Left ventricular diastolic dysfunction in the early stage of chronic kidney disease

Takenori Otsuka (MD)*, Makoto Suzuki (MD, FJCC), Hisao Yoshikawa (MD), Kaoru Sugi (MD, FJCC)

Division of Cardiovascular Medicine, Toho University Ohashi Medical Center, 2-17-6 Ohashi, Meguro-ku, Tokyo 153-8515, Japan

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Summary
Background: The disadvantageous effect of kidney dysfunction on left ventricular (LV) diastolic function is still unknown.
Methods: Forty non-chronic kidney disease (CKD) patients and 202 CKD patients, aged 40—89, were examined by standard echocardiography and the new modality of tissue Doppler imaging. All subjects were divided into 5 groups depending on their estimated glomerular filtration rate (GFR: ml/min/BSA). Classifications by GFR were defined as follows: group 1 (more than 90: normal subjects), group 2 (60—89), group 3 (30—59), group 4 (15—29) and group 5 (less than 15).
Results: There were no significant differences in LV systolic function among the groups. Mitral $E$ velocity was significantly lower in groups 1—4 ($p<0.01—0.02$) compared with group 5. Mitral $A$ velocity was higher in groups 2—5 ($p<0.01—0.04$) compared with group 1. The ratio of mitral $E$ and $A$ velocities ($E/A$) was significantly higher in group 1 ($p<0.02—0.05$) compared with groups 2—5. Deceleration time was significantly shorter in groups 1 and 2 ($p<0.01—0.02$) compared with groups 4 and 5. Furthermore, it was significantly lower in group 5 ($p<0.01$) compared with group 4. Early diastole velocity of mitral annulus (Ea) by tissue Doppler was also higher in group 1 (9.1 ± 2.5; $p<0.01—0.04$) compared with group 2 (7.9 ± 1.7), group 3 (7.9 ± 1.6), group 4 (7.5 ± 2.1), and group 5 (7.6 ± 2.0). Severity of the kidney dysfunction appears to parallel with the rise of $E/Ea$ significantly ($p<0.02$). $A$, $E/A$ and Ea could differentiate between groups 1 and 2 with early stage of CKD.
Conclusions: These data suggest that LV diastolic dysfunction was observed even in patients with early stages of chronic kidney dysfunction. Doppler indices combined with conventional and tissue Doppler methods could detect the subtle changes of diastolic function due to kidney dysfunction.

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* Corresponding author. Tel.: +81 3 3468 1251; fax: +81 3 3468 1269.
E-mail address: nori3649@hotmail.com (T. Otsuka).

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Introduction

Renal dysfunction is closely related to prognosis of cardiovascular disease (CVD) and conversely CVD patients often develop acute renal failure: this association is referred to as the cardio-renal connection. Chronic renal dysfunction has a negative effect on cardiac function and chronic kidney disease (CKD) is an important predictor of adverse outcome and increased morbidity in patients with chronic heart failure (CHF) [1—4]. A stage classification for CKD has been proposed for assessing the degree of severity of renal dysfunction, and recent evidence indicates that a moderate decrease in glomerular filtration rate (GFR) to <60 ml/min/1.73 m² of body surface area is associated with an adverse outcome in CHF patients [1,3].

Tissue Doppler imaging (TDI) is a new tool for assessment of left ventricular systolic and diastolic function in various cardiac diseases. Diastolic dysfunction is frequently observed in CHF patients with or without CKD [5] and TDI has improved assessment of this condition [6]. Left ventricular diastolic dysfunction affects morbidity and mortality in CHF patients with CKD, and echocardiography and tissue Doppler analysis may provide additional diagnostic data on ventricular function [7]. Therefore, the purpose of this study was to evaluate left ventricular diastolic dysfunction in patients with various stages of CKD using conventional echocardiography and TDI.

Methods

Study population

Forty non-CKD patients and 202 CKD patients aged 40—89 were examined by standard echocardiography and TDI. Patients with atrial fibrillation, systolic left ventricular dysfunction, CHF, myocardial infarction, cardiomyopathy, or valvular disorders were excluded from the study. Systolic left ventricular dysfunction is defined as ejection fraction less than 50%.

Demographic and clinical data

Records were reviewed for collection of data for age, gender, blood pressure (BP), hemoglobin (Hb), serum creatinine (Cr), and blood urea nitrogen (BUN). Patients were considered to be hypertensive based on European Society of Hypertension guidelines (≥140/90 mmHg) [8] or if they were taking antihypertensive medication (Table 1).

CKD and estimated GFR

The subjects were divided into 5 groups based on estimated (e)GFR: group 1 (>90), group 2 (60—89), group 3 (30—59), group 4 (15—29), group 5 (<15). Patients in group 2 were defined as having early stage CKD based on the US National Kidney Foundation Kidney Disease Outcome Quality Initiative [9], and those in groups 3—5 were considered to have CKD. Ninety-six patients in group 5 were on dialysis. The eGFR was calculated using the abbreviated Modification of Diet in Renal Disease Study Equation: eGFR (ml/min/1.73 m² of body surface area) = 186 × (serum creatinine in mg/dl)⁻¹.154 × (age in years)⁻⁰.²⁰³ × 0.⁷42 for female subjects [10].

Echocardiography

Echocardiography was performed using a cardiac ultrasound unit (HDI 5000, Phillips, Bothell, WA, USA; Power Vision-8000, Toshiba, Tokyo, Japan) with a 2—3.5 MHz transducer. TDI was performed in all patients with images taken based on the guidelines of the American Society of Echocardiography [11]. Left ventricular end-diastolic, systolic dimensions, end-diastolic, and systolic wall thickness of the interventricular septum and left ventricular wall were determined using standard echocardiographic 2-D and M-mode measurements. Both fractional shortening and left ventricular mass were calculated from the M-mode echocardiogram (Table 2). Mitral inflow velocity was traced and the following variables were derived: peak early (E) and late (A) transmitral flow velocities, the ratio of early to late peak velocities (E/A), and deceleration time of E velocity [12—14]. The echocardiographies of the patient on dialysis were performed before dialysis.

Tissue Doppler imaging

A 6-mm sample volume at the lateral corner of the mitral annulus was used for the apical-four chamber view. Annular velocities were displayed in spectral pulsed-wave TDI. The early peak diastolic annular velocity (Ea) was determined from the TDI recordings and the mitral E/Ea ratio was calculated [6,15—17].

Statistical analysis

One-way analysis of variance (ANOVA) was used to compare continuous variables and a χ² test was used for categorical variables. Data are expressed
Diastolic dysfunction is an abnormality of relaxation, filling, or distensibility of the left ventricle that is associated with augmented cardiovascular mortality [18–20]. Transmitral pulsed Doppler is a non-invasive method of evaluation of diastolic dysfunction, but is influenced by factors such as the loading condition of the left atria and heart rate. In contrast, TDI can be used to measure mechanical wall function directly by calculating the velocity of myocardial longitudinal movement and to mon-
Fig. 1 (A) Mitral E velocity in the five groups of patients. The mitral E velocity was significantly lower in groups 1–4 ($p < 0.02–0.02$) compared with group 5. (B) Mitral A velocity in the five groups of patients. The mitral A velocity was significantly lower in groups 1–4 ($p < 0.01–0.04$) compared with group 5. $E$, Early diastolic mitral inflow velocity; $A$, late diastolic mitral velocity; G1–G5, groups 1–5.

Fig. 2 (A) $E/A$ ratio in the five groups of patients. The ratio of the mitral $E$ and $A$ velocities ($E/A$) was significantly higher in group 1 ($p < 0.02–0.05$) compared with groups 2–5. $E/A$ increased in parallel with the severity of kidney dysfunction except for group 5. (B) Deceleration time (Dec) in the five groups of patients. Dec was significantly shorter in groups 1 and 2 ($p < 0.01–0.02$) compared with groups 4 and 5. Furthermore, it was significantly lower in group 5 ($p < 0.01$) compared with group 4. G1–G5, groups 1–5.

We also found that $E/A$ increased in parallel with the severity of kidney dysfunction, except for patients with very advanced CKD (group 5). $E/A$ was higher in group 5 compared with group 4, although the difference was not significant, and $E$ was significantly lower in groups 1, 2, 3, and 4 compared with group 5. Deceleration time was significantly shorter in groups 1 and 2 compared with groups 4 and 5. Furthermore, it was significantly lower in group 5 compared with group 4. $E/E_a$ also appeared to increase in parallel with the severity of kidney dysfunction. These results suggest that the left ventricle filling pressure may be higher in
group 5 than groups 1, 2, or 3. However, there is a possibility that it is affected by intrinsic volume overload in hemodialysis patients. Even a moderate decline in kidney function is associated with a significantly worse prognosis in patients with underlying CHF [1,3,22], but only a few clinical studies have attempted to elucidate the underlying mechanisms. Diminished renal perfusion is frequently a consequence of hemodynamic changes associated with heart failure and its treatment [23]. In addition to the adverse affects of heart failure on renal function, renal insufficiency adversely affects cardiac function, producing a vicious circle in which renal insufficiency impairs cardiac performance, which then leads to further impairment of renal function. As a result, kidney insufficiency is a major determinant of the progression of heart failure, congestion, recurrent decompensation, and hospitalization. The etiology of heart failure in patients is complex and several factors may be at work in CKD patients [3,24—26].

**Limitations**

We used conventional and TDI methods to assess the left ventricular diastolic function in CKD patients. However, the study also has several limitations. The number of patients was not the same in each group and the duration of renal dysfunction, hypertension, and diabetes was unknown in each group. Secondly, we performed measurements of Ea only in the lateral wall. Thirdly, we did not examine pulmonary vein flow velocity. Therefore, we analyzed the parameters of left ventricular diastolic function by routine echocardiographic examination. These factors may have affected the statistical analysis.

**Conclusion**

Although our study has some limitations, we conclude that left ventricular diastolic dysfunction occurs in patients in the early stage of CKD and that Doppler indices combined with conventional and TDI can be used to detect subtle changes of diastolic function due to kidney dysfunction.

**Conflict of interest**

None of the authors have any relationships with companies or other financial conflicts of interest associated with the work in the manuscript.

**References**


