Diagnosis of Heart Failure with Preserved Heart Failure in the Office Setting: How to Assemble this Puzzle?

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Heart failure with preserved ejection fraction (HFpEF) is the most common form of heart failure (HF) in patients older than 65 years of age, accounting for more than 50% of all cases of HF.[1] However, despite more than 30 years of research on this intriguing and challenging heart disease, there is a lack of consensus on the diagnostic approach and a wide variation in guidelines' criteria.[2,3] This lack of uniformity in the definition and the difficult diagnosis are partly due to an incomplete understanding of the complexity of HFpEF – its pathophysiology, phenotypic heterogeneity and natural history. The 2022 AHA/ACC guideline highlights that evidence supporting increased filling pressures at rest or during exercise is important for the diagnosis of this disease.[3]

Therefore, the diagnosis of HFpEF remains a challenge in clinical practice. When assessing a patient with signs and symptoms of HFpEF, several "pieces" must be considered, as shown in detail in Table 1. It is important to examine the patient, evaluate the comorbidities and risk factors for HFpEF, and to design an accurate approach, not necessarily an invasive or complex one, to establish the correct diagnosis and the best therapeutic approach.

A common situation is that of patients coming to the office with dyspnea and/or exercise intolerance, whose clinical examination and natriuretic peptide levels give rise to diagnostic doubts. The most important step here is the application of the H2FPEF and the HFA-PEFF scores.[5-7] The H2FPEF score is a simple risk score, easy to use in the office setting. The score was first calculated based on the identification of clinical and imaging variables that were independently associated with the invasive diagnosis of HFpEF in a population cohort (Table 2).[6] The odds of HFpEF doubles for each one-unit H2FPEF score increase, with a c-statistic of 0.841.[3] In light of the possibility of HFpEF, the H2FPEF score can be used to either exclude HFpEF among patients with a low score (0-1) or to confirm the diagnosis

Table 1 – Diagnostic tools in heart failure with preserved ejection fraction[4]

Diagnostic tools in HFpEF	Criteria	Remarks
History	Dyspnea / Fatigue/ Orthopnea exertion intolerance Risk factors and comorbidities	Cardinal symptoms Highlights:[5] Exertional dyspnea in more than 90% of patients Fatigue in nearly 60%
Physical examination	- Jugular venous distension - Rales - Edema - Third heart sound	Low sensitivity to clinical signs[5] Edema in approximately 40% of patients Presence of other signs in less than 20%
Natriuretic peptides (NT-proBnp or BNP)	ESC major criteria: NT-proBNP >220 or BNP> 80 (sinus rhythm) NTproBNP >660 or BNP > 240 (AF); ESC minor criteria: NTproBNP >125 or BNP> 35 (sinus rhythm); and NTproBNP > 365 or BNP > 105 (FA)	Nearly 20% of patients with HFpEF by invasive methods have normal NT-proBNP (<125) Sensitivity: 77% Specificity: 53%
Echocardiogram	Diastolic dysfunction Lateral, mitral and septal tissue doppler; e' and E/e' ratio	ESC criteria: Septal e' <7 or lateral e' <10 (<75 years old); Septal e'<5 or lateral e'<7 (≥75 years old); E/e' ratio: ≥15 (major), 9–14(minor)
	Increased left atrial volume (mL/m2)	ESC criteria: **Major:** left atrial volume index >34 (sinus rhythm), >40 (AF); **Minor:** left atrial volume index = 29–34 (sinus rhythm), 34–40 (AF)
Cardiopulmonary test	Markers of functional impairment: peak VO2 and Ve/VCO2 slope	Useful in discriminating HFpEF from non-cardiac dyspnea Sensitivity: 91% Specificity: 51%

HFpEF: heart failure with preserved ejection fraction; ESC: European Society of Cardiology; BNP: B-type natriuretic peptide; NT-pro BNP: N-terminal (NT)-pro hormone BNP; AF: atrial fibrillation. Adapted[4]

Keywords

Heart Failure; Diastolic Heart Failure; Diagnosis.

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Table 2 – Description of the H2FPEF diagnostic algorithm

Clinical variable	Characteristics	Points
H2 - Heavy (obesity) - Hypertension	BMI > 30Kg/m2 2 or more antihypertensive medicines	2 1
F - Atrial fibrillation	Paroxysmal or persistent	3
P - Pulmonary hypertension	PASP>35mmhg (echocardiogram)	1
E - Elder	Age > 60 years	1
F - Filling pressures	E/e'> 9	1

BMI: body mass index; PASP: pulmonary artery systolic pressure. Adapted[6]

of the disease, with reasonable reliability, among patients with higher scores (6-9). However, there remain patients with intermediate scores (in any of the scores), who require further tests.[6]

It is worth pointing out that the therapeutic approach in the office setting has improved with the implementation of scores and tools available. However, clinical examination – symptoms, comorbidities, risk factors and cardinal signs – assessment of natriuretic peptides, echocardiogram and diagnostic scores may not be sufficient to confirm or exclude the diagnosis of HFpEF.

When the basic approach is not sufficient, it is necessary to go beyond. The flowchart presented in the Brazilian guidelines on heart failure (Figure 1) indicates the pathways in this scenario of intermediate probability.[8,9] One more piece needs to be added here. Patient referral for exercise stress echocardiogram, invasive hemodynamic monitoring at rest and during exercise is an indispensable step. Also, it is important to evaluate the etiology of secondary HFpEF, with special attention to the "red flags", in which additional diagnostic tests and specific therapies for infiltrative cardiomyopathies would be needed, as in suspected cardiac amyloidosis.[10]

Conclusion

During the last years, HFpEF has been increasingly recognized as a highly complex syndrome, with different phenotypes, in which the heart is definitely not the only organ affected. Identifying the limitations in assessing these patients was a big step. Current diagnostic approach, putting the pieces together, has certainly enhanced our capacity to diagnose this increasingly prevalent disease. However, not all pieces of this amazing puzzle – the HFpEF – have been identified, and we do not always get to a definite diagnosis in the office; yet, there is still a way to go. In situations where uncertainty remains high after the careful use of available tools, we must go on, with complementary tests (exercise stress and/or diastolic stress test) and referral to specialized centers, and do not stop until all the pieces are put together.

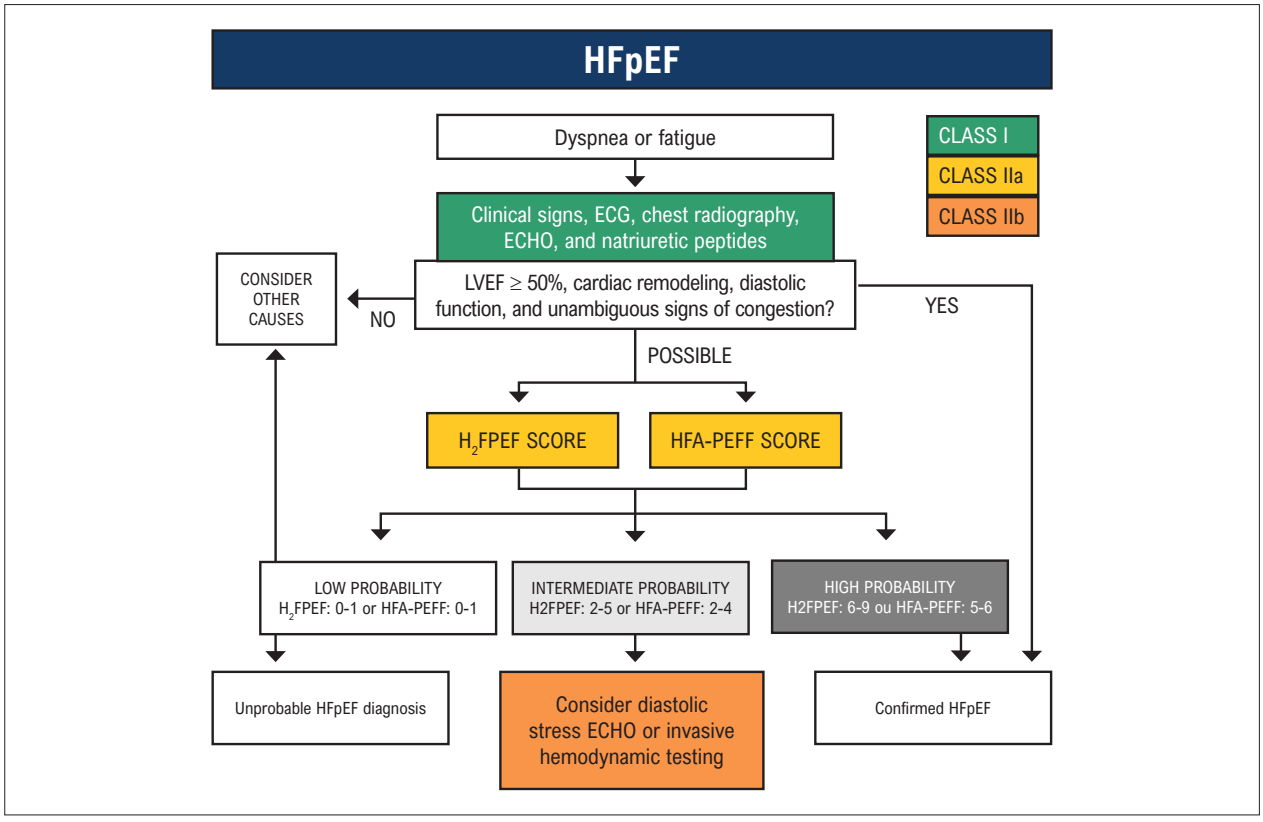

Figure 1 – *Brazilian Society of Cardiology guidelines for the diagnosis of heart failure with preserved ejection fraction (HFpEF).*[9]

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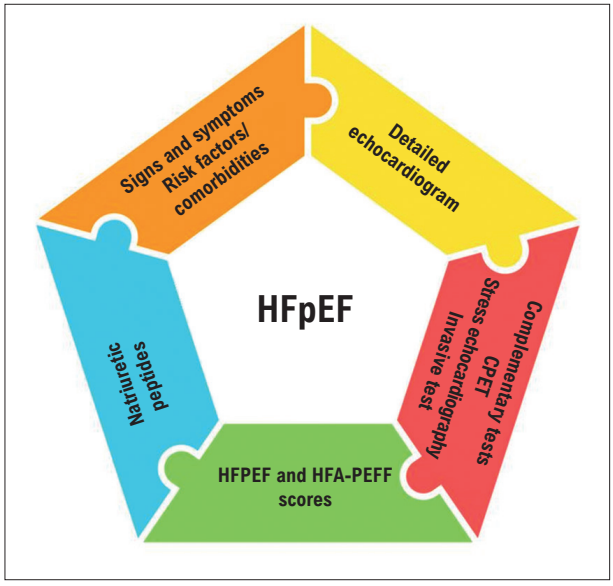

Figure 2 – *Simplified diagnosis of heart failure with preserved ejection fraction (HFpEF) in the office setting – assembling the puzzle; CPET: cardiopulmonary exercise testing.*

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