Original Article

A retrospective study on the clinical significance of cardiac computed tomography in heart failure patients with preserved ejection fraction

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Background: This study investigated the correlation between cardiac function parameters by cardiac computed tomography (CT) and the clinical outcomes of heart failure patients with preserved ejection fraction (HFpEF) to provide experimental data for the diagnosis of HFpEF.

Methods: A total of 157 HFpEF patients admitted to our hospital from January 2017 to January 2019 were retrospectively analyzed. The patients were divided into event and non-event groups according to the occurrence or absence of adverse events. Cardiac function parameters, such as the left ventricular (LV) end-diastolic volume (LVEDV) and LV end-diastolic volume index (LVEDVI), were obtained via CT scan. Also, the N-terminal-pro hormone b-type natriuretic peptide (NT-proBNP) levels in patients' serum were measured using an enzyme linked immunosorbent assay (ELISA) kit, and echocardiographic parameters such as LV posterior wall thickness (LVPWT) were also recorded. Further, Cox regression was employed to analyze factors associated with the clinical outcomes.

Results: Compared with patients in the non-event group, the left ventricular end-diastolic mass (LVM), LVEDVI, left ventricular end-systolic volume index (LVESVI), left atrial end-diastolic volume index (LAEDVI), and left atrial end-systolic volume index (LAESVI) were significantly increased, and the left ventricular total emptying fraction (LVTEF) and left atrial total emptying fraction (LATEF) were markedly decreased in the event group patients. Also, the E/e' and LAEDVI were related factors affecting the clinical outcomes of HFpEF patients. The above indicators displayed a significant predictive for the clinical outcomes of HFpEF patients.

Conclusions: Several cardiac function measures, including LAEDVI, are factors associated with the clinical outcomes of HFpEF patients.

Keywords: Cardiac computed tomography; cardiac function; heart failure with preserved ejection fraction; clinical outcome

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Introduction

Heart failure (HF) refers to a complex group of clinical syndromes caused by abnormal changes in cardiac structure and/or function. Such changes are multifactorial consequences and result in impaired systolic and/or diastolic function. This disease can be divided into HF with reduced EF (HFrEF), HF with preserved EF (HFpEF), and HF with midrange EF (HFmrEF) according to the different left

ventricular (LV) ejection fraction (EF) (1,2). HF has now become a major and growing public health problem (3). A study has shown that more than 70% of HF patients over 65 years of age have preserved EF. The incidence and prevalence of HFpEF increase by 10% every 10 years compared with HFrEF (4). Given the lack of effective treatments, HFpEF remains a common disease with a poor prognosis. Correct diagnosis at an early stage is essential to improving the outcome of this disease (5).

In recent years, computed tomography (CT), an anatomical imaging modality, has been widely used for cardiovascular imaging examinations (6). Recent advances in CT technology and contrast agents (CAs) in clinical and preclinical cardiac imaging have facilitated the development of functional imaging (7). Functional CT can now be achieved through the combination of electrocardiogram gating, allowing a comprehensive assessment of global and regional myocardial function, perfusion, and coronary angiography (8). CT can not only observe the cardiac structure but also accurately report on the vascular condition. A previous study has pointed out that cardiac structure and function are somewhat correlated with quality of life in HFpEF patients (9). However, there is no evidence-based medical research on the correlation between cardiac function indicators detected by CT and the clinical outcomes of HFpEF patients. This study attempts to elaborate on this relationship through clinical trials, and thus, provide a new method for the treatment of HFpEF patients. We present the following article in accordance with the STARD reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-5549/rc).

Highlight box

Key findings

- Several cardiac function measures, including LAEDVI, are factors associated with the clinical outcomes of HFpEF patients and contribute to outcome prediction.

What is known and what is new?

- In recent years, computed tomography (CT), an anatomical imaging modality, has been widely used for cardiovascular imaging examinations.
- This study attempts to elaborate on this relationship through clinical trials, and thus, provide a new method for the treatment of HFpEF patients.

What is the implication, and what should change now?

- Cardiac function indicators obtained by CT scanning can serve as predictive factors of clinical outcomes, and the E/e', LAEDVI, LVM, LVTEF, and LATEF are related factors affecting the clinical outcomes of HFpEF patients.

Methods

Study subjects

A total of 157 HFpEF patients admitted to our hospital from January 2017 to January 2019 were retrospectively analyzed. Their baseline data were collected for further analysis, including gender, age, body mass index (BMI), heart rate (bpm), diastolic blood pressure (mmHg), systolic blood pressure (mmHg), disease duration, New York Heart Association (NYHA) Classification, and past medical history (diabetes, hypertension, hyperlipidemia, coronary heart disease, previous HF, previous myocardial infarction, smoking history, and alcoholism). The patients were divided into an event group (with adverse events) and a non-event group (without adverse events). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by ethics committee of the Affiliated Hospital of Putian University. Individual consent for this retrospective analysis was waived.

The inclusion criteria were as follows: (I) aged ≥18 years old; (II) signs or symptoms of HF; (III) normal or mildly reduced LVEF (LVEF ≥50%); (IV) echocardiography showed abnormal cardiac structure or function; (V) levels of N-terminal-pro hormone b-type natriuretic peptide (NT-proBNP) >125 pg/mL; (VI) cardiac CT data; (VII) complete follow-up data; and (VIII) volunteered to participate in this study and cooperate with the follow-up. Patients who died in the first hospitalization were excluded.

Cardiac CT

All patients were scanned with a third-generation dual-source CT scanner (SOMATOM Force, Siemens Healthineers, Germany). All scans were performed in the craniocaudal direction with patients in the supine position and holding their breath. 85 mL of iodinated CA was injected at 5 mL/s, followed by 25% CA/75% of saline mixture. Before the scan, oral beta-blockers were administered if the patient's heart rate was >60 bpm. Data were analyzed on a dedicated CT workstation.

The following data were obtained directly or indirectly through calculation: LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV), left atrial (LA) end-

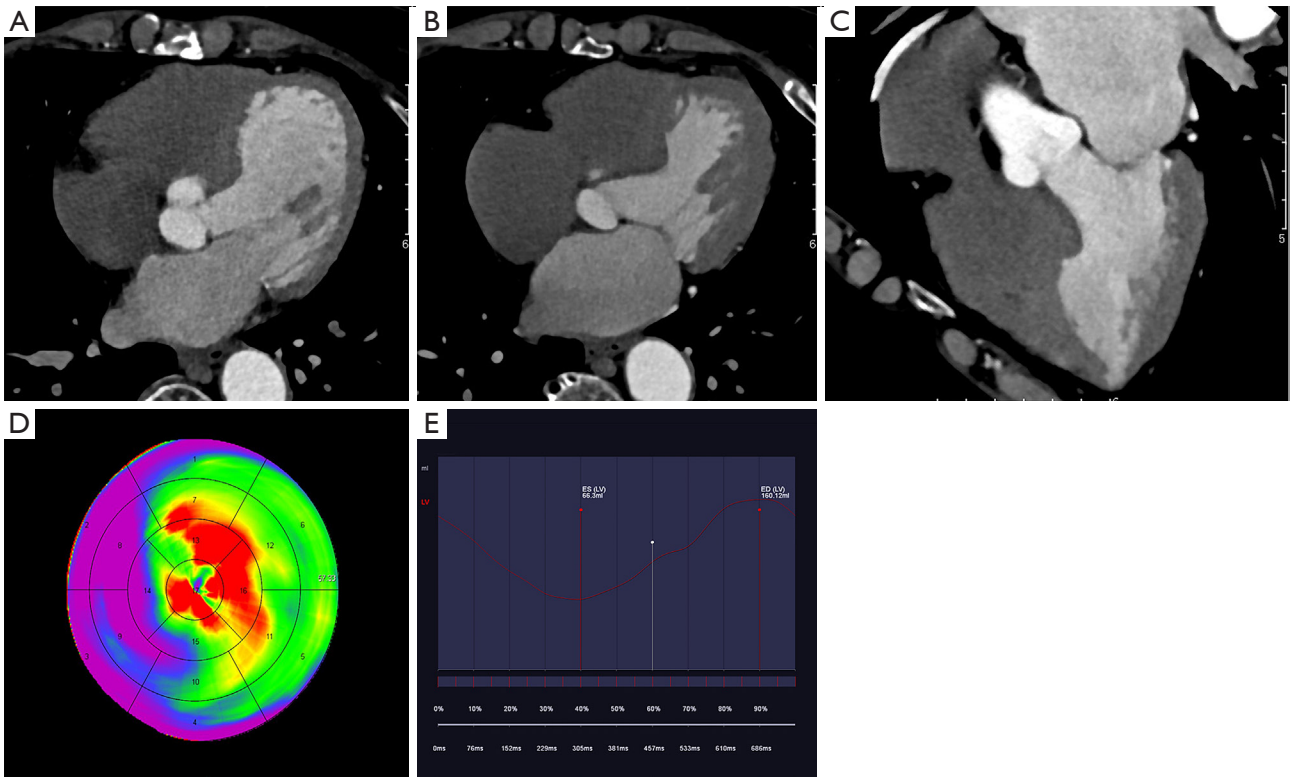

Figure 1 Cardiac computed tomography scan of a patient with HFpEF. (A) End-diastolic four-chamber view; (B) end-systolic four-chamber view; (C) left ventricular long axis; (D) ventricular wall thickening view; (E) ventricular volume view. HFpEF, heart failure patients with preserved ejection fraction.

systolic volume (LAESV), LA end-diastolic volume (LAEDV), LV end-diastolic volume index (LVEDVI), LV end-systolic volume index (LVESVI), LA end-diastolic volume index (LAEDVI), LA end-systolic volume index (LAESVI), LV end-diastolic mass (LVM), LV total emptying fraction (LVTEF), and LA total emptying fraction (LATEF). To determine the reliability of the data, two observers with 5 years of experience in cardiac imaging independently reviewed the echocardiographic images in a blinded manner (10) (*Figure 1*).

Cardiac ultrasound

The cardiac ultrasounds were performed by professional sonographers. The applied ultrasound instrument was GE Vivid 7 (GE, USA), with a probe frequency of 2.0–3.5 MHz. Under M-mode ultrasound, the parasternal long-axis view was taken to measure the LV end-diastolic diameter (LVEDD), LV end-systolic diameter (LVESD), interventricular septum thickness in end-diastole (IVSD), and LV posterior wall thickness (LVPWT). The LV ejection fraction (LVEF) was calculated using the Simpson method, and the ratio of mitral early-diastolic inflow peak velocity (E) to mitral annular early-diastolic peak velocity (e') was calculated.

Detection of serum indicators

After water and food deprivation for more than 12 hours, the patients were subjected to blood collection the next morning. 3 mL of cubital venous blood was drawn into a coagulation tube and then centrifugated to obtain the serum. The serum was collected and stored in a refrigerator at –80 ℃ for subsequent testing. An automatic biochemical analyzer was used to measure the high-sensitivity cardiac troponin I (hs-cTnI), triglyceride (TG), total cholesterol (TC), high-density lipoprotein (HDL), and low-density lipoprotein (LDL). Additionally, the total NT-proBNP level in serum was detected according to the instructions of the ELISA kit (Nanjing Jiancheng Bioengineering Institute,

China), and the absorbance of each well was determined sequentially at a wavelength of 450 nm.

Statistical analysis

Statistical analysis was performed using SPSS software (IBM Corp., Armonk, NY, USA). Data were tested for normal distribution using the Shapiro-Wilk test. Continuous data were expressed as mean ± standard deviation (SD). Cox regression analysis was utilized to assess the factors associated with the composite clinical outcomes. P<0.05 (two-sided) was considered to indicate a statistically significant difference.

Results

General information

A total of 157 patients were enrolled in this study, including 77 in the event group (20 males and 57 females, mean age: 70.97±8.19), and 80 in the non-event group (16 males and 64 females, mean age: 72.17±7.03). There was no significant difference in age, gender, BMI, and disease history (including diabetes, hypertension, smoking, and alcohol history) between the two groups. The event group had significantly higher levels of hs-cTnI (P<0.001) as well as lower IVSD levels and E/e' ratio (both P<0.05) compared with those in the non-event group. However, the levels of TG, TC, and NT-proBNP were not significantly different between the two groups (*Table 1*).

Comparison of cardiac function detected by CT between the two groups

The cardiac CT scan results were further compared between the two groups. The LVEDVI (84.97±3.5, *Figure 2A*), LVESVI (38.61±4.01, *Figure 2B*), LAEDVI (34.38±3.10, *Figure 2C*), LAESVI (57.72±6.65, *Figure 2D*), and LVM (208.02±21.92, *Figure 2E*) were significantly increased in the event group patients compared with the non-event group patients (P<0.05). However, LVTEF (28.1±9.06, *Figure 2F*) and LATEF (31.39±7.00, *Figure 2G*) were markedly lower in the event group than in the non-event group (P<0.05).

Analysis of factors associated with the clinical outcomes of HFpEF patients

Sex, age, hs-cTnI, and cardiac function parameters were correlated with the clinical outcomes of HFpEF patients. The univariate analysis results showed that hs-cTnI, IVSD, E/e', LVEDVI, LVESVI, LAEDVI, LAESVI, LVM, LVTEF, and LATEF were related factors affecting the clinical outcomes of HFpEF patients. In the multivariate analysis, E/e', LAEDVI, LVM, LVTEF, and LATEF were the relevant factors affecting the clinical outcomes of HFpEF patients (*Table 2*).

Discussion

Globally, the prevalence of HFpEF is increasing every year (11,12), and its diagnosis is mainly based on the combination of the E/e' ratio and left ventricular filling pressure (13). However, the accuracy of the measured E/e' ratio is not high in cases involving mitral annular calcification, any mitral valve stenosis, or at least moderate mitral regurgitation (14). Such errors can be avoided by using CT.

HFpEF patients are often accompanied by risk factors and comorbidities such as obesity, hypertension, diabetes, chronic kidney disease, and chronic obstructive pulmonary disease (15). For example, a study (16) showed that obesity and associated cardiometabolic features, including insulin resistance, are closely related to the risk of HFpEF. However, there is currently no clear evidence-based medical research on the factors associated with clinical outcomes in HFpEF patients. In the present study, through CT scanning, we found that the LVM, LVEDVI, LVESVI, LAEDVI, and LAESVI were significantly increased, and LVTEF and LATEF were substantially decreased in the event group, and these indicators reached statistical significance for predicting the clinical outcomes of HFpEF patients.

Further univariate Cox regression analysis revealed that the LVEDVI, LVESVI, LAEDVI, LAESVI, LVM, LVTEF, and LATEF were factors associated with clinical outcomes in HFpEF patients, while multivariate Cox regression analysis identified the E/e', LAEDVI, LVM, LVTEF, and LATEF as influencing factors. A previous study by Ferreira *et al.* (9) showed that health-related quality of life was negatively correlated with LVEDD; combined with these previous results, we suggest that elevated LVEDVI and LVESVI are related to poor prognosis and quality of life in HFpEF patients. Additionally, we observed that several blood parameters showed a downward trend in the event group.

HFpEF patients with elevated B-type natriuretic peptide

Table 1 Clinical baseline characteristics of included patients

Information	Event group (n=77)	Non-event group (n=80)	Statistics	P
Demographic indicators				
Gender (male/female)	20/57	16/64	0.206	0.650
Age (years)	70.97±8.19	72.17±7.03	−0.993	0.322
Body mass index	22.45±1.15	22.69±1.46	−0.991	0.323
Heart rate	71.75±7.97	70.93±8.36	0.638	0.524
Diastolic blood pressure	91.06±10.05	93.40±13.30	−1.258	0.210
Systolic blood pressure	142.32±18.92	143.39±21.83	−0.327	0.744
Course of disease	4.16±1.50	4.27±1.50	−0.461	0.645
NYHA classification (III–IV)	27 (35.1)	30 (36.1)	0.020	0.887
Medical history				
Diabetes	29 (37.7)	36 (43.4)	0.540	0.462
Hypertension	57 (74.0)	59 (71.1)	0.173	0.677
Hyperlipidemia	29 (37.7)	31 (37.3)	0.002	0.967
Coronary heart disease	33 (42.9)	35 (42.2)	0.008	0.930
Previous heart failure	11 (14.3)	15 (18.1)	0.421	0.517
Previous myocardial infarction	10 (13.0)	8 (9.6)	0.449	0.503
Smoking	34 (44.2)	37 (44.6)	0.003	0.957
Alcoholism	36 (46.8)	40 (48.2)	0.033	0.855
Laboratory indicators				
NT-proBNP, pg/mL	909 [625–1,239]	1,000 [702–1,411]	−1.626	0.104
hs-cTnI, ng/mL	22 [15–31]	5.08 [3.01–7.23]	−9.586	<0.001
TG, mmol/L	1.51±0.56	1.59±0.49	−0.926	0.356
TC, mmol/L	4.71±1.16	4.73±1.02	−0.133	0.894
HDL, mmol/L	1.89±0.54	1.80±0.47	1.073	0.285
LDL, mmol/L	2.30±1.13	2.10±0.49	1.419	0.159
Echocardiographic parameters				
LVEDD, mm	46.70±7.61	45.32±7.14	1.180	0.240
LVESD, mm	30.38±5.81	30.34±5.52	0.050	0.960
IVSD, mm	11.61±1.67	12.28±1.61	−2.576	0.011
LVPWT, mm	8.90±1.56	8.46±1.43	1.862	0.064
E/e’	23.47±3.87	25.41±2.99	−3.534	0.001
LVEF, %	52.11±5.68	52.99±5.89	−0.964	0.337

Data are presented as mean ± standard deviation, median [interquartile range], or number (frequency). NT-proBNP, N-terminal-pro hormone b-type natriuretic peptide; hs-cTnI, high-sensitivity cardiac troponin I; TG, triglyceride; TC, total cholesterol; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; IVSD, interventricular septum thickness in end-diastole; LVPWT, left ventricular posterior wall thickness; E/e’, ratio of mitral early-diastolic inflow peak velocity (E) to mitral annular early-diastolic peak velocity (e’); LVEF, left ventricular ejection fraction.

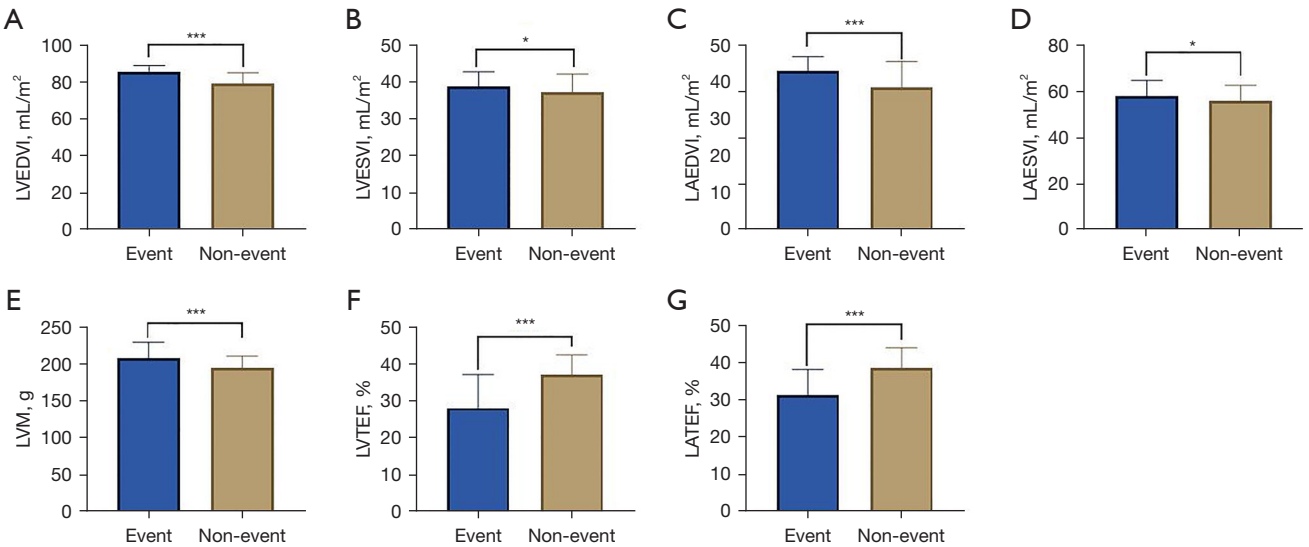

Figure 2 Comparison of cardiac function detected by CT between the event and non-event groups. (A) LVEDVI; (B) LVESVI; (C) LAEDVI; (D) LAESVI; (E) LVM; (F) LVTEF; (G) LATEF. *, P<0.05; ***, P<0.001. LVEDVI, left ventricular end-diastolic volume index; LVESVI, left ventricular end-systolic volume index; LAEDVI, left atrial end-diastolic volume index; LAESVI, left atrial end-systolic volume index; LVM, left ventricular end-diastolic mass; LVTEF, left ventricular total emptying fraction; LATEF, left atrial total emptying fraction; CT, computed tomography.

Table 2 Factors related to composite clinical outcomes

Index	Univariate		Multivariate	
	OR (95% CI)	P	OR (95% CI)	P
Gender	0.846 (0.411–1.742)	0.650	–	–
Age	0.979 (0.940–1.020)	0.320	–	–
Hs-cTnI	1.219 (1.149–1.293)	0.000	1.122 (1.042–1.207)	0.122
IVSD	0.780 (0.643–0.947)	0.012	0.785 (0.423–1.459)	0.444
E/e’	0.849 (0.772–0.935)	0.001	0.826 (0.634–1.076)	0.026
LVEDVI	1.287 (1.184–1.400)	0.000	1.526 (1.140–2.043)	0.135
LVESVI	1.078 (1.005–1.157)	0.036	1.280 (0.991–1.652)	0.058
LAEDVI	1.185 (1.097–1.280)	0.000	1.310 (1.034–1.658)	0.025
LAESVI	1.050 (1.002–1.100)	0.043	1.158 (0.975–1.377)	0.095
LVM	1.035 (1.017–1.053)	0.000	1.127 (0.976–1.282)	0.007
LVTEF	0.819 (0.764–0.877)	0.000	0.729 (0.598–0.889)	0.002
LATEF	0.808 (0.750–0.870)	0.000	0.797 (0.688–0.924)	0.003

hs-cTnI, high-sensitivity cardiac troponin I; IVSD, interventricular septum thickness in end-diastole; E/e’, ratio of mitral early-diastolic inflow peak velocity (E) to mitral annular early-diastolic peak velocity (e’); LVEDVI, left ventricular end-diastolic volume index; LVESVI, left ventricular end-systolic volume index; LAEDVI, left atrial end-diastolic volume index; LAESVI, left atrial end-systolic volume index; LVM, left ventricular end-diastolic mass; LVTEF, left ventricular total emptying fraction; LATEF, left atrial total emptying fraction; OR, odds ratio; CI, confidence interval.

(BNP) levels have an increased risk of hospitalization and death compared to HFpEF patients with normal BNP levels (17). Since BNP levels are easily measured and contribute to identifying HFpEF, elevated BNP levels in the plasma has served as an inclusion criterion in a large number of clinical trials on HFpEF and is even recommended in contemporary guidelines (18). However, in our study, there was no significant difference in the NT-proBNP levels between the two groups, which may be due to ethnic differences in the incidence of HFpEF and the type of HF (19). Notably, our study determined that hs-cTnI was one of the factors associated with clinical outcomes. Lokaj *et al*. (20) demonstrated that hs-cTnI levels ≥17 ng/L represented an increased risk of poor prognosis in patients with HF, and elevated hs-cTnI was a risk factor for HFpEF in Black adults; however, the specific mechanism remains unclear (21).

Our study has some limitations that should be noted. Firstly, this is a single-center study, so the results are somewhat regional and cannot be generalized to other regions. Considering this limitation, the sample size needs to be expanded. Secondly, this study did not analyze whether characteristics such as obesity or diabetes were associated with clinical outcomes in HFpEF patients.

Conclusions

In summary, compared with the non-event group patients, the LVM, LVEDVI, LVESVI, LAEDVI, and LAESVI are significantly increased in HFpEF patients with adverse events, whereas the LVTEF and LATEF are significantly decreased in these patients. Cardiac function indicators obtained by CT scanning can serve as predictive factors of clinical outcomes, and the E/e', LAEDVI, LVM, LVTEF, and LATEF are related factors affecting the clinical outcomes of HFpEF patients.

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Footnote

Reporting Checklist: The authors have completed the STARD reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-5549/rc

Data Sharing Statement: Available at https://atm.amegroups.com/article/view/10.21037/atm-22-5549/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-5549/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by ethics committee of the Affiliated Hospital of Putian University. Individual consent for this retrospective analysis was waived.

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