Some studies have reported on the relationship between coronary plaque and renal function, and it is well known that deteriorating renal function is associated with increased cardiovascular events in patients with chronic kidney disease (CKD).\textsuperscript{1-4}

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In particular, given that coronary plaque morphology is related to the occurrence of a coronary event, the detection of unstable plaque is especially important. Intravascular imaging modalities, as well as non-invasive coronary CT and MRI, have been utilized to detect vulnerable plaque. Some reports have already established plaque evaluation by intravascular ultrasound (IVUS).

Generally, eccentric soft plaque and positive remodeling are found in vulnerable plaque by gray-scale IVUS, and necrotic and lipid rich tissue are more frequently found than in stable plaque by color-coded IVUS. In addition, in 1995 Mintz et al. reported that independent predictors of reference segment calcification were the patient’s age and serum creatinine level.\textsuperscript{5}

In patients with CKD, it has been reported that coronary artery calcification (CAC) is superior in predictive ability of cardiovascular disease risk to carotid intima-media thickness.

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**Figure.** Plaque calcification detected and measured by optical coherence tomography (OCT). Frame level measurement of plaque calcification. Corresponding bright-field (A), fluorescent (B) and OCT (C) images of coronary artery calcification with all calcium borders visualized on OCT and corresponding cryo (D) and OCT (E) measurement tracings of calcium area, angle and depth at 1 degree circumferential intervals. FOCT, frequency-domain optical coherence tomography. (Reproduced with permission from Mehanna E et al.\textsuperscript{16})

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Division of Cardiology, Department of Medicine, Nihon University School of Medicine, Tokyo, Japan

Mailing address: Tadateru Takayama, MD, Division of Cardiology, Department of Medicine, Nihon University School of Medicine, 30-1 Ohyaguchi-kamicho, Itabashi-ku, Tokyo 173-8610, Japan. E-mail: takayama.tadateru@nihon-u.ac.jp

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and the ankle brachial index as an atherosclerosis index. In their IVUS study, Ehara et al. reported in 2004 on the association between spotty calcification and plaque vulnerability in acute coronary syndrome. They highlighted that IVUS allows the identification of vulnerable plaque in coronary arteries, not only by identifying fibrofatty plaque and positive remodeling, but also by identifying a spotty pattern of calcification. Previous virtual histology (VH-) IVUS studies showed that fibrous volume decreased and the dense-calcium volume increased as renal function decreased in either culprit or nonculprit lesions, although plaque volume was comparable among patients with varying degrees of renal function.

In recent years, the progress in coronary CT has facilitated scoring of CAC and its relation to coronary events. Although coronary events occur with soft plaque, it has been reported that a high CAC score is associated with a higher incidence of coronary events. It is considered that the results are somewhat contradictory. The study in terms of coronary plaque in patients with CKD had similar results to the Hisayama-Chou study in that cardiovascular events in CKD patients increased.

In this issue of the Journal, Shimbo et al. report on one of the few IVUS studies of the characteristics of coronary plaque in CKD patients using IB-IVUS, and they show that a reduced eGFR and the presence of proteinuria are significantly associated with the presence of lipid-rich plaques in patients with coronary artery disease. They conclude that the addition of proteinuria to the eGFR may have value in the risk stratification of patients with coronary artery disease and is an important message for the treatment of CKD patients in the practical clinical setting. Miyagi et al. (from the same university) reported a significantly higher lipid volume in patients with CKD, based on results of an IB-IVUS analysis. In the present study, the analysis included not only eGFR but also proteinuria for patients with CKD. However, there was not a significant correlation between lipid volume and the protein-positive degree of proteinuria, and there was not a correlation of the lipid volume of the plaque with proteinuria alone. By multivariable analysis, they determined that the presence of both is important because eGFR and the presence of proteinuria were independent determinants. Also, the evaluation of moderate or severe calcification is insufficient, and therefore the evaluation of coronary lesions using CT does not support the results of this present study because of the cases in this study in which IVUS was performed. Kashiyama et al. reported that the plaque components in patients with CKD using IB-IVUS were the same as in the present study. It suggests that moderate to advanced CKD is associated with coronary plaque progression characterized by greater lipid and fibrotic plaque volumes in nonculprit lesions.

Stone et al. reported that plaque burden >70%, lumen cross-sectional area <4 mm² and VH-thin-cap fibrous atheroma (TCFA) were independent predictors of MACE on IVUS and the incidence of MACE became higher in the PROSPECT study when not only TCFA but also multiple risk factors were increased. Therefore, they determined both vulnerable plaques and significant coronary stenosis as important determinants of poor prognosis.

Mintz et al. showed that calcification had a significant relationship with significant stenosis, as a result of their IVUS analysis of the reference segment of the stenosis. However, moderate or severely calcified lesions were excluded from IVUS analysis in that study, which is a major limitation. As renal dysfunction and the association of calcification have been already reported in a study using CT, a study using IB-IVUS and including not only the vulnerability of the plaque but also the level of calcification was desirable. Quantification of calcification can be evaluated not only by CT but also optical coherence tomography (Figure). Further studies involving a general, comprehensive plaque analysis using IVUS or other imaging modalities in CKD patients and other intravascular imaging may be required.

Disclosures
None.

References
1. Culleton BF, Larson MG, Wilson PW, Evans JC, Parfrey PS, Levy D, et al. Cardiovascular disease and mortality in a community-based cohort with mild renal insufficiency. Kidney Int 1999; 56: 2214 – 2219.
2. 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.
3. Sarnak MJ, Levey AS, Schoolwerth AC, Coresh J, Culleton B, Hamm LL, et al. 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.
4. Gross P, Six I, Kamel S, Massy ZA. Vascular toxicity of phosphate in chronic kidney disease: Beyond vascular calcification. Circ J 2014; 78: 2339 – 2346.
5. Mintz GS, Painter JA, Pichard AD, Kent KM, Satler LF, Popma JJ, et al. Atherosclerosis in angiographically “normal” coronary artery reference segments: An intravascular ultrasound study with clinical correlations. J Am Coll Cardiol 1995; 25: 1479 – 1485.
6. Matsushita K, Sang Y, Ballew SH, Shlipak M, Katz R, Rosas SE, et al. Subclinical atherosclerosis measures for cardiovascular prediction in CKD. J Am Soc Nephrol 2015; 26: 439 – 447.
7. Ehara S, Kobayashi Y, Yoshiyama M, Shimada K, Shimada Y, Fukuda D, et al. Spotty calcification typifies the culprit plaque in patients with acute myocardial infarction: An intravascular ultrasound study. Circulation 2004; 110: 3424 – 3429.
8. Kono K, Fujii H, Nakai K, Goto S, Shiite J, Hirata K, et al. Composition and plaque patterns of coronary culprit lesions and clinical characteristics of patients with chronic kidney disease. Kidney Int 2012; 82: 344 – 351.
9. Motoyama S, Kondo T, Sarai M, Sugihara A, Harigaya H, Sato T, et al. Multislice computed tomographic characteristics of coronary lesions in acute coronary syndromes. J Am Coll Cardiol 2007; 50: 319 – 326.
10. Agaston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M Jr, Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. J Am Coll Cardiol 1990; 15: 827 – 832.
11. Nakano T, Ninomiya T, Sumiyoshi S, Fuji H, Doi Y, Hirakata H, et al. Association of kidney function with coronary atherosclerosis and calcification in autopsy samples from Japanese elders: The Hisayama study. Am J Kidney Dis 2010; 55: 21 – 30.
12. Shimbo Y, Suzuki S, Ishii H, Shibata Y, Tatami Y, Harata S, et al. Association of estimated glomerular filtration rate and proteinuria with lipid-rich plaque in coronary artery disease. Circ J 2015; 79: 2263 – 2270.
13. Miyagi M, Ishii H, Murakami R, Isobe S, Hayashi M, Amano T, et al. Impact of renal function on coronary plaque composition. Nephrol Dial Transplant 2010; 25: 175 – 181.
14. Kashiyama K, Sonoda S, Murakoa Y, Suzuki Y, Kamezaki F, Tsuda Y, et al. Coronary plaque progression of non-culprit lesions after culprit percutaneous coronary intervention in patients with moderate to advanced chronic kidney disease: Intravascular ultrasound and integrated backscatter intravascular ultrasound study. Int J Cardiovasc Imaging 2015; 31: 935 – 945.
15. Stone GW, Maehara A, Lansky AJ, de Bruyne B, Cristea E, Mintz GS, et al. A prospective natural-history study of coronary atherosclerosis. N Engl J Med 2011; 364: 226 – 235.
16. Mehanna E, Bezerra HG, Prabhu D, Brandt E, Chamié D, Yamamoto H, et al. Volumetric characterization of human coronary calcification by frequency-domain optical coherence tomography. Circ J 2013; 77: 2334 – 2340.