Original Article

Difference of Clinical Characteristics between Hypertensive Patients with and without Diastolic Heart Failure: The Roles of Diastolic Dysfunction and Renal Insufficiency

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Clinical characteristics were compared between hypertensive patients with and without heart failure in the absence of reduced ejection fraction (EF) to gain insights into the effects of renal insufficiency on the prevalence of diastolic heart failure. Study subjects consisted of 691 hypertensive patients with an EF>40%. Patients with serum creatinine >2.5 mg/dL were excluded from the study. The Framingham heart failure criteria were met by 198 patients, and competing risks of the prevalence of heart failure were analyzed. The multiple logistic regression analysis revealed that obesity, female gender, creatinine clearance (CCr), and a ratio of transmitral *E* velocity to early diastolic mitral annular velocity (*E*/*E′*)>15 were independently associated with the prevalence of heart failure with preserved EF. Patients with 60≤CCr<90 mL/min represented higher *E*/*E′* ratio and lower *E′* velocity than the patients with CCr≥90 mL/min, although there was no difference in the prevalence of heart failure between the two groups. These indices were not different between the patients with 60≤CCr<90 mL/min and CCr<60 mL/min, although the prevalence of heart failure was higher in the patients with CCr<60 mL/min. The hemoglobin concentration was significantly decreased and the brachial-ankle pulse wave velocity was significantly elevated in patients with CCr<60 mL/min. Thus, progressive left ventricular diastolic dysfunction and renal insufficiency are competing risks of the prevalence of diastolic heart failure in hypertensive patients. Renal insufficiency may exert its effects through the modulation of extracardiac factors such as anemia and arterial stiffening rather than through the promotion of diastolic dysfunction. (*Hypertens Res* 2008; 31: 1865–1872)

***Key Words*: diastolic heart failure, hypertension, renal insufficiency**

Introduction

A large proportion of patients with symptoms of heart failure have a normal or minimally impaired left ventricular (LV) ejection fraction (EF). This syndrome is termed diastolic heart failure (DHF) and is frequently accompanied by hypertension (*1*, *2*). Its incidence has been increasing, and its poor prognosis has not improved during the past two decades (*3*); however, in spite of its clinical burden, the pathophysiology of this disorder is poorly understood.

The close association of renal insufficiency with cardiovas-

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Table 1. Baseline Characteristics of the Patients

	Total (n=691)	HT (n=493)	HTHF (n=198)
Age (years old)	64±13	63±13	67±12*
Female (%)	44	37	61*
Systolic blood pressure (mmHg)	140±22	141±21	139±23
Diastolic blood pressure (mmHg)	74±13	75±12	72±14*
Atrial fibrillation (%)	4	4	5
Body mass index (kg/m^2)	24.2±3.7	23.7±3.3	25.4±4.3*
Coronary artery disease (%)	16	17	16
Diabetes mellitus (%)	34	34	34
Dyslipidemia (%)	51	50	53
CCr (mL/min)	76±36	77±35	72±37
Hemoglobin (g/dL)	13.4±1.8	13.5±1.8	13.0±1.8*
Patients with angiotensin converting enzyme inhibitors (%)	22	20	24
Patients with angiotensin receptor blockers (%)	48	48	48
Patients with β-blockers (%)	29	27	32
Patients with calcium-channel blockers (%)	53	52	60
Patients with statins (%)	32	32	35

Values are expressed as mean±SD. *$p<0.05$ *vs*. HT. HT, hypertensive patients with preserved ejection fraction without heart failure; HTHF, hypertensive patients with diastolic heart failure; CCr, creatinine clearance.

cular diseases has been called cardio-renal syndrome. Hillege *et al*. demonstrated the impact of renal insufficiency on DHF by showing that renal function is an independent predictor of outcomes after the onset of DHF (*4*). Renal impairment is also a powerful predictor of cardiovascular events including hospitalization for heart failure in hypertensive patients (*5*–*7*). However, the onset of heart failure in patients with kidney diseases is principally attributed to LV systolic dysfunction induced by myocardial infarction or long-term hypertension (*8*), and the effects of renal insufficiency on the prevalence of symptomatic heart failure stage without reduced EF remain unclear.

The present study aimed to identify competing risks of the prevalence of DHF in hypertensive patients with preserved EF. As renal insufficiency was identified as one of the competing risks, we also assessed whether the relation between renal insufficiency and the prevalence of DHF was provided through the associated alterations in cardiac structure or function.

Methods

Patients

This retrospective study was approved by the Osaka University Hospital Ethical Committee. Study subjects consisted of 691 hypertensive patients who met the following entry criteria: 1) echocardiographic confirmation of EF>40% (*9*, *10*) between January 2005 and July 2007, 2) no significant valve or lung diseases, 3) available blood sampling data within 3 months before or after echocardiography, 4) serum creatinine ≤2.5 mg/dL, and 5) patients were clinically stable without any changes in symptoms and prescribed medicines for more than 6 months. Medical records were reviewed by cardiologists to assess patient characteristics. In addition, all of the patients were interviewed about their heart failure symptoms based on their Specific Activity Scale questionnaire score at echocardiographic examinations (*11*) and about their histories of previous hospitalization, hypertension, and diabetes mellitus. All of the patients with previous hospitalization were excluded because the reasons for the hospitalization were uncertain in some patients who had been admitted to other hospitals. Following previous clinical studies (*12*, *13*), we defined hypertension as systolic (>140 mmHg) or diastolic (>90 mmHg) blood pressure based on blood pressure recording at the outpatient clinic and ambulatory blood pressure recording, a reported history of hypertension, or use of antihypertensive medications. Heart failure was diagnosed according to the modified Framingham criteria (*11*), and the 691 hypertensive patients with preserved EF were divided into groups without (HT, n=493) and with heart failure (HTHF, n=198). For each participant, cuff blood pressure, height, and weight were measured at echocardiography, and body mass index (BMI) was calculated. Creatinine clearance (CCr) was estimated using the following equation:

$$\begin{aligned}\text{CCr [mL/min]} = {} & (140 - \text{age}) \times \text{body weight [kg]}/ \\ & (72 \times \text{creatinine [mg/dL]}) \\ & \times 0.85 \text{ (if female)}.\end{aligned}$$

Echocardiography

Doppler echocardiography was conducted using commercially available echocardiographic machines as previously described (*14*). Transthoracic two-dimensional Doppler

Table 2. Doppler Echocardiographic Parameters of the Patients

	Total (n=691)	HT (n=493)	HTHF (n=198)
LV end-diastolic dimension (mm)	47±6	48±6	47±6
Posterior wall thickness at end-diastole (mm)	9.1±1.9	9.1±1.9	9.2±1.8
Left atrial dimension (mm)	40±7	40±7	42±6*
LV mass (g)	159±52	159±50	159±57
LV mass/hight$^{2.7}$ (g/m$^{2.7}$)	44±14	43±12	47±16*
Relative wall thickness	0.39±0.10	0.39±0.10	0.40±0.10
Fractional shortening (%)	37±7	37±7	37±8
Ejection fraction (%)	66±9	66±9	67±9
E velocity (cm/s)	70±18	69±19	71±16
A velocity (cm/s)	77±20	75±20	81±22*
E/A ratio	0.96±0.42	0.98±0.44	0.93±0.36
E' velocity (cm/s)	5.8±1.9	6.0±1.9	5.5±1.8*
E/E' ratio	12.8±4.3	12.3±4.3	13.7±4.4*

Values are expressed as mean±SD. *$p<0.05$ *vs*. HT. LV, left ventricular; HT, hypertensive patients with preserved ejection fraction without heart failure; HTHF, hypertensive patients with diastolic heart failure.

echocardiography was recorded with the subjects in the left lateral position and during quiet respiration. In our routine echocardiographic examination, measurements were conducted on-line, and echocardiographic data were observed by a trained sonographer and one or two cardiologists. EF was calculated using a modification of the method of Quinones *et al*. (*15*) as described previously (*14*). In patients with regional wall motion abnormality, the biplane Simpsons' method was used (*16*). LV mass and relative wall thickness were calculated following the formula derived from the data of the American Society of Echocardiography (*16*) as previously described (*14*). LV mass index was calculated as a ratio of LV mass to height$^{2.7}$. In patients with a sinus rhythm, the pulsed Doppler transmitral flow velocity curve was recorded with the sample volume at the mitral tips to measure peak early (E) and late (A) flow velocities. The tissue Doppler imaging of the mitral annulus movement was recorded at septal position to measure peak early diastolic velocity (E') as previously described (*17*, *18*). The ratio of E to E' (E/E') was calculated as a parameter of LV filling pressure and diastolic function (*19*, *20*). The mean±SD of interobserver variability of recordings of Doppler echocardiographic data (n=10) was 1.8±1.4 mm for LV end-diastolic dimension, 1.0±0.7 mm for LV end-systolic dimension, 0.7±0.6 mm for posterior wall thickness at end-diastole, 0.7±0.5 mm for interventricular septal thickness at end-diastole, 1.2±0.8 mm for left atrial dimension, 6.0±4.6 cm/s for E, 3.7±2.0 cm/s for A and 0.6±0.5 cm/s for E'.

Statistical Analysis

Statistics were performed using STATVIEW 5.0 software (SAS Institute Inc., Cary, USA). All data are summarized as mean±SD. Categorical variables were compared by use of χ^2 tests. Continuous variables were compared between groups through analysis of variance with a Bonferroni correction for multiple unadjusted and adjusted comparisons. A logistic regression analysis was used with adjustments for age, gender, BMI, and the presence of other diseases to identify competing risks of the prevalence of DHF. In this study, we used the E/E' ratio as an indirect index of LV filling pressure, which is elevated secondarily to LV diastolic dysfunction. Although the E/E' ratio is a continuous value, its relationship with the LV filling pressure is only modest, and the precise characterization of LV filling pressure in an individual patient cannot be determined using this index (*21*). Thus, the E/E' ratio was utilized as a dichotomized rather than continuous covariable. The diagnostic criteria for dyslipidemia and diabetes mellitus included reported history or medication use, and these factors could not be analyzed in a continuous way. Correlations of the two indices were assessed using linear regression analysis with the least-squares method. A value of $p<0.05$ was considered statistically significant for all analyses.

Results

Baseline Characteristics

The characteristics of the study subjects are presented in Tables 1 and 2. The patients in the HTHF group were older, more often female, and more obese than those in the HT group, and their heart failure stage was New York Heart Association functional class II: 33%, class III: 67%, and class IV: 0%. Hemoglobin was lower in the HFHT patients than in the HT patients. There was no difference in systolic blood pressure, medication use, or the prevalence of coronary artery disease, diabetes mellitus, and dyslipidemia between the two groups. CCr tended to be low, although not significantly so, in the HFHT patients compared to the HT patients (p=0.07).

Table 3. Multivariate Analysis of Determinants of DHF

	Relative risk (95% CI of the estimates)	*p* value
Age	1.00 (0.97–1.02)	n.s.
Female	3.03 (1.81–5.06)	<0.0001
Body mass index	1.26 (1.16–1.37)	<0.0001
Coronary artery disease	1.46 (0.76–2.80)	n.s.
Diabetes mellitus	0.81 (0.49–1.34)	n.s.
Dyslipidemia	0.65 (0.40–1.05)	n.s.
LV end-diastolic dimension	0.98 (0.93–1.02)	n.s.
Posterior wall thickness at end-diastole	0.96 (0.84–1.10)	n.s.
E/E' ratio>15	1.79 (1.05–3.06)	0.033
CCr	0.99 (0.98–1.00)	0.026

DHF, diastolic heart failure; CI, confidence interval; LV, left ventricular; CCr, creatinine clearance.

There was no difference in LV end-diastolic dimension, EF, LV mass, relative wall thickness, or E/A ratio between the two groups. LV mass index, left atrial dimension, and E/E' ratio were higher, and the E' velocity was lower in the HTHF than in the HT patients.

Competing Risks of the Prevalence of DHF

Multivariate logistic regression analysis was conducted to determine competing risks of the prevalence of DHF among the following factors: age, gender, BMI, history of coronary artery disease, diabetes mellitus, or dyslipidemia, LV end-diastolic dimension, posterior wall thickness at end-diastole, elevated LV filling pressure secondary to diastolic dysfunction (E/E' ratio>15 (*21*)), and renal function (CCr) (Table 3). The analyses showed that female gender, higher BMI, higher E/E' ratio, and renal insufficiency were independently associated with the prevalence of DHF in hypertensive patients without reduced EF.

The Relationship between Renal Insufficiency and the Prevalence of DHF

To investigate the relationship between renal insufficiency and the prevalence of DHF in hypertensive patients, 691 patients were divided into three groups according to CCr (CCr≥90 mL/min, 60≤CCr<90 mL/min and CCr<60 mL/min).

The LV end-diastolic dimension, E' velocity, and E/A ratio were significantly lower, and the E/E' ratio was significantly higher in patients with 60≤CCr<90 mL/min than in patients with CCr≥90 mL/min after adjusting for age, gender, BMI, and systolic blood pressure. There was no difference in LV posterior wall thickness or relative wall thickness, and the prevalence of heart failure was similar between the two groups.

Patients with CCr<60 mL/min had a greater chance of being female and had a higher prevalence of heart failure. BMI progressively decreased and age increased with the reduction of CCr. After adjusting for age, gender, BMI, and systolic blood pressure, the exacerbation of renal dysfunction and the increase in the prevalence of DHF were associated with the reduction of hemoglobin, but not with changes in LV end-diastolic dimension, E/E' ratio, E' velocity, or E/A ratio compared to patients with 60≤CCr<90 mL/min. In a very small number of patients (CCr≥90 mL/min; $n=16$, 60≤CCr<90 mL/min; $n=17$, CCr<60 mL/min; $n=9$), the brachial-ankle pulse wave velocity (baPWV) was measured using a non-invasive automatic waveform analyzer (model BP-203RPE II; Omron Healthcare Co. Ltd., Kyoto, Japan) as previously described (*22*, *23*) to assess the relation between arterial stiffening and renal insufficiency. The baPWV was increased with the reduction of CCr (CCr≥90 mL/min; 1,532±233 cm/s, 60≤CCr<90 mL/min; 1,755±381 cm/s, CCr<60 mL/min; 1,852±473 cm/s), and a statistical difference was observed between the patients with CCr<60 mL/min and CCr≥90 mL/min ($p=0.032$).

There was no significant difference in serum sodium, potassium, and C-reactive protein among the groups.

Discussion

The current study analyzed the competing risks of the prevalence of symptomatic heart failure stage, *i.e.*, DHF, in hypertensive patients with preserved EF. The DHF patients were older; more often female; more obese; and presented with lower hemoglobin level and E' velocity and greater left atrial dimension, LV mass index, and E/E' ratio than the hypertensive patients without heart failure. CCr tended to be low, although not significantly so, in the DHF patients. After adjusting for age, gender, and BMI, all of which are well known as clinically characteristic factors of DHF (*1*, *2*, *24*), the reduction of CCr and the increase in E/E' ratio were independently associated with the prevalence of DHF (Table 3). The patients with CCr<60 mL/min showed higher prevalence of DHF than those with 60≤CCr<90 mL/min, but there was no difference in LV structural or functional indices between the groups (Table 4). In patients with CCr<60 mL/

Table 4. Relationship between CCr and Biological or Echocardiographic Data

	CCr≥90 mL/min (n=174)	60≤CCr<90 mL/min (n=278)	CCr<60 mL/min (n=239)	p value[§]
Prevalence of heart failure (%)	24	25	36	0.008
Age (years old)	52±12	65±10*	72±8*,†	
Female (%)	36	44	49	0.020
Systolic blood pressure (mmHg)	137±19	142±23	140±21	
Body mass index (kg/m^2)	26.1±4.3	24.1±3.3*	23.0±3.1*,†	
Coronary artery disease (%)	14	16	19	n.s.
Diabetes mellitus (%)	40	35	30	n.s.
Dyslipidemia (%)	54	51	49	n.s.
CCr (mL/min)	122±36	74±8*	44±10*,†	
Serum sodium (mEq/L)	140±2	141±2	141±3	
Serum potassium (mEq/L)	4.2±0.3	4.2±0.3	4.3±0.4	
Serum C-reactive protein (mg/dL)	0.1±0.1	0.1±0.2	0.1±0.4	
Hemoglobin (g/dL)[#]	14.1±1.8	13.5±1.5*	12.6±1.8*,†	
LV end-diastolic dimension (mm)[#]	50±5	46±5*	46±6*	
Posterior wall thickness at end-diastole (mm)[#]	9.2±1.9	8.9±1.7	9.2±1.9	
Left atrial dimension (mm)[#]	41±6	39±6*	40±7	
LV mass/hight$^{2.7}$ (g/m$^{2.7}$)[#]	45±16	42±11*	45±13†	
Relative wall thickness[#]	0.38±0.09	0.39±0.09	0.41±0.12*	
Ejection fraction (%)[#]	65±10	68±8*	67±9	
E/A ratio[#]	1.1±0.4	0.9±0.3*	0.9±0.4*	
E' velocity (cm/s)[#]	6.8±2.1	5.9±1.8*	5.5±1.6*	
E/E' ratio[#]	11.0±3.5	12.6±4.2*	13.6±4.3*	

Values are expressed as mean±SD. *p<0.05 *vs*. CCr≥90 mL/min, †p<0.05 *vs*. 60≤CCr<90 mL/min. §p value was shown in the right column only for the relative frequencies. #Echocardiographic data are adjusted by age, gender, body mass index and systolic blood pressure. CCr, creatinine clearance; LV, left ventricular.

min, hemoglobin was decreased, and the baPWV was elevated.

LV Diastolic Dysfunction and DHF

This study showed that the increase in E/E' ratio, an index of LV filling pressure and stiffness regardless of LV systolic function (*19*, *20*), was independently related to the prevalence of DHF in hypertensive patients with preserved EF (Table 3). In addition, the E' velocity, an index of LV relaxation (*25*), was lower in the DHF patients than in the hypertensive patients without heart failure (Table 2). These results suggest that promotion of diastolic dysfunction independently increases the prevalence of symptomatic heart failure in hypertensive patients with preserved EF. Our conclusion is partly in agreement with a previous study that showed that LV diastolic function was impaired in patients with clinical diagnosis of DHF compared to control subjects without cardiovascular disease (*26*). All subjects in this study had hypertension, and the LV mass index was greater in the DHF patients than in the hypertensive patients without heart failure (Table 2). Our animal experiments and a recent clinical study have demonstrated that progressive LV hypertrophy is associated with the development of LV fibrosis (*27*, *28*), and LV fibrosis plays a crucial role in the enhancement of LV stiffness and the transition from asymptomatic diastolic dysfunction to DHF (*27*, *29*, *30*). LV hypertrophy was not independently associated with the prevalence of DHF (Table 3), and the noninvasive assessment of LV fibrosis is currently difficult. However, previous and current results suggest that the progression of LV diastolic dysfunction is at least partly induced by pressure-overload–induced LV hypertrophy and fibrosis and results in the increased incidence of heart failure symptoms in hypertensive patients with preserved EF.

Renal Insufficiency and DHF

Renal insufficiency is a powerful predictor of high mortality and morbidity in patients with DHF as well as heart failure patients with reduced EF (*4*). The current study expanded the previous study by demonstrating that renal impairment is one of the competing risks of the prevalence of DHF in hypertensive patients without reduced EF. Renal insufficiency is highly associated with hypertension and coronary artery events, and the frequent hospitalization for heart failure of patients with kidney diseases has been explained by LV systolic dysfunction induced by chronic pressure overload or myocardial infarction. The subjects in this study included

only patients with preserved EF, and the value of EF and the prevalence of coronary artery disease were not different between patients with and without heart failure. Thus, renal insufficiency is likely associated with the prevalence of DHF independent of coronary artery events or LV systolic dysfunction in hypertensive patients.

This study showed that the E/E' ratio was higher and the E' velocity was lower in hypertensive patients with $60 \leq CCr < 90$ mL/min than in those with $CCr \geq 90$ mL/min. The smaller LV end-diastolic dimension in spite of the higher E/E' ratio in the patients with $60 \leq CCr < 90$ mL/min may indicate the less LV compliance. Thus, renal insufficiency even at the early stage may play a role in the induction of LV diastolic dysfunction. However, this may not be the principal reason for the close association between renal impairment and the prevalence of DHF because 1) the prevalence of DHF was not increased in the patients with $60 \leq CCr < 90$ mL/min compared to those with $CCr \geq 90$ mL/min (Table 4), and 2) the decrease in CCr below 60 mL/min was associated with the increased prevalence of DHF without the changes in E/E' ratio or E' velocity (Tables 3 and 4). Verma *et al*. recently suggested that diastolic dysfunction is an important mediator of increased risk associated with renal impairment in patients with myocardial infarction (*31*), which is partly incompatible with our conclusion. Their conclusion was drawn on the basis of data of LV mass index and left atrial volume, both of which are only indirect measures of LV diastolic function. In this study, we assessed tissue Doppler imaging for a more robust measure of LV diastolic function, and the difference in the measures of diastolic function may partly explain the discrepancy. In addition, the study subjects of the previous study were patients with myocardial infarction and most patients had reduced EF. This study enrolled only hypertensive patients with preserved EF, and the difference in the characteristics of the study subjects might also explain the discrepancy.

Hemoglobin levels were lower in the DHF patients than in the hypertensive patients without heart failure (Table 1), and the progression of renal insufficiency was associated with anemia (Table 4). Previous studies have also shown that serum creatinine and the prevalence of anemia were higher in DHF patients than in hypertensive patients without heart failure (*13*), and anemia exacerbated the prognosis of DHF patients (*32*, *33*). Thus, renal insufficiency may increase the prevalence of DHF partly through the induction of anemia in hypertensive patients without reduced EF. Maurer *et al*. concluded that anemia induced DHF through volume overload because LV end-diastolic dimension was greater in the DHF patients than in hypertensive patients without heart failure (*13*). However, the LV end-diastolic dimension was small in patients with renal insufficiency and low hemoglobin in this study (Table 4), and thus, anemia was unlikely to induce DHF through volume overload. Anemia leads to excessive myocardial work to compensate for reduced tissue oxygen delivery (*34*), and this may result in chronic exercise intolerance and dyspnea on exertion, both of which are symptoms of heart failure.

Anemia may be an important mediator of the increased prevalence of DHF with renal insufficiency; however, there may be other mediators. The baPWV correlates well with the invasively measured aortic pulse wave velocity (*35*), which is known as an indicator of arterial stiffness (*36*, *37*). In this study, the baPWV was increased with the decrease in CCr, although these data were available in only some of the study subjects; this result is compatible with the current hypotheses (*8*). Elevated arterial stiffness is associated with an impairment of exercise tolerance (*38*), and thus, a close relation between renal insufficiency and arterial stiffening may also explain the association of renal insufficiency with the prevalence of heart failure symptoms in hypertensive patients with preserved EF.

Aging, Obesity, and DHF

It is well known that the prevalence of DHF increases with age (*3*). The current study showed that mean age of the patient group with low CCr, high baPWV, and a high prevalence of DHF was significantly high (Table 4). Hees *et al*. showed declining LV filling reserve with aging (*39*), suggesting that aging is associated with LV stiffening. Although renal insufficiency was associated with the prevalence of DHF independently of aging (Table 3), our results still suggest that aging promotes renal dysfunction and vascular stiffening and increases the risk of DHF. Another risk factor for heart failure is obesity (*40*), and this study also showed that BMI was significantly higher in the patients with DHF than in the patients without DHF (Table 1). In contrast, the group with low CCr and a high prevalence of DHF had lower BMI in this study (Table 4). Recently, the association of low BMI with increased mortality in heart failure patients has been reported as reverse epidemiology (*41*, *42*). The mechanisms of reverse epidemiology remain controversial, and further studies are necessary to clarify the relationship between BMI and renal dysfunction and DHF

Study Limitation

There are several limitations to this study. First, this study is retrospective in nature. It is difficult to prove cause-and-effect between the competing risks and the incidence of DHF, and thus mechanistic interpretations based on the current study may be limited. Further prospective studies are necessary. In addition, this study is not community-based and enrolled only hypertensive patients referred for echocardiographic examination. Thus, the current study subjects might be more frequently symptomatic than community-based hypertensive patients, and the absolute value of the prevalence of each factor may not be representative of all patients with hypertension in Japan. Second, the baPWV was measured only in a part of the study subjects. However, the relationship between renal

function and baPWV was compatible with current hypotheses (*8*). Third, renal dysfunction may well increase the prevalence of heart failure through volume overload. However, we only assessed LV end-diastolic dimension, and could not get insight into the effects of renal dysfunction on volume load in this retrospective study. Fourth, one of the criteria of hypertension in this study is the use of antihypertensive medications as was done in previous studies (*12*, *13*), and thus, patients treated with antihypertensive medicines for reasons other than hypertension may be defined as hypertensive in this study. In addition, the data were collected without withholding medications. However, there was no association of any of the medications with the prevalence of DHF in this study, and the effects of the medications were adjusted in the multivariate logistic regression analysis. Thus, we believe that the effects of the definition of hypertension or the medications on the results of this study may be small, if any are present at all.

Conclusion

Progressive LV diastolic dysfunction and renal insufficiency are competing risks of the prevalence of DHF in hypertensive patients with preserved EF. Although renal insufficiency is partly related to diastolic dysfunction, its principal effects in the symptomatic heart failure stage are likely exerted through extracardiac factors, such as anemia and arterial stiffening, rather than through the promotion of diastolic dysfunction.

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