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Review article

Heart failure with preserved ejection fraction: current status, diagnostic criteria and therapeutic challenges

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ABSTRACT

Introduction: Heart failure with preserved ejection fraction accounts for approximately half of all heart failure cases, and its prevalence is increasing due to population aging and the high burden of cardiovascular comorbidity. Unlike the reduced ejection fraction subtype, its diagnosis and treatment are challenging.

Objective: To analyze the clinical, diagnostic, and therapeutic aspects, as well as the main controversies described in heart failure with preserved ejection fraction.

Methods:A narrative review of the literature published between 2020 and 2025 in PubMed/MEDLINE, Scopus, SciELO, and Google Scholar. Clinical guidelines, systematic

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reviews, clinical trials, and relevant observational studies were included. Priority was given to information on echocardiographic morphofunctional and hemodynamic variables, diagnostic criteria, and available therapies.

Results: Heart failure with preserved ejection fraction is characterized by diastolic dysfunction, left ventricular hypertrophy, and increased left atrial volume. Echocardiography allows the assessment of morphofunctional and hemodynamic variables essential for diagnosis and follow-up. Current pharmacological treatments have not demonstrated a consistent reduction in mortality; However, diuretics and comorbidity management improve symptoms and reduce hospitalizations. Pathophysiological heterogeneity and variability in diagnostic criteria constitute the main clinical challenges.

Conclusions: Heart failure with preserved ejection fraction is a common and complex syndrome that requires comprehensive assessment through echocardiography and personalized management of comorbidities. Further studies are needed to characterize normal echocardiographic findings during aging, understand the natural history of the disease, and develop more effective therapeutic strategies.

Keywords: Heart failure; Preserved ejection fraction; Diastolic dysfunction; diagnosis; treatment.

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Introduction

Heart failure (HF) represents one of the main cardiovascular health problems worldwide due to its high prevalence, impact on quality of life, frequent hospitalizations, and high mortality. (1) In recent decades, it has been recognized that approximately half of patients with HF have a normal or preserved left ventricular ejection fraction (LVEF), a condition known as heart failure with preserved ejection fraction (HFpEF).

Recognition of this condition has progressively increased, particularly in aging populations and in patients with comorbidities such as hypertension, obesity, diabetes mellitus, and chronic kidney disease. However, despite its growing clinical relevance, HFpEF is a complex and heterogeneous syndrome whose pathophysiology, diagnostic criteria, and therapeutic approach remain a subject of debate.

Unlike heart failure with reduced ejection fraction (HFrEF), where therapies have been shown to decrease mortality and hospitalizations, in heart failure with preserved ejection fraction (HFpEF) available treatments have shown limited results in terms of survival, which has generated significant clinical and scientific challenges. (2,3)

The objective of this narrative review is to analyze the clinical, diagnostic, therapeutic aspects and the main controversies described in heart failure with preserved ejection fraction.

Method

A narrative review of the scientific literature on HFpEF was conducted. The literature search was performed in recognized biomedical databases, including PubMed/MEDLINE, Scopus, SciELO, and Google Scholar. Search terms in Spanish and English related to the topic were used, including: heart failure with preserved ejection fraction, HFpEF, diastolic dysfunction, echocardiography, diagnosis, management, treatment, and guidelines. Articles published in the last five years were prioritized, including systematic reviews, clinical trials, observational studies, and clinical practice guidelines issued by international scientific societies. (Table 1).

The inclusion criteria considered relevant publications addressing epidemiological, pathophysiological, diagnostic, and therapeutic aspects of HFpEF, as well as studies evaluating the role of morphological, functional, and hemodynamic echocardiographic variables in the diagnosis and follow-up of this condition. Duplicate publications, studies

with incomplete information, or those whose subject matter was not directly related to the objective of the review were excluded.

HFpEF was defined as a patient with clinical manifestations of HF according to the Framingham criteria and a left ventricular ejection fraction ≥ 50% from an echocardiographic point of view.

The collected information was critically analyzed and synthesized for the purpose of identifying the main scientific advances, current controversies and knowledge gaps in relation to ICFEp.

Table 1 Bibliographic search strategy used in the review

Database	Main descriptors	Boolean operators	Type of documents	Search period
PubMed/ MEDLINE	Heart failure with preserved ejection fraction; HFpEF; Diastolic dysfunction; Echocardiography; Diagnosis; Treatment	AND / OR	Reviews, clinical trials, clinical guidelines	2020–2025
Scopus	Heart failure with preserved ejection fraction; Echocardiographic parameters; Diastolic function; Cardiac remodeling	AND / OR	Original articles, reviews	2020–2025
SciELO	Heart failure with preserved ejection fraction; Diastolic dysfunction; Echocardiography	AND / OR	Original articles and reviews	2020–2025
Google Scholar	HFpEF; Diagnosis; Echocardiography; Management	AND / OR	Relevant scientific reviews and documents	2020–2025

Legend: HFpEF, heart failure with preserved systolic function/Heart failure with preserved systolic function.

Ethical considerations

This study is a narrative review of the scientific literature based exclusively on information previously published in academic and scientific sources. Consequently, no direct intervention was performed on humans or animals, nor were any identifiable individual clinical data used.

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Development

Heart failure with preserved ejection fraction (HFpEF) currently accounts for approximately 50% of heart failure cases in clinical practice, and its prevalence continues to rise due to population aging and the increase in risk factors.cardiometabolic. It is associated with high morbidity, frequent hospitalizations and an annual mortality rate of approximately 15%. (4,5)

This syndrome is particularly common in elderly patients, women, with a history of high blood pressure, obesity, diabetes mellitus, chronic kidney disease, and atrial fibrillation.

Although traditionally considered a “less severe” form of heart failure, recent studies show that mortality and hospitalization rates are comparable to those observed in patients with HFrEF.

In addition, patients with HFpEF have a high burden of symptoms, mainly exertional dyspnea, exercise intolerance and pulmonary congestion, which leads to a significant deterioration in quality of life and frequent hospital readmissions.

The pathophysiology of HFpEF is complex and multifactorial. It has traditionally been associated with left ventricular diastolic dysfunction, characterized by alterations in ventricular distensibility and relaxation, which translates into increased myocardial stiffness. (6-8)

However, recent research suggests that multiple pathophysiological mechanisms are involved, including: (5, 6)

- Ventricular diastolic dysfunction.
- Left ventricular hypertrophy.
- Endothelial dysfunction.
- Systemic inflammation.

- Coronary microvascular alterations.
- Increased arterial stiffness.
- Cardiorenal and cardiopulmonary interactions.

In many cases, HFpEF develops as a result of the interaction between systemic comorbidity and structural changes of cardiovascular aging.

Fluid overload may be absent, particularly in patients receiving diuretic treatment for hypertension. This can lead to misdiagnosis of mild disease.

On the other hand, age-related dyspnea is quite common, which can lead to overdiagnosis of this disease.

Consensus guidelines recommend that the diagnosis of heart failure be ruled out in patients with B-type natriuretic peptide (BNP) levels below 100 ng/L or proBNP levels below 400 ng/L, as these have a high negative predictive value (97%). (7)

One of the main challenges in the study of HFpEF lies in the absence of uniform diagnostic criteria.

Various scientific societies recommend different diagnostic algorithms (Table 2); among which the following stand out:

- European Society of Cardiology (ESC) criteria. (8) Integrated clinical diagnosis.
- HFA-PEFF algorithm. (9) Validation of the scale in the Barandiarán serieset al, (8) showed that a low score can rule out HFpEF with a sensitivity of 99% and a negative predictive value of 73%. The diagnostic accuracy of the score is 0.90 (0.84-0.96), by the area under the receiver operating characteristic (ROC) curve.
- H2FPEF scale; in the external validation of this score, the H2FPEF score had good discriminatory performance with an area under the ROC curve of 0.88 in a validation cohort where the prevalence of HFpEF was 64%. It uses 6 clinical and echocardiographic

variables including age > 60 years, body mass index >30 kg/m2, hypertension with ≥ 2 antihypertensive medications, atrial fibrillation, E/e' ratio > 9 and pulmonary artery systolic pressure > 35 mmHg.

- The Alberta HEART study demonstrated that the H2FPEF model's score range allows for the application of separate cut-off points to confirm or rule out the diagnosis of HFpEF, with acceptable discriminatory power (c-statistic > 0.8). (10)

Table 2. Comparison of diagnostic criteria for heart failure with preserved ejection fraction.

Criterion	ESC	HFA-PEFF	H2FPEF
Ejection fraction	≥ 50%	≥ 50%	≥ 50%
Symptoms of IC	Required	Required	Required
Biomarkers	Elevated BNP / NT-proBNP	Biomarker-based scoring	Indirectly included
Structural alterations	Left ventricular hypertrophy or left atrial dilation	Structural scoring system	Not explicit
Diastolic parameters	TDI: High E/e', reduced e' speed	Functional domain with score	Not explicit
Clinical factors	Not included	Partially included	Age, obesity, atrial fibrillation, hypertension
Diagnostic result	Integrated clinical diagnosis	A score ≥ 5 confirms ICFEp	scale ≥ 6 high probability

Legenda: BNP / NT-proBNP. Brain natriuretic peptide (BNP) / N-terminal pro-B-type brain natriuretic peptide (NT-proBNP).

ESCEuropean Society of Cardiology.

HFA-PEFF Algorithm(Heart Failure Association Pre-test assessment. (Pre-test assessment of the HFA-PEFF (Heart Failure Association).

H2FPEF scale Includes: obesity (H); use of ≥ 2 antihypertensive drugs (H); atrial fibrillation (F); pulmonary hypertension (P); age > 60 years (E); and E/e' > 9 (F).

In general, the diagnosis of ICFEp requires the presence of three fundamental elements: (3,4,11, 12)

- Symptoms and signs of heart failure.
- Preserved left ventricular ejection fraction (≥ 50%).
- Objective evidence of structural or functional cardiac alterations, primarily diastolic dysfunction.

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Importance of evaluating echocardiographic morphofunctional and hemodynamic variables in HFpEF.

In this context, echocardiographic assessment allows the identification of characteristic structural changes, evaluation of ventricular diastolic function, and indirect estimation of intracardiac hemodynamic conditions. (Table 3).

Table 3. Main echocardiographic variables in the evaluation of HFpEF. (3,4,9, 13)

Variable type	Echocardiographic parameter	Clinical significance
Morphological	Left ventricular mass index > 110 g/m2	Left ventricular hypertrophy
Morphological	Left atrial volume index > 34 mL/m2	Marker of chronic elevation of filling pressures
Functional	E/A ratio of the mitral flowgram ≤ 0.8 or ≥ 2.0	Diastolic filling assessment Diastolic dysfunction
Functional	e' velocity (Tissue Doppler)	Myocardial relaxation
Hemodynamics	E/e' ratio > 8	Estimated left ventricular filling pressure (Estimated left atrial pressure/pulmonary capillary pressure) > 14 mmHg
Hemodynamics	Pulmonary artery systolic pressure > 30 mmHg	Detection of secondary pulmonary hypertension

Legend: ICFEp heart failure with preserved ejection fraction

These variables are essential not only to confirm the diagnosis, but also to understand the pathophysiology of the syndrome and guide therapeutic decisions.

Morphological variables

Morphological variables provide information on cardiac structural changes associated with pressure or volume overload and ventricular remodeling. (20,21)

Among the most relevant are:

- Left ventricular hypertrophy, generally secondary to chronic high blood pressure.
- Increased left atrial volume index (LAVI), considered a marker of chronic elevation of filling pressures.
- Increased left ventricular mass index.

- Geometric alterations of the left ventricle (LV), including concentric remodeling.

Left atrial (LA) dilation is one of the most robust indicators of chronic diastolic dysfunction and is associated with an increased risk of atrial fibrillation and adverse cardiovascular events. (14)

Functional variables

Echocardiographic functional assessment allows characterization of left ventricular diastolic function, a central aspect in the pathophysiology of HFpEF.

Among the most commonly used parameters are:

- E/A ratio of the transmitral flow E/A.
- Myocardial relaxation velocity (e') by tissue Doppler.
- E/e' ratio**,**used as an estimator of ventricular filling pressures > 14.
- Left atrial strain ≤ 18%.
- Transmitral flow deceleration time.

Integrating these parameters allows for the identification of diastolic dysfunction patterns and the estimation of the severity of alterations in ventricular relaxation. (15,16)

Echocardiographic hemodynamic variables

In addition to structural and functional variables, echocardiography allows for the indirect estimation of various hemodynamic variables that reflect the interaction between the left ventricle, the left atrium, and the pulmonary circulation.

Among the most relevant are: estimated pulmonary artery systolic pressure, left ventricular filling pressures, E/e' ratio as a marker of left atrial pressure, and tricuspid regurgitation jet velocity > 2.8 m/s. (3,4,10-12,17)

These variables are particularly important in patients with HFpEF, since the increase in filling pressures may initially manifest during exercise or under conditions of hemodynamic stress, which explains the frequent presence of exertional dyspnea in these patients.

The 2025 American Society of Echocardiography (ASE) guidelines (18) propose aupdated approach with early identification of impaired myocardial relaxation, definedby reducing the e' velocity of the mitral annulus≤ 6.5 cm/s, or a septal e' velocity ≤ 6 cm/s or a lateral e' velocity ≤ 7 cm/s when only one measurement is availableIt also incorporates the recommendation to use age-adjusted cut-off points, which reflects an explicit recognition of the influence of aging on diastolic parameters and contributes to improving the clinical accuracy of the diagnosis.

Following this initial step, the evaluation focuses on identifying markers suggestive of elevated left ventricular filling pressures and cardiac chamber remodeling. These include an average E/e' ratio > 14, an E/A ratio ≤ 0.8 or ≥ 2 in mitral flow, a peak tricuspid regurgitation velocity > 2.8 m/s, and a left atrial volume index (LAVI) > 34 mL/m². The concomitant presence of impaired relaxation and any of these parameters supports the diagnosis of diastolic dysfunction. (19) This diagnosis can also be established even in the absence of obvious relaxation impairment when at least two additional markers are documented.

Validation studies demonstrate the limited performance of the IVAI as a single marker of LV filling pressures, underscoring the need for a multiparametric approach. (20) Accordingly, algorithm validation analyses consistently support the combined use of two or more complementary indices to improve diagnostic reliability. (21)

Taken together, the ASE 2025 recommendations reinforce the concept that the diagnosis of diastolic dysfunction and HFpEF should be based on a comprehensive approach that combines echocardiographic findings, biomarkers, and pretest clinical probability. (22)

Despite the methodological advances introduced, gaps remain related to the prospective validation of the algorithm in different clinical settings and the need for more sensitive criteria for early detection of the disease.

Therefore, the current challenge lies not only in perfecting diagnostic tools, but also in optimizing their integration within clinical decision models that allow for a more precise characterization of the HFpEF phenotype.

Furthermore, the integration of echocardiographic parameters with biomarkers and clinical variables contributes to improving risk stratification and optimizing therapeutic management.

Current treatment

Unlike what was observed in HFrEF, most clinical trials conducted in patients with HFpEF have not demonstrated significant benefits in reducing mortality.

Consequently, the treatment focuses primarily on:

1. Control of pulmonary congestion. Diuretics are the most effective treatment for relieving symptoms related to pulmonary and peripheral congestion (Furosemide and Spironolactone are among the most effective).
2. Comorbidity management. Appropriate treatment of concomitant diseases plays a fundamental role in disease control, particularly: hypertension, diabetes mellitus, atrial fibrillation, obesity, and chronic kidney disease.
3. Blood pressure control. High blood pressure is one of the most important factors in the development and progression of HFpEF, so its strict control is a priority therapeutic goal.

Clinical trials evaluating the use of renin-angiotensin system inhibitors, mineralocorticoid receptor antagonists, and beta-blockers in heart failure with preserved ejection fraction (HFpEF) have yielded heterogeneous and generally inconsistent results. In recent years,

sodium-glucose cotransporter 2 (SGLT2) inhibitors have shown promising results in reducing hospitalizations, representing a new therapeutic perspective in this population. (23) In particular, the EMPEROR-Preserved trial (24) demonstrated a significant reduction in the combined risk of cardiovascular death at the expense of a reduction in hospitalizations. (Table 4).

The 2023 update to the heart failure (HF) guidelines published by the European Society of Cardiology (8), which focused on the recommendations issued in 2021, incorporated significant changes based on the most recent scientific evidence. Among the main changes is the recommendation to use sodium-glucose cotransporter 2 (SGLT2) inhibitors and finerenone, a selective non-steroidal mineralocorticoid receptor antagonist, for the prevention of HF in patients with chronic kidney disease associated with diabetes mellitus. Furthermore, the indication for SGLT2 inhibitors as a therapeutic pillar across the entire spectrum of LVEF is being expanded, reflecting a paradigm shift in the contemporary pharmacological approach to this clinical syndrome.

Table 4. Relevant clinical trials in heart failure with preserved ejection fraction

Study	Year	Drug	Main results
PEP-CHF (9.25)	2006	Perindopril	No significant reduction in mortality
CHARM-Preserved (26)	2003	Candesartan	Modest reduction in hospitalizations
I-PRESERVE Trial (27)	2008	Irbesartan	No benefit in mortality
TOPCAT (28	2014	Spironolactone	Reduction in hospitalizations due to heart failure
PARAGON-HF (29)	2019	Sacubitril/valsartan	Profit trend, not significant
EMPEROR-Preserved (24)	2021	Empagliflozin	Reduction in the combined risk of cardiovascular death or hospitalization for heart failure by 21%
DELIVER Trial (23)	2022	Dapagliflozin	Significant reduction in hospitalizations for heart failure

Legend

PEP-CHF The perindopril in elderly people with chronic heart failure (PEP-CHF) study.
CHARM-Preserved Candesartan in Heart failure Assessment of Reduction in Mortality and morbidity.
I-PRESERVE Trial Irbesartan in Heart Failure and Preserved Ejection Fraction.
TOP ATT Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist.
PARAGON-HF Angiotensin–Neprilysin Inhibition in Heart Failure with Preserved Ejection Fraction.

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EMPEROR-Preserved Empagliflozin in Heart Failure with a Preserved Ejection Fraction.
DELIVER Trial: Dapagliflozin in heart failure with mildly reduced ejection fraction or preserved

Although some studies have shown a reduction in the rate of hospitalizations for heart failure, a significant benefit on overall survival has not been conclusively demonstrated. The prognosis of patients with HFpEF is closely related to the clinical severity at the time of diagnosis and the context in which the disease is detected. It is estimated that approximately one in ten patients dies within five years of diagnosis; however, this proportion can increase to nearly one in three in those cases first identified during an episode of hospitalization for decompensated heart failure. (30-32)

From a comparative perspective, some observational studies have shown that HFpEF is associated with lower long-term cardiovascular mortality compared to HFrEF, with an adjusted odds ratio of 0.79 (95% CI: 0.67–0.95). (33) Consistently, a meta-analysis that included patients from 31 studies reported an adjusted odds ratio for all-cause mortality of 0.68 (95% CI: 0.64–0.71) in HFpEF versus HFrEF. Furthermore, in patients older than 60 years with type 2 diabetes mellitus, overall mortality in incident cases of HFpEF was lower compared to that observed in HFrEF (1.51 vs. 3.31 per 100 person-years). (34)

Current controversies

Despite advances in research, multiple controversies surrounding ICFEp persist.

Heterogeneity of the syndrome: HFpEF does not represent a single disease, but a heterogeneous set of clinical phenotypes, which makes it difficult to develop uniform diagnostic and therapeutic strategies.

Diagnostic definition: the lack of consensus in diagnostic criteria generates variability in the identification of patients and limits the comparison between studies.

Value of echocardiography: there are uncertainties regarding the interpretation of echocardiographic parameters in elderly patients and in differentiating between physiological cardiac aging and disease.

Limitations of the article

The main limitations stem from its narrative review nature, which may imply heterogeneity in the selection and interpretation of scientific evidence. The variability in diagnostic criteria and methodological designs of the analyzed studies limits the comparability of results and the robustness of conclusions.

Conclusions

Heart failure with preserved ejection fraction is a common and complex clinical syndrome that presents a significant challenge to contemporary cardiology. Despite its high prevalence and impact on cardiovascular morbidity and mortality, significant uncertainties remain regarding its pathophysiology, diagnosis, and treatment. The variability in diagnostic criteria and the limited efficacy of available therapies in terms of survival underscore the need for continued research into this condition.

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Conflicts of interest

The authors declare that there are no financial, personal or professional conflicts of interest that may have influenced the performance or interpretation of the results of this study.

Authorship contribution

Julio Cesar Gonzalez Cesar: conceptualization, formal analysis, research methodology, project management, writing – original draft, writing – revision and editing.

Julio Alberto Pérez Domínguez:conceptualization, formal analysis, research methodology, writing, review, supervision, validation.

Raúl Leyva Castro:resources, formal analysis, research, methodology, validation.

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