

Diastolic dysfunction and chronic kidney disease

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In patients with chronic kidney disease (CKD), cardiovascular disease is the most common cause of death. Patients with CKD have a high burden of conventional risk factors that are closely related to accelerated atherosclerosis, left ventricular (LV) dilatation with hypertrophy, systolic dysfunction, and high LV filling pressure. Furthermore, primary disorders of the cardiac and renal system cause deterioration in each other via direct or indirect injuries through several complex mechanisms [1]. In CKD patients, retention of sodium and water often causes cardiac problems. CKD is closely related to LV hypertrophy and fibrosis, which is closely associated with stiff ventricles and abnormalities in ventricular relaxation. Thus, a small increase in preload can result in significantly increased left atrial and pulmonary vein pressures, thereby causing pulmonary edema even with normal LV systolic function.

Echocardiography enables the evaluation of the diastolic stiffness of the ventricle [2]. The most important variables are the transmitral pulsed wave Doppler flow and mitral annular tissue Doppler signal [3]. Measuring the transmitral pulsed wave is the first step in evaluating diastolic dysfunction,

but it is influenced by factors such as the load on the left atrium and heart rate. By contrast, tissue Doppler imaging (TDI) can assess myocardial function directly at the level of the mitral annulus by measuring the velocity along the longitudinal myocardial axis, which is influenced less by the loading conditions. Therefore, TDI can be used to more effectively monitor myocardial function.

During diastole, transmitral Doppler flow can be classified into four stages: isovolumic relaxation time, early filling phase (E), diastasis, and atrial contraction. The E velocity correlates positively with the LV filling pressure in heart failure and correlates inversely with LV relaxation, while in the broader community, the abnormalities are non-linear because the measurement is affected by both myocardial relaxation and filling pressure. Mitral annular TDI measures myocardial velocity, which is characterized by a peak systolic velocity (s'), early diastolic velocity (e'), and late diastolic velocity (a' , during atrial contraction). Of these, e' is inversely related to LV relaxation. The E/e' ratio is the ratio of (LV filling pressure/LV relaxation) and LV relaxation, and is correlated with the LV filling pressure. Values of $E/e' > 15$ indicate an elevated filling pressure or left atrial pressure, whereas $E/e' < 8$

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is considered a normal LV filling pressure or left atrial pressure. To complete LV filling and achieve an end-diastolic volume sufficient for adequate stroke volume in patients who have LV relaxation abnormalities or a stiff LV, the left ventricle requires filling pressures higher than normal [2]. The value of E/e' is the most powerful prognosticator in most cardiac disorders, including both systolic and diastolic heart failure, myocardial infarction, cardiomyopathy, LV hypertrophy, and subclinical myocardial disease [3,4].

Despite its usefulness, the measurement of E/e' has pitfalls [5,6]. Some investigators have proposed that E/e' does not represent the LV filling pressure in some conditions, especially in decompensated advanced systolic heart failure with large LV volumes, worse cardiac indices, significant mitral regurgitation, regional wall motion abnormalities in the basal segments, a prosthesis in the mitral area, constrictive pericarditis, or after cardiac resynchronization therapy. Nevertheless, TDI is a sensitive, load-independent measure of LV relaxation and is a widely used echocardiographic methodology. Although E/e' is a good index of the LV filling pressure, a high E/e' is not always associated with diastolic dysfunction. In fact, diastolic dysfunction means that the LV fills at higher pressures. In patients with CKD, this condition is more frequent because of the increased LV systolic and diastolic stiffness associated with ventricular hypertrophy and fibrosis. This condition is particularly common in hemodialysis patients. As a consequence of fibrosis, relaxation becomes slower and LV compliance decreases, manifesting as a decrease in the e' velocity on TDI. Meanwhile, the increased sodium and water retention associated with CKD increases the E velocity. Consequently, a high E/e' is closely associated with the presence of heart failure and is good index for the future development of heart failure regardless of renal function.

Kim et al. [7] investigated echocardiographic parameters for estimating the LV filling pressure as a prognosticator in CKD. They suggested that E/e' could predict mortality and cardiovascular events in CKD patients with diastolic dysfunction. We have a large dataset on the ability of E/e' to predict adverse outcomes of heart failure in patients with either decreased or normal renal function. In the general population, diastolic dysfunction has become more prevalent than

systolic dysfunction. However, not all patients who have diastolic dysfunction develop clinical heart failure. Diastolic heart failure is more common in heart failure with a LV ejection fraction of more than 50% [2].

The relationship between myocardial fibrosis and diastolic dysfunction has been evaluated in many cardiac diseases, but few data exist for patients with end-stage renal disease [8]. In the present study, 39% of the patients had decreased LV systolic function, and a significant proportion had undergone maintenance dialysis. Thus, this study included a heterogeneous population and did not focus on only diastolic heart failure. Furthermore, the enlarged left atrium and high E/e' in the study populations indicates that these patients had long-standing elevated LV filling pressures. Therefore, we should not extrapolate these data to all patients with stable CKD.

In conclusion, although the ratio of the transmitral inflow (E velocity) to the tissue velocity (e') may be imperfect in some circumstances, it is a robust marker for predicting the LV filling pressure and therefore a powerful prognosticator in heart failure with CKD. Nevertheless, the annular tissue velocity must still be measured in patients who have annular calcification related to renal failure.

Conflict of interest

No potential conflict of interest relevant to this article is reported.

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