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ORIGINAL RESEARCH

Assessing Established Diagnostic Markers of HFpEF in Older Patients Presenting with Acute Dyspnoea in the Emergency Department

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Background: Heart failure with preserved ejection fraction (HFpEF) is common yet diagnostically challenging in older adults presenting with acute dyspnoea to the emergency department (ED). This study evaluated the diagnostic performance of established markers used in HFpEF assessment, including echocardiographic indices, NT-proBNP, and the H_2FPEF score, in identifying newly diagnosed HFpEF in this population.

Methods: Between September 2024 and May 2025, we conducted a prospective observational study of patients aged ≥60 years presenting to the ED of a tertiary hospital in Vietnam with acute dyspnoea. HFpEF was identified using the 2021 European Society of Cardiology (ESC) guidelines, which served as the gold-standard diagnostic framework. Baseline characteristics were compared between HFpEF and non-HFpEF groups, and the diagnostic performance of candidate markers was assessed using receiver operating characteristic curve analysis.

Results: Among 280 enrolled patients, 118 (42.1%) were newly diagnosed with HFpEF. Sociodemographic, geriatric, clinical, and comorbidity characteristics were comparable between groups. Patients with HFpEF had significantly higher NT-proBNP levels (median 2205 pg/mL vs 150 pg/mL, p<0.001), left ventricular mass index (LVMI) (118.0 ± 12.1 g/m^2 vs 93.4 ± 15.9 g/m^2, p<0.001), and H_2FPEF scores (median 7 vs 4, p<0.001). NT-proBNP ≥760 pg/mL (AUC 0.979, 95% confidence interval [CI] 0.964–0.994; Youden index 0.91), LVMI ≥108 g/m^2 (AUC 0.889, 95% CI 0.851–0.927; Youden index 0.62), and an H_2FPEF scores ≥6 (AUC 0.861, 95% CI 0.818–0.903; Youden index 0.71) demonstrated strong discriminatory performance. Diastolic indices alone showed poor discriminatory ability (AUC <0.55).

Conclusion: In older adults presenting with acute dyspnoea, NT-proBNP, LVMI, and the H_2FPEF score demonstrated good discriminatory ability for newly diagnosed HFpEF. However, the diagnostic performance of NT-proBNP and LVMI should be interpreted with caution, as both are included in the ESC diagnostic framework. Diastolic indices showed limited diagnostic value, likely because diastolic abnormalities were also common among non-HFpEF patients, highlighting an important methodological constraint.

Keywords: HFpEF, NT-proBNP, H_2FPEF score, emergency department, older adults

Background

Heart failure with preserved ejection fraction (HFpEF) has emerged as a major public health concern, accounting for nearly half of all heart failure (HF) cases worldwide.[1] It is particularly prevalent among older adults and is associated with substantial morbidity, impaired quality of life, and frequent hospitalisations.[2] Despite its high prevalence and clinical burden, HFpEF remains one of the most diagnostically challenging syndromes in cardiovascular medicine, especially in acute care settings. The diagnostic difficulty arises from its heterogeneous pathophysiology, frequent coexistence of multiple comorbidities, and considerable symptom overlap with other cardiopulmonary disorders, particularly among older individuals.[3] One key example is atrial fibrillation (AF), a common age-related comorbidity

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that can significantly influence natriuretic peptide concentrations and diastolic parameters, sometimes independently of HFpEF, thereby increasing diagnostic complexity in this population.[4]

In the emergency department (ED), accurate and timely recognition of HFpEF is essential for guiding appropriate management. However, diagnosis in older adults presenting with acute dyspnoea is often hampered by non-specific clinical manifestations. Recent evidence suggests that the integration of multiple diagnostic domains, including clinical features, biochemical markers and imaging indices, may improve diagnostic accuracy. N-terminal pro B-type natriuretic peptide (NT-proBNP) is an established biomarker of myocardial stress and is recommended by international guidelines as part of the diagnostic evaluation for suspected HF.[5] The H_2FPEF score offers a pragmatic composite tool that has demonstrated utility in diverse clinical settings.[6] Echocardiography remains central to HFpEF assessment, particularly for identifying structural cardiac abnormalities and evaluating diastolic function or elevated left ventricular filling pressures.[7]

In the emergency setting, assessing the individual diagnostic contribution of NT-proBNP and structural or functional echocardiographic indices may be particularly valuable when full application of the European Society of Cardiology (ESC) diagnostic algorithm is not immediately feasible. These markers are often available early and can support the initial clinical assessment while more comprehensive investigations are being arranged. However, because NT-proBNP and structural cardiac abnormalities form part of the ESC 2021 HFpEF diagnostic criteria, a degree of diagnostic circularity may arise when their performance is evaluated.[5] Recognising this methodological issue is important for placing the interpretation of these markers within the wider diagnostic framework for HFpEF.

Evidence on the performance of established HFpEF markers in the ED remains limited, particularly in low- and middle-income countries where healthcare resources may be constrained.[8] Most existing studies have focused on chronic HFpEF or heterogeneous patient populations rather than specifically on older adults with acute presentations,[9] in whom rapid diagnosis is both challenging and clinically important. To address this gap, the present study aimed to evaluate the diagnostic value of established HFpEF markers, including echocardiographic indices, NT-proBNP and the H_2FPEF score, in older adults presenting with acute dyspnoea to the ED.

Methods

Study Design, Population, and Setting

We conducted a prospective observational study in the ED of Thong Nhat Hospital, a tertiary care centre in Ho Chi Minh City, Vietnam. Patient screening and enrolment were carried out between September 2024 and May 2025. The study protocol was approved by the Institutional Ethics Committee of Thong Nhat Hospital (Approval No. 119/2024/CN-BVTN-HĐĐĐ). Written informed consent was obtained from all participants or their legal representatives in accordance with the Declaration of Helsinki. Clinical trial registration was not applicable.

Patients aged ≥60 years who presented with acute dyspnoea were screened for eligibility. Eligible participants underwent baseline clinical assessment, echocardiography and laboratory testing. Exclusion criteria were as follows: (1) a prior diagnosis of HF, (2) left ventricular ejection fraction (LVEF) <50% on the index echocardiogram, (3) acute coronary syndrome, (4) active malignancy, (5) pulmonary embolism, (6) primary moderate-to-severe mitral or aortic valve disease, (7) septic shock, and (8) refusal to participate.

Diagnosis of HFpEF

In this study, the gold standard for confirming HFpEF was a composite diagnostic algorithm based on the 2021 ESC guidelines.[5] This required the presence of signs or symptoms of HF such as dyspnoea, orthopnoea, peripheral oedema or pulmonary crackles, a LVEF ≥50%, and objective evidence of cardiac structural or functional abnormalities consistent with left ventricular diastolic dysfunction or elevated left ventricular filling pressures, including raised natriuretic peptides. Patients who did not meet the ESC criteria for HFpEF were categorised as the non-HFpEF group, and their final diagnoses were recorded.

According to the ESC guidelines, the likelihood of HFpEF increases when more structural or functional abnormalities are present. For this study, HFpEF was diagnosed only when all three required components were fulfilled.[5] These components included structural cardiac abnormalities, diastolic dysfunction or elevated left ventricular filling pressures, and elevated NT-proBNP. Structural abnormality required at least one abnormal parameter, including increased left ventricular mass index (LVMI) defined as ≥95 g/m^2 for women or ≥115 g/m^2 for men, or increased relative wall thickness (RWT) defined as >0.42. Diastolic dysfunction or elevated left ventricular filling pressure was considered present when at least one of the following criteria was met: increased left atrial volume index (LAVI) defined as >34 mL/m^2 in sinus rhythm or >40 mL/m^2 in AF, elevated average E/e′ defined as ≥14, or maximal tricuspid regurgitation velocity (TR Vmax) ≥2.8 m/s or pulmonary artery systolic pressure (PASP) ≥35 mmHg. The biomarker criterion required elevated NT-proBNP defined as ≥300 pg/mL in sinus rhythm or ≥739 pg/mL in AF.[10]

Data Collection

Baseline sociodemographic, geriatric, clinical and comorbidity characteristics were collected through direct patient interviews and review of medical records. Age was categorised as <75 or ≥75 years, and sex as men or women. Body mass index (BMI) was classified according to the World Health Organisation guidelines for the Asia Pacific region.[11] Clinical symptoms and signs were documented by a cardiologist with more than five years of clinical experience. Blood pressure was recorded at ED admission, and New York Heart Association (NYHA) class was determined based on functional status during the preceding week.

Functional status was assessed using the Katz Activities of Daily Living and the Lawton Instrumental Activities of Daily Living indices. Patients were considered functionally limited if they were unable to complete ≥1 task in each respective index. Frailty was evaluated using the Clinical Frailty Scale, with a score ≥5 (range 1 to 9) indicating frailty. Cognitive impairment was defined as a Mini Mental State Examination score <24.

Transthoracic echocardiography was performed within 8 hours of admission in haemodynamically stable patients who were not receiving vasopressors. All examinations were conducted using a Sonoscape X5 system (SonoScape Medical Corp.) by a cardiologist with 10 years of experience and a routine workload of at least 100 studies per week, who was fully blinded to NT-proBNP values and all other clinical information at the time of imaging. Studies with suboptimal image quality were jointly reviewed with a second cardiologist of equivalent expertise, and patients were excluded if consensus could not be reached. Measurements were performed according to the guidelines of the American Society of Echocardiography and the European Association of Cardiovascular Imaging.[12] LVEF was assessed using Simpson's biplane method. Left ventricular hypertrophy (LVH) patterns were classified as: (1) normal geometry defined as normal LVMI and RWT, (2) concentric remodelling defined as normal LVMI with increased RWT, (3) eccentric hypertrophy defined as increased LVMI with normal RWT, and (4) concentric hypertrophy defined as increased LVMI and RWT.

The H_2FPEF score was calculated for all participants based on its six components, including BMI, use of anti-hypertensive medications, AF, age, the E/e′ ratio and PASP. Each component was assigned its predefined point value, yielding a total score from 0 to 9. In the original scoring system, a score of 0 to 1 indicates low probability of HFpEF, a score of 2 to 5 indicates intermediate probability and a score of 6 to 9 indicates high probability.[13,14] For this study, a score ≥6 was considered suggestive of HFpEF. Laboratory testing, including NT-proBNP, was performed at ED presentation in accordance with hospital protocols. Blood samples were collected within 1 hour of admission, and NT-proBNP was measured using a chemiluminescent immunoassay (Cobas Pro e801 analyser, Roche Diagnostics).

Statistical Analysis

Categorical variables were expressed as frequencies and percentages. Continuous variables were summarised as mean ± standard deviation (SD) or median with interquartile range (IQR), depending on the distribution assessed by the Shapiro–Wilk test. Comparisons between the HFpEF and non HFpEF groups were conducted using Student's *t* test or the Mann–Whitney *U*-test for continuous variables, and the Chi-square test or Fisher's exact test for categorical variables. The diagnostic performance of NT-proBNP, the H_2FPEF score and echocardiographic indices for HFpEF was evaluated using the area under the receiver operating characteristic (ROC) curve (AUC). Optimal cut-offs were derived from ROC curves using the Youden index [(sensitivity + specificity) – 1]. A two tailed p value <0.05 was considered statistically significant. All statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA).

Sample Size

Sample size was initially calculated using a single population proportion formula: $n = Z^2_{1-\alpha/2}*[p*(1-p)/d^2]$, where n was the required minimum sample size, $Z_{1-\alpha/2}$ was 1.96 for $\alpha = 0.05$ with a 95% confidence interval, and d was the precision, which was set at 0.06. A value of p = 0.5 was selected to yield the maximum variance of 0.25. This calculation resulted in a minimum required sample size of 267 participants. To ensure adequate precision for estimating diagnostic accuracy, we also applied the method proposed by Hajian Tilaki using a two sided $\alpha = 0.05$ and a desired confidence interval half width of d = 0.05.[15] Based on an anticipated AUC of 0.85, the minimum total sample size required was 232 participants, including 116 participants in each group.

Results

During the study period, 429 older patients presented to the ED with acute dyspnoea. Of these, 149 were excluded due to a prior diagnosis of HF (n = 19), LVEF <50% on index echocardiography (n = 50), acute coronary syndrome (n = 31), pulmonary embolism (n = 2), primary severe mitral or aortic valve disease (n = 7), active malignancy (n = 14), septic shock (n = 25) or refusal to participate (n = 1). The enrolment process is shown in Figure 1.

A total of 280 patients met the inclusion criteria. The median age was 78 years (IQR 71.3–85.8; range 61–102), and 118 patients (42.1%) were newly diagnosed with HFpEF. Baseline sociodemographic, geriatric, BMI and comorbidity characteristics were comparable between the HFpEF and non HFpEF groups (Table 1). Among patients in the non HFpEF group, alternative causes of acute dyspnoea included acute pulmonary infections (n = 87), exacerbations of chronic lung disease (n = 13), anaemia (n = 5), uncontrolled hypertension (n = 36) and arrhythmias (n = 21).

At ED presentation, median systolic and diastolic blood pressures, NYHA class distribution and the prevalence of exertional dyspnoea, orthopnoea, paroxysmal nocturnal dyspnoea, chest pain, peripheral oedema and pulmonary crackles did not differ significantly between the two groups. In contrast, the median H_2FPEF score was significantly higher in the HFpEF group, with 93.2% classified as high probability compared with 22.2% in the non HFpEF group. Median NT-proBNP concentrations were also markedly higher in patients with HFpEF, with all values exceeding guideline recommended thresholds, whereas only 7.4% of non HFpEF patients met these thresholds (Table 2).

LVEF was preserved in both groups, with no significant difference in median values. However, structural and functional cardiac abnormalities were significantly more common in HFpEF patients. Increased LVMI, RWT and LAVI were observed more frequently in the HFpEF group. Left ventricular geometry patterns were distinct between

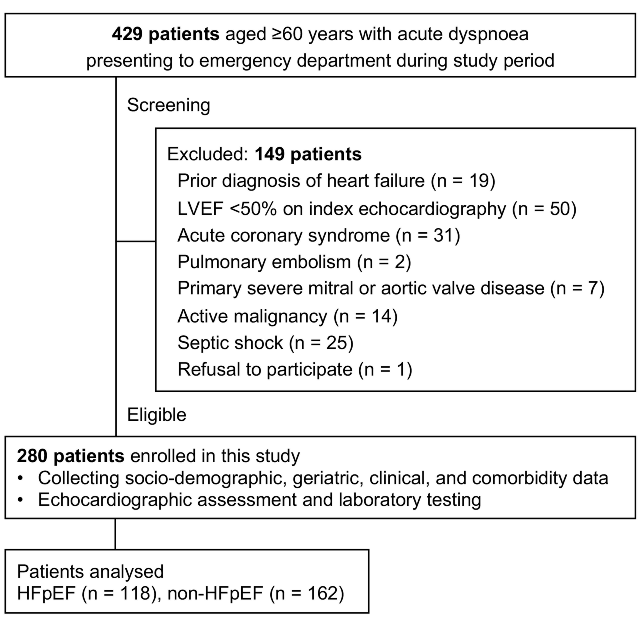

Figure 1 Flow chart of the enrolment of participants.

Table 1 Sociodemographic, Geriatric, and Medical History Characteristics of Participants

Characteristics	Total (n = 280)	HFpEF (n = 118)	Non-HFpEF (n = 162)	p
Sociodemographic characteristics				
Age, years	78.0 (71.3–85.8)	79.0 (71.0–86.0)	78.0 (71.8–85.3)	0.583
Men, n (%)	136 (48.6)	56 (47.5)	80 (49.4)	0.809
BMI groups, n (%)				0.616
Underweight	37 (13.2)	17 (14.4)	20 (12.3)	
Normal	131 (46.8)	54 (45.8)	77 (47.6)	
Overweight	29 (10.4)	15 (12.7)	14 (8.6)	
Obese	83 (29.6)	32 (27.1)	51 (31.5)	
Geriatric characteristics, n (%)				
Limitations in ADLs	115 (41.1)	42 (35.6)	73 (45.1)	0.140
Limitations in IADLs	95 (33.9)	38 (32.2)	57 (35.2)	0.612
Frailty	206 (73.6)	84 (71.2)	122 (75.3)	0.493
Cognitive impairment	82 (29.3)	28 (23.7)	54 (33.3)	0.086
Medical history, n (%)				
Hypertension	256 (91.4)	106 (89.8)	150 (92.6)	0.517
Dyslipidaemia	204 (72.9)	87 (73.7)	117 (72.2)	0.892
Chronic coronary syndromes	203 (72.5)	85 (72.0)	118 (72.8)	0.893
History of stroke	21 (7.5)	9 (7.6)	12 (7.4)	1.000
Atrial fibrillation	158 (56.4)	67 (56.8)	91 (56.2)	1.000
Diabetes mellitus	103 (36.8)	40 (33.9)	63 (38.9)	0.452
Anaemia	145 (51.8)	63 (53.4)	82 (50.6)	0.717
Chronic pulmonary diseases	25 (8.9)	9 (7.6)	16 (9.9)	0.672
Chronic kidney disease	138 (49.3)	60 (50.8)	78 (48.1)	0.717
Stages of chronic kidney disease				0.558
Stage 3a	55 (19.6)	21 (17.8)	34 (21.0)	
Stage 3b	59 (21.1)	25 (21.2)	34 (21.0)	
Stage 4–5	24 (8.6)	14 (11.8)	10 (6.1)	

Notes: Categorical variables are described as frequencies (n) and percentages (%). Age is presented as median and interquartile range (25–75th percentile). Chi-square test was used to compare categorical variables. The Mann–Whitney test was used to compare two medians of age.
Abbreviations: ADLs, activities of daily living; BMI, body mass index; IADLs, instrumental activities of daily living.

groups, with eccentric and concentric hypertrophy predominating in HFpEF patients, whereas normal geometry and concentric remodelling were more common among non HFpEF individuals. TR Vmax and PASP values were significantly higher in the HFpEF group, and nearly all HFpEF patients demonstrated elevated PASP. Diastolic dysfunction or elevated left ventricular filling pressures was present in all HFpEF patients compared with 79.0% of non HFpEF patients (Table 3).

Table 2 Clinical Characteristics and Laboratory Findings of Participants

Characteristics	Total (n = 280)	HFpEF (n = 118)	Non-HFpEF (n = 162)	p
Clinical characteristics				
SBP at admission, mmHg	143 (138–147)	143 (137–147)	142 (138–147)	0.663
DBP at admission, mmHg	83 (81–86)	83 (81–87)	83 (81–86)	0.999
NYHA class before admission, n (%)				0.349
I–II	247 (88.2)	107 (90.7)	140 (86.4)	
III	33 (11.8)	11 (9.3)	22 (13.6)	
Exertional dyspnoea, n (%)	172 (61.4)	71 (60.2)	101 (62.3)	0.711
Paroxysmal nocturnal dyspnoea, n (%)	66 (23.6)	25 (21.2)	41 (25.3)	0.477
Orthopnoea, n (%)	76 (27.1)	29 (24.6)	47 (29.0)	0.419
Chest pain, n (%)	64 (22.9)	28 (23.7)	36 (22.2)	0.775
Peripheral oedema, n (%)	88 (31.4)	35 (29.7)	53 (32.7)	0.605
Pulmonary crackles, n (%)	70 (25.0)	27 (22.9)	43 (26.5)	0.576
H_2FPEF score	6 (4–7)	7 (6–7)	4 (3–5)	<0.001
Interpretation of H_2FPEF				<0.001
Intermediate probability of HFpEF	134 (47.9)	8 (6.8)	126 (77.8)	
High probability of HFpEF	146 (52.1)	110 (93.2)	36 (22.2)	
Laboratory findings				
NT-proBNP, pg/mL	493 (127–2034)	2205 (1316–7297)	150 (62–287)	<0.001
Elevated NT-proBNP, n (%)	130 (46.4)	118 (100)	12 (7.4)	<0.001
Serum sodium, mmol/L	137 (134–139)	137 (135–139)	137 (134–140)	0.860

Notes: Categorical variables are described as frequencies (n) and percentages (%). Continuous variables are presented as median and interquartile range (25–75th percentile). Chi-square test or Fisher's exact test was used to compare categorical variables. The Mann–Whitney test was used to compare two medians.

Abbreviations: DBP, diastolic blood pressure; NT-proBNP, N-terminal pro–B-type natriuretic peptide; NYHA, New York heart association; SBP, systolic blood pressure.

Table 3 Echocardiographic Characteristics of Participants

Characteristics	Total (n = 280)	HFpEF (n = 118)	Non-HFpEF (n = 162)	p
LVEF, %	65 (58–70)	65 (58–70)	66 (57–70)	0.575
LVIDd, mm	45 (41–50)	45 (42–50)	45 (40–50)	0.219
LVMI, g/m^2	103.8 ± 18.8	118.0 ± 12.1	93.4 ± 15.9	<0.001
Increased LVMI, n (%)	139 (49.6)	110 (93.2)	29 (17.9)	<0.001
RWT	0.38 (0.33–0.45)	0.41 (0.33–0.49)	0.37 (0.33–0.43)	0.051
Increased RWT, n (%)	91 (32.5)	50 (42.4)	41 (25.3)	0.003
Structural abnormalities, n (%)	177 (63.2)	118 (100)	59 (36.4)	<0.001

(*Continued*)

Table 3 (Continued).

Characteristics	Total (n = 280)	HFpEF (n = 118)	Non-HFpEF (n = 162)	p
Phenotypes of LVH, n (%)				<0.001
Normal	103 (36.8)	0 (0)	103 (63.6)	
Concentric Remodelling	38 (13.6)	8 (6.8)	30 (18.5)	
Eccentric Hypertrophy	86 (30.7)	68 (57.6)	18 (11.1)	
Concentric Hypertrophy	53 (18.9)	42 (35.6)	11 (6.8)	
LAVI, mL/m^2	29 (25–35)	32.5 (28–39)	27 (24–31)	<0.001
Increased LAVI, n (%)	41 (14.6)	24 (20.3)	17 (10.5)	0.026
TR Vmax, m/s	2.8 (2.5–2.8)	2.8 (2.8–2.8)	2.6 (2.1–2.8)	<0.001
Increased TR Vmax	189 (67.5)	117 (99.2)	72 (44.4)	<0.001
PASP, mmHg	40 (28–40)	40 (40–40)	32.5 (20–40)	<0.001
Increased PASP, n (%)	198 (70.7)	117 (99.2)	81 (50.0)	<0.001
Septal e', cm/s	4.9 (4–6.2)	4.7 (4–5.7)	5.1 (3.9–6.3)	0.711
Lateral e', cm/s	7.4 (6–9.3)	7.1 (6.1–8.6)	7.6 (6.0–9.5)	0.714
Average e', cm/s	6.1 (5–7.7)	5.9 (5.0–7.1)	6.3 (4.9–7.9)	0.725
E/e' ≥14, n (%)	184 (65.7)	83 (70.3)	101 (62.3)	0.202
LV diastolic dysfunction or raised LV filling pressure, n (%)	246 (87.9)	118 (100)	128 (79.0)	<0.001

Notes: Categorical variables are described as frequencies (n) and percentages (%). LVMI is described using means and standard deviations. Other continuous variables are presented as median and interquartile range (25–75th percentile). Chi-square test or Fisher's exact test was used to compare categorical variables. The Student's *t*-test was used to compare two means of LVMI. The Mann–Whitney test was used to compare two medians.
Abbreviations: LAVI, left atrial volume index; LV, left ventricular; LVEF, left ventricular ejection fraction; LVIDd, left ventricular internal diameter in diastole; LVH, left ventricular hypertrophy; LVMI, left ventricular mass index; PASP, pulmonary artery systolic pressure; RWT, relative wall thickness; TR, tricuspid regurgitation.

ROC analysis showed that NT-proBNP (AUC 0.979), LVMI (AUC 0.889) and the H_2FPEF score (AUC 0.861) were the most accurate diagnostic markers for HFpEF. An NT-proBNP cut off ≥760 pg/mL provided excellent diagnostic performance, with sensitivity of 95.8% and specificity of 95.7%. TR Vmax ≥2.8 m/s and PASP ≥40 mmHg demonstrated only moderate diagnostic utility, with both showing an AUC of 0.792 (Table 4 and Figure 2).

Table 4 Diagnostic Value of Echocardiographic Indices, NT-proBNP, and the H_2FPEF Score for Newly Diagnosed HFpEF in Older Adults Presenting with Dyspnoea

Variable	AUC (95% CI)	Optimal Cut-off	Sensitivity (%)	Specificity (%)	Youden Index
NT-proBNP	0.979 (0.964–0.994)	≥760	95.76	95.68	0.91
LVMI	0.889 (0.851–0.927)	≥108	80.51	81.48	0.62
H_2FPEF score	0.861 (0.818–0.903)	≥6	93.22	77.78	0.71
TR Vmax	0.792 (0.748–0.835)	≥2.8	99.15	55.56	0.55
PASP	0.792 (0.748–0.835)	≥40	99.15	55.56	0.55
LAVI	0.709 (0.647–0.770)	≥32	57.63	75.31	0.33

(*Continued*)

Table 4 (Continued).

Variable	AUC (95% CI)	Optimal Cut-off	Sensitivity (%)	Specificity (%)	Youden Index
Average e'	0.488 (0.419–0.556)	<4.6	90.68	19.14	0.10
Lateral e'	0.487 (0.418–0.556)	<5.4	92.37	17.28	0.11
Septal e'	0.487 (0.418–0.556)	<3.7	90.68	19.14	0.10
Average E/e'	0.541 (0.473–0.609)	<13.8	72.03	37.65	0.10

Abbreviations: AUC, area under the receiver operating characteristic curve; CI, confidence interval; E/e′, ratio of early mitral inflow velocity to mitral annular early diastolic velocity; LAVI, left atrial volume index; LVMI, left ventricular mass index; PASP, pulmonary artery systolic pressure; TR, tricuspid regurgitation.

Discussion

In this prospective study of 280 older adults presenting to the ED with acute dyspnoea, 42.1% were newly diagnosed with HFpEF according to the 2021 ESC criteria. To minimise diagnostic overlap with other causes of dyspnoea, we applied the full ESC composite diagnostic algorithm, ensuring that elevated NT-proBNP alone was not sufficient for diagnosis and that only patients who fulfilled all structural and functional criteria were classified as having HFpEF. Despite this rigorous approach, the evaluation of acute dyspnoea in older adults remains challenging because multimorbidity is common in this population.[16] In our study, nine patients admitted for pneumonia had elevated NT-proBNP together with structural abnormalities and echocardiographic evidence of diastolic dysfunction or elevated filling pressures, which resulted in their classification as HFpEF. This overlap reflects the clinical reality in acute care, where dyspnoea often arises from several coexisting conditions.[17] Although immediate treatment typically focuses on the primary precipitating cause, identifying concomitant HFpEF remains important for optimising haemodynamic management and ensuring comprehensive care.

Although baseline sociodemographic, geriatric, comorbidity and most clinical characteristics were comparable between the HFpEF and non HFpEF groups, notable differences were observed in laboratory and echocardiographic findings. Patients with HFpEF had substantially higher NT-proBNP concentrations, greater LVMI, more frequent structural abnormalities, larger LAVI, higher PASP and higher H_2FPEF scores. ROC analysis identified NT-proBNP,

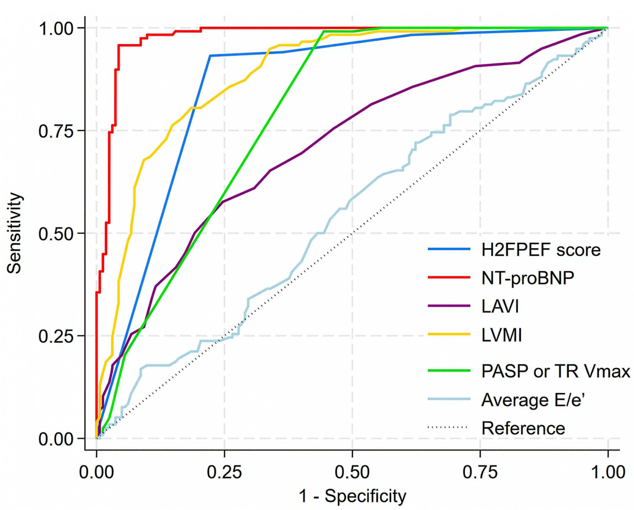

Figure 2 ROC curves of markers for newly diagnosed HFpEF in older adults presenting with dyspnoea. The composite gold standard diagnosis of HFpEF is not included in the ROC curves because it yields a binary outcome and does not provide continuous values for ROC analysis.

Abbreviations: E/e′, ratio of early mitral inflow velocity to mitral annular early diastolic velocity; LAVI, left atrial volume index; LVMI, left ventricular mass index; NT-proBNP, N-terminal pro–B-type natriuretic peptide; PASP, pulmonary artery systolic pressure; TR, tricuspid regurgitation.

LVMI and the H_2FPEF score as the strongest individual diagnostic markers, each demonstrating excellent discriminative performance.

Incidence of HFpEF in Older Adults Hospitalised with Acute Dyspnoea

Our study identified a notably high proportion of newly diagnosed HFpEF among older adults presenting to the ED with acute dyspnoea, based entirely on the gold standard ESC composite diagnostic criteria. This finding is consistent with the broader epidemiological landscape in which HFpEF accounts for approximately half of all HF cases in the general population,[18] with even higher proportions reported in some older studies. Previous research in Western populations has described variable incidence rates of HFpEF among older ED attendees with acute dyspnoea, ranging from 28% to 45%,[19,20] depending on the diagnostic criteria and study design. For instance, the European Heart Failure Pilot Survey reported that HFpEF constituted 38% of acute HF admissions,[21] while the ARIC study identified HFpEF in up to 50% of hospitalised patients aged ≥65 years.[22] In Asia, available data are more limited. However, the ATTEND registry in Japan reported that 45% of acute HF cases were HFpEF,[23] which suggests a comparable, and in some contexts even greater, prevalence in non Western settings. The incidence observed in our study aligns with these findings and reinforces the view that HFpEF represents a substantial proportion of acute dyspnoea presentations in the ED.

Several factors may contribute to this high proportion. First, the demographic profile of our study population, with a median age of 78 years and high rates of comorbidities such as hypertension and AF, closely reflects the risk profile for HFpEF reported internationally. Second, the use of the 2021 ESC diagnostic algorithm, which incorporates natriuretic peptide levels, echocardiographic structural indices and diastolic function indices, likely increased diagnostic sensitivity compared with older criteria. It is also noteworthy that our exclusion criteria removed patients with known HF or reduced ejection fraction, which enriched the study population for first-time HFpEF diagnoses. This methodological approach may partly explain the relatively high proportion of new diagnoses compared with studies that include recurrent admissions or patients with mixed ejection fraction phenotypes. In addition, cultural and healthcare access factors in Vietnam may delay the recognition of early HF, resulting in a larger pool of undiagnosed individuals who present with more advanced symptoms during acute episodes. This finding reinforces the observation that HFpEF is common among older adults presenting with acute dyspnoea, particularly in the context of multimorbidity. Identifying HFpEF at the index presentation has important implications for both acute and long-term management. In the acute setting, recognising HFpEF helps guide haemodynamic decisions, optimise diuretic use and support the management of coexisting precipitants such as infection or uncontrolled hypertension. In the longer term, establishing a diagnosis of HFpEF enables appropriate follow-up and optimisation of comorbidity management, which may reduce the risk of future decompensation.

Comparisons between the HFpEF and non HFpEF groups in our study showed that baseline sociodemographic, geriatric and clinical characteristics alone did not effectively differentiate the two populations. This finding reinforces the understanding that history taking and physical examination by themselves are insufficient for accurate diagnosis in the ED,[24] particularly in older adults whose symptoms are frequently shaped by multiple comorbid conditions. Taken together, our results provide important epidemiological data from a low to middle-income country context and demonstrate that HFpEF is both prevalent and often newly recognised among older adults presenting with acute dyspnoea in the ED.

Diagnostic Markers of HFpEF in Older Adults Hospitalised with Acute Dyspnoea

Diagnostic Value of NT-proBNP

In our study, NT-proBNP was the strongest individual marker for newly diagnosed HFpEF, with an AUC of 0.979 and excellent sensitivity and specificity at a cut-off of ≥760 pg/mL. These results are consistent with previous evidence showing that NT-proBNP is a reliable biomarker of myocardial stress and elevated intracardiac pressures.[25] In contrast to structural or purely functional echocardiographic indices, NT-proBNP directly reflects neurohormonal activation and ventricular wall stress,[26] both of which are central to the pathophysiology of HFpEF.

The diagnostic strength of NT-proBNP in our study likely reflects several underlying factors. First, natriuretic peptide release occurs in response to both pressure and volume overload,[27] which are central features of the haemodynamic profile in HFpEF. Older adults with HFpEF frequently have chronically elevated ventricular filling pressures, even during asymptomatic periods, and this contributes to persistently increased NT-proBNP concentrations. Second, NT-proBNP is less affected by short-term changes in loading conditions than Doppler-derived indices.[28] Although fluid shifts and respiratory mechanics may alter E/e′ or TR Vmax over a short time frame, NT-proBNP tends to integrate haemodynamic stress over longer periods and therefore provides a more stable diagnostic signal in the acute setting.

Importantly, NT-proBNP retains diagnostic usefulness in the presence of comorbidities that are common in older adults, including hypertension, AF and chronic kidney disease, although interpretation requires caution in individuals with severe renal impairment in whom baseline values may be chronically elevated. In our study, the discriminatory performance of NT-proBNP remained high despite the substantial prevalence of AF, which highlights its robustness in this diagnostically challenging subgroup. Although NT-proBNP should not be interpreted in isolation, its incorporation into an ED-based diagnostic approach for older adults with acute dyspnoea has the potential to expedite diagnostic decision making, guide initial management and improve clinical outcomes. Future research should explore the incremental prognostic value of NT-proBNP when combined with structural markers and composite scoring systems, as well as its role in post discharge risk stratification.

Diagnostic Value of H_2FPEF Score

The H_2FPEF score was also identified as a strong diagnostic marker for HFpEF in our study. Median H_2FPEF scores were substantially higher in patients with HFpEF than in those without the condition, and 93.2% of individuals in the HFpEF group were classified as having a high probability of HFpEF. This result is consistent with previous studies demonstrating the utility of the H_2FPEF score in both outpatient and inpatient settings, and it extends its applicability to acutely unwell older adults presenting to the ED. The strong performance observed in our study is likely related to the high prevalence of major risk factors among participants with HFpEF, particularly hypertension, AF and structural cardiac abnormalities, which are heavily weighted within the score.

The appeal of the H_2FPEF score in the emergency care setting lies in its simplicity, speed and minimal resource requirement. Most of its component variables can be obtained from clinical history, basic echocardiography and the electrocardiogram. This makes the score particularly valuable in low- and middle-income country settings where access to advanced imaging modalities and specialist interpretation may be limited. Although its performance did not exceed that of NT-proBNP in our study, the multidimensional structure of the H_2FPEF score allows it to capture aspects of HFpEF pathophysiology that are not reflected by biomarkers alone. Future research should evaluate whether incorporating the H_2FPEF score into ED-based diagnostic algorithms can reduce the time to diagnosis.

Diagnostic Value of Echocardiographic Indices

In the present study, LVMI was one of the strongest echocardiographic markers of newly diagnosed HFpEF in older adults presenting to the ED with acute dyspnoea. This finding highlights the clinical importance of structural cardiac assessment in acute care, particularly in older patients whose haemodynamic status may be transiently altered.

The diagnostic strength of LVMI is likely related to its role as a stable indicator of chronic myocardial remodelling. LVH is a central component of HFpEF pathophysiology and develops in response to long-standing haemodynamic stressors such as systemic hypertension, increased arterial stiffness and age-related myocardial changes. In contrast to diastolic function indices, which can be influenced by acute changes in haemodynamics, preload, afterload and intrathoracic pressures, LVMI is relatively unaffected by short-term physiological fluctuations. In acute settings where volume status and loading conditions may vary considerably, the stability of structural measures provides a diagnostic advantage.

Our findings are consistent with recognised HFpEF phenotypes, in which concentric left ventricular remodelling and hypertrophy are highly prevalent. In the echocardiographic substudy of the TOPCAT trial, for example, 78% of participants had an elevated relative wall thickness and 44% fulfilled criteria for concentric LVH.[29] Similarly, the ASIAN HF registry reported high rates of LVH among patients with HFpEF, particularly women.[30] By identifying LVH, LVMI effectively functions as a quantitative marker of the chronic pressure overload and myocardial fibrosis that characterise the HFpEF myocardium. In our study, patients with HFpEF had an average LVMI of approximately 118 g/

m^2 compared with approximately 93 g/m^2 in those without HFpEF. This substantial difference reflects the degree of structural remodelling present in HFpEF. We propose that LVMI provides a valuable structural anchor within the diagnostic framework. When increased, it strongly suggests that a patient's dyspnoea may be rooted in long standing hypertensive heart disease or related processes, even when the patient is clinically euvolaemic or exhibits equivocal signs.

Diastolic parameters showed low discriminatory performance in our study because diastolic abnormalities were also common among patients who did not meet the ESC criteria for HFpEF. Indices such as the E/e′ ratio, TR Vmax and LAVI are susceptible to haemodynamic variability in acutely unwell patients. Factors including intravascular volume shifts, respiratory variation, tachyarrhythmias and acute pulmonary processes can alter diastolic filling patterns and Doppler derived measurements over short periods. These physiological fluctuations reduce the specificity of diastolic indices for HFpEF, particularly in older adults with multiple comorbidities. In addition, diastolic dysfunction is intrinsically prevalent in ageing populations because of myocardial stiffening and vascular changes,[31] which further limits its diagnostic precision. In our study, nearly 80% of patients without HFpEF met echocardiographic criteria for diastolic dysfunction or elevated filling pressures. This finding illustrates why these parameters contributed little to distinguishing HFpEF from other causes of acute dyspnoea.

Several limitations of our study should be acknowledged. First, this was a single centre study conducted in a Vietnamese tertiary hospital and limited to patients aged ≥60 years. Therefore, the findings may not be fully generalisable to other clinical settings or to younger populations. Second, we excluded individuals with any prior diagnosis of HF or with LVEF <50% to focus specifically on new onset HFpEF. Although this approach enriched the study for first-time diagnoses, it may have introduced spectrum bias. Third, because eligibility required dyspnoea severe enough to warrant hospital admission and in hospital evaluation, our sample primarily reflects patients with moderate-to-severe symptoms and may not represent those with milder or subacute presentations. Fourth, we did not systematically follow patients after discharge and therefore cannot comment on the prognostic implications of the assessed markers or on longer term outcomes. Fifth, although echocardiography formed a central component of the diagnostic protocol and was performed by experienced operators, image acquisition and measurement may still vary in the emergency setting. Moreover, we did not evaluate inter observer or intra observer variability. This is important because several key structural parameters, including LVMI and RWT, are sensitive to measurement technique and may vary between operators. Sixth, several markers examined in this study, such as NT-proBNP and structural cardiac indices, are intrinsic parts of the ESC 2021 diagnostic criteria, which introduces incorporation bias and may overestimate their diagnostic performance. Finally, due to sample size constraints, we were unable to conduct multivariable analyses or subgroup sensitivity analyses to determine whether any marker provides independent diagnostic value beyond the ESC framework. Larger, multi centre studies are needed to validate these findings and to better assess the independent diagnostic contribution of individual markers.

Conclusion

In this prospective study of older adults presenting to the ED with acute dyspnoea, 42.1% were newly diagnosed with HFpEF, highlighting its substantial burden in geriatric emergency care. NT-proBNP, the H_2FPEF score and LVMI demonstrated clear diagnostic separation between patients with and without HFpEF, although their performance should be interpreted with caution because NT-proBNP and structural abnormalities form part of the ESC reference standard. Diastolic indices showed limited discriminatory utility, which is consistent with the high prevalence of diastolic abnormalities among older individuals with multiple comorbidities. Interpretation of several diagnostic markers is further complicated by the high rate of AF in this population, as it influences natriuretic peptide concentrations and Doppler-based indices independently of HFpEF. Overall, these findings emphasise the value of biochemical and structural markers in the assessment of suspected HFpEF in the ED, while underscoring the need to interpret their diagnostic accuracy within the methodological and population-related constraints of this clinical setting.

Data Sharing Statement

The dataset used and analyzed in the current study is available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

The study was carried out in accordance with the ethical principles stated in the Declaration of Helsinki. The Institutional Ethics Committee of Thong Nhat Hospital approved this study, ensuring strict anonymity of participants during data analysis (Approval No. 119/2024/CN-BVTN-HĐĐĐ). Written informed consent was obtained from all participants or their legal representatives.

Consent for Publication

All participants gave written consent, that the results of the study including their anonymised data maybe published.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no competing interests.

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