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ORIGINAL ARTICLE

A two-phase approach to identifying HFpEF in heart failure patients: Risk score evaluation and decision tree development

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Abstract

Aims Heart failure (HF) with preserved ejection fraction (HFpEF) poses significant diagnostic challenges due to its complex aetiology and overlapping symptoms with other HF types. The heterogeneity of HFpEF, compounded by frequent comorbidities, complicates diagnosis. This study aimed to enhance HFpEF prediction through a two-phase approach: a simplified risk score and a decision tree model.

Methods and results In Phase 1, an 8-point risk score based on accessible clinical parameters was developed. In Phase 2, we conducted comprehensive predictive modelling using decision tree analysis. Data from 560 HF patients were analysed. It achieved an accuracy of 63.13% (sensitivity: 62.87%, specificity: 54.24%). In Phase 2, a decision tree model using broader clinical variables improved accuracy to 73.04% (sensitivity: 53.89%, specificity: 81.17%).

Conclusions This dual framework provides tools for both quick screening and detailed risk stratification in various clinical settings.

Keywords Clinical decision support; Heart failure; Heart failure with preserved ejection fraction; Risk score; Screening

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Introduction

Heart failure (HF) remains a major public health challenge worldwide, affecting millions and contributing to significant morbidity and mortality.[1,2] Heart failure with preserved ejection fraction (HFpEF), according to ESC guidelines, is a distinct and increasingly recognized phenotype, with studies indicating a rising trend in its prevalence.[3–5]

Despite advancements in HF treatment, HFpEF presents a unique diagnostic and therapeutic challenge due to its heterogeneous nature and complex pathophysiology.[6] This diversity in presentation and underlying mechanisms often complicates the early identification and stratification of patients with HFpEF, as well as limits the effectiveness of standard HF therapies.[5–7] Accurate prediction and timely recognition of HFpEF among HF patients could improve clinical outcomes by facilitating interventions specifically tailored to the nuances of HFpEF.[8,9]

Current diagnostic approaches such as the H2FPEF score developed by Reddy et al.[10] and the HFA-PEFF algorithm from the ESC[11] have demonstrated good diagnostic accuracy but present limitations in clinical settings. The H2FPEF score was designed to distinguish HFpEF from non-cardiac causes of dyspnoea rather than differentiating between HF subtypes, while the HFA-PEFF algorithm requires complex diagnostic testing including detailed echocardiography and biomarkers. These limitations highlight the need for simpler yet effective tools that can be easily implemented in various clinical settings, particularly when specialized diagnostic resources are limited.

Current methods for assessing HFpEF risk typically rely on general heart failure markers, which may not fully capture

the unique characteristics of this particular subtype.[8,12] While several risk scores have been developed to estimate the likelihood of HFpEF, there is still room for improvement in their specificity. To further enhance prediction accuracy and risk stratification for HFpEF, it is important to continue exploring and developing new assessment methods.

The primary objective of this study is to improve HFpEF prediction among HF patients through the development and validation of a novel risk score and a decision tree model, using a dual approach that combines both simplified screening and comprehensive risk stratification to support various clinical needs.

Methods

Participants

The study group included 560 patients with diagnosed heart failure (70% male, 30% female, mean age M ± SD = 67.4 ± 12.3 years). Clinical data were collected and analysed from two groups of patients treated at the University Clinical Hospital in Wroclaw: hospitalized patients from the Cardiology Clinic and outpatients from the Heart Failure Outpatient Clinic. This study used a retrospective cohort design analysing data collected prospectively during standard clinical care. The study was conducted between January 2022 and January 2024. Inclusion criteria were (1) a confirmed diagnosis of heart failure based on clinical and diagnostic criteria according to ESC guidelines, (2) age ≥18 years and (3) patient consent to participate and for the use of their medical information. We excluded patients with significant valvular heart disease, pulmonary arterial hypertension, constrictive pericarditis, primary cardiomyopathies or history of heart transplant.

Data collection

The initial objective of the study was to develop a simplified version of the H2FPEF diagnostic score, designed to estimate the likelihood of HFpEF. The original H2FPEF score consisted of six criteria: obesity (BMI $>$ 30 kg/m^2), atrial fibrillation, age $>$60 years, treatment with ≥2 antihypertensive medications, e/e' ratio $>$9 and pulmonary artery systolic pressure $>$35 mmHg. Our goal was to create a more accessible clinical tool by eliminating the echocardiographic criteria (e/e' ratio $>$9 and pulmonary artery systolic pressure $>$35 mmHg), which can be challenging to obtain in some clinical settings due to image quality issues, measurement variability, or limited resource availability. This simplified version was subsequently tested in a cohort of 560 heart failure patients to evaluate its diagnostic utility and practical application across various clinical settings.

For Phase 1 of the study, we selected the eight parameters based on a comprehensive literature review of established HFpEF risk factors and clinical predictors, focusing on variables that are easily accessible in routine clinical practice and do not require specialized testing. We developed an 8-point HFpEF risk score based on easily accessible clinical parameters [female sex, dyspnoea, age $>$60 years, body mass index (BMI) $>$ 30 kg/m^2, multimorbidity defined as the presence of at least three chronic diseases, paroxysmal or persistent atrial fibrillation (AF), hypertension requiring at least two antihypertensive medications, and chronic kidney disease with eGFR $<$ 60 mL/min/1.73 m^2]. Each positive response contributed one point to the total score.

For Phase 2 of the study, we included a broader set of variables known to be associated with heart failure phenotypes based on prior research, and selected the final variables for our decision tree model through statistical significance testing. A range of sociodemographic (sex and age) and clinical data were analysed, including HF phenotype, left ventricular ejection fraction (LVEF), BMI, heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), New York Heart Association (NYHA) class, dyspnoea, haemoglobin level, NT-proBNP, eGFR, creatinine level and medications (ACEI/ARB/ARNI, beta-blockers and diuretics). Additional clinical factors included smoking status, diabetes mellitus, chronic obstructive pulmonary disease (COPD) or asthma, coronary artery disease, hypertension, chronic kidney disease, stroke, AF, and multimorbidity. All data were obtained from patients' electronic medical records.

Ethical consideration

This study was conducted in accordance with the Declaration of Helsinki and approved by the Bioethics Committee of the Wroclaw Medical University. Written informed consent was obtained from participants prior to their inclusion in the study. All patient data were anonymized to ensure confidentiality.

Statistical methods

The statistical methods applied included ROC curve analysis, where sensitivity, specificity and accuracy were calculated at various cut-off points to assess discriminative ability and identify the optimal threshold for the developed 8-item risk score. The Hosmer–Lemeshow goodness-of-fit test was performed to assess calibration of the risk score model. To stratify patients into groups with differing probabilities of HFpEF, the Conditional Inference Tree (CTree)[13] algorithm was used. The analysis was conducted with a significance level of 0.05, interpreting *P*-values below 0.05 as statistically significant. All calculations were performed using R software (version 4.4.1)[14] with the partykit package.[15]

Table 1 Sociodemografhic and clinical characteristics of the study group

Parameter		Overall (N = 560)
Phonotype of HF	HFrEF and HFmrEF	393 (70.18%)
	HFpEF	167 (29.82%)
LVEF (%)	Mean (SD)	41 (13.12)
	Median (quartiles)	40 (30–52)
	Range	13–75
	n	560
Age (years)	Mean (SD)	67.4 (12.3)
	Median (quartiles)	70 (63–75)
	Range	23–91
	n	560
Sex	Women	169 (30.18%)
	Men	391 (69.82%)
BMI (kg/m^2)	Mean (SD)	29.1 (5.9)
	Median (quartiles)	28.2 (24.9–32.3)
	Range	17.9–68.2
	n	556
BMI	Normal weight	148 (26.4%)
	Overweight	197 (35.9%)
	Obesity	215 (38.4%)
Heart rate (b.p.m.)	Mean (SD)	77 (16.52)
	Median (quartiles)	75 (65–86)
	Range	37–150
	n	559
SBP (mmHg)	Mean (SD)	128 (20.48)
	Median (quartiles)	127 (113–140.25)
	Range	80–197
	n	560
DBP (mmHg)	Mean (SD)	78 (13.58)
	Median (quartiles)	77 (69–85)
	Range	46–155
	n	559
NYHA class	I	74 (13.21%)
	II	218 (38.93%)
	III	176 (31.43%)
	IV	92 (16.43%)
Dyspnoea	No	292 (52.14%)
	Yes	268 (47.86%)
Hgb (g/dL)	Mean (SD)	13.5 (1.93)
	Median (quartiles)	13.7 (12.2–14.8)
	Range	7.1–18.5
	n	560
NT-proBNP (pg/mL)	Mean (SD)	4273 (8512)
	Median (quartiles)	1998 (736–4203)
	Range	60–70 000
	n	557
eGFR (mL/min/1.73 m^2)	Mean (SD)	69 (26)
	Median (quartiles)	68 (53–88)
	Range	5–147
	n	560
Creatinine [mg/dL]	Mean (SD)	1.35 (1.42)
	Median (quartiles)	1.06 (0.84–1.33)
	Range	0.53–22.5
	n	560
ACEI/ARB/ARNI	No	52 (9.29%)
	Yes	508 (90.71%)
Beta-blockers	No	15 (2.68%)
	Yes	545 (97.32%)
Diuretics	No	71 (12.68%)
	Yes	489 (87.32%)
Active nicotinism	No	444 (79.29%)
	Yes	116 (20.71%)
Diabetes mellitus	No	266 (47.50%)
	Yes	294 (52.50%)
COPD/Asthma	No	480 (85.71%)
	Yes	80 (14.29%)
Coronary artery disease	No	272 (48.57%)
	Yes	288 (51.43%)
Hypertension	No	100 (17.86%)
	Yes	460 (82.14%)
Chronic kidney diseases	No	393 (70.18%)
	Yes	167 (29.82%)
After stroke	No	509 (90.89%)
	Yes	51 (9.11%)
Atrial fibrillation	No	274 (48.93%)
	Yes	286 (51.07%)
Multimorbidity	No	97 (17.32%)
	Yes	463 (82.68%)

Results

Patient characteristics

Table 1 presents the characteristics of 560 patients, with a classification by heart failure phenotype [HFpEF, heart failure with mild-range ejection fraction (HFmrEF) and heart failure with reduced ejection fraction (HFrEF)]. It includes data on key parameters such as LVEF, age, sex, BMI, heart rate, blood pressure, dyspnoea and multimorbidity. It also highlights the frequency of selected comorbidities and medication use. Additionally, it reports the distribution of patients across NYHA classes and other clinical variables such as NT-proBNP, eGFR, creatinine and haemoglobin levels.

Predictive analysis of the proposed model for HFpEF risk assessment (Phase 1)

The area under the ROC curve (AUC) is 0.612 (*Figure 1*). The Hosmer–Lemeshow test showed adequate calibration of the model (χ^2 = 9.83, P = 0.28). The optimal cutoff point for the number of points is 5. The rule stating that if there are 5 or more 'yes' responses, HFpEF is likely to occur, has a sensitivity of 62.87% and has a specificity of 54.24%. The overall accuracy is 63.13%, indicating that this percentage of patients was correctly diagnosed.

Table 2 shows the individual contributions of the eight variables in our simplified risk score model. Female sex (OR 2.13, 95% CI 1.46–3.11, $P < 0.001$), age >60 years (OR 1.87, 95% CI 1.22–2.86, P = 0.004) and atrial fibrillation (OR 1.94, 95% CI 1.33–2.84, $P < 0.001$) were the strongest predictors of HFpEF in our model. While diabetes mellitus showed a trend toward association with HFpEF in univariate analysis (OR 1.33, 95% CI 0.92–1.92, P = 0.13), it did not reach statistical significance for inclusion in our final model.

Figure 1 ROC curve illustrating the diagnostic accuracy of the proposed model for HFpEF risk assessment.

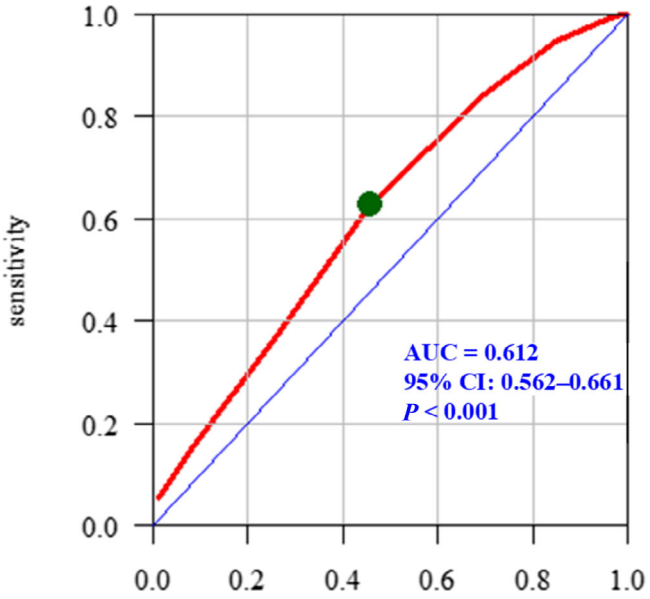

Table 2 Univariate analysis of predictors included in the simplified HFpEF risk score

Parameter	Odds ratio	95% CI	*P*-value
Female sex	2.13	1.46–3.11	<0.001
Dyspnoea	1.42	0.98–2.05	0.064
Age >60 years	1.87	1.22–2.86	0.004
BMI > 30 kg/m^2	1.55	1.07–2.26	0.022
Multimorbidity	1.68	0.95–2.99	0.078
Atrial fibrillation	1.94	1.33–2.84	<0.001
Hypertension (≥2 medications)	1.76	1.09–2.84	0.021
CKD (eGFR <60 mL/min/1.73 m^2)	1.38	0.94–2.03	0.102
Diabetes mellitus[a]	1.33	0.92–1.92	0.131

[a]Not included in the final risk score model.

Algorithm to develop a prediction model for HFpEF risk assessment (Phase 2)

Assuming that a probability above 50% read from the decision tree indicates HFpEF, and a probability below 50% indicates HFmrEF or HFrEF, this rule has a sensitivity of 53.89% and a specificity of 81.17% (*Figure 2*). In comparison, it is slightly less sensitive but significantly more specific than the previously described proposed model for assessing the risk of HFpEF. The overall accuracy of the decision tree is 73.04%, meaning that this percentage of patients was correctly diagnosed. *Table 3* presents a comparison between two models, emphasizing their respective performance metrics, including sensitivity, specificity and overall accuracy.

Discussion

Our two-phase analysis of HFpEF prediction reveals several important findings in the context of existing literature and current clinical approaches. When examining traditional risk scores, our initial score's modest performance (AUC = 0.612) aligns with challenges reported in previous scoring systems. For comparison, the H2FPEF score developed by Reddy et al. achieved higher discrimination (AUC = 0.841) in their validation cohort, focusing on distinguishing HFpEF from non-cardiac causes of dyspnoea rather than other forms of heart failure.[10] Similarly, while the HFA-PEFF scoring system from the ESC demonstrated better diagnostic accuracy, it requires more complex diagnostic testing including echocardiographic parameters and biomarkers.[11] This substantial difference in performance highlights the challenge of developing a simplified tool while maintaining accuracy, particularly when distinguishing between heart failure subtypes rather than between cardiac and noncardiac causes of symptoms.

The relatively lower performance of our simplified score emphasizes a crucial point also demonstrated by Lip et al.[16] while simplification of diagnostic criteria may improve clinical applicability, it often comes at the cost of accuracy, as seen in other cardiovascular risk scores like CHADS2 versus CHA2DS2-VASc for atrial fibrillation.[17]

Regarding machine learning approaches, our decision tree model's performance (accuracy 73.04% and specificity 81.17%) compares favourably with other machine learning

Figure 2 The decision tree model for diagnosing HFpEF. ACEI/ARB, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers; AF, atrial fibrillation; CAD, coronary artery disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate (measured in mL/min/1.73 m^2); Hgb, haemoglobin; HR, heart rate; HT, hypertension; Multimorb., multimorbidity; NYHA, New York Heart Association functional classification; Sex, Gender (Male - M, Female - F).

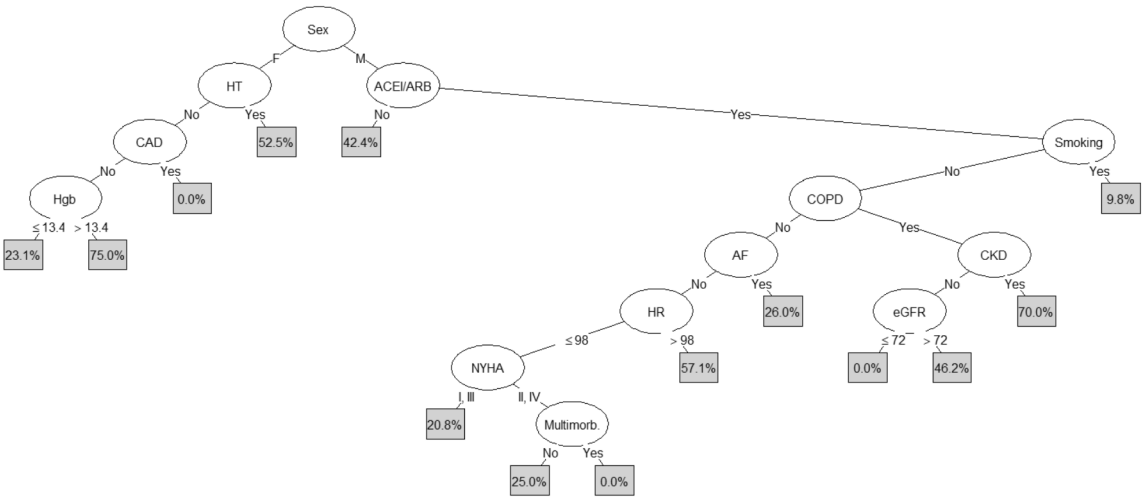

Table 3 Comparison of the analysed models for diagnosing HFpEF

	The proposed risk model	The decision tree model
Sensitivity	62.87%	53.89%
Specificity	54.24%	81.17%
The overall accuracy	63.13%	73.04%

approaches in HFpEF prediction. As reviewed by Ahman et al., recent studies using random forests and neural networks have reported similar accuracy ranges of 70%–75%.[17] The high specificity of our model stands out when compared with Segar et al. random forest model at 76% specificity[18] and Zhang et al. deep learning approach at 79% specificity.[19] Our decision tree's primary split on gender aligns with emerging literature on sex-specific differences in HFpEF. Lam et al. have highlighted distinct pathophysiological pathways in male versus female patients.[20] Our model's structure provides quantitative support for these observations and suggests different diagnostic approaches may be needed based on gender.

The importance of gender as the primary discriminating factor in our model suggests potential value in developing sex-specific HFpEF diagnostic and risk stratification approaches. Based on our findings, the pathophysiological pathways leading to HFpEF appear to differ significantly between men and women, with hypertension playing a more prominent role in women while treatment patterns and cardiac remodelling may be more influential in men. This supports growing evidence for the need to tailor diagnostic algorithms and treatments based on gender differences in cardiovascular disease phenotypes.

The prominent role of ACEI/ARB use in our tree model provides interesting insights when compared to recent clinical trials. While the PARAGON-HF trial showed overall neutral results for sacubitril/valsartan in HFpEF, it did demonstrate benefit in specific subgroups, particularly in patients with LVEF between 45% and 57% and in women.[21] This heterogeneity in treatment response aligns with our model's identification of medication use as an important stratification factor, suggesting that treatment patterns may have diagnostic value because they reflect physicians' assessment of underlying phenotypes. While the PARAGON-HF trial showed limited overall benefit with sacubitril/valsartan in HFpEF, our findings suggest that ACEI/ARB (in men) use might be an important stratification factor in diagnostic algorithms. Our model's handling of comorbidities reveals patterns that both support and challenge existing literature. Hypertension's role (in our analysis only in women) as a key predictor aligns with pathophysiological models proposed by Paulus and Tschöpe, supporting the systemic inflammation hypothesis in HFpEF development.[22] Furthermore, the interaction between COPD/asthma and kidney function in our model suggests more complex relationships than previously described in singular risk factor analyses.

From a methodological perspective, our dual approach differs from previous studies that typically focus on either simplified scores or complex algorithms. Similar dual-methodology approaches have proven successful in other areas of cardiovascular medicine, as demonstrated by Fox et al. in the development of the GRACE score for acute coronary syndromes.[23]

Limitations

This study has several limitations that should be considered. First, the sample size, while adequate, may not fully represent the broader population of heart failure patients, limiting the generalizability of the findings. Additionally, the study relied on retrospective data, which may introduce biases and limit the ability to draw causal conclusions. We acknowledge the need for external validation of our models in different healthcare settings and geographic regions to confirm their generalizability and robustness. We are currently planning a multicentre validation study to address this important limitation. The novel risk score and decision tree model, although promising, have not yet been externally validated, and their accuracy may vary in different clinical settings. Furthermore, the decision tree model, while demonstrating higher specificity, showed slightly lower sensitivity, which may affect its performance in identifying all patients at risk for HFpEF. The inclusion of treatment variables (ACEI/ARB use) as predictors in our decision tree model may introduce circular reasoning, as medication choice might have been influenced by the known or suspected heart failure phenotype. However, this reflects real-world clinical decision-making and may still provide valuable information for phenotype prediction. Lastly, the study did not explore the long-term impact of using these predictive models on patient outcomes, which warrants further investigation.

Implication for practice

This study highlights the importance of improving risk assessment for HFpEF. Our findings offer clinicians two complementary tools that can be applied based on available resources and specific needs: a simplified clinical score for rapid screening in resource-limited settings, and a more detailed decision tree model for comprehensive risk stratification when more data are available. The identification of sex-specific pathways in our model suggests that gender-specific approaches to HFpEF diagnosis may improve accuracy, with particular attention to hypertension in women and treatment patterns in men. Additionally, the moderate performance of our simplified score reminds clinicians that when feasible, incorporating echocardiographic and laboratory parameters significantly improves diagnostic accuracy.

The proposed dual-phase approach offers a new perspective on how predictive tools can enhance the identification and stratification of HFpEF risk. While further research and validation are needed, this method could provide valuable insights for clinicians, supporting more accurate evaluation and decision-making. Continued exploration of new assessment tools is essential to better understand and manage HFpEF, ultimately leading to improved patient care.

Conclusions

Our two-phase analysis demonstrates that while a simplified risk score has limited predictive value for HFpEF, a decision tree model can achieve superior accuracy. The combination of approaches provides a comprehensive framework for HFpEF prediction in heart failure patients, offering both simple screening tools and sophisticated risk stratification methods. The hierarchical nature of the decision tree model provides insights into the relative importance of different clinical factors and their interactions. Implementation of this dual approach could improve the identification and management of HFpEF patients in various clinical settings.

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Conflict of interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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