Case Report

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Heart Failure with Preserved Ejection Fraction: A Case Report

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Abstract

Background: The prevalence of Heart Failure with Preserved Ejection Fraction (HFpEF) currently reaches 50% of heart failure cases and continues to increase every year. HFpEF is an important clinical condition, but the diagnosis is far more challenging than Heart Failure with Reduced Ejection Fraction (HFrEF), and there has not been any proven effective treatment. In this case presentation, the latest HFpEF diagnosis and therapy will be discussed.

Case Illustration and Discussion: A man and a woman came to the emergency room with signs and symptoms of congestion suggestive of heart failure. Additional examination was performed to support the working diagnosis of HFpEF, namely ECG, NTproBNP and echocardiography. HFA-PEFF scores of the first and second patient was 3 and 4 respectively. During hospitalization, diuretics was given to overcome congestion according to guidelines, as well as ACE-inhibitor and beta-blocker. Both patients were also screened for cardiovascular and non-cardiovascular comorbidities, and were given appropriate therapy.

Conclusion: The diagnosis of HFpEF does not have a gold standard yet, meanwhile, the HFA-PEFF scoring can be used. Recommended HFpEF therapy includes diuretics for congestion and management of comorbidities. Several studies of HFpEF treatment are ongoing.

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Keywords: heart failure with preserved ejection fraction, HFpEF

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Background

The prevalence of Heart Failure with Preserved Ejection Fraction (HFpEF) currently reaches 50% of all cases of heart failure and continues to increase by 1% per year.1 ASIAN-HF study found that HFpEF occurred mostly in the elderly, those with atrial fibrillation, metabolic disease, and diabetes. Whereas in Indonesia, HFrEF (Heart Failure with Reduced Ejection Fraction) is more frequent with ischemic etiology. However, with aging population and increasing prevalence of HFpEF risk factors such as hypertension, obesity, and diabetes, HFpEF will be the most common phenotype of heart failure.[2,3]

Differentiation of heart failure patients based on ejection fraction is important because of the differences in etiology, demographic, comorbidity, and response to therapy. When compared to HFrEF patients, more HFpEF patients are older, female, and have a history of hypertension and atrial fibrillation, whereas a history of myocardial infarction is less common.[1,2]

HFpEF is a condition that is difficult to diagnose and treat. Also, most hospitalizations in HFpEF patients are caused by non-cardiovascular causes, with the same mortality as HFrEF. There is no proven scoring or treatment for HFpEF yet, however, in 2019, the Heart Failure Association of the European Society of Cardiology (HFA ESC) released the HFA-PEFF diagnosis algorithm.[2]

Case Illustrations 1

Mr. DT, a 55-year old man was admitted to the emergency room with chief complaint of breathlessness for two days before admission. There was dyspnoea on exertion, orthopnoea, and paroxysmal nocturnal dyspnoea. Patient felt frequent fatigue and activity intolerance for a month before admission. Other complaints were palpitations, bloating, and edema of both lower extremities. There were no chest pain, nausea, or vomiting reported.

He had a history of hypertension and smoking. He was newly admitted to NCC Harapan Kita. Possible trigger of the decompensated heart failure was suboptimal treatment. Patient's only medication was amlodipine 1x5 mg that he sometimes bought from the pharmacy by himself.

On physical examination patient was fully alert, moderately ill with blood pressure of 128/91 mmHg, heart rate was 132 bpm, respiratory rate of 24 times per minute, temperature was 37ºCelcius, and peripheral oxygen saturation was 94%. Body height was 155 cm, body weight 62.4 kg, with BMI 25.6. There was distended JVP. Heart examination revealed normal first and second heart sounds, no murmur, and no gallop. Lung examination revealed vesicular pulmonary sounds with crackles on both lung bases. Abdominal examination revealed hepatomegaly and minimal ascites. Extremities examination revealed bilateral pitting edema.

Laboratory examination revealed mild anemia with haemoglobin level of 11.1 g/dL and mild leukocytosis. There was reduced renal function with creatinine serum level of 2.16 mg/dL and eGFR was 32 mL/min/1.73m². There was hyperglycemia of 256 g/dL. Sodium was only slightly reduced with value of 134 mmol/L.

Electrocardiography showed sinus tachycardia with heart rate of 132 bpm, normal axis, normal P wave, PR interval 0.12 s, QRS duration 0.10 s, pathologic Q wave in leads II, III, aVF. Chest X-ray revealed cardiothoracic ratio 54%, dilated aortic segment, normal pulmonary segment, downward apex, and pulmonary vascular congestion.

Echocardiographic examination revealed left ventricular ejection fraction of 54% with concentric left ventricular hypertrophy and diastolic dysfunction grade 1. The global wall motion was normal and right

Table 1. Laboratory findings of Mr. DT at admission.

Name	Result	Value
Hemoglobin	11.1	g/dL
Hematocrit	32.3	%
Leukocyte	11 610	cells/mm^3
Thrombocyte	182 000	cells/mm^3
Urea	49.2	mg/dL
BUN	23	mg/dL
Creatinine	2.16	mg/dL
estimated GFR	32	mL/min/1.73m^2
Blood glucose	256	g/dL
Sodium	134	mmol/L
Potassium	3.8	mmol/L
Chloride	97	mmol/L
Calcium total	2.19	mmol/L
Magnesium	2.5	mmol/L

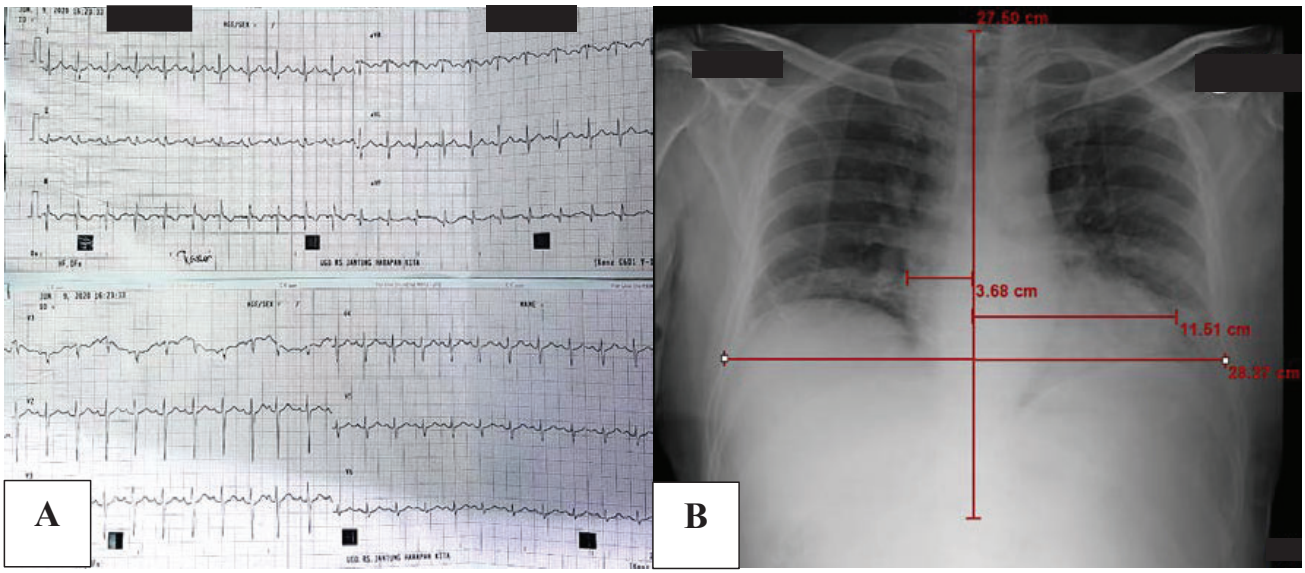

Figure 1. A. ECG of Mr. DT at admission; **B.** chest X-ray of Mr. DT at admission.

ventricular contraction was good with TAPSE of 21 mm. Septal e' was 5.3 cm/s, lateral e' 11.6 cm/s, average E/e' 9.1, LAVI (left atrial volume index) 18 mL/m², LVMI (left ventricular mass index) 127 g/m², and RWT (relative wall thickness) 0.47.

Based on history taking, physical examination, and supporting examination, patient was diagnosed with acute decompensated heart failure in HFpEF due to hypertensive heart disease with hyperglycemia, grade 1 hypertension, and renal insufficiency.

Patient was initially treated with furosemide 20 mg iv and continued with 2x40 mg IV, ramipril 1x2.5 mg, and insulin drip 2 units/hour. During treatment in the ward, diuretic was optimized to 3x60 mg IV. Blood glucose was well-controlled and insulin was switched to metformin 2x500 mg. NT-pro BNP was tested on the third day with result of 68.

During hospitalization, the clinical condition of the patient improved. Furosemide was down-titrated to oral 1x40 mg, ramipril increased to 1x10 mg, and bisoprolol was initiated at 1x1.25 mg. On the seventh day, patient was discharged with euvolemic and stable hemodynamic condition. Drugs given during discharge were furosemide 1x40 mg, ramipril 1x10 mg, bisoprolol 1x1.25 mg, simvastatin 1x20 mg, and metformin 2x500 mg. Patient was educated to limit fluid intake up to 1500 mL/day and to return for follow up in the polyclinic one week later.

Case Illustrations 2

Mrs. S, a 66-year old woman was admitted to the emergency room with chief complaint of breathlessness for one month before admission. There was dyspnoea on exertion, orthopnea, and paroxysmal nocturnal dyspnea. Patient felt frequent fatigue and activity intolerance for three months before admission. There was also edema of both lower extremities. There were no chest pain, nausea, or vomiting reported.

She had a history of hypertension and menopause. Patient was newly admitted to NCC Harapan Kita with possible trigger of failure was suboptimal treatment. Patient routinely went to a nearby clinic and was given furosemide 1x40 mg, captopril 3x25 mg, and amlodipine 1x5 mg.

On physical examination patient was fully alert, moderately ill with blood pressure of 135/71 mmHg, heart rate 90 bpm, respiratory rate of 24 times per minute, temperature 37-degree Celsius, and oxygen saturation 98%. Body height was 143 cm, body weight 74.6 kg, with BMI 36.2. There was distended JVP. Heart examination revealed normal first and second heart sounds, no murmur, and no gallop. Lung examination revealed vesicular pulmonary sounds with crackles on both lung bases. Abdominal examination revealed hepatomegaly and extremities examination revealed bilateral pitting edema.

Laboratory examination revealed mild anemia with hemoglobin level of 11.9 g/dL and mild leukocytosis. There was hypokalemia with value of 2.9 mmol/L. Electrocardiography showed sinus rhythm with heart rate of 94 bpm, left axis deviation, normal P wave, PR interval 0.15 s, QRS duration 0.09 s, and normal ST-T segment. Chest X-ray revealed cardiothoracic ratio 74%, dilated aortic segment, normal pulmonary segment, downward apex, and congestion.

Echocardiographic examination revealed left ventricular ejection fraction of 57% with concentric left ventricular hypertrophy and diastolic dysfunction grade 1. Wall motion was global normokinetic and right ventricular contraction was good with TAPSE of 18 mm. Septal e' was 4.7 cm/s, lateral e' 5.8 cm/s, average E/e' 9.1, LAVI 26 mL/m², LVMI 126 g/m², and RWT 0.45.

Based on the history taking, physical examination, and supporting examination, patient was diagnosed with acute decompensated heart failure in HFpEF due to hypertensive heart disease, hypertension with controlled blood pressure, hypokalemia, and obesity.

Patient was initially treated with furosemide 40 mg iv and continued with 2x20 mg iv, ramipril 1x10 mg, and spironolactone 1x25 mg. During treatment in the ward, diuretic was optimized to 10 mg/hour and spironolactone increased to 1x50 mg. Oral glucose tolerance test result was 119 and 199, therefore patient was given metformin 2x500 mg. Potassium level improved to 3.7. Bisoprolol was also initiated at 1x1.25 mg.

During hospitalization, clinical condition of the patient improved. NT-proBNP was tested on the fifth day with result of 43. Furosemide was down-titrated to 2x40 mg, and bisoprolol was up-titrated to 1x2.5 mg. On the sixth day, patient was discharged with euvolemic and stable hemodynamic condition. Drugs given during discharge were furosemide 2x40 mg, ramipril 1x10 mg, bisoprolol 1x2.5 mg, spironolactone 1x50 mg, and metformin 2x500 mg. Patient was educated to limit fluid intake up to 1800 mL/day and to return for follow up in the polyclinic one week later

Table 2. Laboratory findings of Mrs. S at admission.

Name	Result	Value
Haemoglobin	11.9	g/dL
Haematocrit	35.7	%
Leukocyte	11 000	cells/mm³
Thrombocyte	325.000	cells/mm³
Urea	25.7	mg/dL
BUN	12	mg/dL
Creatinine	0.89	mg/dL
estimated GFR	68	mL/min/1.73m²
Blood glucose	148	g/dL
Sodium	138	mmol/L
Potassium	2.9	mmol/L
Chloride	97	mmol/L

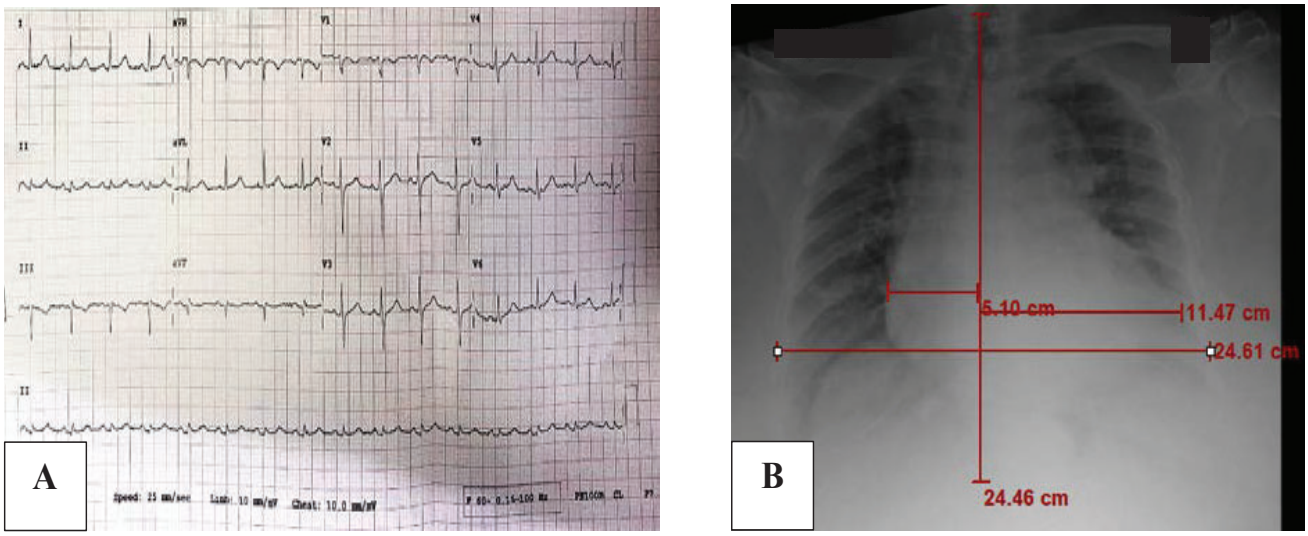

Figure 2. A. ECG of Mrs. S at admission; **B**. chest X-ray of Mrs. S at admission.

Discussion

Heart Failure with Preserved Ejection Fraction

Heart Failure with Preserved Ejection Fraction (HFpEF) was previously referred to as heart failure with normal systolic function or diastolic heart failure. Diastolic dysfunction itself is a myocardial relaxation disorder and impaired left ventricular compliance which causes an increase in left ventricular end-diastolic pressure (LVEDP). Diastolic heart failure is diastolic dysfunction accompanied with signs and symptoms of heart failure. HFpEF does not only consist of diastolic dysfunction, but also abnormalities of regional contractility and chronotropic incompetence, causing dyspnea and intolerance during activity. [1,4]

The definition of HFpEF from the ESC are symptoms and/or signs with left ventricular ejection fraction more than or equal to 50%, accompanied with elevated levels of natriuretic peptides and at least one additional criterion (relevant structural heart disease or diastolic dysfunction).[2]

Typical symptoms of heart failure include breathlessness, orthopnoea, paroxysmal nocturnal dyspnoea, reduced exercise tolerance, fatigue, tiredness, increased time to recover after exercise, and ankle swelling. Meanwhile, specific signs of heart failure are elevated jugular venous pressure, hepatojugular reflux, gallop rhythm, and laterally displaced apical impulse. These signs and symptoms are often harder to identify and interpret in patients with obesity, advanced age, and chronic lung disease.[2]

Elevated levels of natriuretic peptides can support the diagnosis of heart failure. In non-acute setting, the upper limit of normal of B-type natriuretic peptide (BNP) is 35 pg/mL and for N-terminal pro-BNP (NT-proBNP) is 125 pg/mL. While in an acute setting, higher values are used (BNP >100 pg/mL, NT-proBNP >300 pg/mL).[2]

Diagnosis of HFpEF

In 2019, the Heart Failure Association of the European Society of Cardiology (HFA ESC) released the HFA-PEFF algorithm to diagnose HFpEF. The steps are Pretest assessment, Echocardiographic and natriuretic peptide score, Functional testing in case of uncertainty, and Final etiology.[5]

First, in breathless patients, assess the signs and symptoms. Patients with HFpEF usually experience reduced exercise tolerance and fatigue. ECG increases the likelihood of heart failure, but has low specificity. Atrial fibrillation (AF) is particularly predictive of HFpEF. In both patients, the pre-test results are suggestive of HFpEF, therefore the HFA-PEFF score can be calculated using echocardiography and NT-proBNP level.[2,5]

The HFA-PEFF score consists of three components: functional, morphological, and biomarker. Biomarker is further divided into sinus rhythm (SR) and atrial fibrillation (AF) because NP levels in patients with AF on average are 3 times higher than in patients with SR. Major criteria accounts for two points, while minor criteria accounts for one point.

In the first patient, major functional criteria and minor morphological criteria were fulfilled, adding up to 3 points. While the second patient fulfilled major functional and morphological criteria, resulting in 4 points. Both patients needed diastolic stress test or invasive hemodynamic measurements to confirm the diagnosis of HFpEF.[5] However, in these two patients additional testing was not performed. Furthermore, to identify the etiology, ergometry and cardiac magnetic resonance (CMR) can be performed. Possible etiologies include chronotropic incompetence, ischemia, or cardiomyopathy.

Natriuretic peptides may be affected by various factors. Beside atrial fibrillation, increasing age and renal failure can also increase NP. On the other hand, NP levels may be low in obese or euvolemic patients. In both patients, NT-proBNP was tested on the third and fifth days of treatment, when the patient's condition was probably euvolemic. In the first patient, renal insufficiency has improved on the third day, while the second patient is obese. In addition, NP values also tend to be lower in HFpEF because left ventricular hypertrophy (LVH) tends to normalize wall stress. These factors might cause normal NT-proBNP values in both patients.[2,5]

Treatment of HFpEF

Hospitalizations in HFpEF patients are mostly due to comorbidities, therefore it is very important to screen patients for cardiovascular and non-cardiovascular

comorbidities, then they should be treated accordingly. To relieve signs and symptoms of congestion, diuretics can be given, with the same principle as HFrEF. As for other therapies, none has been proven effective. There was not enough evidence relating to beta-blockers and mineralocorticoid receptor antagonists for treating HFpEF. Data was also inconsistent for ACE-inhibitors and ARBs.[2,6,7]

Typical demographics and co-morbidities associated with HFpEF are advanced age, arterial hypertension, AF, female gender, kidney dysfunction, metabolic syndrome, obesity, physical deconditioning, pulmonary disease, pulmonary hypertension, and sleep apnea. Hypertension and age are important risk factors for HFpEF. Increasing age causes arterial stiffness, resulting in systolic hypertension.[2] Whereas obesity was reported in 34% of patients in the I-PRESERVE study.[8] Data from the MESA (Multi-Ethnic Study of Atherosclerosis) study showed that EF usually increases with age and is higher in women than in men.[9] Central obesity is also associated with arterial stiffness and concentric LVH, especially in women. However, hospitalization and mortality were reported to be lower in women, with better prognosis in women without AF, renal insufficiency, angina pectoris, and severe NYHA class.[2,8,10]

In this case, the male patient had hypertension and kidney dysfunction, while the female patient had advanced age, hypertension, metabolic syndrome, and obesity. Heart failure was treated with ACE inhibitors, beta-blockers, and diuretics, according to the recommendation by the ESC. Both patients were also pre-diabetic and were given metformin, as the first line anti-diabetic medication in HFpEF.[2]

Several studies have been conducted to investigate effective treatments in reducing mortality and hospitalization due to heart failure in HFpEF. Several of the studies found significant results. However, this is in contrast to many studies on HFrEF where mortality dropped significantly.[2]

Current ongoing study on HFpEF treatment is PARAGON-HF, comparing valsartan and sacubitril/valsartan or angiotensin receptor-neprilysin inhibitor (ARNI), primarily to examine the effects of sacubitril itself. Another consideration from the researchers to compare those drugs is that the majority of patients in the study and the general population have already used ARBs. The result was no significant difference in hospitalization for heart failure and cardiovascular mortality in the valsartan and ARNI groups with p = 0.059. Statistically, the effect of ARNI was not significant, but in subgroup analysis it was found that ARNI provided better results in the female population and also patients with LVEF below 57% or the median EF in this study.[11]

Conclusion

A man and woman with HFpEF and HHD, came to the emergency room with signs and symptoms of congestion. Additional examination was performed to support the diagnostic criteria, namely ECG, NTproBNP and echocardiography. HFA-PEFF scores of the first and second patient was 3 and 4 respectively. During hospitalization, diuretics was given to overcome congestion according to guidelines, as well as ACE-inhibitor and beta-blocker. Both patients were also screened for cardiovascular and non-cardiovascular comorbidities, and were given appropriate therapy. The diagnosis of HFpEF does not have a gold standard yet, meanwhile the HFA-PEFF scoring can be used. Recommended HFpEF therapy includes diuretics for congestion and management of comorbidities. Several studies of HFpEF treatment are ongoing.

References

1. Oktay A, Shah S. Diagnosis and Management of Heart Failure with Preserved Ejection Fraction: 10 Key Lessons. Curr Cardiol Rev. 2014;11:42-52.
2. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2016;37:2129-2200m.
3. Tromp J, Tay WT, Ouwerkerk W, Teng THK, Yap J, MacDonald MR, Leineweber K, McMurray JJV, Zile MR, Anand IS, Lam CSP. Multimorbidity in patients with heart failure from 11 Asian regions: A prospective cohort study using the ASIAN-HF registry. PLoS Med. 2018;15:1-22.
4. Lam CSP. What is normal in HFNEF?: The case for HFpEF. JACC Hear Fail. 2014;2:541-543.
5. Pieske B, Tschöpe C, De Boer RA, Fraser AG, Anker SD, Donal E, et al. How to diagnose heart failure

with preserved ejection fraction: The HFA-PEFF diagnostic algorithm: A consensus recommendation from the Heart Failure Association (HFA) of the European Society of Cardiology (ESC). Eur Heart J. 2019;40:3297-3317.
6. Mullens W, Damman K, Harjola VP, Mebazaa A, Brunner-La Rocca HP, Martens P, Testani JM, Tang WHW, Orso F, Rossignol P, Metra M, Filippatos G, Seferovic PM, Ruschitzka F, Coats AJ. The use of diuretics in heart failure with congestion — a position statement from the Heart Failure Association of the European Society of Cardiology. Eur J Heart Fail. 2019;21:137-155.
7. Senni M, Paulus WJ, Gavazzi A, Fraser AG, Díez J, Solomon SD, et al. New strategies for heart failure with preserved ejection fraction: the importance of targeted therapies for heart failure phenotypes. Eur Heart J. 2014;35:2797-2811d.
8. Massie BM, Carson PE, McMurray JJ, Komajda M, McKelvie R, Zile MR, Anderson S, Donovan M, Iverson E, Staiger C, Ptaszynska A. Irbesartan in patients with heart failure and preserved ejection fraction. N Engl J Med. 2008;359:2456-2467.
9. Cheng S, Fernandes VRS, Bluemke DA, McClelland RL, Kronmal RA, Lima JAC. Age-related left ventricular remodeling and associated risk for cardiovascular outcomes the multi-ethnic study of atherosclerosis. Circ Cardiovasc Imaging. 2009;2:191-198.
10. Lam CSP, Carson PE, Anand IS, Rector TS, Kuskowski M, Komajda M, McKelvie RS, McMurray JJ, Zile MR, Massie BM, Kitzman DW. Sex differences in clinical characteristics and outcomes in elderly pati