Left Atrial Enlargement: An Unfavorable Cardiorenal Omen

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Chronic kidney disease (CKD) is a major public health problem worldwide, and cardiovascular disease remains the leading cause of morbidity and mortality among patients with CKD (1). The cardiovascular mortality risk is demonstrable at each stage of CKD due to both traditional risk factors and those specific to kidney disease. There has been rapidly growing interest in the past decade in the relation between heart and kidney dysfunctions, popularly termed “cardiorenal syndrome” (2). The cardiac alterations develop early during the course of CKD, attributed mainly to volume and pressure overloads associated with a variety of metabolic and neurohumoral abnormalities. Accordingly, pathologic cardiac remodeling, including cellular, structural and functional changes, is frequently identified in patients with CKD, and associated with disease progression and poor prognosis (1, 3).

Echocardiography is an established non-invasive method for estimating the risk for cardiovascular complications and for guiding treatment of CKD patients. It is particularly helpful in risk stratification and monitoring (4, 5). Several left ventricular (LV) structural and functional parameters, such as the left ventricular mass index (LVMI), ejection fraction (LVEF) and LV chamber volume, have been shown to be valuable prognosticators of cardiovascular events and adverse outcomes in CKD patients (4-6). Although less well studied than LV abnormalities, an enlarged left atrium (LA) has recently been identified as another useful indicator for unfavorable cardiovascular outcomes in various pathologic conditions, including atrial fibrillation, stroke, heart failure, cardiovascular and all-cause mortality (7-9).

The LA mechanical function, in a close interdependence with LV, plays a key role in maintaining optimal cardiac performance through its “reservoir,” “conduit,” and “booster pump” phasic properties. LV hypertrophy, LV systolic and diastolic dysfunctions, valvular heart disease, dysrhythmias, extracellular volume expansion, hypertension and diabetes mellitus are all regarded as underlying mechanisms leading to LA remodeling in the CKD population (9, 10). Particularly in subjects without primary atrial pathology and mitral valve disease, increased LA volume always leads to increased wall tension as a result of elevated LV filling pressure. The progressive deterioration of myocardial diastolic properties causes an elevation of LV filling pressures (9). Therefore, LA enlargement has been proposed as a sensitive integrator of severity and chronicity of diastolic dysfunction, which is highly prevalent in CKD patients (9-11). Indeed, close monitoring of LA size has been suggested to provide valuable prognostic information beyond established echocardiographic markers for high cardiovascular risk. Notably, in both the initial survey and the longitudinal analysis, the predictive power of LA enlargement is higher than that provided by LVMI and LV function (8-11).

In this issue of Acta Nephrologica, Yang et al. demonstrated a statistical correlation between LA enlargement and the rate of renal function decline in a cohort of patients with CKD stages 3 to 5 (12). They suggested that increased LA diameter, as measured by M-mode echocardiography, was independently associated with rapid progression of renal dysfunction in moderate to advanced CKD patients. There are several explanations for such association. First, hypertension is an influential risk factor for both progression of kidney and heart dysfunction. It is well known that hypertension is associated with LA size in hypertensive patients (9). Salt and fluid
overload with extracellular volume expansion complicating CKD also contributes to LV preload and increased LA size (10). Additionally, diabetes mellitus, another strong progression risk factor in CKD, can also inflict direct and indirect insults to the myocardium and influence cardiac remodeling, leading to an enlarged LA. Diastolic dysfunction has been observed in up to 40% of individuals with diabetes and correlates significantly with poor glycemic control (13). In the evolution of diabetic complications over time, the severity of LA enlargement will possibly correspond with decline in renal function. Finally, some abnormalities in chronic inflammation, oxidative stress, endothelial function, electrolyte homeostasis, mineral metabolism, natriuretic peptides and activation of the renin-angiotensin-aldosterone system are often present and may contribute to pathologic cardiac remodeling and LA structural alterations in CKD patients (8-11, 14).

Two-dimensional and Doppler echocardiography is a well-established practice for the assessment of LA size and function. Measurement of anteroposterior LA linear dimension by M-mode, as applied in the study of Yang et al., is simple, convenient and widely employed in clinical practice but not reliably accurate, given that the LA is not a symmetrically shaped three-dimensional structure. Moreover, because LA enlargement may not occur in a uniform fashion, one-dimensional assessment for LA diameter does not reflect true LA size (9, 15). For these reasons, the LA diameter as the sole measure of LA size may be misleading and should be accompanied by LA volume determination in both clinical practice and research. Recent guidelines from the American Society of Echocardiography have recommended quantification of LA size using LA volume measured by biplane two-dimensional echocardiography. Such a standardized approach for LA volume assessment, indexed by body surface area, will be pivotal for reproducible measures and communication of LA size between laboratories (15).

Although echocardiography is recommended as a valuable and helpful tool for risk stratification and monitoring in CKD patients, facilities for echocardiography are not widely available in many clinics because of cost and technical limitations. The utility of biochemical assays for diagnosing anatomic and functional alterations of the heart is a growing and promising clinical research area over the past decade. Natriuretic peptides, including atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP), have emerged as important biomarkers with an established role in the diagnosis of congestive heart failure (16). Recent studies have shown that circulating ANP, BNP and N-terminal fragment (NT-proBNP) are strongly related to LA volume and predict progression in LA enlargement and associated alterations in LV mass and function among patients with end-stage renal disease (17, 18).

In conclusion, LA enlargement in general is an ominous prognostic sign in CKD patients. Longitudinal studies are warranted to refine the prognostic utility of LA echocardiographic parameters and to establish causality between LA size and progressive decline in renal function. Furthermore, because factors predisposing to LA enlargement in CKD are in part modifiable by pharmacological and non-pharmacological interventions, studies are also needed to determine whether managing LA enlargement may serve as a useful therapeutic target for improving cardiovascular and renal outcomes.

References


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