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Editorial

A New Factor for Vascular Calcification in Chronic Kidney Disease:

Computed Tomography-Based Renal Parenchymal Volume

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Vascular calcification usually occurs in large and medium-sized muscular arteries and arterioles and is common in dialysis patients and nondialysis chronic kidney disease (CKD) patients. It is likely to lead to cardiovascular disease risk in these patient populations[1]. The prevalence of vascular calcification among CKD patients is generally higher than that in the general population. The extent of vascular calcification seems to be more severe as the stage of CKD progresses and the estimated glomerular filtration rates (eGFRs) go down; the severity of vascular calcification is the strongest in long-term dialysis patients[2, 3]. These findings indicate a close relationship between renal dysfunction and vascular calcification in CKD patients.

There are two types of vascular calcification in CKD patients: intimal and medial. Intimal calcification is the result of an inflammatory process and is a manifestation of advanced atherosclerosis. It is mainly associated with a marked reduction in endothelial function and reactivity and is partly associated with a reduced coronary flow reserve[4]. Spotty intimal calcification in the coronary arteries may play a role in the occurrence of acute coronary syndrome[5]. Medial calcification is partly due to increased serum calcium, phosphate, and vitamin D concentrations. In contrast to intimal calcification, medial calcification is not associated with atherosclerosis. Medial calcification decreases vascular distensibility, leading to increased arterial stiffness[6]. Increased arterial stiffness due to medial calcification contributes to left ventricular hypertrophy, myocardial ischemia, and microcirculatory disturbance in important organs such as the brain, heart, or kidneys[7]. In an autopsy study by Nakamura, *et al.*[8], coronary calcification is mainly due to intimal calcification, particularly in nondialysis CKD patients; this finding indicates that coronary calcification is closely related to atherosclerotic changes[9]. In contrast, vascular calcification found in large and medium-sized arteries is mainly due to medial calcification and partly due to intimal calcification derived from atherosclerotic lesions. Intimal calcification progresses with the CKD stage, whereas medial calcification appears from CKD stage 3 and progresses at CKD stages 4/5 and further on dialysis[10] (**Fig. 1**). Intimal and medial calcifications have been associated with increased mortality, although intimal calcification is more closely associated with the increased occurrence of cardiovascular events and cardiovascular-related mortality.

Ichii *et al.* investigated the relationship between the progression of vascular calcification and renal function and/or morphological changes in 70 asymptomatic CKD patients[11]. Annualized variations of the coronary artery calcification score (CACS) were associated with the CACS at baseline and the presence of diabetes mellitus and those of the abdominal aortic calcification index (ACI) were associated with the ACI at baseline and the presence of hypertension. Annualized variations of the computed tomography (CT)-based renal parenchymal volume index were inversely related with the annualized variations of the CACS and the ACI, whereas the eGFR and annualized variations of the eGFR were not associated with the progression of vascular calcification. The authors concluded that the degree of vascular calcification at baseline and in the presence of diabetes and hypertension and changes in renal parenchymal volume strongly affected the progression of vascular calcification in CKD patients.

Generally, risk factors for vascular calcification

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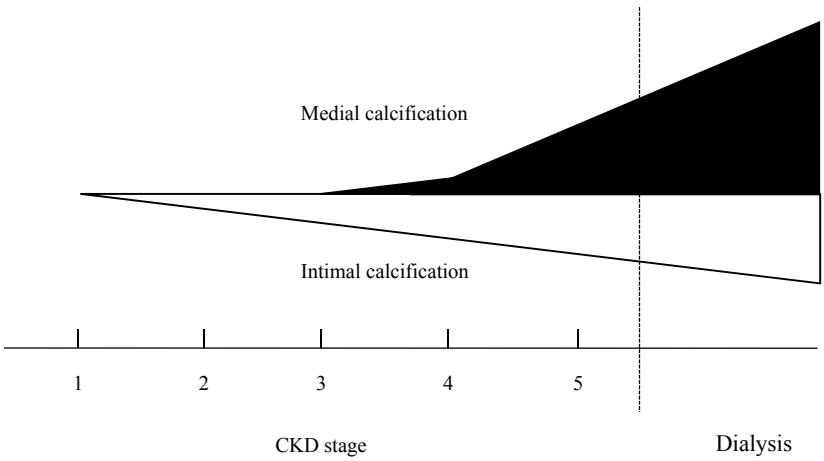

Fig. 1. Progression of vascular calcification in CKD stages

include the following: increasing age, dialysis vintage for dialysis patients, hyperphosphatemia, positive net calcium and phosphate balance and calcium intake[12], high calcium-phosphate product, vitamin D therapy, diabetes, or dyslipidemia. Ichii *et al.* reported changes in renal parenchymal volume as a new factor for vascular calcification[11]. In contrast, the eGFR and changes in the eGFR were not included as a risk factor for calcification in their study. The eGFR is generally an approved indicator of renal function; however, serum creatinine levels are influenced by muscle mass and the nutritional status. In contrast, the CT-based renal parenchymal volume might reflect renal dysfunction more correctly than the eGFR. Changes in the renal parenchymal volume would be associated with renal endocrine and tubular function in addition to filtration ability because renal atrophy develops because of glomerulosclerosis, tubular atrophy, and interstitial fibrosis. Renal parenchymal atrophy may cause imbalance in the levels of humoral factors regulating vascular calcification including α-klotho, fibroblast growth factor-23, or 1,25-dihydroxyvitamin D_3[13].

The inhibition of vascular calcification is important for reducing the occurrence of cardiovascular events and improving the prognosis of CKD patients. Although the study by Ichii *et al.*[11] was conducted in a single center and included a small number of patients, they were the first to show the importance of changes in the CT-based renal parenchymal volume in the progression of intimal and medial calcifications. We need to verify the involvement of this new factor for vascular calcification in CKD patients.

Conflict of Interest

None.

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