Antihypertensive treatment improves left ventricular diastolic function in patients with chronic kidney disease

KU-LIN LI[1], RU-XING WANG[2], MIN DAI[2], JUAN LU[2], JING XUE[3] and XIANG-JUN YANG[1]

[1]Department of Cardiology, First Affiliated Hospital of Soochow University, Suzhou, Jiangsu 215006;
Departments of [2]Cardiology and [3]Nephrology, Wuxi People's Hospital Affiliated to Nanjing Medical University,
Wuxi, Jiangsu 214002, P.R. China

Abstract. In patients with chronic kidney disease (CKD), hypertension (HP) is associated with the development of left ventricular (LV) diastolic dysfunction. However, the impact of antihypertensive treatment on LV diastolic function has not been well studied in CKD patients. Recently, two-dimensional speckle-tracking echocardiography (2DSTE) has emerged as a sensitive and quantitative assessment of LV diastolic function. The present study used 2DSTE to investigate the effects of antihypertensive treatment on LV diastolic function in patients with CKD and untreated HP. The study comprised 134 patients with CKD and untreated HP. The patients received blood pressure (BP)-lowering therapy for six months. The patients were clinically and echocardiographically evaluated at baseline and after 6 months of therapy. It was found that the mean systolic BP (SBP) and diastolic BP (DBP) at baseline were 154.0±7.0 and 92.6±10.2 mmHg, respectively, decreasing to 121.2±7.3 and 74.6±10.4 mmHg, respectively (P<0.05 for both) after the 6-month treatment period. Moreover, the mean peak LV strain rate during the isovolumetric relaxation period (SR_{IVR}) and early diastole (SR_E) improved following treatment (from 0.23±0.10 to 0.42±0.10 sec^{-1} and from 0.58±0.25 to 1.07±0.24 sec^{-1}, respectively; P<0.05 for both). Notably, the patients with CKD stage ≥3 were more likely to demonstrate an improvement in diastolic speckle-tracking parameters than those with CKD stage 1 or 2. For the entire population, the change (Δ) in B-type natriuretic peptide (BNP) level correlated with changes in echocardiographic parameters between baseline and follow-up, among which ΔSR_{IVR} presented the highest correlation coefficient (r=-0.73, P<0.01). On multivariate analysis, the independent predictors of ΔSR_{IVR} were found to include baseline CKD stage, SBP and SR_{IVR}. This study demonstrated that LV diastolic function was improved in CKD patients following antihypertensive treatment, particularly in patients with CKD stage ≥3, higher baseline SBP and worse LV diastolic function. These results highlight the importance of BP reduction in the treatment of CKD.

Introduction

Chronic kidney disease (CKD) is an important public health problem, affecting 10-15% of the adult general population. CKD has a negative effect on cardiac function and frequently leads to anomalies in left ventricular (LV) structure and function. Cardiovascular disease-related mortality is the most common cause of mortality in patients with CKD (1-5). LV diastolic dysfunction, characterized by abnormalities of ventricular filling, including decreased diastolic distensibility and impaired relaxation, is a very common structural abnormality in patients with CKD and is independently associated with morbidity and mortality (2,3). Previous studies have shown that LV function deterioration in CKD patients progresses in a predictable fashion, with LV diastolic dysfunction usually preceding LV systolic dysfunction (5-7). These findings suggest that maintaining LV diastolic function may be critical for preventing cardiac failure in CKD patients (6,7).

CKD frequently coexists with traditional cardiovascular risk factors, hypertension (HP) being the most common. HP can be either a cause or a consequence of CKD. Specifically, HP is known to play an important role in causing LV diastolic dysfunction. Several trials have demonstrated the benefit of blood pressure (BP) control in slowing the progression of kidney disease and improving clinical outcomes, particularly in patients with CKD stage ≥3 (4,8); however, the mechanisms involved remain unknown. Diastolic dysfunction is considered as an important pathophysiological intermediate to heart failure and represents a attractive target for cardiovascular disease prevention (4-7). However, to the best of our knowledge, the impact of antihypertensive treatment on LV diastolic function has never been analyzed in CKD patients.

Newly developed two-dimensional speckle tracking echocardiography (2DSTE) is based on tracking of the speckles produced by the interaction of ultrasound with the ventricular structures and quantitatively analyzes global and regional myocardial motion. Global diastolic strain rate (SR)

Correspondence to: Dr Xiang-Jun Yang, Department of Cardiology, First Affiliated Hospital of Soochow University, 188 Shi Zi Street, Suzhou, Jiangsu 215006, P.R. China
E-mail: yangxjjs@126.com

measurements, averaged from all LV segmental SRs at the same time, have been validated to be accurate in the assessment of diastolic function and advantageous over the traditional tissue Doppler approach (9,10). In light of this evidence, 2DSTE was chosen for use in the current study to evaluate the effect of antihypertensive treatment on LV diastolic function in patients with CKD.

Materials and methods

Study population. Initially, 172 consecutive patients with newly diagnosed and untreated hypertension with decreased estimated glomerular filtration rate (eGFR) or elevated albuminuria levels were recruited from the outpatient department of Wuxi People's Hospital Affiliated to Nanjing Medical University (Wuxi, China), among whom 152 patients met standard clinical criteria for CKD (11). BP was measured in a sitting position (measurements were made after a 5-min rest in a sitting position with a certified mercury sphygmomanometer; an average of three measurements made at an interval of ≥2 min was used in the analysis). Patients underwent clinical assessment that included an evaluation of their symptoms and physical condition prior to enrollment. HP was diagnosed and treated in accordance with the Seventh Report of the Joint National Committee on the Prevention, Detection, Evaluation and Treatment of High Blood Pressure; the goal of antihypertensive treatment is to attain a BP <130/80 mmHg (12). Antihypertensive agents, namely β-blockers, diuretics, calcium channel blockers (CCBs), angiotensin receptor blockers (ARBs) and angiotensin converting enzyme inhibitors (ACEIs), were titrated to the maximal tolerated dose and used in combination when the BP goal was not reached. BP treatment was checked every 2 weeks and continued for 6 months. The following indicators were used as exclusion criteria: clinically significant coronary artery disease, any valvular diseases, atrial fibrillation, anticipated dialysis initiation within 6 months, LV ejection fraction (EF) <50% and poor-quality imaging on echocardiography. A total of 18 patients were excluded on the basis of these exclusion criteria; therefore, the final study population consisted of 134 hypertensive patients with stable CKD (73 males and 61 females; mean age, 50.8±11.5 years). Blood samples were obtained from all participants and laboratory tests were performed to determine the levels of hemoglobin, fasting glucose, total cholesterol, low-density lipoprotein cholesterol (LDL), triglyceride and B-type natriuretic peptide (BNP). eGFR was calculated by the Modification of Diet in Renal Disease equation (13). The final protocol was approved by the Human Ethics Committee of Wuxi People's Hospital Affiliated to Nanjing Medical University. Written informed consent was obtained from all subjects. All patients were treated with antihypertensive drugs and underwent two separate transthoracic echocardiographic exams at baseline and after 6 months of therapy.

Echocardiographic evaluation. Baseline and follow-up echocardiographic exams were performed using a Vivid 7 ultrasound system (GE Medical Systems, Milwaukee, WI, USA). Two-dimensional measurements were performed according to the American Society of Echocardiography recommenda-

tions (14) and included LV ejection fraction (LVEF) by the biplane method of discs, maximal left atrial (LA) volume by the method of discs and LV mass (LVM) calculated using the Devereux formula. Maximal LA volume and LVM were indexed to body surface area. Tissue Doppler imaging at the septal side of the mitral annulus was used to specify early diastolic (E') mitral annular velocity. Mitral inflow measurements included peak early (E) and peak late (A) velocities and the deceleration time (DT) of E (14). The E/A and E/E' ratios were subsequently calculated. Three cardiac cycles were measured and averaged for all Doppler measurements.

Grayscale images of apical views were obtained with frame rates >80 Hz for strain analysis by 2DSTE (Fig. 1). Recordings were processed with acoustic-tracking software (EchoPAC PC version 110.0.0, GE Healthcare) allowing off-line semi-automated speckle-based strain analyses. Longitudinal LV strain rates were measured by 2DSTE as previously reported (9,10). Peak systolic strain rate (SR_{SYS}), peak strain rate during isovolumetric relaxation period (SR_{IVR}) and early diastole (SR_E) were calculated by averaging the values of each of the 18 segments, which were derived from the 6 segments of each of the 3 apical views (2-chamber, 4-chamber, and apical long-axis views). The ratio of E and SR_{IVR} was calculated. All measurements of heart structure and performance were averaged over 3 cardiac cycles.

Intraobserver and interobserver variation. A total of 15 randomly selected subjects were independently assessed by two echocardiologists to identify variability between and within observers in the measurement of 2DSTE parameters.

Statistical analysis. Distribution of data was assessed using a one-sample Kolmogorov-Smirnov test. Data are reported as mean ± standard deviation (SD) for normally distributed continuous variables, median (quartile 1-quartile 3) for skew-distributed continuous variables, and frequencies for categorical variables. For numerical variables, an independent sample t-test and the Mann-Whitney U test were used for inter-group comparisons. A comparison of the clinical and echocardiographic variables before and after treatment was performed by paired sample t-test or Wilcoxon signed-rank test. Spearman's correlation analysis was used to assess the strength of the association between variables with non-normal distributions. Multivariate linear regression analyses (backward) were performed with significant variables in univariate analysis to determine the independence. Inter- and intra-observer agreements were assessed with intra- and inter-class correlation coefficients. For all tests, a P-value <0.05 was considered significant. All statistical analyses were performed using SPSS statistical software, version 15.0 (SPSS Inc., Chicago, IL, USA).

Results

Characteristics of the study population. A cohort of 134 non-dialyzed CKD patients was included (73 males and 61 females; mean age, 50.8±11.5 years). Of these participants, 36 patients (26.9%) had stage 1 CKD, 38 patients (28.4%) had stage 2 CKD, 44 patients (32.8%) had stage 4 CKD and 16 patients (11.9%) had stage 5 CKD. Subjects were categorized into two groups based on the CKD stage. These were group I

Table I. Baseline and follow-up demographic and clinical variables.

Characteristics	Total (n=134)		Group I (n=74)		Group II (n=60)	
	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up
Age (years)	50.8±11.5		48.8±11.6		52.9±11.2	
Male/female (n/n)	73/61		40/34		33/27	
BSA (m^2)	1.77±0.35	1.77±0.35	1.76±0.37	1.76±0.36	1.78±0.33	1.77±0.34
Systolic BP (mmHg)	154.6±7.6	124.0±7.3[a]	150.4±5.6	122.9±6.5[a]	159.8±6.4[b]	125.4±8.0[a,b]
Diastolic BP (mmHg)	92.6±10.2	74.6±10.4[a]	90.5±9.3	73.8±9.3[a]	94.9±10.7[b]	75.4±11.5[a]
Heart rate (bpm)	72.7±6.8	70.7±6.9	72.0±6.6	70.2±7.0	73.5±7.0	71.3±6.7
Total cholesterol (mmol/l)	4.7±1.2	4.4±0.8	4.4±1.0	4.3±0.8	4.6±1.0	4.4±0.9
LDL cholesterol (mmol/l)	2.3±0.7	2.2±0.6	2.3±0.6	2.2±0.7	2.4±0.7	2.2±0.6
Hemoglobin (g/l)	116.7±23.9	117.7±22.5	120.0±21.5	118.2±21.9	113.0±25.9	117.1±23.3
Glucose (mmol/l)	6.4±1.4	6.7±1.7	6.4±1.5	6.3±1.4	6.7±1.7	6.5±1.8
eGFR (ml/min/1.73 m^2)	61.8±24.3	65.9±24.1	81.2±10.8	84.7±11.7	37.9±11.8[b]	42.7±11.4[a,b]
BNP (pg/ml)	205 (179,265)	172 (155,200)[a]	179 (172,190)	158 (148,165)[a]	272 (242,287)[b]	202 (195,212)[a,b]
Smoking history, n (%)	25 (18.7)		15 (20.2)		10 (16.7)	
Diabetes mellitus, n (%)	50 (37.3)		27 (36.5)		23 (38.3)	
Dyslipidemia, n (%)	56 (41.8)		30 (40.5)		26 (43.3)	
ARBs or ACEIs, n (%)	61 (45.5)		38 (51.4)		28 (38.3)	
β-blockers, n (%)	58 (43.3)		27 (36.5)		31 (51.7)	
CCBs, n (%)	95 (70.9)		48 (64.8)		47 (73.4)	
Diuretics, n (%)	49 (74.6)		51 (68.9)		49 (81.7)	

BSA, body surface area; BP, blood pressure; bpm, beats per minute; LDL, low-density-lipoprotein; eGFR, estimated glomerular filtration rate; BNP, B-type natriuretic peptide; ACEIs, angiotensin converting enzymes inhibitors; ARBs, angiotensin receptor blockers; CCBs, calcium channel blockers. [a]$P<0.05$ compared with baseline; [b]$P<0.05$ compared with group I. Data are presented as mean ± standard deviation for normally distributed continuous variables, median (quartile 1-quartile 3) for skew-distributed continuous variables and frequencies for categorical variables.
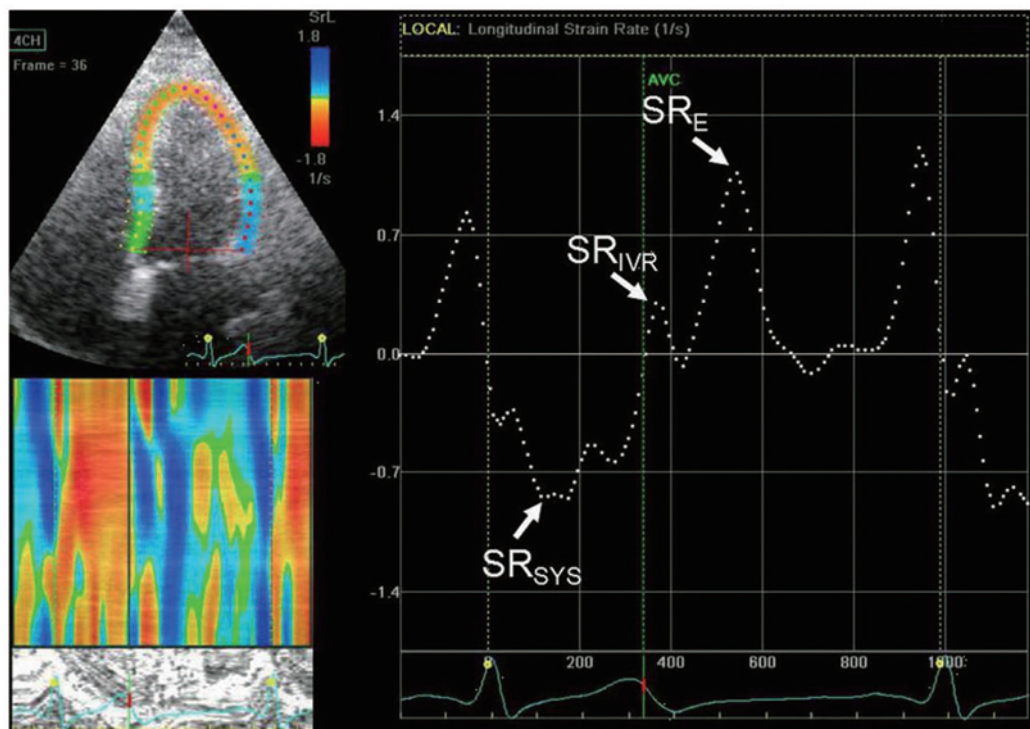

Figure 1. Longitudinal global strain rate of the left ventricle. AVC, aortic valve closure; SR_{SYS}, LV peak systolic strain rate; SR_{IVR}, LV peak strain rate during the isovolumetric relaxation period; SR_E, LV peak strain rate during early diastole.

Table II. Baseline and follow-up echocardiographic parameters in the study population.

Parameters	Total (n=134)		Group I (n=74)		Group II (n=60)	
	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up
LA volume index (ml/m^2)	36.2±5.9	33.1±5.9[a]	35.7±5.7	32.8±5.9[a]	36.8±6.0	33.5±5.8[a]
LV end-diastolic dimension (mm)	49.6±2.8	49.2±2.7	48.9±2.7	48.5±2.9	50.6±2.8	50.0±2.6
LV MI (g/m^2)	95.1±26.7	93.0±25.7	87.3±19.0	86.7±18.7	104.7±31.6	100.7±30.7
LV ejection fraction (%)	68.0±8.9	68.7±11.4	68.5±7.5	69.4±10.0	67.2±10.3	67.8±12.9
Mitral deceleration time (msec)	208.1±50.0	212.5±45.4	210.5±46.7	214.8±42.3	205.2±53.8	209.6±49.2
E velocity (m/sec)	73.4±28.4	71.0±22.5	72.9±33.1	70.1±12.4	74.1±21.4	72.2±31.7
A velocity (m/sec)	62.5±23.9	59.2±29.7	60.8±34.2	59.9±26.2	64.7±30.6	60.9±33.7
E/A	1.2±0.2	1.3±0.3	1.2±0.2	1.3±0.3	1.2±0.3	1.3±0.3
E' velocity (m/sec)	8.4±3.3	9.9±3.1[a]	8.7±3.8	10.0±2.0[a]	8.0±2.4	9.9±4.0[a]
E/E'	9.0±1.8	8.2±1.2[a]	8.5±1.5	8.1±0.9	9.5±2.0[b]	8.2±1.5[a]
SR$_{SYS}$ (sec^{-1})	-0.80±0.06	-0.82±0.07	-0.81±0.06	-0.83±0.06	-0.80±0.06	-0.81±0.09
SR$_{IVR}$ (sec^{-1})	0.23±0.10	0.42±0.10[a]	0.30±0.07	0.43±0.08[a]	0.13±0.03[b]	0.41±0.11[a]
SR$_E$ (sec^{-1})	0.58±0.25	1.07±0.24[a]	0.76±0.17	1.08±0.20[a]	0.34±0.13[b]	1.04±0.27[a]
E/SR$_{IVR}$(m)	3.8±1.8	1.7±0.4[a]	2.3±0.7	1.7±0.2[a]	5.6±1.0[b]	1.8±0.5[a]

LA, left atrial; LV, left ventricular; MI, mass index; E, mitral early diastolic velocity; A, mitral late diastolic velocity; E', early diastolic mitral annular velocity; SR$_{SYS}$, average of peak LV systolic strain rate; SR$_{IVR}$, average of peak LV strain rate during isovolumetric relaxation; SR$_E$, average of peak LV strain rate during early diastole. [a]$P<0.05$ compared with baseline; [b]$P<0.05$ compared with group I. Data are presented as mean ± standard deviation.

Table III. Comparison of changes in diastolic parameters and plasma BNP levels between the two groups.

Parameters	Group I (n=74)	Group II (n=60)	P-value
ΔLA volume index (ml/m^2)	-2.7 (-3.0, -2.6)	-3.2 (-3.7, -2.6)	0.17
Deceleration time (msec)	-8.0 (-41.2, 27.2)	-6.0 (-34.8, 19.5)	0.61
ΔE/A	0.04 (-0.13, 0.17)	-0.01 (-0.14, 0.17)	0.81
ΔE/E'	-0.01 (-0.78, 0.16)	-1.40 (-1.83, -0.50)	<0.01
ΔSR$_{IVR}$ (sec^{-1})	0.15 (0.10, 0.19)	0.31 (0.27, 0.34)	<0.01
ΔSR$_E$ (sec^{-1})	0.35 (0.25, 0.47)	0.75 (0.69, 0.84)	<0.01
ΔE/SR$_{IVR}$ (m)	-0.08 (-0.10, -0.04)	-0.39 (-0.45, -0.35)	<0.01
ΔBNP(pg/ml)	-21 (-28, -17)	-71 (-78, -48)	<0.01

LA, left atrial; E, mitral early diastolic velocity; A, mitral late diastolic velocity; E', early diastolic mitral annular velocity; SR$_{IVR}$, average of peak LV strain rate during isovolumetric relaxation; SR$_E$, average of peak LV strain rate during early diastole; BNP, B-type natriuretic peptide. Data are reported as median (quartile 1-quartile 3).

(CKD stage 1 or 2; n=74) and group II (CKD stage ≥3; n=60). Table I presents a detailed list of demographic and clinical variables at baseline and follow-up. Following antihypertensive treatment, 69 patients achieved their target BP in group I (93.2%), and 53 patients in group II (88.3%). Notably, participants in group II at study entry were older, had higher systolic BP (SBP) and diastolic BP (DBP), as well as higher BNP levels; however, SBP, DBP and the level of BNP declined from baseline to follow-up in the two groups.

Baseline and follow-up echocardiographic results. Table II lists comprehensive list of echocardiographic measurements

at baseline and follow-up. LVEF and SR$_{SYS}$ at baseline and follow-up were similar across the two groups. Compared with group I, higher E/E' and E/SR$_{IVR}$ ratios, and lower SR$_{IVR}$ and SR$_E$ indicated more severe baseline diastolic dysfunction in group II. Over the study period, the E/E' ratio was similar between baseline and follow-up in group I, but was decreased at follow-up in group II; however, there were no significant differences in E velocity, A velocity, E/A ratio or DT. Although SR$_{IVR}$ and SR$_E$ improved from baseline to follow-up in both groups, the ratio of E/SR$_{IVR}$ decreased. As shown in Table III, the patients in group II were more likely to demonstrate improvements in diastolic speckle-tracking parameters

Table IV. Clinical predictors for the difference of SR_{IVR} between the baseline and follow-up using univariate and multivariate linear regression analyses.

Variables	Univariate			Multivariate		
	B	95% CI	P-value	B	95%CI	P-value
Age	0.23	0.09, 0.37	<0.01			
Baseline CKD stage	8.78	7.78, 9.78	<0.01	4.11	1.79, 6.44	<0.01
ΔeGFR	0.17	-0.02, 0.35	0.04			
Baseline systolic BP	0.71	0.54, 0.89	<0.01	0.15	0.02, 0.28	0.02
ΔSystolic BP	0.69	0.56, 0.82	<0.01	0.20	0.08, 0.33	<0.01
Baseline diastolic BP	0.16	-0.02, 0.33	0.03			
ΔDiastolic BP	2.04	1,35, 2.73	<0.01			
Baseline LVMI	0.09	0.02, 0.15	<0.01			
Baseline SR_{IVR}	-0.75	-0.86, -0.64	<0.01	-0.26	-0.44, -0.08	<0.01

CI, confidence interval; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; BP, blood pressure; LVMI, left ventricular mass index; SR_{IVR}, average of peak LV strain rate during isovolumetric relaxation.

following treatment compared with those in group I. Plasma levels of BNP, as a biomarker of diastolic function, decreased throughout the study; however, the reduction was greater in group II. Therefore, these analyses indicate an association between the plasma BNP levels and echocardiographic parameters.

Association between BNP levels and echocardiographic parameters. In groups I and II, the BNP level was correlated with SR_{IVR} (r=-0.77, P<0.01), E/SR_{IVR} (r=0.69, P<0.01), SR_E (r=-0.68, P<0.01), E/E' (r=0.53, P<0.01) and LA volume index (LAVI) (r=0.47, P<0.01) at baseline. The differences (Δ) of clinical and echocardiographic parameters prior to and following treatment were determined by subtracting the values at follow-up from the values at baseline. There were significant correlations between ΔBNP and $ΔSR_{IVR}$ (r=-0.73, P<0.01), $ΔE/SR_{IVR}$ (r=0.64, P<0.01), $ΔSR_E$ (r=-0.66, P<0.01), ΔE/E' (r=0.57, P<0.01) and ΔLAVI (r=0.51, P<0.01). Among these parameters, SR_{IVR} and $ΔSR_{IVR}$ presented the highest correlation coefficient.

Predictors of $ΔSR_{IVR}$. To control for potential confounding variables in the data, univariate and multivariate linear regression analyses of $ΔSR_{IVR}$ were used to evaluate potential predictive factors for change of diastolic function. In univariate analyses, it was found that age, baseline CKD stage, SBP, DBP, LVMI, ΔSBP and ΔDBP each were significantly associated with $ΔSR_{IVR}$ (Table IV). On multivariable analysis, baseline CKD stage, SBP and ΔSBP were positively associated with $ΔSR_{IVR}$ (P<0.01), and baseline SR_{IVR} was inversely associated with $ΔSR_{IVR}$ (P<0.01).

Reproducibility. The interobserver correlation coefficients [95% confidence interval (CI)] were good for SR_{IVR} [0.93 (0.93-0.99)] and SR_E [0.97 (0.91-0.99)]. The intraobserver correlation coefficients (95% CI) were also good for SR_{IVR} [0.98 (0.95-0.99)] and SR_E [0.96 (0.89-0.98)].

Discussion

To the best of our knowledge, this is the first study to demonstrate that LV diastolic function improves with antihypertensive treatment in patients with CKD using 2DSTE. Notably, antihypertensive treatment was particularly efficacious among patients with CKD stage ≥3.

E/E' has been shown to be useful in predicting elevated LV filling pressures in clinical studies; however, E/E' has a significant gray zone and is less reliable in preserving LVEF >50% due to several factors (9,15). Firstly, there are well-known limitations of Doppler-based methods such as the angle dependency, which has the potential for significant errors with angulations >20°. Secondly, regional wall motion abnormalities in the sampling region may lead to low annular velocities on tissue Doppler despite near normal LV relaxation. Thirdly, another important limitation of this approach is the potential effect of LA pressure (9,15,16). Since E' occurs during the early phase of LV filling, not only LV relaxation, but also LA pressure has an important impact on its value. Furthermore, Andersen *et al* found there was not a strong correlation between changes in E/E' and changes in LV filling pressure (17). Conversely, the global LV diastolic SR collected using 2DSTE may overcome all the aforementioned limitations and provide a more complete reflection of overall LV diastolic function than E/E' (9,10,15-17). Notably, this measurement reflects the total performance of all LV segments. Therefore, in the present study, the E/E' ratio was similar between baseline and follow-up in group I, However, significant changes in LV diastolic performance over the study period were revealed following 2DSTE evaluation in these patients.

The BNP assessment used in this study has been validated as a highly sensitive and accurate method for the detection of LV diastolic dysfunction and applied in patients with CKD (18,19). In previous studies concerning HP or CKD, patients with an improvement in LV diastolic function exhibited a reduction in BNP plasma concentration after

treatment (19-21). The present study found significant changes in BNP concentrations and echocardiographic parameters in patients with CKD following antihypertensive treatment, suggesting an improvement of LV diastolic function. Among these echocardiographic parameters, ΔSR_{IVR} presented the highest correlation with ΔBNP, suggesting that SR_{IVR} might have better diagnostic value than traditional echo indices in detecting changes in LV diastolic function. SR_{IVR} is obtained directly from the ventricular myocardium during the isovolumetric relaxation period (when the mitral valve is closed), meaning that problems related to valvular pathology and LA pressure, which undermine other echocardiographic parameters, are circumvented (9,22).

Patients with CKD have a much greater cardiovascular risk than the general population. Moreover, HP is common in these patients and an important independent risk factor of LV diastolic dysfunction (2,4,8). Previous literature suggests that the mechanism underlying the impairment of LV diastolic function in patients with CKD and HP may be due to increased transmyocardial wall stress, which can produce subendocardial ischemia, thus increasing myocardial stiffness and reducing myocardial deformation in diastole. As BP decreases following medical treatment, LV wall stress also decreases, thus decreasing LV stiffness and improving myocardial diastolic function (8,15). Antihypertensive agents reduce endothelial dysfunction and microvascular disease, which has been shown to contribute to a worsening of cardiovascular risk factors and may also play a role in the pathophysiological process that leads to accelerated cardiovascular disease in patients with CKD (8). This effect may result in greater benefit than that achieved by BP-lowering alone. Studies have reported the benefits of antihypertensive treatment on cardiovascular and renal outcomes in CKD patients, and absolute risk reductions in people with CKD stage ≥3 have been found to be greater than those in people with CKD of stages 1 and 2 (4,8). The present study found significantly improved LV diastolic function in patients with CKD following 6 months of antihypertensive treatment. Notably, the patients with CKD stage ≥3 were more likely to demonstrate improvements in diastolic parameters than the others. On multivariate analysis, baseline CKD stage and BP were positively associated with ΔSR_{IVR} (P<0.01), and baseline SR_{IVR} was inversely associated with ΔSR_{IVR}. These results suggest the importance of BP reduction in this population, particularly with CKD stage ≥3, higher BP and LV diastolic dysfunction.

Several limitations of this study should be considered. The sample was small (134 patients), but the careful selection and recruitment of newly diagnosed and untreated hypertensive individuals is a major challenge in this field. Further confounding the recruitment efforts, patients with severe renal dysfunction and LV systolic dysfunction were excluded from this study. Consequently, the relatively small number of total subjects that was analyzed lessened the power and interpretation of the findings. The patients were not followed for clinical outcomes (such as readmission for clinical events, mortality or stroke), which meant that it was not possible to assess permit associations between the speckle-tracking parameters and outcomes. Furthermore, albuminuria was only assessed at some of the visits during the course of the trial, making it impossible to assess the changes in albuminuria and its

interaction with echocardiographic parameters (9). Although the results achieved statistical significance, further follow-up investigation and confirmation in a larger sample are required to validate the findings.

Overall, in the present sample of individuals with CKD, a significant improvement in LV diastolic function was obtained following antihypertensive therapy, which was demonstrated to be more effective in patients with CKD stage ≥3, higher baseline SBP and worse LV diastolic function.

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