Echocardiography in Heart Failure with Preserved Ejection Fraction: From Primary Care to Tertiary Hospitals

Marcelo Iorio Garcia[1,2,3]
Universidade Federal do Rio de Janeiro,[1] Rio de Janeiro, RJ – Brazil
Hospital Pró-Cardíaco,[2] Rio de Janeiro, RJ – Brazil
Clínica São Vicente da Gávea,[3] RJ – Brazil

Introduction

Heart failure (HF) is a highly prevalent and incident clinical syndrome that mostly affects older adults. It is one of the main causes of hospital admission, which is a strong prognostic marker, considering that approximately 50% of hospitalized patients will be readmitted within 6 months.[1]

HF with preserved ejection fraction (HFpEF) is hemodynamically defined as an inability of the heart to meet adequate metabolic demands under normal filling pressures. This concept is fundamental, given that patients with normal left ventricular (LV) ejection fraction (EF) (> 50%) usually have normal cardiac output, but are only able to maintain this output at the expense of increased filling pressures. Some patients are known to show signs of congestion at rest, but the vast majority only presents clinical symptoms during effort.[2]

Echocardiography (ECHO) is the main tool used in this population. It is highly available, noninvasive, and easily applicable. However, EF assessment alone may not be sufficient to support the presence of HFpEF.

Concepts in the diagnosis of heart failure with preserved ejection fraction

HFpEF is currently defined as a clinical syndrome of HF with LVEF > 50% in the absence of a previously reduced EF. Patients' symptoms fundamentally result from increases in LV filling pressures at rest or during effort. Documenting this increase in pressure using practical and reproducible means is one of the major challenges in the diagnostic process. Guidelines define HFpEF according to:[3]

1. Presence of signs and symptoms of HF
2. LVEF ≥ 50%
3. Absence of syndromes "simulating" HFpEF
4. Evidence of increased filling pressures or correlated noninvasive markers (elevated E/e′ ratio, increased left atrial volume, and increased levels of natriuretic peptides)

Keywords

Heart Failure; Prognosis; Diagnosis.

Mailing Address: Marcelo Iorio Garcia •
Rua Euclides Figueiredo, casa 2. Postal Code 22261-070, Jardim Botânico, RJ - Brazil
E-mail: miriogarcia@gmail.com
Manuscript received August 18, 2022, revised manuscript August 30, 2022, accepted August 30, 2022

DOI: https://doi.org/10.36660/abchf.20220056

Clinical syndromes that mimic heart failure with preserved ejection fraction

Patients with HFpEF are typically older, obese, and female and have predisposing comorbidities such as hypertension, metabolic syndrome, lung disease, and renal failure. Differentiating a cardiac origin from noncardiac conditions is very difficult for the physician when faced with patients with nonspecific symptoms suggestive of HF, such as fatigue, reduced effort capacity, dyspnea on exercise, and lower limb edema. This is a very common problem in clinical practice.

Diagnostic scores

Two diagnostic algorithms – the H_2FPEF score and the HFA-PEFF algorithm of the European Society of Cardiology[4,5] – assess pre-test probability in order to distinguish HFpEF from dyspnea of noncardiac origin. The combination of clinical and laboratory data, including electrocardiogram and ECHO analysis, will estimate whether the probability of HFpEF is low, intermediate, or high. The Emerging Topics Update of the Brazilian Heart Failure Guideline[6] has objectively summarized this line of reasoning (Tables 1 and 2). Figure 1 shows how to apply these scores.

Echocardiography

We will now describe the main objective of our review, which consists of extracting the greatest number of data from this great diagnostic tool. Notice the amount of information obtained from ECHO when creating the HFA-PEFF score for HFpEF diagnosis (Table 2). In addition to ventricular diameters and LVEF calculation, an estimate of the pulmonary artery systolic pressure (PASP), the E/e′ ratio by tissue Doppler, the indexed left atrial volume (LAV), the indexed LV mass, the relative wall thickness (RWT) and, if possible, the study of myocardial deformation (global longitudinal strain) will be obtained. The accuracy of the variables provided by the ECHO will be analyzed, as well as how to use them.

Ejection fraction

LVEF should be obtained from a biplanar study, classically using Simpson's method.[7] The limitations of using EF assessment alone in decision making have been previously described.[8] However, in the setting of HF, a LVEF > 50% is considered significant, thus starting the clinical reasoning within the HFpEF model.

Estimation of mean left atrial pressure in patients with normal ejection fraction

Careful quantification of cavity dimensions and volumes is extremely important before estimating filling pressures. The presence of structural changes, such as LV hypertrophy and/or left atrial (LA) dilatation, indicates a more marked cavity remodeling. The correct assessment of diastolic function will allow an adequate extraction of volume data. Diastolic dysfunction is a combination of abnormal ventricular relaxation, myocyte deformation, and LA function, culminating in elevated filling pressures.

The first step consists of analyzing the mitral flow pattern, known as the E/A ratio. In many cases, this pattern alone may be sufficient. Patients with an E/A ratio ≤ 0.8 and an E wave velocity ≤ 50 cm/s have a normal mean LA pressure, whereas those with an E/A ratio ≥ 2 have an elevated LA pressure. In intermediate cases, other variables will be used, such as the E/e' ratio, indexed LAV, and peak tricuspid regurgitation velocity (TRV)[9] (Figures 2 and 3).

The relationship between flow velocity in early diastole (E wave, measured by pulsed Doppler) and mitral annular velocity (e' wave, which represents mean septal and lateral annular velocities, measured by tissue Doppler) reflects the mean capillary pressure (CP). An E/e' ratio ≥ 15 at rest has good diagnostic sensitivity in identifying an elevated CP, reinforcing the likelihood of HFpEF as the etiology of symptoms. However, an E/e' ratio in the intermediate range (9-14) is much less sensitive and should not be used as an isolated echocardiographic parameter; the entire diagnostic algorithm should be used instead.[10]

This algorithm showed good accuracy (84%) in identifying patients with HFpEF when applied to those with normal LVEF and complaints of fatigue during effort. Clinical evaluation, which included chest radiography and N-terminal B-type natriuretic peptide levels, was only 64% accurate. The use of these echocardiographic variables was also evaluated with regard to the prediction of hospital readmission in 30 days. When the E/e' ratio was added to the clinical score, there was a 29% increase in the prediction of readmission risk.[11]

Patterns of diastolic dysfunction are also prognostic markers, as they show changes in left atrial compliance, with atrial dilatation, mitral regurgitation, and atrial fibrillation (AF), the so-called progressive atrial remodeling (Figure 4). The indexed LAV represents a marker of chronic remodeling and is much more accurate than the diameter measure. In patients in sinus rhythm without valve disease, an indexed LAV > 34 mL/m^2 was an independent predictor of death, HF, and stroke.[12,13] Different cut-off values are recommended for the indexed LAV in patients in sinus rhythm and patients with AF. Table 2 shows major and minor criteria according to the indexed LAV.

The PASP is calculated by peak TRV, using the modified Bernoulli equation (PASP = 4 x TRV squared, added to the estimated right atrial pressure). Elevated PASP, especially if associated with right ventricular (RV) dysfunction, is an important variable of poor prognostic in HFpEF.[14] A peak TRV > 2.8 m/s indicates elevated PASP and represents an indirect marker of diastolic dysfunction.[15]

Table 1 – H_2FPEF score for the diagnosis of heart failure with preserved ejection fraction

	CLINICAL VARIABLE	CHARACTERISTICS	POINTS
H_2	Heavy Hypertension	BMI > 30 2 or more anti-hypertensive drugs	2 1
F	Atrial fibrillation	Paroxysmal or persistent	3
P	Pulmonary hypertension	PASP > 35 mm Hg (echocardiogram)	1
E	Older patients	Age > 60 years	1
F	Filling pressures	E/e' > 9	1

Source: Marcondes Braga et al[6]. BMI: body mass index; PASP: pulmonary artery systolic pressure.

Structural changes

Initial studies suggested that patients with HFpEF have concentric LV hypertrophy, which leads to reduced

Table 2 – HFA-PEFF score for the diagnosis of heart failure with preserved ejection fraction

Criteria	Major (2 points)	Minor (1 point)
Functional	Septal e' < 7 Lateral e' < 10 or E/e' > 15 or TRV > 2.8 m/s (PASP > 35 mm Hg)	E/e' 9-14 or GLS < 16%
Morphological	Indexed LAV > 34 mL/m^2 or LV mass 149/122 g/m^2 (M/W) and RWT > 0.42	Indexed LAV 29-34 mL/m^2 or LV mass > 115/95 g/m^2 (M/W) or IVS or PW ≥ 12 mm
Biomarker (sinus rhythm)	NT-proBNP > 220 pg/mL or BNP > 80 pg/mL	NT-proBNP 125-220 pg/mL or BNP 35-80 pg/mL
Biomarker (atrial fibrillation)	NT-proBNP > 660 pg/mL or BNP > 240 pg/mL	NT-proBNP 365-660 pg/mL or BNP 105-240 pg/mL

GLS: global longitudinal strain; IVS: intraventricular septum; LAV: left atrial volume; M: men; NT-proBNP: N-terminal pro–B-type natriuretic peptide; PASP: pulmonary artery systolic pressure; PW: posterior wall; RWT: relative wall thickness; TRV: tricuspid regurgitation velocity; W: women. Source: Marcondes Braga et al.[6]

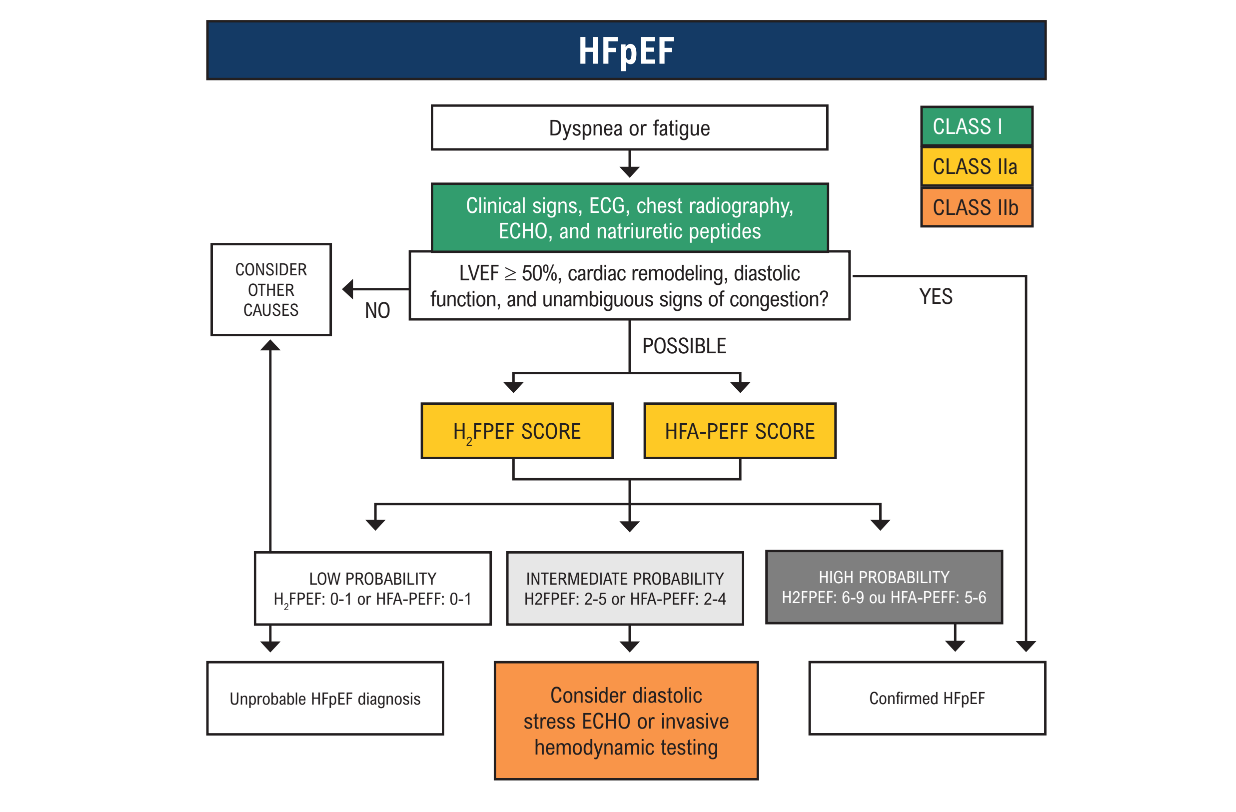
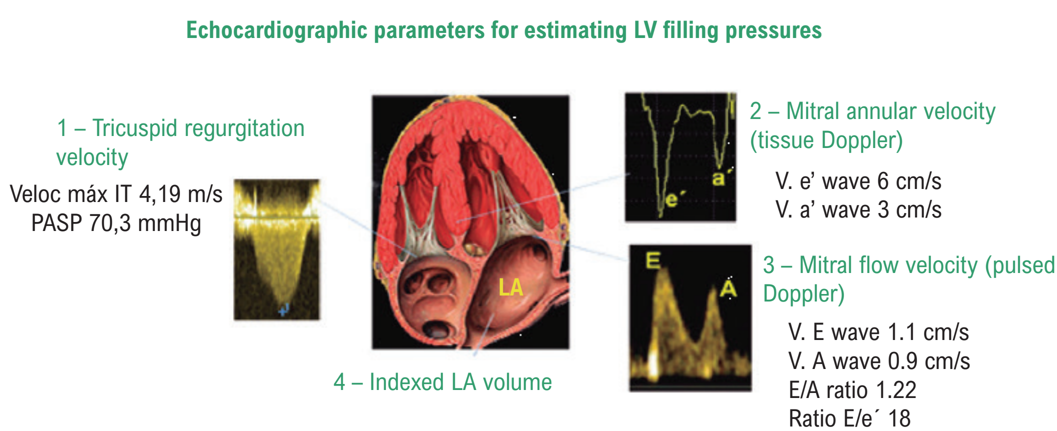


Figure 1 – *Diagnostic flowchart of heart failure with preserved ejection fraction (HFpEF). ECG: electrocardiogram; ECHO: echocardiography; LVEF: left ventricular ejection fraction. Source: Marcondes Braga et al.*[6]



Assessed parameter	Cut-off value
Peak tricuspid regurgitation velocity	> 2.8 m/s
E/e' ratio	> 14
Indexed LA volume	> 34 mL/m^2

Figure 2 – *Diastole and volume estimation in heart failure. LA: left atrial; LV: left ventricular; PASP: pulmonary artery systolic pressure. Source: adapted from Nagueh SF.*[9]

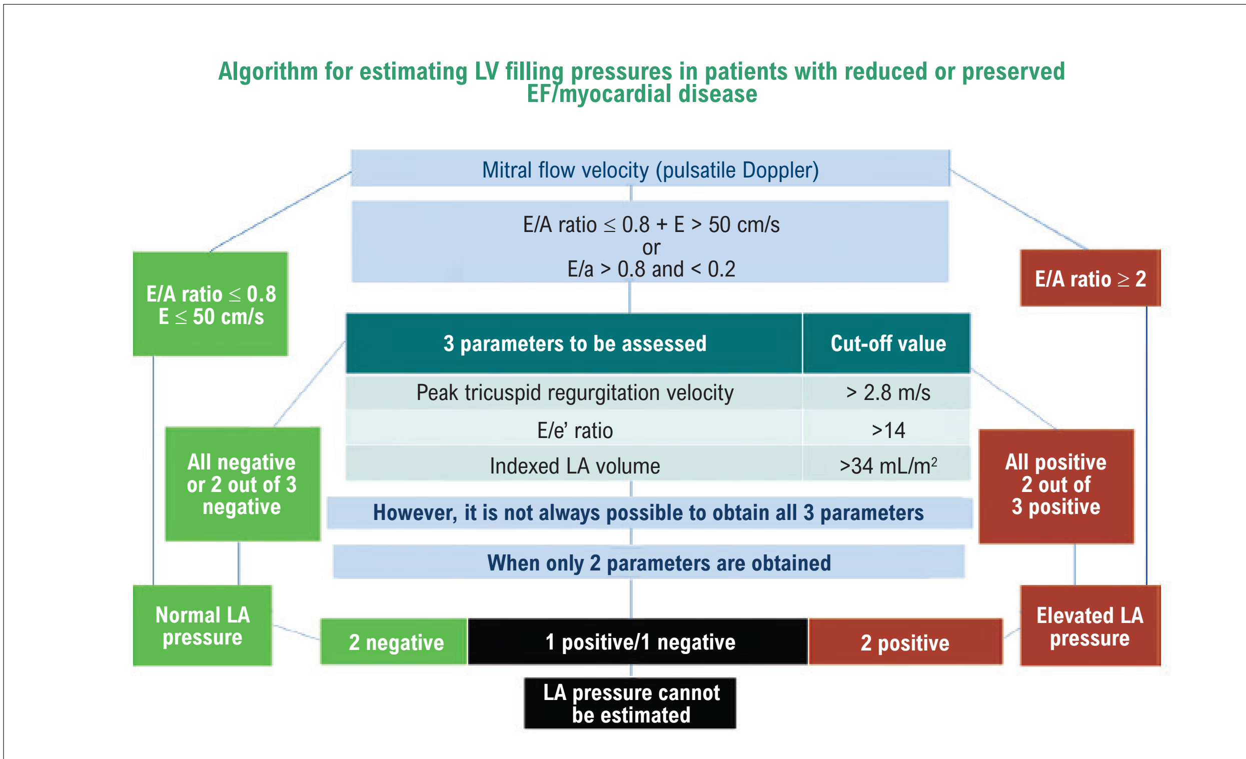


Figure 3 – *Diagnostic algorithm based on echocardiographic data. EF: ejection fraction; LA: left atrial; LV: left ventricular. Source: adapted from Nagueh SF.*[9]

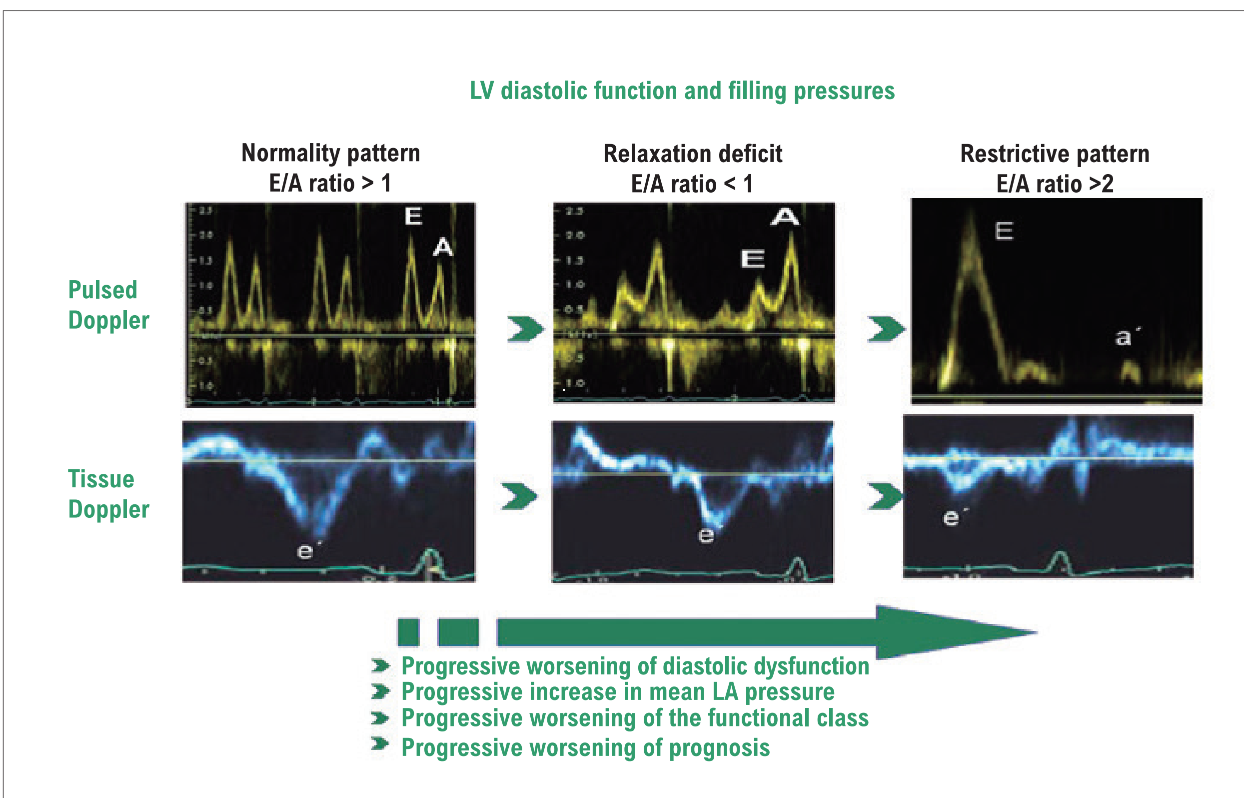


Figure 4 – *Patterns of diastolic dysfunction. LA: left atrial; LV: left ventricular. Source: personal archive.*

distensibility and, consequently, elevated filling pressures.[16] In addition, indexed LV mass has also shown a modest relationship with invasive measurement of filling pressures (r = 0.41-0.48).[17,18] However, several studies have shown that many patients with HFpEF exhibit concentric remodeling in the absence of hypertrophy or normal ventricular geometry.[19-21] Corroborating this affirmation, LV hypertrophy was recently shown to be highly specific (88%) but not very sensitive (26%) in the diagnosis of HFpEF, meaning that the absence of LV hypertrophy does not rule out HFpEF.[3] LV geometry is often classified using RWT, which consists of multiplying the LV posterior wall thickness (PWT) by 2 and dividing it by its end-diastolic diameter (EDD) (RWT = 2xEPP/PWT). There are four different patterns, described in Figure 5.

According to Table 2, assigned points differ according to mass and RWT values. Table 3 summarizes the accuracy of the main markers used.

When evaluating LV morphology, pathologies that mimic HFpEF should be excluded. Whenever significant hypertrophy is identified, the diagnosis of amyloidosis should be considered, especially in the presence of pericardial effusion or apical sparing pattern (the LV apex is "spared" from involvement) by global longitudinal strain.[22] In a series of patients with thicknesses > 12 mm, amyloidosis accounted for 13% of hospitalized patients with "HFpEF".[23] Figure 6 shows an example of amyloidosis.

Diastolic stress echocardiography – assessment of patients with dyspnea, normal left ventricular ejection fraction, and normal left atrial pressure at rest

Much of the difficulty in diagnosing HFpEF is associated with the fact that filling pressures are often normal at rest and only become elevated during exercise testing. Thus, invasive cardiopulmonary exercise testing has emerged as the gold standard to confirm or exclude the diagnosis of HFpEF as a cause of dyspnea.[24,25] Recent studies have evaluated whether similar data can be obtained noninvasively using diastolic stress ECHO.[26] Information acquisition during effort can unmask systolic and diastolic dysfunction. The most frequently studied parameters are the E/e' ratio and peak TRV, which indicate increases in CP and PASP, respectively. The European Association of Cardiovascular Imaging and the American Society of Echocardiography recommend a staged protocol, preferably on a semi-supine bicycle, until the patient reaches the predicted

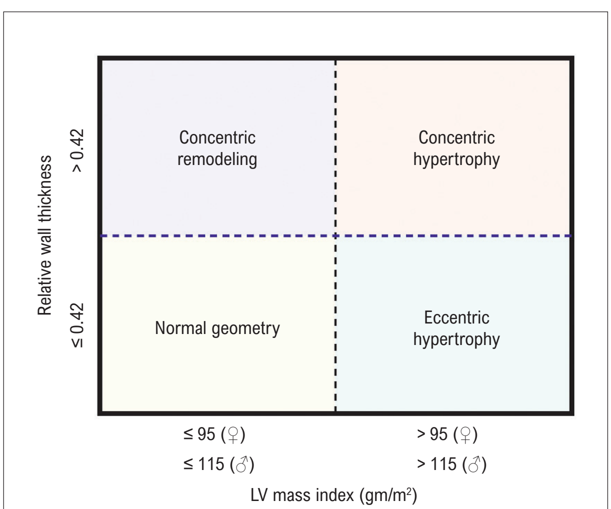


Figure 5 – *Patterns of ventricular geometry. Source: adapted from Lang RM.*[7]

Table 3 – Objective evidence of structural and functional cardiac abnormalities consistent with the presence of diastolic dysfunction/elevated left ventricular filling pressures

Parameter	Cut-off values	Observations
Indexed LV mass Relative wall thickness	> 115/95 g/m² (M/W) > 0.42	Although the presence of concentric remodeling or hypertrophy is a marker of HFpEF, the absence of hypertrophy does not exclude the diagnosis of HFpEF
Indexed LA volume	> 34 mL/m² (sinus rhythm)	In the absence of valve disease, LA dilation reflects chronically elevated LV filling pressures (in AF, the threshold is > 40 mL/m²)
E/e' ratio at rest	> 9	Sensitivity of 78% and specificity of 59% for the presence of HFpEF confirmed by invasive exercise testing. If a higher cut-off value (> 13) is used, the sensitivity is reduced to 46%, but with greater specificity (86%)
Peak tricuspid regurgitation velocity at rest	> 2.8 m/s	Sensitivity of 54% and specificity of 85% for the presence of HFpEF confirmed by invasive stress test

LA: left atrium; AF: atrial fibrillation; HFpEF: heart failure with preserved ejection fraction; LV: left ventricle. Source: adapted from McDonagh.[3]

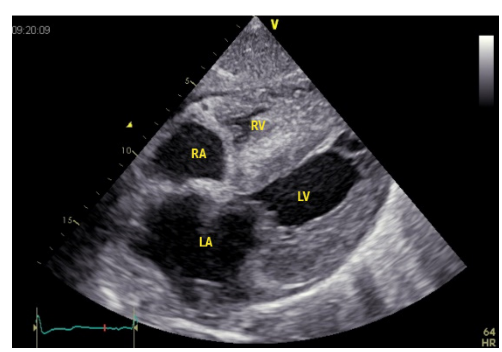


Figure 6 – *Cardiac amyloidosis with extensive myocardial infiltration, valves, and interatrial septum. RV: right ventricle; RA: right atrium; LV: left ventricle; LA: left atrium. Source: personal archive.*

maximum heart rate or develops limiting symptoms. The test is considered abnormal if the E/e′ ratio at peak stress is ≥ 15, with or without TRV > 3.4 m/s. It should be noted that increased TRV alone should not be used for the diagnosis of HFpEF, as it may simply represent a normal hyperdynamic response to effort, caused by increased pulmonary flow, even in the absence of diastolic dysfunction.[27-29]

In the presence of inconclusive results, one should consider performing an invasive stress test, measuring CP at rest and during effort (algorithm described in Figure 1).

Special cases

In patients with AF, the determination of the diastolic function pattern is compromised, given the absence of the A wave. However, filling pressures may be estimated using the E/e′ ratio or other variables. In cases of high filling pressures, the E-wave deceleration time and the isovolumetric relaxation time (IVRT) will be reduced.

In patients with pulmonary hypertension who develop RV overload, ventricular interdependence is usually altered, with a paradoxical septal movement. In these cases, only the lateral mitral annular velocity should be used, as the septal annular velocity will be reduced.

Another common situation, especially among older adults, is mitral annular calcification, which considerably reduces e′ wave velocity, overestimating the E/e′ ratio. In these cases, the E/A pattern on pulsed Doppler and the IVRT should be used instead of the E/e ratio.[30,31]

Conclusions

Diagnosing HFpEF is not simple, and the interaction between the clinician and the echocardiographer plays a key role in this process. The examiner has great responsibility and may even screen some patients in the outpatient setting, identifying higher risk phenotypes. Identifying specific imaging features can reduce the time until diagnosis; however, in most cases, clinical suspicion will be raised in a detailed report. There are controversies about the best indexes for obtaining LV filling pressures noninvasively, which are often tested in different settings and with different objectives. The adequate use of each discussed marker, respecting their limitations, will be of great value for the clinician in their etiological search.

Author Contributions

Critical revision of the manuscript for important intellectual content: Garcia MI

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any thesis or dissertation work.

Ethics approval and consent to participate

This article does not contain any studies with human participants or animals performed by any of the authors.

References

1. Owan TE, Hodge DO, Herges RM, Jacobsen SJ, Roger VL, Redfield MM. Trends in Prevalence and Outcome of Heart Failure with Preserved Ejection Fraction. N Engl J Med. 2006;355(3):251-9. doi: 10.1056/NEJMoa052256.
2. Almeida Junior GL, Xavier SS, Garcia MI, Clausell N. Hemodynamic Assessment in Heart Failure: Role of Physical Examination and Noninvasive Methods. Arq Bras Cardiol. 2012;98(1):e15-21. doi: 10.1590/s0066-782x2012000100020.
3. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2021 ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure. Eur Heart J. 2021;42(36):3599-726. doi: 10.1093/eurheartj/ehab368.
4. Reddy YNV, Carter RE, Obokata M, Redfield MM, Borlaug BA. A Simple, Evidence-Based Approach to Help Guide Diagnosis of Heart Failure With Preserved Ejection Fraction. Circulation.;138(9):861-70. doi: 10.1161/CIRCULATIONAHA.118.034646.
5. Pieske B, Tschöpe C, de Boer RA, Fraser AG, Anker SD, Donal E, et al. How to Diagnose Heart Failure with Preserved Ejection Fraction: The HFA-PEFF Diagnostic Algorithm: A Consensus Recommendation from the Heart Failure Association (HFA) of the European Society of Cardiology (ESC). Eur Heart J. 2019;40(40):3297-317. doi: 10.1093/eurheartj/ehz641.
6. Marcondes-Braga FG, Moura LAZ, Issa VS, Vieira JL, Rohde LE, Simões MV, et al. Emerging Topics Update of the Brazilian Heart Failure Guideline - 2021. Arq Bras Cardiol. 2021;116(6):1174-1212. doi: 10.36660/abc.20210367.
7. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2015;28(1):1-39. doi: 10.1016/j.echo.2014.10.003.
8. Garcia MI. Repensando a Definição de Insuficiência Cardíaca Baseada na Fração de Ejeção: Reflexões com Impacto na Terapêutica. ABC Heart Fail Cardiomyop. 2022;2(1):76-79.
9. Nagueh SF. Non-invasive Assessment of Left Ventricular Filling Pressure. Eur J Heart Fail. 2018;20(1):38-48. doi: 10.1002/ejhf.971.
10. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF 3rd, Dokainish H, Edvardsen T, et al. Recommendations for the Evaluation of Left Ventricular Diastolic Function by Echocardiography: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging. 2016;17(12):1321-60. doi: 10.1093/ehjci/jew082.
11. Thavendiranathan P, Yingchoncharoen T, Grant A, Seicean S, Landers SH, Gorodeski EZ, et al. Prediction of 30-day Heart Failure-specific Readmission Risk by Echocardiographic Parameters. Am J Cardiol. 2014;113(2):335-41. doi: 10.1016/j.amjcard.2013.09.025.
12. Melenovsky V, Hwang SJ, Redfield MM, Zakeri R, Lin G, Borlaug BA. Left Atrial Remodeling and Function in Advanced Heart Failure with Preserved or Reduced Ejection Fraction. Circ Heart Fail. 2015;8(2):295-303. doi: 10.1161/CIRCHEARTFAILURE.114.001667.

13. Almeida P, Rodrigues J, Lourenço P, Maciel MJ, Bettencourt P. Left Atrial Volume Index is Critical for the Diagnosis of Heart Failure with Preserved Ejection Fraction. J Cardiovasc Med (Hagerstown). 2018;19(6):304-9. doi: 10.2459/JCM.0000000000000651.

14. Gorter TM, van Veldhuisen DJ, Bauersachs J, Borlaug BA, Celutkiene J, Coats AJS, et al. Right Heart Dysfunction and Failure in Heart Failure with Preserved Ejection Fraction: Mechanisms and Management. Position Statement on Behalf of the Heart Failure Association of the European Society of Cardiology. Eur J Heart Fail. 2018;20(1):16-37. doi: 10.1002/ejhf.1029.

15. Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K, et al. Guidelines for the Echocardiographic Assessment of the Right Heart in Adults: A Report from the American Society of Echocardiography Endorsed by the European Association of Echocardiography, a Registered Branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. J Am Soc Echocardiogr. 2010;23(7):685-713. doi: 10.1016/j.echo.2010.05.010.

16. Zile MR, Baicu CF, Gaasch WH. Diastolic Heart Failure--Abnormalities in Active Relaxation and Passive Stiffness of the Left Ventricle. N Engl J Med. 2004;350(19):1953-9. doi: 10.1056/NEJMoa032566.

17. Kasner M, Westermann D, Steendijk P, Gaub R, Wilkenshoff U, Weitmann K, et al. Utility of Doppler Echocardiography and Tissue Doppler Imaging in the Estimation of Diastolic Function in Heart Failure with Normal Ejection Fraction: A Comparative Doppler-conductance Catheterization Study. Circulation. 2007;116(6):637-47. doi: 10.1161/CIRCULATIONAHA.106.661983.

18. Dokainish H, Nguyen JS, Sengupta R, Pillai M, Alam M, Bobek J, et al. Do Additional Echocardiographic Variables Increase the Accuracy of E/e' for Predicting Left Ventricular Filling Pressure in Normal Ejection Fraction? An Echocardiographic and Invasive Hemodynamic Study. J Am Soc Echocardiogr. 2010;23(2):156-61. doi: 10.1016/j.echo.2009.11.015.

19. Sharifov OF, Schiros CG, Aban I, Denney TS, Gupta H. Diagnostic Accuracy of Tissue Doppler Index E/e' for Evaluating Left Ventricular Filling Pressure and Diastolic Dysfunction/Heart Failure With Preserved Ejection Fraction: A Systematic Review and Meta-Analysis. J Am Heart Assoc. 2016;5(1):e002530. doi: 10.1161/JAHA.115.002530.

20. Borlaug BA, Lam CS, Roger VL, Rodeheffer RJ, Redfield MM. Contractility and Ventricular Systolic Stiffening in Hypertensive Heart Disease Insights into the Pathogenesis of Heart Failure with Preserved Ejection Fraction. J Am Coll Cardiol. 2009;54(5):410-8. doi: 10.1016/j.jacc.2009.05.013.

21. Lam CS, Roger VL, Rodeheffer RJ, Bursi F, Borlaug BA, Ommen SR, et al. Cardiac Structure and Ventricular-vascular Function in Persons with Heart Failure and Preserved Ejection Fraction from Olmsted County, Minnesota. Circulation. 2007;115:1982-990.

22. Phelan D, Collier P, Thavendiranathan P, Popović ZB, Hanna M, Plana JC, et al. Relative Apical Sparing of Longitudinal Strain Using Two-dimensional Speckle-tracking Echocardiography is Both Sensitive and Specific for the Diagnosis of Cardiac Amyloidosis. Heart. 2012;98(19):1442-8. doi: 10.1136/heartjnl-2012-302353.

23. González-López E, Gallego-Delgado M, Guzzo-Merello G, Haro-Del Moral FJ, Cobo-Marcos M, Robles C, et al. Wild-type Transthyretin Amyloidosis as a Cause of Heart Failure with Preserved Ejection Fraction. Eur Heart J. 2015;36(38):2585-94. doi: 10.1093/eurheartj/ehv338.

24. Maron BA, Cockrill BA, Waxman AB, Systrom DM. The Invasive Cardiopulmonary Exercise Test. Circulation. 2013;127(10):1157-64. doi: 10.1161/CIRCULATIONAHA.112.104463.

25. Givertz MM, Fang JC, Sorajja P, Dimas V, Forfia PR, Kapur NK, et al. Executive Summary of the SCAI/HFSA Clinical Expert Consensus Document on the Use of Invasive Hemodynamics for the Diagnosis and Management of Cardiovascular Disease. J Card Fail. 2017;23(6):487-91. doi: 10.1016/j.cardfail.2017.04.013.

26. Obokata M, Kane GC, Reddy YN, Olson TP, Melenovsky V, Borlaug BA. Role of Diastolic Stress Testing in the Evaluation for Heart Failure With Preserved Ejection Fraction: A Simultaneous Invasive-Echocardiographic Study. Circulation. 2017;135(9):825-38. doi: 10.1161/CIRCULATIONAHA.116.024822.

27. Lancellotti P, Pellikka PA, Budts W, Chaudhry FA, Donal E, Dulgheru R, et al. The Clinical Use of Stress Echocardiography in Non-ischaemic Heart Disease: Recommendations from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. Eur Heart J Cardiovasc Imaging. 2016;17(11):1191-229. doi: 10.1093/ehjci/jew190.

28. Belyavskiy E, Morris DA, Url-Michitsch M, Verheyen N, Meinitzer A, Radhakrishnan AK, et al. Diastolic Stress Test Echocardiography in Patients with Suspected Heart Failure with Preserved Ejection Fraction: A Pilot Study. ESC Heart Fail. 2019;6(1):146-53. doi: 10.1002/ehf2.12375.

29. Nagueh SF, Chang SM, Nabi F, Shah DJ, Estep JD. Cardiac Imaging in Patients With Heart Failure and Preserved Ejection Fraction. Circ Cardiovasc Imaging. 2017;10(9):e006547. doi: 10.1161/CIRCIMAGING.117.006547.

30. Mitter SS, Shah SJ, Thomas JD. A Test in Context: E/A and E/e' to Assess Diastolic Dysfunction and LV Filling Pressure. J Am Coll Cardiol. 2017;69(11):1451-64. doi: 10.1016/j.jacc.2016.12.037.

31. Andersen OS, Smiseth OA, Dokainish H, Abudiab MM, Schutt RC, Kumar A, et al. Estimating Left Ventricular Filling Pressure by Echocardiography. J Am Coll Cardiol. 2017;69(15):1937-48. doi: 10.1016/j.jacc.2017.01.058.