measurement			
Minimum lumen diameter, mm	2.0±0.4	1.9±0.5	0.058
Minimum lumen area, mm^2	3.3±1.5	2.9±1.3	0.027*
Reference lumen diameter, mm	3.1±0.6	3.1±0.6	0.642
Reference lumen area, mm^2	7.9±3.0	7.8±2.9	0.736
Diameter stenosis, %	37.2±0.6	40.8±8.2	0.001*

CASS indicates coronary artery surgery segment; CKD, chronic kidney disease; LAD, left anterior descending artery; LCX, left circumflex artery; OCT, optical coherence tomography; and RCA, right coronary artery.

*P<0.05.

OCT Findings

Comparisons of quantitative OCT findings between non-CKD and CKD are shown in Figure 4. Plaques in the CKD patients had a wider lipid arc (156.7±34.6°; median=150.0° [25th–75th percentile, 133.0°–178.0°; non-CKD] versus 172.9±37.9°; 170.0° [144.3–191.0°; CKD]; P=0.006), a longer lipid length (8.0±4.7 mm; 7.0 mm [4.3–10.8 mm; non-CKD] versus 9.5±4.6 mm; 8.0 mm [6.8–11.9 mm; CKD]; P=0.015), and a larger lipid index (1248.4±782.8 mm°; 1069.2 mm° [590.0–1744.4 mm°; non-CKD] versus 1716.1±1116.2 mm°; 1257.8 mm° [1105.2–1978.1 mm°; CKD]; P=0.003). Fibrous cap thickness was not significantly different between the groups (93.4±45.5; 80.0 [63.0–117.0; non-CKD] versus 87.9±33.0; 80.0 [63.0–99.3; CKD]; P=0.268). The prevalence of OCT plaque characteristics is shown in Figure 5. The prevalence of lipid-rich plaques was similar between the groups, as was the prevalence of macrophage accumulations, microchannels, and thin-cap fibroatheroma. However, calcification, cholesterol crystals, and disruption were more frequently observed and thrombus tended to be more frequent in the CKD group. Although the baseline patient characteristics were different between the non-CKD and CKD groups, quantitative and qualitative OCT findings were not adjusted for other factors because the primary purpose was to make a direct comparative description of the plaque characteristics. No correlation between eGFR and lipid index was observed (P=0.102; r=0.061; Figure 6).

Univariate and Multivariate Linear Regression Models for Lipid Index

Table 3 shows the univariate and multivariate linear regression models. In the univariate model, the presence of ACS,

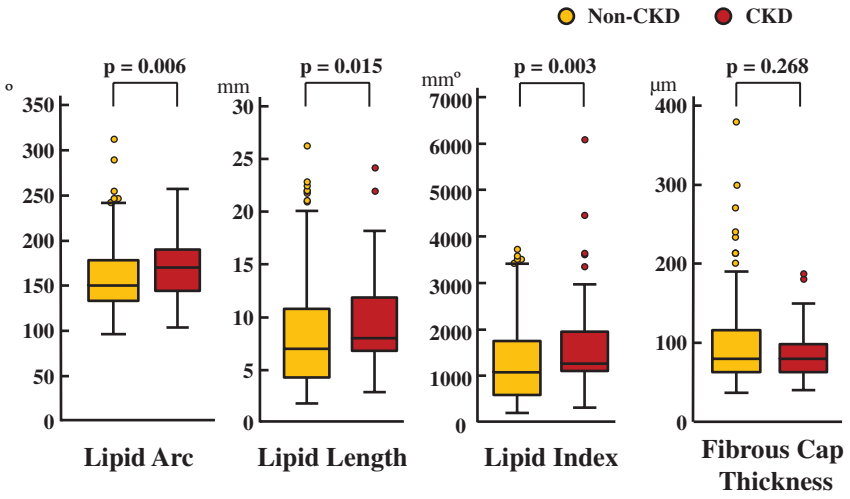

Figure 4. Quantitative optical coherence tomography findings. Compared with non–chronic kidney disease (CKD) plaques, plaques with CKD had a wider lipid arc and a larger lipid index. However, fibrous cap thickness was not significantly different between the groups.

diabetes mellitus, and nonuse of statin were all associated with a larger lipid index. The multivariate linear regression model demonstrated that only lower eGFR and diabetes mellitus were independent risk factors for a larger lipid index after adjustment for other factors.

Clinical Follow-up Data

The 1-year follow-up rate was 96.5%. Thirteen patients (4.5%) had clinical events: 1 (0.3%) noncardiac death, 10 (3.5%) percutaneous coronary interventions, and 2 coronary artery bypass grafts (0.7%). Only 1 patient with CKD underwent percutaneous coronary intervention during the follow-up period.

Discussion

The present study demonstrated that nonculprit plaques in patients with CKD had a larger lipid index as compared with non-CKD patients. The presence of calcification, cholesterol crystals, and disruption was more frequently observed in CKD patients. The multivariate linear regression model demonstrated that a lower eGFR and diabetes mellitus were independently associated with a larger lipid index.

Plaque Characteristics in CKD Patients

CKD is recognized as an independent risk factor for cardiovascular events, including ACS.[1–3] A previous postmortem study demonstrated that a lower eGFR level is associated with a greater percentage of advanced coronary atherosclerosis, defined as American Heart Association types IV to VI.[7] Moreover, integrated backscatter intravascular ultrasound studies demonstrated that a lower eGFR level is related to a higher percentage of lipid volume and a lower percentage of fibrous volume.[23,24] In the present study, plaques in CKD patients had a wider lipid arc, a longer lipid length, and a larger lipid index. Although a correlation between eGFR and lipid index was not observed, the multivariate linear regression model demonstrated that a lower eGFR was an independent risk factor for a larger lipid index after adjustment for other factors.

In the present study, the prevalence of thin-cap fibroatheroma and macrophage accumulations did not differ between the groups. The subgroup analysis of the PROSPECT study also demonstrated that the prevalence of *Virtual Histology*-derived thin-cap fibroatheroma was not significantly different,

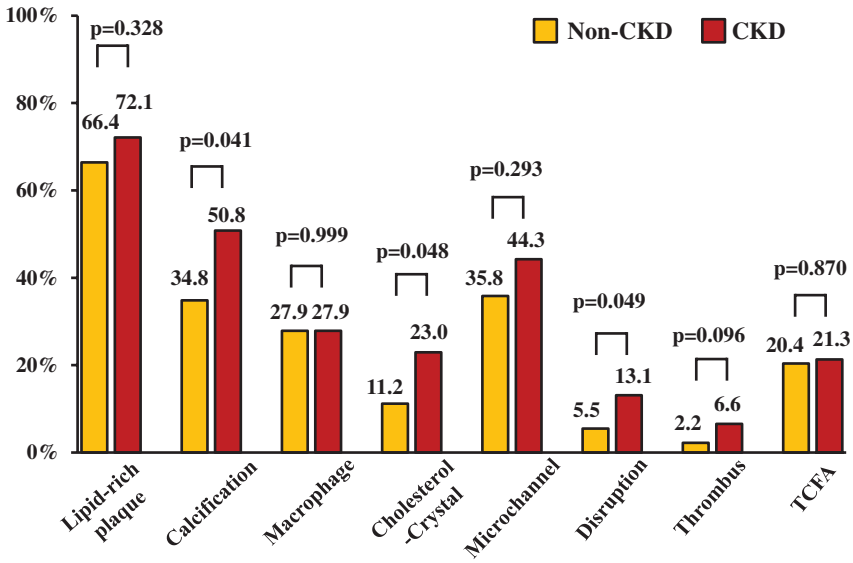

Figure 5. Qualitative optical coherence tomography findings. Compared to non–chronic kidney disease (CKD) plaques, plaques with CKD had a higher prevalence of calcification, cholesterol crystals, and disruption. Thrombus tended to be more frequently observed in the CKD group. TCFA indicates thin-cap fibroatheroma.

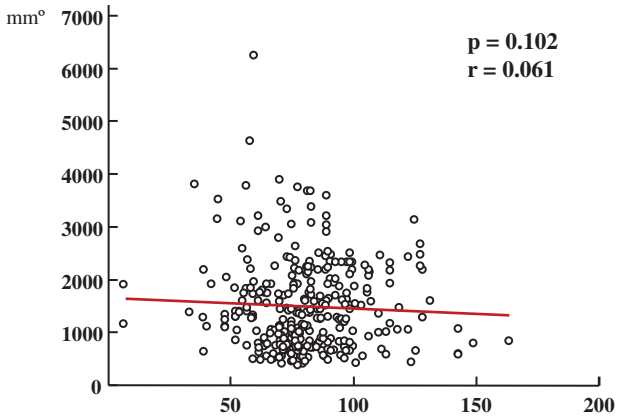

Figure 6. Scatterplot of estimated glomerular filtration rate (eGFR; *x* axis) and lipid index (*y* axis). No correlation between eGFR and lipid index was observed (*P*=0.102; *r*=0.061).

although plaques in CKD patients had a higher plaque burden with a greater necrotic core and a higher frequency of dense calcium.[8]

Nonculprit plaques were selected because it is often challenging to acquire optimal-quality images in the presence of luminal thrombus and severe stenosis. In that case, operators may be more likely to perform OCT after predilatation or stenting. In the registry database, culprit lesion images of optimal quality were acquired in 36.8% of ACS patients and in 59.7% of non-ACS patients. However, several studies have shown that nonculprit lesions have morphological characteristics similar to culprit lesions as detected by angiography,[25] intravascular ultrasound,[26] angioscopy,[27] and coronary thermography.[28,29]

Calcification and Cholesterol Crystals

We identified several differences in coronary atherosclerotic plaque composition between patients with and without CKD. The prevalence of calcification and cholesterol crystals was higher in CKD patients as compared with non-CKD patients. In previous autopsy,[6,7] intravascular ultrasound,[8] and computed tomography angiography[30,31] studies, calcification was more frequently observed in plaques of CKD patients compared with those in non-CKD. It has been reported that the uremic state is associated with numerous metabolic abnormalities and endocrine disturbances, including abnormalities in calcium, phosphate metabolism, and inflammatory syndrome. These dysfunctions occur early in the course of CKD and contribute to the development and progression of vascular calcification and atherosclerosis.[32]

Cholesterol crystals play an important role in the atherosclerotic process[33] and serve as a marker for advanced atherosclerotic lesions.[34] On OCT images, cholesterol crystals are observed as thin, linear lesions of high intensity, usually associated with lipid-rich plaque. A previous autopsy study demonstrated that there were strong associations between cholesterol crystals and plaque disruption, thrombus, and plaque size; moreover, cholesterol crystals were significantly associated with clinical events.[35] In the present study, cholesterol crystals were more frequently observed in plaques of CKD patients compared with those of non-CKD. The present results also suggest that CKD patients have advanced plaques in their coronary trees.

Table 3. Univariate and Multivariate Linear Regression Models for Lipid Index

	Univariate Model		Multivariate Model	
	β Coefficient	*P* Value	β Coefficient	*P* Value
eGFR	−4.2	0.102	−6.0	0.034*
Age	−3.1	0.510	−4.5	0.465
ACS	389.2	0.002*	272.9	0.050
Hypertension	113.3	0.334	204.3	0.059
Hyperlipidemia	40.5	0.800	141.1	0.273
Smoking	155.9	0.212	63.1	0.604
Diabetes mellitus	480.5	<0.001*	461.7	<0.001*
LVEF	−9.0	0.203	−9.9	0.093
Hb	−17.2	0.707	−23.8	0.617
LDL-C	−0.4	0.756	−0.9	0.446
HDL-C	−2.3	0.541	−0.2	0.951
Triglycerides	0.4	0.411	0.2	0.699
Statin	−367.2	0.008*	−240.9	0.173
ACE-I/ARB	−159.1	0.127	−121.9	0.252
β-Blocker	−161.0	0.145	−148.9	0.284
% DS	5.6	0.452	3.6	0.560

ACE-I indicates angiotensin-converting enzyme inhibitor; ACS, acute coronary syndrome; ARB, angiotensin II receptor blocker; DS, diameter stenosis; eGFR, estimated glomerular filtration rate; Hb, hemoglobin; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; and LVEF, left ventricular ejection fraction.

*$P<0.05$. *P* values are from the inference using the generalized estimating equation–based sandwich SE estimates.

Disruption and Thrombus

In the present study, the prevalence of disruption in nonculprit plaques was higher in the CKD group as compared with the non-CKD group, and thrombus tended to be more frequent in the CKD group. Plaque disruption exposes thrombogenic substrates to circulating blood, leading to local thrombus formation. When thrombus is not occlusive, the disruption can be silent without causing ischemia or myocardial necrosis. The thrombus will then be organized, resulting in sudden plaque growth. A pathological study showed evidence of multiple plaque ruptures before a clinical event, indicating that the majority of plaque disruptions are silent.[36] Several intracoronary imaging studies have reported that plaque rupture was observed not only in the culprit lesion but also in nonculprit sites. A 3-vessel OCT study demonstrated that 35.3% of ACS patients and 12.6% of non-ACS patients had disruption in nonculprit lesions[10]; a 3-vessel intravascular ultrasound study reported 8% of ACS plaques and 4% non-ACS plaques.[37] Tanaka et al[38] reported that multiple plaque disruption was associated with systemic inflammation and that patients with multiple plaque rupture had poor prognoses. Although plaque disruption with thrombus formation is thought to be the main underlying mechanism of ACS, the significance of disruption and thrombus on OCT in CKD patients is still unknown. To the best of our knowledge, our

study is the first to demonstrate the prevalence of plaque disruption and thrombus in CKD plaques; further investigation, including the clinical significance of plaque disruption and thrombus, is warranted.

Patients with CKD are more likely to die of cardiovascular disease than to require dialysis.[39] Therefore, reduction of morbidity and mortality in patients with CKD requires strict management of these patients' cardiovascular disease risk factors. The National Kidney Foundation's Kidney Disease Outcome Quality Initiative guidelines recommend an A_{1c} level of <7% with diabetes mellitus,[40] a blood pressure goal of <130/80 mm Hg,[41] and low-density lipoprotein-cholesterol levels <100 mg/dL.[42] All of these recommendations are related to antiatherosclerosis effects. In the present study, plaques in CKD patients had a larger lipid index. Moreover, the multivariate linear regression model demonstrated that a lower eGFR was an independent risk factor for a larger lipid index. We could not find any relationship between lipid data and follow-up clinical events; it is possible that this lack of relationship is related to the small number of subjects and short follow-up period. However, aggressive lipid management would probably have an additional value in CKD patients.

Limitations

First, patients in this registry were selected for OCT by the operator, introducing the possibility of selection bias. Second, exact measurements of necrotic core and plaque burden by OCT are not possible because of the relatively shallow axial penetration. Third, calcification, macrophage accumulations, cholesterol crystals, microchannel, disruption, and thrombus were not quantified or rigorously validated. Fourth, although the baseline patient characteristics were different between patients with and without CKD, quantitative and qualitative OCT findings were not adjusted for other factors because the primary purpose was to make a direct comparative description of the plaque characteristics. Fifth, the sample size for this study was limited, especially with regard to the small number of CKD patients. Sixth, OCT imaging did not include whole coronary artery segments. Seventh, the duration of CKD has been linked with poor outcomes and affected plaque morphology; however, the patient-reported duration of CKD was not collected in the registry. Eighth, the very proximal segment was not visualized because of the proximal occlusion balloon when the time domain OCT system was used. Although 2 OCT systems were used (frequency domain and time domain OCT system) in the present study, the percentage of imaged plaques by each modality and the plaque distribution were not significantly different between the CKD and non-CKD groups. Ninth, 5 patients on hemodialysis (8 plaques) were not included because of the small number. Tenth, the culprit lesions were identified by the operators at each site. Finally, we collected data only from nonculprit plaques.

Conclusions

Compared with non-CKD patients, patients with CKD had a larger lipid index and a higher prevalence of calcium, cholesterol crystals, and disruption. Thrombus tended to be more frequently observed in the CKD group. Multivariate linear regression model demonstrated that a lower eGFR was an independent risk factor for a larger lipid index.

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CLINICAL PERSPECTIVE

Chronic kidney disease (CKD) promotes the development of atherosclerosis and increases the risk of cardiovascular disease. Although pathology studies have demonstrated that coronary atherosclerosis and calcification are more frequent and severe in patients with CKD, the underlying mechanism for poor outcomes and higher recurrent ischemic events in CKD patients has not been fully elucidated. In the current study, we attempted to clarify these underlying mechanisms using a high-resolution intravascular imaging modality: optical coherence tomography. Indeed, compared with non-CKD patients, patients with CKD had a wider lipid arc, a larger lipid index, and a higher prevalence of calcium, cholesterol crystals, and disruption. Thrombus tended to also be more frequent in the CKD group. Multivariate linear regression model demonstrated that a lower estimated glomerular filtration rate was an independent risk factor for a larger lipid index. The present study demonstrated that coronary atherosclerosis was more complex in patients with CKD compared with non-CKD.