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COMMENT

Central hemodynamics and left ventricular hypertrophy in chronic kidney disease

Naoki Nakagawa[1] · Naoyuki Hasebe[1]

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It is well known that chronic kidney disease (CKD) is one of the most important risk factors for cardiovascular events worldwide [1, 2]. A major driver is increased aortic stiffness, which is a strong independent predictor of cardiovascular mortality in this population. Aortic stiffening is a potentially modifiable biomarker of cardiovascular dysfunction, and it is used in risk stratification of patients with CKD and end-stage renal disease [3–6]. Pulse wave velocity (PWV) is an indirect measure of stiffness and the accepted standard for noninvasive assessment of aortic stiffness. The clinical significance of PWV is thought to be related to not only structural changes within the vascular wall but also adverse hemodynamic effects [7]. These include an increase in systolic blood pressure and pulse pressure (PP) and, hence, an increase in the dynamic left ventricular (LV) load. Meanwhile, a decreased glomerular filtration rate (GFR) may cause latent volume retention in patients with earlier stages of CKD. Furthermore, various factors that deteriorate vascular function, such as the renin–angiotensin–aldosterone system, homocysteine, oxidative stress, and inflammation, are reportedly activated not only in patients with end-stage renal disease but also in those with earlier stages of CKD [2, 8].

Recent advances in technology have enabled the noninvasive evaluation of central hemodynamics. The central blood pressure represents the true load imposed on the heart, kidney and brain. An elevation of the central blood pressure has a direct adverse impact on the target organ and, therefore, on the cardiovascular prognosis in patients with hypertension [4, 9]. A decrease in the central blood flow can cause organ dysfunction and failure. The central pressure and flow dynamics are conventionally regarded as unidirectional, from the heart to the periphery. However, current evidence suggests that they should be recognized as a bidirectional interplay between the central and peripheral arteries. In particular, the pressure pulse wave is not only transmitted forward to the periphery but also reflected backward to the central aorta [10]. The flow pulse wave is also composed of the forward and reverse components. Aortic stiffening and arteriolar remodeling, due to hypertension, not only augment the central pressure by increasing the wave reflection but may also alter the central bidirectional flow, inducing hemodynamic damage/dysfunction in susceptible organs. Therefore, central hemodynamic monitoring has the potential to provide a diagnostic and therapeutic basis for the prevention of systemic target organ damage and to offer personalized therapy suitable for arterial properties of each patient with hypertension [10].

LV hypertrophy (LVH) is also common and is a strong predictor of cardiovascular events in patients with CKD [11, 12]. LVH is also known to be preventable or even reversible by controlling the blood pressure and volume in patients with CKD [13]. Although it is well known that the arterial stiffness gradient is inverted during the CKD progression, central hemodynamic pressure profiles and their association with LVH in CKD have not been fully examined.

In this issue of *Hypertension Research*, Takenaka et al. [14] demonstrate a relationship between the pulse amplification (PA) and LVH according to CKD stages in 2020 hypertensive patients who underwent echocardiography and measurement of their serum creatinine levels as a subanalysis in the second version of the Antihypertensives and Blood Pressure of Central Artery study in Japan (ABC-J II study) [15]. Brachial systolic and diastolic blood pressures were measured using oscillometric methods (HEM-9000AI; Omron Healthcare, Kyoto, Japan) in a sitting position after at least a 5-min rest, which was similar to the methods used in the Systolic Blood Pressure Intervention Trial (SPRINT) [16].

✉ Naoki Nakagawa
naka-nao@asahikawa-med.ac.jp

[1] Division of Cardiology, Nephrology, Pulmonology and Neurology, Department of Internal Medicine, Asahikawa Medical University, Asahikawa, Japan

First, they showed that the central PP was higher at CKD stages 3a–5 than at stage 1, whereas the brachial PP was higher at stage 3b and later than at stage 1, suggesting that the central PP was more significantly elevated in earlier stages of CKD than the brachial PP was. Second, they performed multiple regression analysis for PA, which was defined as a ratio of brachial PP/central PP. Interestingly, compared with that at CKD stage 1, the adjusted PA at CKD stages 3a and 3b was significantly lower. However, the adjusted PA at CKD stage 1 was similar to that at CKD stages 4 and 5. Similar trends were observed when PA was adjusted for all variables, suggesting that the CKD progression inverted PA. Third, they assessed LV parameters according to CKD stages and demonstrated that the LV thickness and mass index were greater at CKD stage 3b and later than at CKD stage 1, whereas only the LV end-diastolic diameter was greater at CKD stage 5 that at CKD stage 1. These results are consistent with the data of previous reports, indicating that GFR generally decreases with age and the pressure and volume load, augmented by renal dysfunction, and directly increases arterial stiffness, the LV mass, and the left atrial size [3, 12]. Finally, they discussed ventricular–vascular coupling and an impedance mismatch in CKD. In early stages of CKD, the reflection wave increases, mainly due to increases in peripheral arterial stiffness. During CKD progression, the aorta stiffens more progressively than peripheral arteries do, thereby reversing the arterial stiffness gradient. In advanced CKD, preferential increases in proximal aortic stiffness (afterload mismatch) account for both an inverted PA and high brachial PP (low arterial compliance).

The central PP seems particularly important for patients with CKD. It has been reported that each 10 ml/min per 1.73 m^2 decrement in the estimated GFR was associated with an increase in the central PP of ~2.5 mmHg in a large patient cohort with mild to moderate CKD [4]. Other investigators have shown that the central PP was an independent predictor of the progression to end-stage renal disease in CKD patients [17]. Furthermore, some prospective studies have investigated the predictive capability of central pressure indices for cardiovascular prognosis in patients with end-stage renal disease [18, 19]. Most of the studies have confirmed that the central PP and augmentation index predict future cardiovascular events more accurately than, or independently of, the brachial pressure [10, 20]. Further studies are needed to better understand the synergistic impact of central hemodynamics and LVH on cardiovascular events in patients with CKD.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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