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Incidence and risk factors of heart failure with preserved ejection fraction in elderly patients with hypertension

Min Chen[1*], Wentao Li[2] and Qin Ran[1]

Abstract

Background Heart failure with preserved ejection fraction (HFpEF) poses a significant clinical challenge, especially in older patients with HT. This study aimed to identify the factors influencing HFpEF occurrence in elderly patients with HT.

Methods Elderly patients with HT were categorized into two groups: no HFpEF group and HFpEF group based on HFpEF diagnosis. Demographic, clinical, laboratory and echocardiographic data was conducted. Logistic regression analysis and joint prediction modeling were used to identify predictive factors for HFpEF.

Results Several factors were associated with HFpEF, including age, body mass index, duration of HT, atrial fibrillation (AF), chronic kidney disease (CKD), stroke, systolic blood pressure (SBP), serum creatinine (SCr), N-terminal pro brain natriuretic peptide (NT-proBNP), heart rate, serum sodium, low density lipoprotein cholesterol (LDL-c), triglyceride, left ventricular ejection fraction (LVEF), E/e' ratio, left atrial diameter, tricuspid regurgitation velocity, mitral regurgitation and C-reactive protein (CRP) levels. The joint prediction model shown high accuracy, with an area under the curve (AUC) of 0.840.

Conclusions This study provided insights into the incidence rate and risk factors of HFpEF in elderly patients with HT. Key determinants included age, blood pressure, biomarkers, and echocardiographic parameters.

Keywords Incidence rate, Risk factors, HFpEF, Elderly, Hypertension

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Introduction

Heart failure with preserved ejection fraction (HFpEF) has become a complex and common clinical condition, particularly among older individuals with hypertension (HT) [1, 2]. As the population continues to age, the burden of HFpEF is expected to increase, necessitating a comprehensive understanding of its incidence rate and associated risk factors [3, 4]. HFpEF, characterized by diastolic dysfunction and maintained left ventricular ejection fraction (LVEF), accounts for a substantial portion of heart failure cases, especially in the elderly population [5–7]. With a complex pathophysiology involving comorbidities, aging-related changes, and inflammatory

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processes, HFpEF presents unique diagnostic and therapeutic challenges [8, 9]. HT, as a prevalent cardiovascular risk factor, is intricately linked to the development and progression of HFpEF, further emphasizing the need for detailed investigation into the incidence rate and specific risk factors of HFpEF in elderly patients with HT [10–12]. Recent studies have highlighted the importance of statistical models in predicting survival time and identifying risk factors for patients with heart failure. For instance, Ashine et al. [13] used Bayesian methods to evaluate the survival time of heart failure patients, demonstrating the potential of advanced statistical approaches in this field. Similarly, Ashine et al. [14] applied a Bayesian accelerated failure time (AFT) shared frailty model combined with integrated nested Laplace approximation to estimate time-to-death and identify risk predictors for heart failure patients. These studies highlight the value of complex statistical techniques in understanding the heterogeneity of heart failure outcomes and identifying high-risk patients. However, despite these advancements, there remains a need for comprehensive risk prediction models specifically targeting elderly HT patients with HFpEF. Current research has largely focused on individual risk factors and their associations with HFpEF, but there is a lack of integrated approaches that consider the interplay between demographic, clinical, laboratory, and echocardiographic factors [15]. To address this gap, our study aimed to conduct a thorough analysis of these factors to identify predictive elements linked to HFpEF in elderly patients with HT.

Methods

Study design and population

This study employed a retrospective case-control design. Elderly patients with HT admitted to our hospital between January 2020 and May 2023 were stratified into two groups based on the development of HFpEF: the no HFpEF group and HFpEF group. Patients in the HFpEF group met the diagnostic criteria for HFpEF outlined by the European Society of Cardiology [16]. The no HFpEF group consisted of patients without heart failure. Inclusion Criteria: (1) patients exhibited signs of left atrial or right atrial enlargement or left ventricular hypertrophy on echocardiography, and were diagnosed with primary HT based on the diagnostic criteria in the "Chinese Guidelines for the Prevention and Treatment of Hypertension" (systolic blood pressure > 140mmHg and diastolic blood pressure > 90mmHg) [17]; (2) patients had a disease duration of > 5 years, were receiving treatment with one of the following medications: diuretics, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, angiotensin receptor-neprilysin inhibitors, calcium channel blockers or beta-blockers, and had a LVEF of ≥ 50% on echocardiography; (3) age ≥ 65 years;

(4) patients were conscious and in a stable condition. Exclusion Criteria: (1) patients with heart failure with reduced ejection fraction (HFrEF) and heart failure with mid-range ejection fraction (HFmrEF) (LVEF < 50%); (2) patients with various secondary HT or severe infectious diseases; (3) patients with coronary artery stenosis exceeding 50%; (4) patients who had a history of myocardial infarction, heart valve disease, chronic kidney insufficiency, dilated cardiomyopathy, hypertrophic cardiomyopathy, or rheumatic heart valve disease within the previous three months; (5) patients with malignant tumors.

Date collection

Data was systematically obtained from medical records. Moreover, 5 mL of fasting venous blood was drawn from the patient's elbow, and serum separation was performed. Serum levels of hemoglobin, serum creatinine (SCr), N-terminal pro-brain natriuretic peptide (NT-proBNP), serum sodium and serum potassium were measured using a fully automatic biochemical analyzer (BS-280, Mindray, China). C-reactive protein (CRP) levels were quantified using the enzyme-linked immunosorbent assay (ELISA). Blood plasma, obtained after heparin anticoagulation and centrifugation, was used to assess total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-c), and high-density lipoprotein cholesterol (HDL-c) using enzymatic colorimetric techniques.

Echocardiographic examination

Echocardiography was performed using an ultrasound diagnostic instrument equipped with an M5Sc 2D probe (2-4.5 MHz) and a 4Vc 4D probe (2.5-4 MHz). Patients were positioned in the left lateral decubitus position. During image acquisition, patients were instructed to breathe calmly or, if necessary, to hold their breath to ensure clear and stable images. The following measurements were taken: LVEF, left atrial diameter, E/e' ratio and heart rate. Pulsed-wave Doppler sampling at the mitral valve orifice was used to assess of mitral regurgitation. Continuous-wave Doppler measured tricuspid regurgitation velocity.

Statistical analysis

Using G*Power 3.1.9.7, the "Means: Difference between two independent means (two groups)" option under t tests was selected for Post hoc analysis. The settings were as follows: Two tails mode, Effect size d = 0.6, α err prob = 0.05. Subsequently, the sample sizes of the two groups were entered, and the Power (1-β err prob) was calculated, resulting in a Power of 0.867. SPSS 29.0 statistical software (SPSS Inc., Chicago, IL, USA) was utilized for data analysis. Normally distributed continuous data

Table 1 Demographic characteristics

Parameter	No HFpEF group (n=110)	HFpEF group (n=35)	t/χ²	P
Age (years)	68.45±4.12	70.24±3.78	2.392	0.020
Gender				
Male	55 (50.00%)	16 (45.71%)	0.061	0.804
Female	55 (50.00%)	19 (54.29%)		
Body mass index (kg/m²)	26.91±6.56	30.25±6.89	2.533	0.014
Smoking	40 (36.36%)	14 (40.00%)	0.035	0.852
Drinking	35 (31.82%)	12 (34.29%)	0.004	0.949
Duration of hypertension (years)	10.58±3.57	11.97±2.96	2.299	0.025
Diabetes	30 (27.27%)	15 (42.86%)	2.329	0.127
CAD	20 (18.18%)	10 (28.57%)	1.171	0.279
AF	15 (13.64%)	11 (31.43%)	4.567	0.033
CKD	10 (9.09%)	9 (25.71%)	5.067	0.024
Stroke	5 (4.55%)	6 (17.14%)	4.348	0.037
PAD	25 (22.73%)	9 (25.71%)	0.018	0.893

Note: CAD=Coronary artery disease; AF=Atrial fibrillation; CKD=Chronic kidney disease; PAD=Peripheral arterial disease

Table 2 Clinical characteristics of study participants

Parameter	No HFpEF group (n=110)	HFpEF group (n=35)	t	P
SBP (mm/Hg)	140.23±10.26	145.23±12.15	2.195	0.033
DBP (mm/Hg)	94.46±3.48	96.26±3.59	2.645	0.009
SCr (mg/dL)	1.12±0.27	1.27±0.33	2.468	0.017
NT-proBNP (pg/mL)	472.14±50.17	520.46±100.28	2.743	0.009
Heart rate (bpm)	78.23±5.49	80.47±6.47	1.851	0.070
Hemoglobin (g/dL)	14.13±1.03	13.85±1.25	1.175	0.245

Note: SBP=Systolic Blood Pressure; DBP=Diastolic Blood Pressure; SCr=Serum Creatinine; NT-proBNP=N-terminal pro-brain natriuretic peptide

were presented in the format (mean±SD). Categorical data were represented using [n (%)] and the chi-square test was employed. Normal distribution of continuous variables was evaluated using the Shapiro-Wilk method. A two-sided $P<0.05$ was considered statistically significant. Covariates demonstrating significant differences in both the difference analysis were included in the logistic regression analysis. Variables with differences in logistic regression analysis were included receiver operating characteristic (ROC) analysis. The predictive value of each index for the occurrence of HFpEF in elderly patients with HT was evaluated using the area under the curve (AUC).

Results

Demographic characteristics
Based on the table, elderly patients with HT with HFpEF had a significantly higher mean age (70.24±3.78 vs. 68.45±4.12 years, $P=0.020$), higher body mass index (30.25±6.89 vs. 26.91±6.56, $P=0.014$), longer duration of hypertension (11.97±2.96 vs. 10.58±3.57 years, $P=0.025$), higher proportion of atrial fibrillation (31.43% vs. 13.64%, $P=0.033$), higher proportion of chronic kidney disease (25.71% vs. 9.09%, $P=0.024$) and higher proportion of stroke(17.14% vs. 4.55%, $P=0.037$) compared

to those without HFpEF (Table 1). No significant differences were found in gender distribution, smoking habits, drinking habits, diabetes prevalence, coronary artery disease, and peripheral arterial disease between the two groups ($P>0.05$).

Clinical characteristics
The HFpEF group showed significantly higher systolic blood pressure (145.23 vs. 140.23 mmHg, $P=0.033$) and diastolic blood pressure (96.26 vs. 94.46 mmHg, $P=0.009$) compared to the non-HFpEF group (Table 2). SCr and NT-proBNP levels were also significantly higher in the HFpEF group. However, no differences were found in heart rate and hemoglobin levels between the two groups.

Laboratory tests
In the elderly hypertensive patient population, the HFpEF group showed significantly lower serum sodium levels ($P=0.005$), HDL cholesterol levels ($P=0.026$) and higher LDL cholesterol levels ($P=0.005$), triglycerides ($P=0.012$) and CRP ($P=0.028$) compared to the non-HFpEF group (Table 3). However, no significant variations were found in the serum potassium and total cholesterol levels.

Table 3 Laboratory tests of study participants

Parameter	No HFpEF group	HFpEF group	t	P
	(*n* = 110)	(*n* = 35)		
Serum sodium (mmol/L)	140.25 ± 2.48	138.52 ± 3.14	2.978	0.005
Serum potassium (mmol/L)	4.18 ± 0.36	4.28 ± 0.47	1.19	0.24
TC (mmol/L)	5.23 ± 0.85	5.57 ± 0.96	1.828	0.073
LDL-c (mmol/L)	3.16 ± 0.67	3.58 ± 0.75	2.947	0.005
HDL-c (mmol/L)	1.15 ± 0.31	1.04 ± 0.23	2.268	0.026
Triglycerides (mmol/L)	1.48 ± 0.57	1.83 ± 0.71	2.626	0.012
CRP (mg/L)	3.09 ± 0.58	3.51 ± 1.05	2.275	0.028

Note: TC = Total Cholesterol; LDL-c = low-density lipoprotein cholesterol; HDL-c = high-density lipoprotein cholesterol; CRP = C-reactive protein

Table 4 Echocardiographic parameters of study participants

Parameter	No HFpEF group	HFpEF group	t/χ^2	P
	(*n* = 110)	(*n* = 35)		
LVEF (%)	53.36 ± 5.14	50.26 ± 8.13	2.12	0.040
E/e' Ratio	10.65 ± 2.69	12.38 ± 3.24	2.851	0.006
Left Atrial Diameter (mm)	38.26 ± 3.51	40.27 ± 5.16	2.152	0.037
Tricuspid Regurgitation Velocity (m/s)	2.08 ± 0.53	2.38 ± 0.72	2.293	0.026
Mitral Regurgitation				
Mild	58 (52.73%)	10 (28.57%)	6.229	0.044
Moderate	42 (38.18%)	20 (57.14%)		
Severe	10 (9.09%)	5 (14.29%)		

Note: LVEF = Left Ventricular Ejection Fraction

Echocardiographic parameters

The HFpEF group showed a significantly reduced LVEF (*P* = 0.040) and elevated E/e' ratio (*P* = 0.006), left atrial diameter (*P* = 0.037) and tricuspid regurgitation velocity (*P* = 0.026) compared to the non-HFpEF group (Table 4). In addition, mitral regurgitation in the no HFpEF group was mainly mild, while in the HFpEF group, it was predominantly moderate (*P* = 0.044).

Logistic regression analysis

Age, body mass index, duration of hypertension, atrial fibrillation, chronic kidney disease, stroke, systolic blood pressure, SCr levels, NT-proBNP, heart rate, serum sodium, LDL cholesterol, triglyceride levels, LVEF, E/e' ratio, left atrial diameter, tricuspid regurgitation velocity, mitral regurgitation and CRP levels all demonstrated significant correlations with HFpEF in elderly patients with HT (Table 5).

ROC analysis

The predictive value of each risk factor for the occurrence of HFpEF in elderly patients with HT was comprehensively evaluated. Sensitivities and specificities were computed for each parameter, resulting in specific values for the AUC and the Youden index (Table 6). Among the parameters assessed, the AUC ranged from 0.563 to 0.678, demonstrating varying degrees of predictive power, with diastolic blood pressure and NT-proBNP showing relatively higher AUC values. These results offer

valuable perspective on how these risk factors could be utilized to predict the onset of HFpEF in elderly individuals with HT. Finally, this study combined significant predictive risk factors to construct a joint model for predicting the occurrence of HFpEF in elderly patients with HT. The results demonstrated an AUC value of 0.840 for the joint model (Fig. 1), suggesting that the combined factors model holds a significantly high predictive ability for the occurrence of HFpEF in elderly patients with HT.

Discussion

The frequency and determining factors of HFpEF in elderly individuals with HT have gained increasing attention in cardiovascular medicine. This retrospective case-control study aimed to clarify the frequency and risk factors for HFpEF in elderly patients with HT. The demographic characteristics of the study participants revealed several notable associations between age, body mass index, duration of hypertension, atrial fibrillation, chronic kidney disease, stroke, and the occurrence of HFpEF. The logistic regression analysis underscored the significant predictive value of these demographic factors in relation to HFpEF, with age, body mass index, duration of hypertension, atrial fibrillation, chronic kidney disease, and stroke emerging as independent risk factors for the development of HFpEF. These findings align with existing literature [18–20], emphasizing the cumulative impact of aging, comorbidities, and cardiovascular risk factors on HFpEF pathogenesis. Notably, the observed correlations

Table 5 Logistic regression analysis between risk factors and HFpEF in elderly patients with HT

Parameter	Odds ratio	95%CI	P
Age	1.120	1.016–1.244	0.026
Body mass index	1.076	1.017–1.143	0.013
Duration of Hypertension	1.129	1.008–1.274	0.041
AF	2.903	1.166–7.124	0.02
CKD	3.462	1.257–9.48	0.015
Stroke	4.345	1.227–16.064	0.022
SBP	1.044	1.007–1.084	0.021
DBP	1.119	1.046–1.204	0.002
SCr	6.745	1.709–29.331	0.008
NT-proBNP	1.010	1.005–1.017	< 0.001
Heart Rate	1.070	1.001–1.146	0.049
Serum Sodium	0.783	0.666–0.908	0.002
LDL-c	2.385	1.36–4.375	0.003
Triglycerides	2.591	1.356–5.214	0.005
LVEF	0.920	0.86–0.98	0.011
E/e' Ratio	1.237	1.079–1.435	0.003
Left Atrial Diameter	1.136	1.031–1.264	0.013
Tricuspid Regurgitation Velocity	2.463	1.261–5.087	0.011
Mitral Regurgitation	1.918	1.089–3.436	0.025
CRP	2.197	1.296–3.899	0.005

Note: AF=Atrial Fibrillation; CKD=Chronic Kidney Disease; SBP=Systolic Blood Pressure; DBP=Diastolic Blood Pressure; SCr=Serum Creatinine; NT-proBNP=N-terminal pro-brain natriuretic peptide; LDL-c=low-density lipoprotein cholesterol; LVEF=Left Ventricular Ejection Fraction; CRP=C-reactive protein

Table 6 The predictive value of each risk factor for the occurrence of HFpEF in elderly patients with HT

Parameter	Sensitivities	Specificities	AUC	Youden index
Age	0.486	0.755	0.619	0.241
Body mass index	0.771	0.509	0.644	0.28
Duration of Hypertension	0.914	0.327	0.61	0.241
AF	0.314	0.864	0.589	0.178
CKD	0.257	0.909	0.583	0.166
Stroke	0.171	0.955	0.563	0.126
SBP	0.771	0.464	0.629	0.235
DBP	0.743	0.609	0.678	0.352
SCr	0.314	0.964	0.622	0.278
NT-proBNP	0.571	0.836	0.655	0.407
Serum Sodium	0.429	0.891	0.663	0.32
LDL-c	0.629	0.673	0.659	0.302
Triglycerides	0.429	0.891	0.646	0.320
LVEF	0.543	0.727	0.621	0.270
E/e' Ratio	0.629	0.655	0.651	0.284
Left Atrial Diameter	0.657	0.618	0.631	0.275
Tricuspid Regurgitation Velocity	0.743	0.536	0.635	0.279
Mitral Regurgitation	0.714	0.527	0.622	0.241
CRP	0.314	1.000	0.63	0.314

Note: AF=Atrial Fibrillation; CKD=Chronic Kidney Disease; SBP=Systolic Blood Pressure; DBP=Diastolic Blood Pressure; SCr=Serum Creatinine; NT-proBNP=N-terminal pro-brain natriuretic peptide; LDL-c=low-density lipoprotein cholesterol; LVEF=Left Ventricular Ejection Fraction; CRP=C-reactive protein

and predictive associations emphasize the importance of comprehensive geriatric assessment and targeted management strategies for elderly patients with HT at risk of HFpEF.

Elevated blood pressure has been widely recognized as a major factor in the development and progression of HFpEF [21–23]. This investigation revealed that the clinical features of the HFpEF group exhibited notably elevated levels of both systolic and diastolic blood pressure in comparison to the non-HFpEF group. Moreover, the logistic regression analysis validated the predictive significance of systolic and diastolic blood pressure concerning the occurrence of HFpEF, underscoring the pivotal role of HT in the pathophysiology of HFpEF. These
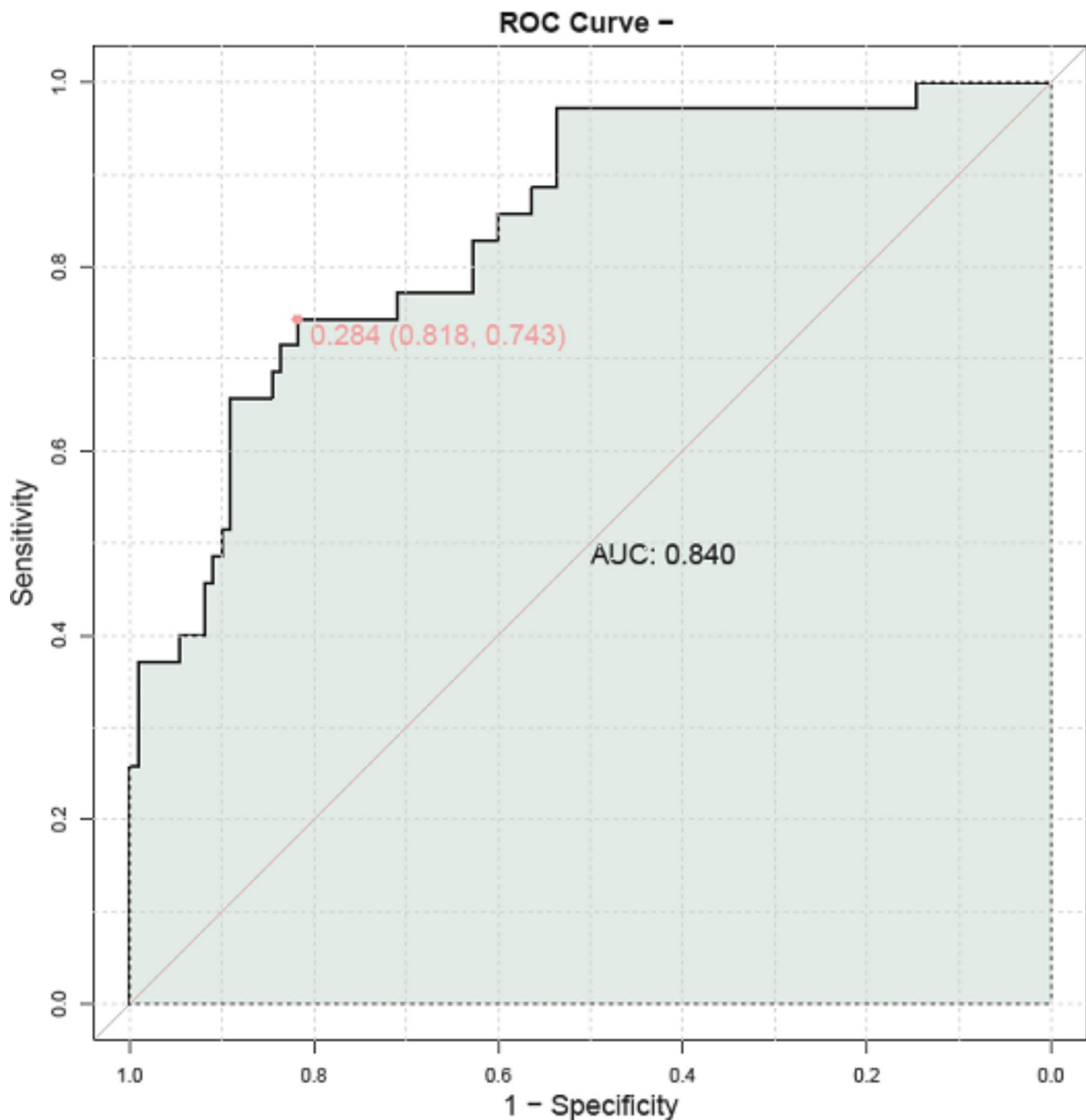
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Fig. 1 ROC curve analysis of joint prediction model for HFpEF in elderly patients with HT

findings highlight the importance of aggressive blood pressure control and targeted antihypertensive therapies in mitigating the risk of HFpEF in elderly patients with HT.

The laboratory examinations in this research offered valuable perspectives on the correlation between particular biomarkers and HFpEF in elderly individuals with HT. Notably, serum Cr and NT-proBNP emerged as strong predictors of HFpEF occurrence, consistent with their established roles as markers of renal function and cardiac

stress, respectively. Additionally, the correlation between serum sodium levels and HFpEF implies a possible connection between electrolyte imbalances and cardiac dysfunction in these patients. These results underscore the potential utility of renal and cardiac biomarkers in risk stratification and prognostication in elderly patients with HT at risk of HFpEF.

Echocardiographic parameters are crucial in diagnosing and characterizing HFpEF [24–26], and the findings from this study align with established echocardiographic

features of HFpEF. Specifically, the HFpEF group demonstrated significantly lower LVEF, higher E/e' ratio, left atrial diameter and tricuspid regurgitation velocity compared to the non-HFpEF group. Significantly, these echocardiographic parameters were recognized as important indicators of HFpEF occurrence in the logistic regression analysis, emphasizing their diagnostic and prognostic significance in elderly individuals with HT who are suspected of having HFpEF. These findings emphasize the central role of echocardiography in the comprehensive assessment of elderly patients with HT at risk of HFpEF, supporting the incorporation of these parameters into risk prediction models and clinical decision-making algorithms.

Inflammatory markers have garnered increasing attention in the context of HFpEF, reflecting the intertwined relationships between inflammation, endothelial dysfunction, and cardiovascular disease [27–29]. In this investigation, higher CRP levels were observed in the HFpEF group, suggesting a possible pro-inflammatory environment associated with HFpEF in elderly individuals with HT. The logistic regression analysis further confirmed the predictive value of CRP, underscoring their potential as novel targets for risk stratification and therapeutic interventions in HFpEF. These findings support the rationale for exploring anti-inflammatory strategies in the management of HFpEF and highlight the need for further research into the mechanistic links between inflammation, HT, and HFpEF pathophysiology.

The logistic regression equation facilitated the identification of a constellation of risk factors and biomarkers associated with HFpEF in elderly patients with HT. Notably, these findings reflect the multifaceted nature of HFpEF pathogenesis and underscore the importance of a multidimensional approach to risk assessment and management in this patient population. The joint prediction model constructed in this study further demonstrated a significantly high predictive value, with an AUC of 0.873. This underscores the potential utility of integrating demographic, clinical, laboratory and echocardiographic into a comprehensive risk prediction model for HFpEF, offering a practical tool for risk stratification and prognostication in real-world clinical settings.

The study has several limitations that should be recognized. First, its retrospective nature could have introduced inherent biases and limitations in the collection and analysis of data. Moreover, the study cohort was derived from a single-center setting, potentially limiting the generalizability of the findings to wider patient populations. Currently, the combined prediction model in this study has not been validated in an independent external dataset. Although internal validation results show that the model has high predictive performance, external validation is a critical step to assess the model's generalizability. Future studies should use independent cohort data to externally validate the model to ensure its stability and reliability across different populations. Despite including multiple important risk factors in the model, there may still be unconsidered confounding factors. For example, lifestyle factors (such as diet and physical activity), socioeconomic status, and medication adherence can significantly influence the development of HFpEF. Due to data limitations, these factors were not included in our analysis. Future research should further explore these potential confounders and incorporate them into the model to enhance predictive accuracy. Additionally, the observational design of the study precludes causal inferences, and further prospective studies were warranted to confirm the predictive value of the identified risk factors and biomarkers in relation to HFpEF occurrence in elderly patients with HT.

Conclusions

In conclusion, this study provides valuable insights into the frequency and risk factors of HFpEF in elderly patients with HT. Key determinants include age, blood pressure, biomarkers and echocardiographic parameters. These findings have implications for risk assessment, early identification, and targeted interventions. Future research should validate these findings in diverse population and explore additional confounders to improve clinical outcomes for HFpEF patients.

Abbreviations

HFpEF	Heart failure with preserved ejection fraction
HT	Hypertension
LVEF	Left ventricular ejection fraction
HFrEF	Heart failure with reduced ejection fraction
HFmrEF	Heart failure with mid-range ejection fraction
SCr	Serum creatinine
NT-proBNP	N-terminal pro-brain natriuretic peptide
CRP	C-reactive protein
ELISA	Enzyme-linked immunosorbent assay
TC	Total cholesterol
TG	Triglycerides
HDL-c	High-density lipoprotein cholesterol
LDL-c	Low-density lipoprotein cholesterol
ROC	Receiver operating characteristic
AUC	Area under the curve
CAD	Coronary artery disease
AF	Atrial fibrillation
CKD	Chronic kidney disease
PAD	Peripheral arterial disease
SBP	Systolic blood pressure
DBP	Diastolic blood pressure

Declarations

Ethics approval and consent to participate
This study received approval from the Institutional Review Board and Ethics Committee of Chengdu Seventh People's Hospital. Informed consent was waived for this retrospective study because it solely utilized de-identified patient data, which had no potential harm or impact on patient care. The Institutional Review Board and Ethics Committee of Chengdu Seventh People's Hospital granted approval for this waiver in accordance with the regulatory and ethical guidelines governing retrospective research studies.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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