



# Clinical Usefulness of the HFA-PEFF Diagnostic Scoring System in Identifying Late Elderly Heart Failure With Preserved Ejection Fraction Patients

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**Background:** Diagnosis of heart failure with preserved ejection fraction (HFpEF) remains challenging in elderly. This study investigated the diagnostic ability of the HFA-PEFF scoring system in elderly patients (>75 years of age).

**Methods and Results:** This study enrolled 286 subjects aged >75 years (130 men; mean [ $\pm$ SD] age 81.5 $\pm$ 5.1 years): 95 healthy controls, 98 with hypertension (HT), and 93 with HFpEF. The HFA-PEFF score was calculated as a sum of points in functional, morphological, and biomarker domains. In the HFpEF group, 84%, 84%, and 70% of subjects met the major functional, morphological, and biomarker criteria for HFpEF, respectively. Thus, 73 subjects with HFpEF (78%) were diagnosed as having HFpEF using the HFA-PEFF scoring system. In contrast, among the healthy controls and subjects with HT, 52% and 72%, respectively, met the major functional criteria for HFpEF, 28% and 53%, respectively, met the morphological criteria, and 0% and 24%, respectively, met the biomarker criteria. As such, 32 subjects with HT (33%) were diagnosed with HFpEF. Even in the healthy control group, 72% were classified as having an intermediate probability of HFpEF, and 3 were diagnosed with HFpEF.

**Conclusions:** In the late elderly, the HFA-PEFF scoring system diagnosed subjects with HFpEF precisely. In addition, this scoring system may be able to detect early stage HFpEF in the subclinical population.

**Key Words:** Diastolic function; Echocardiography; Elderly; Heart failure with preserved ejection fraction (HFpEF); Natriuretic peptide

Japan, Italy, and Germany already have a super-aged society, and it is projected that there will be a global increase in the proportion of the aged population, primarily the late elderly (i.e., those aged  $\geq 75$  years).<sup>1,2</sup> In the elderly, heart failure (HF) with preserved ejection fraction (HFpEF) is the major phenotype of HF.<sup>3-5</sup> Therefore, reducing the incidence and slowing the progress of HFpEF, as well as preventing death from this disease, have become social issues. However, awareness of HFpEF is low, even among healthcare professionals.<sup>4</sup> Diagnosis of HFpEF in elderly patients with comorbidities and no obvious signs of central fluid overload is challenging, particularly in the late elderly. Left ventricular (LV) diastolic dysfunction is the main pathophysiology in HFpEF, but is not essential in HFpEF.<sup>5-10</sup> HFpEF is a clinical syndrome, and its heterogeneity may make diagnosis difficult.<sup>11</sup> Recently, the Heart Failure Association (HFA) of the European Society of Cardiology proposed a new algorithm, the HFA-PEFF score, to identify HFpEF based on a comprehensive diagnostic workup using the HFA-PEFF scoring system.<sup>12,13</sup> Because in the real world HFpEF is more common in the

late elderly, the value of the HFA-PEFF scoring system has to be validated in this population.

The Japanese eLderly data Of Normal echocardiography (J-LONG) study was designed to establish normal value for echocardiographic parameters in the late elderly (i.e., those aged >75 years) because of a lack of such values in this population.<sup>14</sup> In addition to healthy controls, the J-LONG study also enrolled patients with hypertension (HT) and those with HFpEF. The aim of the present study, using data from the J-LONG study, was to investigate the diagnostic ability of the HFA-PEFF scoring system in patients with HFpEF aged >75 years.

## Methods

### Study Population

Participants were enrolled in the J-Long study between April 2017 and March 2019. In all, 402 subjects aged >75 years were enrolled, including 130 healthy controls, 115 with HT, 93 with HFpEF, and 64 with aortic stenosis. HT was defined as an office blood pressure of at least 140 mmHg

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systolic or 90 mmHg diastolic, a home blood pressure of at least 135 mmHg systolic or 85 mmHg diastolic in untreated cases, or currently receiving antihypertensive medication. Subjects with HFpEF were defined as those with a history of hospitalization for HF, those currently undergoing HF treatment, and those with a left ventricular ejection fraction (LVEF) of  $\geq 50\%$  at the time of registration in whom there were no underlying diseases of HF, such as hypertrophic cardiomyopathy, amyloidosis, sarcoidosis, constrictive pericarditis, advanced mitral valve disease, advanced aortic valve disease, and pulmonary arterial and chronic thromboembolic pulmonary HT. After excluding subjects with aortic stenosis, participants with complete datasets to enable assessment of the HFA-PEFF score were screened for inclusion in this study. Finally, 286 subjects (130 men; mean  $[\pm SD]$  age  $81.5 \pm 5.1$  years, range 75–98 years) were enrolled in this study: 95 healthy controls, 98 with HT, and 93 with HFpEF. The main reason for exclusion from the study was the lack of B-type natriuretic peptide (BNP) data.

This study investigation conformed to the principles outlined in the Declaration of Helsinki. The study was approved by the Ethics Committee of the University of Tsukuba (Reference no. H28-119), as well as the local ethics committee of each participating institute. Informed consent was obtained from all subjects before they were included in the study.

### Echocardiographic Data

All images were reviewed offline by the headquarter using vendor-independent 2D Cardiac Performance Analysis software (TomTec Imaging System, Munich, Germany).

Comprehensive echocardiographic studies were performed according to established guidelines.<sup>15,16</sup> LV end-diastolic diameter (LVDd), interventricular septum thickness (IVSTd), posterior wall thickness (PWTd), and LV end-systolic diameter (LVDs) were measured in parasternal long-axis views. LV volumes and LVEF were measured by the disk summation method from the apical 4- and 2-chamber views. Relative wall thickness was calculated as  $(2 \times \text{PWTd} / \text{LVDd})$ . LV mass (LVM) was calculated using Devereux's formula. Maximum left atrial volume (LAV) was measured by the disk summation method from the apical 4- and 2-chamber views. LVM and LAV were corrected for body surface area (LVMI and LAVI, respectively). The tissue Doppler-derived early diastolic mitral annular velocity ( $e'$ ) was measured at septal and lateral wall sites in the apical 4-chamber view. The ratio of early diastolic mitral inflow velocity (E) to  $e'$  ( $E/e'$ ) was calculated as the mean of septal and lateral  $E/e'$ . Tricuspid regurgitation peak velocity (TRV) was derived from peak tricuspid regurgitation jet velocity.

Speckle tracking echocardiography (STE) was performed using the TomTec Imaging System. In an end-systolic frame, a region of interest was traced on the endocardial cavity interface using a point-and-click approach. The region of interest was automatically selected to approximate the myocardium between the endocardium and epicardium. The region of interest was adjusted further to ensure that all myocardial regions were included. Then, the software captured the myocardium, automatically tracking its motion and thickening in subsequent frames. Finally, the myocardium was divided into 6 segments in each plane. For assessment of LV global longitudinal strain (GLS), the mean of the longitudinal systolic negative peak values obtained from the 18 LV segments in the apical 4-, 3-, and

2-chamber views was calculated. Segments were discarded if tracking was of poor quality.

### Calculation of the HFA-PEFF Score

The HFA-PEFF score was calculated using the proposed algorithm,<sup>12</sup> which assigns 2 points for a major criterion and 1 point for a minor criterion within each functional, morphological, and biomarker domain (**Supplementary Figure**). A total score of 5 or 6 is considered to be diagnostic of HFpEF, whereas scores of 0 or 1 are considered to indicate that a diagnosis of HFpEF is very unlikely. Patients with scores in the range 2–4 are considered as being at intermediate probability of having HFpEF; specifically, HFpEF could not be diagnosed in these patients using the HFA-PEFF scoring system.

As a diagnostic control for HFpEF to examine the added value of a comprehensive evaluation using the HFA-PEFF score, the Doppler echocardiographic algorithm for the evaluation of LV diastolic function of the American Society of Echocardiography (ASE) and the European Association of Cardiovascular Imaging (EACVI) was used.<sup>16</sup>

### Statistical Analysis

Variables were compared between groups using 1-way analysis of variance (ANOVA) with a post hoc Tukey-Kramer test. Student's t-tests were used to compare continuous variables between 2 groups, whereas  $\chi^2$  tests were used to compare categorical variables between groups. Statistical analyses were performed using SPSS ver. 25 (SPSS Inc., Chicago, IL, USA).

## Results

### Clinical Characteristics

The clinical characteristics of the healthy control, HT, and HFpEF groups are summarized in **Table 1**. Age and sex distributions did not differ among groups. Systolic blood pressure was higher in the HT than HFpEF group, and diastolic blood pressure was lower in the HFpEF than other groups. Atrial fibrillation (AF) was observed in approximately one-quarter of subjects in the HFpEF group. Hemoglobin, albumin, and estimated glomerular filtration rate (eGFR) were lower in the HFpEF than other groups.

### Comparisons of Echocardiographic Parameters and BNP Concentrations

As indicated in **Table 2**, both LVDd and LVDs were larger in the HFpEF than other groups. In addition, IVSTd and PWTd were greater in the HFpEF than healthy control group. LVEF was lowest in the HFpEF than in the other 2 groups.

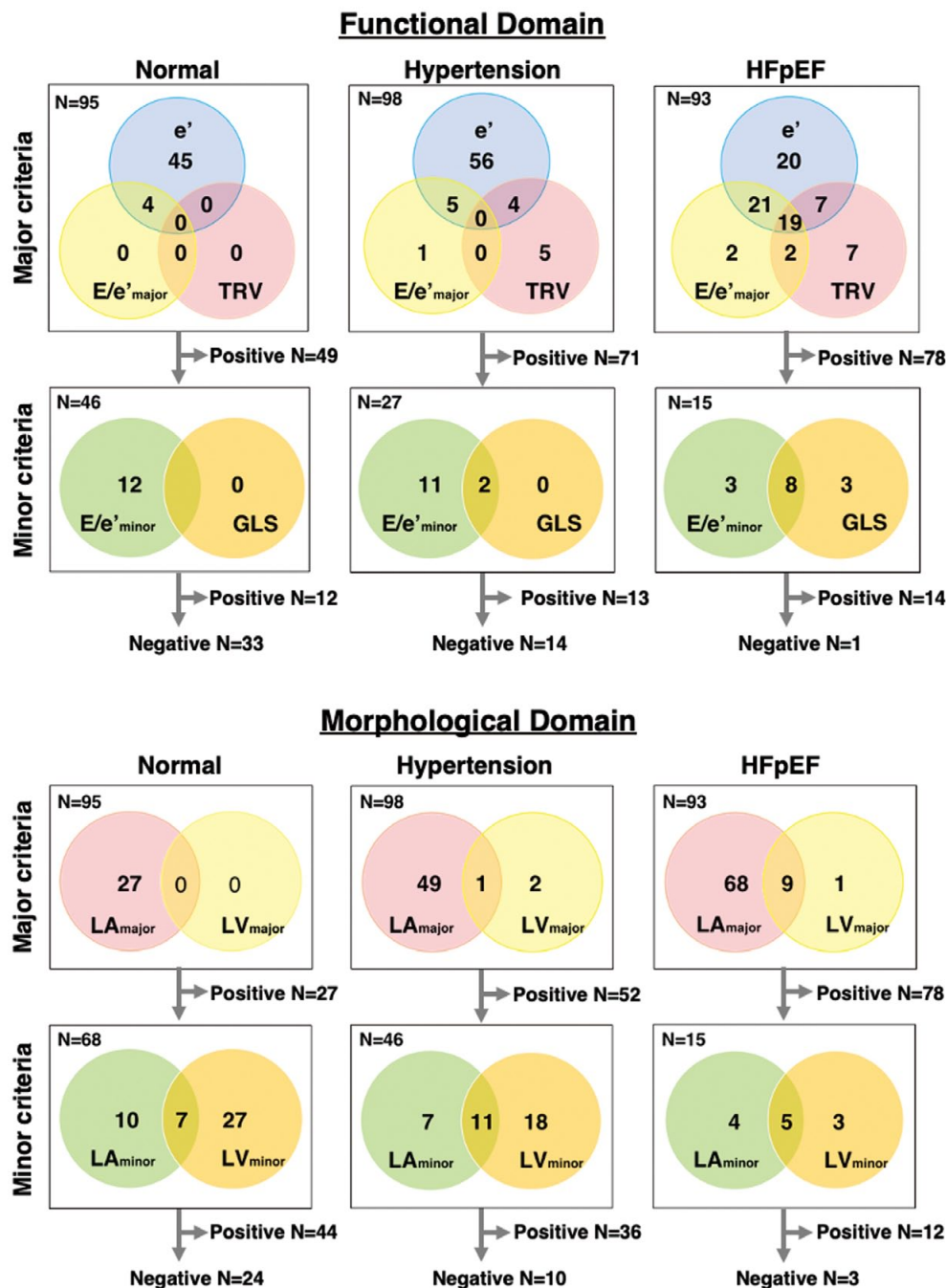
Of the functional parameters contributing to the HFA-PEFF score,  $e'$  at the septum was smaller in the HFpEF than healthy control group but did not differ from that in the HT group; there was no significant difference in  $e'$  at the lateral wall among the 3 groups.  $E/e'$  and TRV were significantly higher in the HFpEF than other groups. Adequate speckle tracking to obtain GLS was confirmed in 5,066 (98.6%) segments, with significant differences in GLS among the 3 groups. Of the morphological parameters, although there were no differences in LAVI in subjects with AF between the HT and HFpEF groups, among subjects with sinus rhythm, LAVI was significantly larger in the HFpEF than other groups. Similar results were observed for LVMI, although relative wall thickness did

	Healthy control (n=95)	Hypertension (n=98)	HFpEF (n=93)	P value
Age (years)	79.4±4.4	80.5±3.9	80.5±3.2	0.08
Male sex	42 (44)	44 (45)	44 (47)	0.90
BSA (m <sup>2</sup> )	1.52±0.15	1.53±0.18	1.49±0.17	0.40
BMI (kg/m <sup>2</sup> )	23.3±2.9	23.3±3.3	22.4±4.1	0.13
SBP (mmHg)	129±14	137±16 <sup>†</sup>	127±21	0.002
DBP (mmHg)	71±10	71±12	66±14*	0.006
HR (beats/min)	70±11	70±12	66±12	0.056
Hypertension	0	98 (100)	76 (82)	<0.001
Diabetes	0	24 (25)	27 (29)	<0.001
AF	0	7 (7.1)	24 (26)	<0.001
Hemoglobin (g/dL)	13.1±1.3	12.9±1.5	11.5±1.8*	<0.001
Albumin (g/dL)	4.1±0.3	4.1±0.4	3.6±0.6*	<0.001
eGFR (mL/min/1.73m <sup>2</sup> )	59.3±15.5	55.1±16.1	45.5±16.9*	<0.001

Unless indicated otherwise, data are given as the mean±SD or n (%). \*P<0.001 compared with the other groups; <sup>†</sup>P<0.01 compared with the HFpEF group. AF, atrial fibrillation; BMI, body mass index; BSA, body surface area; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HFpEF, heart failure with preserved ejection fraction; HR, heart rate; SBP, systolic blood pressure.

	Healthy control (n=95)	Hypertension (n=98)	HFpEF (n=93)	P value
<b>Echocardiographic parameters</b>				
LVDd (mm)	42.5±5.1	44.3±5.2	46.3±6.2 <sup>†††</sup>	<0.001
LVDs (mm)	26.2±3.8	27.3±3.8	29.6±6.3 <sup>†††</sup>	<0.001
IVSTd (mm)	9.0±1.3	9.3±1.6	9.8±2.1 <sup>‡</sup>	0.004
PWTd (mm)	8.9±1.2	9.4±1.6	9.7±1.8 <sup>‡</sup>	0.002
LVEF (%)	67.8±5.8	66.0±6.4	63.3±8.1 <sup>†††</sup>	<0.001
E (cm/s)	59.8±13.2	64.7±20.2	82.5±27.6*	<0.001
E/A	0.7±0.2	0.7±0.2 (n=90)	1.0±0.5* (n=67)	<0.001
<b>e' (cm/s)</b>				
At the septum	5.7±1.4	5.3±1.5	4.9±1.8 <sup>‡</sup>	0.002
At the lateral wall	7.4±2.1	7.0±2.0	6.8±2.6	0.15
E/e'	9.6±2.7	10.7±3.1	15.8±8.2*	<0.001
TRV (m/s)	2.3±0.3 (n=82)	2.4±0.4 (n=82)	2.6±0.5* (n=88)	<0.001
GLS (%)	21.0±3.2	18.9±3.1 <sup>††</sup>	14.5±3.9*	<0.001
<b>LAVI (mL/m<sup>2</sup>)</b>				
Sinus rhythm	31.8±13.0	36.1±14.2	49.2±17.0*	<0.001
AF	–	54.7±21.5	61.4±24.7	0.52
<b>LVMi (g/m<sup>2</sup>)</b>				
Males	81.3±15.9	95.9±19.8 <sup>‡</sup>	110.6±39.1 <sup>†††</sup>	<0.001
Female	79.4±18.6	86.4±21.6	104.0±33.5*	<0.001
RWT	0.43±0.08	0.43±0.10	0.43±0.10	0.94
<b>BNP (pg/mL)</b>				
Sinus rhythm	15.8 [22.0, 30.5]	41.2 [25.0, 79.5] <sup>††</sup>	146.7 [87.6, 294.6]*	<0.001
AF	–	140.2 [67.1, 223.0]	191.5 [117.0, 400.9]	<0.001

Unless indicated otherwise, data are given as the mean±SD or median [interquartile range]. \*P<0.001 compared with all other groups; <sup>†</sup>P<0.01, <sup>††</sup>P<0.001 compared with the healthy control; <sup>‡</sup>P<0.05 compared with the hypertensive group. AF, atrial fibrillation; BNP, B-type natriuretic peptide; E, early diastolic mitral inflow velocity; E/A, the ratio of E to A; e', early diastolic velocity of mitral annulus; E/e', the average of ratio of E to septal e' and ratio of E to lateral e'; HFpEF, heart failure with preserved ejection fraction; GLS, global longitudinal strain; IVSTd, intraventricular septal thickness at end-diastole; LAVI, indexed left atrial volume; LVDd, left ventricular (LV) end-diastolic dimension; LVDs, LV end-systolic dimension; LVEF, LV ejection fraction; LVMi, indexed LV mass; PWTd, posterior wall thickness at end-diastole; RWT, relative wall thickness; TRV, tricuspid regurgitation peak velocity.



**Figure 1.** Venn diagrams showing the number of patients who met each major and minor criterion in the functional and morphological domains of the HFA-PEFF scoring system among the 95 healthy controls (normal), 98 hypertensive subjects, and 93 subjects with heart failure with preserved ejection fraction (HFpEF). E/e', ratio of early (E) diastolic mitral inflow velocity to velocity of mitral annuls (e'); GLS, left ventricular (LV) global longitudinal strain; LA<sub>major</sub>, major criterion of left atrial volume index (LAVI); LA<sub>minor</sub>, minor criterion of LAVI; LV<sub>major</sub>, major criterion of LV remodeling; LV<sub>minor</sub>, minor criterion of LV remodeling; TRV, tricuspid regurgitation peak velocity.

not differ between the 3 groups. There were significant differences in BNP concentrations among the 3 groups for subjects in sinus rhythm and for those with AF.

#### Positive Rate of HFA-PEFF Score Components

Venn diagrams in **Figure 1** and **Table 3** summarize the num-

ber of subjects who met each criterion in the HFA-PEFF scoring system. In the functional domain, subjects meeting (vs. not meeting) the e' criterion were more common in each group. In contrast, a greater proportion of subjects in the HFpEF than other groups met the E/e' major criterion and the TRV criterion. There were significant differences

<b>Table 3. Subjects in the Healthy Control, Hypertensive, and HFpEF Groups Positive for Components of the HFA-PEFF Scoring System</b>				
	<b>Healthy control (n=95)</b>	<b>Hypertension (n=98)</b>	<b>HFpEF (n=93)</b>	<b>P value</b>
<b>Functional domain</b>				
e' at septum <7 cm/s	78 (82)	84 (86)	81 (87)	0.61
e' at lateral wall <10 cm/s	83 (87)	86 (88)	78 (84)	0.69
e' at septum <7 cm/s or e' at lateral wall <10 cm/s	89 (94)	94 (96)	85 (91)	0.44
e' at septum <5 cm/s	25 (26)	45 (46)	52 (56)	<0.001
e' at lateral wall <7 cm/s	38 (40)	55 (56)	54 (58)	0.02
<b>Major criteria</b>				
e' at septum <5 cm/s or e' at lateral wall <7 cm/s (for patients ≥75 years)	49 (52)	65 (66)	67 (72)	0.01
E/e' ≥15	4 (4.2)	6 (6.1)	44 (47)	<0.001
TRV >2.8 m/s	0	9 (9.2)	35 (38)	<0.001
Subjects meeting major criteria	49 (52)	71 (72)	78 (84)	<0.001
<b>Minor criteria (n=88)*</b>				
E/e' 9–14	12 (26)	13 (48)	11 (73)	0.004
GLS (absolute value) <16%	0	2 (7.4)	11 (73)	<0.001
Subjects meeting minor criteria	12 (26)	13 (48)	14 (93)	<0.001
<b>Morphological domain</b>				
LVMI ≥149 g/m <sup>2</sup> in men, ≥122 g/m <sup>2</sup> in women	1 (1.0)	3 (3.1)	17 (19)	<0.001
RWT >0.42	44 (46)	47 (48)	40 (44)	0.83
<b>Major criteria</b>				
LAVI >34 mL/m <sup>2</sup> in sinus rhythm, >40 mL/m <sup>2</sup> in AF	27 (28)	50 (51)	77 (83)	<0.001
RWT >0.42 and LVMI ≥149 g/m <sup>2</sup> in men or ≥122 g/m <sup>2</sup> in women	0	3 (3.1)	10 (11)	0.001
Subjects meeting the major criteria	27 (28)	52 (53)	78 (84)	<0.001
<b>Minor criteria (n=129)*</b>				
RWT >0.42	32 (47)	27 (59)	5 (33)	0.19
LAVI 29–34 mL/m <sup>2</sup> in sinus rhythm, 34–44 mL/m <sup>2</sup> in AF	17 (25)	18 (39)	9 (60)	0.02
LVMI ≥115 g/m <sup>2</sup> in men, ≥95 g/m <sup>2</sup> in women	6 (8.8)	9 (20)	5 (33)	0.04
Wall thickness ≥12 mm	0	5 (11)	1 (6.7)	0.02
Subjects meeting the minor criteria	44 (65)	36 (78)	12 (80)	0.21
<b>Biomarker domain</b>				
<b>Major criterion</b>				
BNP >80 pg/mL in sinus rhythm, >240 pg/mL in AF	0	23 (24)	65 (70)	<0.001
<b>Minor criterion (n=198)*</b>				
BNP 35–80 pg/mL in sinus rhythm, 105–240 pg/mL in AF	20 (21)	36 (48)	20 (71)	<0.001

Data are given as the number of subjects with percentages in parentheses. \*Subjects meeting the major criterion were excluded. Abbreviations as in Table 2.

in the prevalence of subjects who met each major criterion, although the number of subjects who met the major criteria was primarily dependent on the e' criterion, with more than half of the healthy control group even meeting this criterion (**Figure 1**). In contrast, with regard to minor criteria, the positive rate for meeting the GLS criterion was more specific for HFpEF than the minor criterion of E/e' (**Figure 1**). However, the addition of the GLS criterion changed the diagnosis from intermediate probability to HFpEF in only 2 cases.

In the morphological domain, the major criterion of LAVI differentiated the 3 groups well. In contrast, few subjects met the major criterion of LV concentric hypertrophy, even in the HFpEF group. Among the remaining subjects, those meeting the minor criteria were more common in the 3 groups with no significant differences in prevalence among the groups.

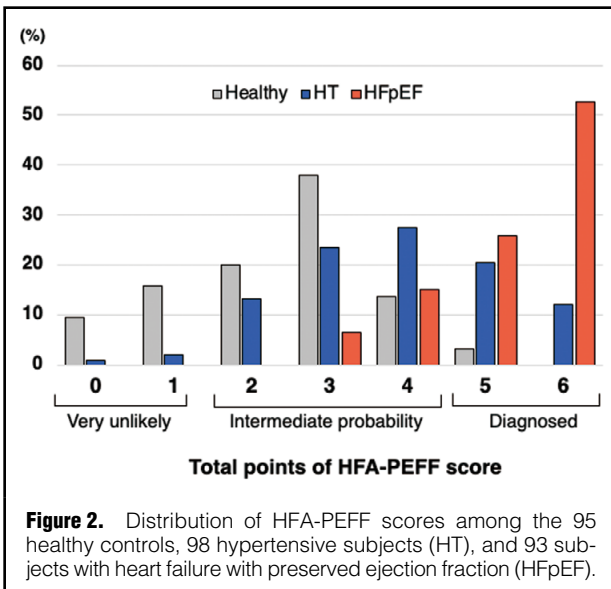
In the biomarker domain, both major and minor criteria differentiated the 3 groups well.

**Figure 2** summarizes the distribution of HFA-PEFF

scores in each group. In the HFpEF group, 73 subjects (78%) had a total score of 5 or 6, which was diagnostic of HFpEF. In contrast, in the healthy control group, only 3 subjects (3.2%) were diagnosed with HFpEF. In the HT group, 32 subjects (33%) were diagnosed with HFpEF. In both the healthy control and HT groups, there were fewer subjects with a score of 0 or 1, considered to indicate that a diagnosis of HFpEF was very unlikely, and most subjects in these groups were classified as being of intermediate probability, with scores ranging between 2 and 4.

#### **Reclassification of Subjects According to the HFA-PEFF Score**

**Figure 3** shows the reclassification of subjects in different LV diastolic dysfunction groups, determined with the ASE/EACVI algorithm, according to HFA-PEFF scores. In the HFpEF group, 24 of 26 patients (92%) in the ASE/EACVI intermediate probability group were reclassified as “HFpEF diagnosed” based on HFA-PEFF scores, with no subjects reclassified as “HFpEF very unlikely”. In the healthy control group, 43 of 67 subjects (64%) with normal



LV diastolic function according to the ASE/EACVI algorithm were reclassified into the intermediate probability group based on HFA-PEFF scores. In the HT group, 42 of 45 patients (93%) with normal LV diastolic function according to the ASE/EACVI algorithm were reclassified into the intermediate probability or HFpEF diagnosed groups using HFA-PEFF scores.

### Discussion

This study investigated the ability of the HFA-PEFF score to diagnose HFpEF in the late elderly through comparisons with healthy control subjects and subjects with HT. The major findings of this study are that: (1) the proportion of subjects meeting the HFA-PEFF criteria differed significantly among the 3 groups, although some criteria showed a relatively high rate of conformable cases even in the normal and HT groups; (2) the HFA-PEFF score diagnosed HFpEF subjects as HFpEF with high probability;

(3) one-third of subjects with HT were diagnosed with HFpEF regardless of the presence of LV diastolic dysfunction; and (4) two-thirds of healthy control subjects and subjects HT were classified as being of “intermediate probability” rather than “very unlikely” to have HFpEF.

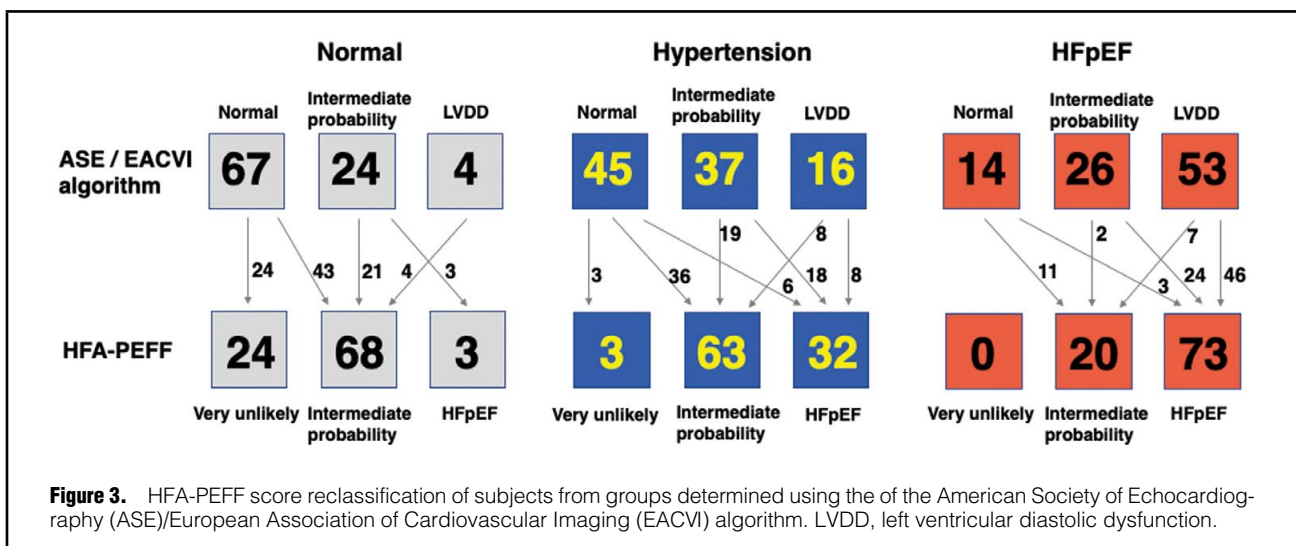
### Characteristics of Late Elderly HFpEF Subjects

Among HFpEF subjects in this study, the prevalence of AF was higher, there was a tendency for lower heart rate, hemoglobin, eGFR, and GLS were lower, LV diastolic dysfunction was prominent, there was more LA dilatation and LV hypertrophic remodeling, and plasma BNP concentrations were higher than in the other groups. These characteristics are consistent with the clinical features of HFpEF reported previously, and the HFpEF subjects enrolled in this study were considered to be a typical HFpEF population, even though they were restricted to the elderly aged  $\geq 75$  years.<sup>4,5,10</sup>

### HFA-PEFF Score Components in Elderly HFpEF Subjects

Because myocardial relaxation abnormality is essential for LV diastolic dysfunction,<sup>6-8</sup>  $e'$  is used as a major component in the HFA-PEFF scoring system.<sup>12,17</sup> However, there was no significant difference in the prevalence of subjects who met the general criterion of  $e'$  in the algorithm of LV diastolic functional evaluation ( $e'$  at the septum  $< 7$  cm/s or  $e'$  at the lateral wall  $< 10$  cm/s), indicating that this level of myocardial relaxation abnormality is common even in the subclinical late elderly. Therefore, the stricter criteria for the elderly aged  $\geq 75$  years in the HFA-PEFF scoring system (i.e.,  $e'$  at the septum  $< 5$  cm/s or  $e'$  at the lateral wall  $< 7$  cm/s) helped distinguish HFpEF from healthy control and HT subjects. However, the fact that more than half of all subjects (even in the healthy control group) still met the  $e'$  criterion is a possible limitation using the tissue Doppler method to evaluate myocardial diastolic dysfunction. Rather, parameters strongly suggesting elevated LV filling pressure, including high  $E/e'$ , TRV, and LAVI, were more specific for HFpEF.<sup>16</sup>

Using GLS as a parameter is a feature of the HFA-PEFF scoring system and is the first time GLS has been used in an algorithm for the diagnosis of HFpEF. GLS has been used to evaluate myocardial dysfunction in subclinical



subjects and patients with preserved LVEF.<sup>5,18–21</sup> Although there have not been sufficient studies investigating the use of GLS for HFpEF, in this study we confirmed the ability of GLS to distinguish HFpEF. Unfortunately, satisfying the GLS criterion in this algorithm contributed little to the HFpEF diagnosis. Because GLS was able to discriminate between the 3 groups across all subjects (Table 2), if it is used as a first-line criterion, GLS may make a greater contribution to identifying HFpEF. Larger studies are needed to evaluate the value of GLS as a key component of the HFA-PEFF score in the assessment of HFpEF.

### Advantage of Comprehensive Evaluation by the HFA-PEFF Score

The present study demonstrated the ability of the HFA-PEFF scoring system to diagnose HFpEF. Just as the definition of HFpEF has historically depended on LV diastolic dysfunction, the results of the present study support the presence of advanced LV diastolic dysfunction determined by echocardiography as an important component of HFpEF. However, the key point of the HFA-PEFF scoring system is that it also uses advanced morphological analysis and assessment of BNP concentrations to diagnose HFpEF in subjects without advanced LV diastolic dysfunction.

Another interesting finding of this study is that one-third of HT subjects, who had no prior HF events, were diagnosed with HFpEF based on the HFA-PEFF score. The prevalence of HFpEF in this study was larger than a previous validation study in which the number of control subjects was smaller and the subjects were younger than in the present study.<sup>13</sup> The progression from HT to HF is well known, and the main pathophysiology is LV diastolic dysfunction rather than systolic dysfunction.<sup>22</sup> In addition, patients with LV diastolic dysfunction but without a diagnosis of HF are common in the clinical setting.<sup>9</sup> Interestingly, in the present study, three-quarters of reclassifications to HFpEF were observed in HT subjects without LV diastolic dysfunction according to the ASE/EACVI algorithm, suggesting the advantage of performing a comprehensive evaluation using the HFA-PEFF score. Therefore, a workup with the HFA-PEFF scoring system may contribute to a more precise diagnosis of early stage HFpEF in elderly patients with HT who have not been diagnosed with HF. Although stress tests or invasive hemodynamic evaluations may be needed to determine HF status, classification as HFpEF may be the first step in preventing the progression of HF status.

Finally, the scoring system often classified subjects in the healthy control and HT groups as being in the “intermediate probability” group. Previous studies have reported that hemodynamic assessment during exercises in patients with or suspected HFpEF is useful in diagnosing symptoms on exertion, elucidating the pathophysiological mechanism, and predicting the prognosis.<sup>23–26</sup> The HFA-PEFF algorithm recommends that the population without a definite diagnosis proceeds to the next diagnostic step, such as exercise stress echocardiography or invasive hemodynamic measurements, which is an important point from the perspective of preventive medicine in subclinical cases.

### Study Limitations

Because this study was a cross-sectional study, we could not evaluate the usefulness of the function tests in identifying HFpEF among a subclinical but undiagnosed HFpEF

population; further longitudinal studies are needed to address this issue.

This study was limited to the late elderly, therefore another algorithm with an aging criterion was not assessed for comparison.<sup>26</sup> Furthermore, we did not collect information about medications, so the effects of medications on the HFA-PEFF algorithm could not be assessed. Finally, subjects with a previous history of cardiovascular disease were excluded from this study, except for HFpEF patients. However, because the study was performed in an elderly population, it is possible that the subjects may have had occult coronary artery disease, which may have had an effect on diastolic function.

### Conclusions

In the late elderly (aged >75 years), workup with echocardiography and BNP evaluations as part of the HFA-PEFF algorithm was able to identify subjects with HFpEF with high probability. In addition, most of the healthy control late elderly and subjects with HT were also classified as having HFpEF or having an intermediate probability of HFpEF, suggesting that the HFA-PEFF scoring system could contribute to the detection of early stage HFpEF in the subclinical late elderly.

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### Disclosures

N.O. is the Associate Editor for *Circulation Journal*. The remaining authors have no conflicts of interest to declare.

### IRB Information

This study was approved by the Ethics Committee of the University of Tsukuba (Reference no. H28-119).

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## Appendix

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## Supplementary Files

Please find supplementary file(s);  
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