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# Echocardiographic Features of Heart Failure with Preserved Ejection Fraction

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**Abstract:**
The ejection fraction (EF) is at or above 50% in about half of heart failure patients. The etiology of heart failure with preserved ejection fraction (HFpEF) is still somewhat contentious, and there are no evidence-based management guidelines in place, despite the condition's high prevalence, morbidity, and economic impact. Older women with a history of systolic hypertension, many of whom have heart hypertrophy and obesity, make up the bulk of HFpEF patients. Only a small percentage of them acquire clinical HFpEF, and the majority do not exhibit any heart failure (HF) symptoms, even if they may have preclinical disease. Increased ventricular end-systolic stiffness (elastance), vascular stiffening (17–19), and abnormal diastolic function have all been linked, although it's not obvious which characteristics are most distinct and independent.

**Keywords:** Echocardiographic Features, Heart Failure, Preserved Ejection Fraction.

## Introduction:

Heart failure with preserved ejection fraction is common, a frequent clinical condition, is rising in tandem with the increased load of comorbidities and aging in the population (1). More than half of individuals with unexplained exertional dyspnea who are referred for invasive evaluation ultimately develop HFpEF, while more than 70% of patients with prevalent heart failure over 65 have normal ejection fraction (2). The assessment and treatment of HFpEF heavily relies on cardiovascular imaging, especially echocardiography (3).

Echocardiography, which provides vital information on heart structure, function, and hemodynamics, is performed on nearly all patients with a clinical suspicion of developing HFpEF (3). Risk stratification for outcomes; (2) management, which includes using imaging to assess hemodynamic status and identify underlying pathophysiologic phenotypes; and (3) diagnosis, which entails determining whether a patient's unexplained dyspnea actually has HFpEF or another cardiac or non-cardiac cause. These are the most important issues that can be practically addressed. This chapter critically assesses the role of echocardiography in treating patients with or suspected of having HFpEF, taking into account these three groups (4).

## Diastolic Dysfunction and HFpEF:

Although the terms diastolic dysfunction and HFpEF are commonly used interchangeably, they are not the same thing. HFpEF requires the presence of high filling pressures, either at rest or

during activity, to maintain systemic perfusion (5). The pathophysiology of HFpEF is complex, despite the fact that diastolic dysfunction is a major component. A number of factors, such as diastolic dysfunction, impaired contractile reserve, impaired atrial function, relative pericardial restraint, and abnormal ventricular vascular coupling, contribute to the increase in pulmonary venous and left-sided filling pressures (6). Elevations in LV filling Pressures worsen dyspnea feelings, decrease exercise capacity (7), and raise the risk of HF hospitalization and death in HFpEF (8). The etiology of HFpEF is therefore thought to be based on diastolic dysfunction (6). An increase in viscoelastic LV diastolic chamber stiffness, a prolonging of relaxation in early diastole, or a combination of the two is known as diastolic dysfunction. Not every patient with diastolic dysfunction has or will develop clinical HFpEF because LV relaxation and compliance reductions are a normal part of aging (9). Just 12% of participants in a prospective cohort trial who had severe diastolic dysfunction at the time of first evaluation went on to develop clinical HFpEF throughout the six-year follow-up period. Diastolic dysfunction is not evident on echocardiograms in around one-third of HFpEF patients who are enrolled in treatment trials (10).

Accordingly, current research has indicated that echocardiographic classification of diastolic dysfunction should not be utilized alone for diagnostic purposes, even though it is predictive and helpful in predicting incident HFpEF (11).

**Echocardiography to Identify Increased Filling Pressure:**

The last sign of issues with diastolic function is an increase in LV filling pressures. Filling pressures have been estimated using a variety of echocardiographic indices, but the E/e' is by far the most studied (11). The diagnostic accuracy of the E/e' ratio in HFpEF is called into question because a recent meta-analysis revealed only a modest correlation (pooled r = 0.56) between E/e' and invasively obtained resting filling pressures across studies (3). In patients with sustained EF, thirty studies have found relationships between E/e' and invasive filling pressure, ranging in strength from 0.02 to 0.87. Despite its erratic and usually weak relationship with filling pressure, E/e' has been demonstrated to have prognostic value in patients with HFpEF (10).

Transmitral flow (TMF), which is driven by the LA-LV pressure gradient during diastole, can be used to identify high filling pressure in patients with normal sinus rhythm. TMF is commonly classified as normal, poor relaxation, pseudonormal, and restrictive filling patterns. Because TMF is affected by LA pressure, the E/A ratio shows a U-shaped relationship with LV filling pressure. The biphasic connection of the E/A ratio makes it difficult for clinicians to differentiate between normal and pseudonormal patterns, thus they must rely on other echocardiographic indices, such as the E/e' ratio (4).

LV filling pressures have also been linked to other indicators. LV end-diastolic pressure (LVEDP) and end-diastolic LV operative compliance are measured by pulmonary vein (PV) Reversals of Doppler flow during atrial contraction. When the resistance to end-diastolic atrial contraction is raised, the flow reversal into the PV is extended relative to the forward flow period. Increased LVEDP has been linked to variations in these periods longer than 20 to 30 milliseconds, with an 87% diagnostic sensitivity and an 85% specificity. Reasonable correlations between invasively measured LV filling pressure and backward and forward PV flow time in patients with maintained EF have been found in six investigations (r = 0.39–0.70). Despite the apparent benefits of these data, It is often not technically feasible to capture the PV Doppler flow in a diagnostic-quality manner, and other PV metrics, such as systolic and diastolic flow velocities, are less accurate. Therefore, as filling pressure indicators, PV Doppler indices have not gained much traction (12). Determining the downstream consequences of elevated left-sided filling pressures on the LA is an alternate technique for evaluating their long-term implications. Through atrioventricular coupling, LV diastolic performance is linked to both atrial operational compliance and atrial

volume. LA remodeling and dysfunction are caused by LV diastolic dysfunction, which results in chronic resistance to LA emptying. Instead of reflecting immediate pressures, LA volume is believed to represent the long-term repercussions of an increase in LV filling pressure (13).

Compared to other indices like E/e' and PV Doppler, Since the LA volume index is a chronic indicator, there are weaker relationships between it and ambient LV filling pressures (r = 0.10–0.49). This does not mean that the cumulative effects of filling pressure do not affect HFpEF outcome, even though the LA volume index has a less correlation with HFpEF outcome than E/e'. Instead, it emphasizes the need to evaluate LA burden using a different metric, like LA reservoir strain, which is discussed later (14).

According to earlier research, concentric hypertrophy is seen in individuals with HFpEF, which raises filling pressure by increasing passive chamber stiffness. The invasively recorded LV filling pressure and the LV mass index have a moderately strong connection (r = 0.41–0.48; P<.001). The latest guidelines from the European Society of Cardiology (ESC) include a higher LV mass index as one of the criteria for diagnosing HFpEF. However, community-based research and trial supplemental studies have shown that some people with HFpEF have concentric remodeling without hypertrophy or even normal LV shape. (15).

According to a recent study, LV hypertrophy was found to be highly specific (88%) but poorly sensitive (26%), meaning that its absence cannot be used to rule out the diagnosis of HFpEF. Other differential diagnoses that mimic HFpEF should be carefully ruled out when assessing LV morphology (Table 1). Amyloidosis should always be suspected when there is noticeable LV hypertrophy, especially if there is a pericardial effusion or an apical sparing pattern of LV strain. Amyloidosis was found in 13% of hospitalized "HFpEF" Among a group of patients who have LV hypertrophy that is more than or equal to 12 mm. This distinction from HFpEF is particularly important in light of the development of new treatments for cardiac amyloid (16).

**Table (1):** Differential diagnoses of HFpEF and their echocardiographic clues.

| Differential Diagnosis | Echocardiographic Clues |
|---|---|
| **Hypertrophic cardiomyopathy** | Asymmetric hypertrophy, ↑↑LV wall thickness, LVOT obstruction, SAM |
| **Restrictive cardiomyopathy** | Small LV cavity, ↑LV wall thickness, sparkling myocardium, apical sparing, severely reduced tissue Doppler, PE |
| **Pulmonary arterial hypertension** | ↑RVSP with no sign of increased LV filling pressure, isolated right heart dilatation, PA dilatation, RVOT Doppler midsystolic notch |
| **Constrictive pericarditis** | Pericardial thickening, septal bounce, annulus paradoxus and annulus reversus, ↑respiratory variation in mitral/ tricuspid flow, absence of IVC collapse |
| **Valvular heart disease** | Morphologic valvular abnormalities, color Doppler |
| **Coronary artery disease** | Regional wall motion abnormality and thinning |
| **Chronic thromboembolic pulmonary hypertension** | ↑RVSP with no sign of increased LV filling pressure, isolated right heart dilatation, PA dilatation, RVOT Doppler midsystolic notch |
| **High-output HF** | ↑Doppler-derived cardiac output |

IVC = inferior vena cava; LVOT = left ventricular outflow obstruction; PA = pulmonary artery; PE = pericardial effusion; RVOT = right ventricular outflow; SAM = systolic anterior motion of the mitral valve.

LV filling pressure has also been estimated using strain and strain rate imaging. The ratio of mitral E velocity to longitudinal diastolic strain rate during early diastole (E/SRE) demonstrated a reasonable connection with invasively acquired filling pressure, with high sensitivity and specificity (E/SRE >11.5, 91%, and 78%, respectively). In one investigation, E/SRE outperformed E/e' as a predictor of cardiovascular outcomes (17). Smaller investigations have observed correlations between filling pressures and LV GLS (18). Left atrial longitudinal strain during ventricular systole serves as a representation of atrial reservoir function, which is decreased in HFpEF (19). Although invasive filling pressure and LA reservoir strain have been found to be highly correlated in one study (r = -0.79) in patients with maintained EF (20), their capacity to distinguish between HFpEF and noncardiac dyspnea has not yet been investigated. Reduced GLS (> -16%), on the other hand, has been linked to negative outcomes in HFpEF **(21)**.

**Optimal Use of Echocardiography in Diagnosis of HFpEF:**

When pulmonary congestion, peripheral edema, and jugular vein distention are evident in individuals with overt congestion at rest, the diagnosis of HFpEF is clear and does not require echocardiography. On the other hand, diagnosing euvolemic patients with exertional dyspnea is more difficult. As previously mentioned, several echocardiographic indices are connected with filling pressures, and correlational analyses are crucial for demonstrating the degree of relationship between two variables. However, from a diagnostic standpoint, the ability of a test to distinguish between cases and controls is more significant than basic correlative analyses (22).

An elevated E/e' ratio has been found to have a high specificity for identifying high LV filling pressure (77%–100%), suggesting that it may be useful in ruling out HFpEF when elevated. However, the E/e' ratio is not a useful test for ruling out HFpEF because of its low sensitivity (0%–73%). Since poorer relaxation is expected to follow high filling pressures, it has been proposed that an increase in E/e' be accompanied by an impairment in e' velocity. This more stringent

criterion will only worsen sensitivity even though it might boost specificity (23).

As an additional measure of diastolic dysfunction, An high LA volume index has been recommended by expert consensus, with a cut point of greater than 34 mL/m2. When examined prospectively, an extended LA volume index (>34 mL/m2) is specific (83%) for HFpEF but also has poor sensitivity (49%), much like E/e'. One potential cause for worry is how to appropriately allometrically adjust LA volume to body size in obese patients, who comprise the bulk of the HFpEF population. A linear adjustment of the LA volume index to body surface area may understate LA remodeling in obese people since the quotient falls as body mass increases. Another aspect that complicates the determination of LA volume is atrial fibrillation. Since recent research has shown that atrial fibrillation in patients with dyspnea is highly predictive of the presence of underlying HFpEF, this is less of an issue, at least in terms of diagnosis (24).

To diagnose HFpEF, the current guidelines suggest using a variety of diastolic function indices. These methods have been proven to have poor sensitivity despite having excellent specificity. The authors have developed a simple measure to predict the existence of HFpEF in more than 500 individuals with unexplained dyspnea. Even though many echocardiographic variables were predictive of HFpEF diagnosis when taken into consideration separately, the combination of elevated E/e’ (>9) and RVSP (>35 mmHg) was additive to clinical characteristics, such as older age, larger BMI, number of antihypertensive medications, and history of atrial fibrillation in multivariable analyses (H2FPEF score). This approach retained its remarkable discriminatory ability after validation in a different test cohort (area under the curve, 0.886; P<.0001). Therefore, although though a number of echocardiographic indications are associated with the presence or absence of HFpEF, it seems that the combination of E/e' and RVSP is the most effective method to inform the noninvasive diagnosis (24).

Using the echocardiography data (increased E/e' and RVSP), older age, obesity, and the use of two antihypertensive drugs, the approach concludes that HFpEF is the 92% likely cause of exertional dyspnea. Patients with extremely low odds, on the other hand, can be ruled out, and further investigation is necessary to determine the cause. As will be covered later, To identify the cause of exertional dyspnea, dynamic stress testing is required to evaluate an abnormal increase in filling pressure (Fig. 1). An exercise catheterization examination confirmed the diagnosis of HFpEF in this case, showing a normal pulmonary capillary wedge pressure (PCWP) at rest (11 mmHg) but markedly raised filling pressures with effort (30 mm Hg) (11).

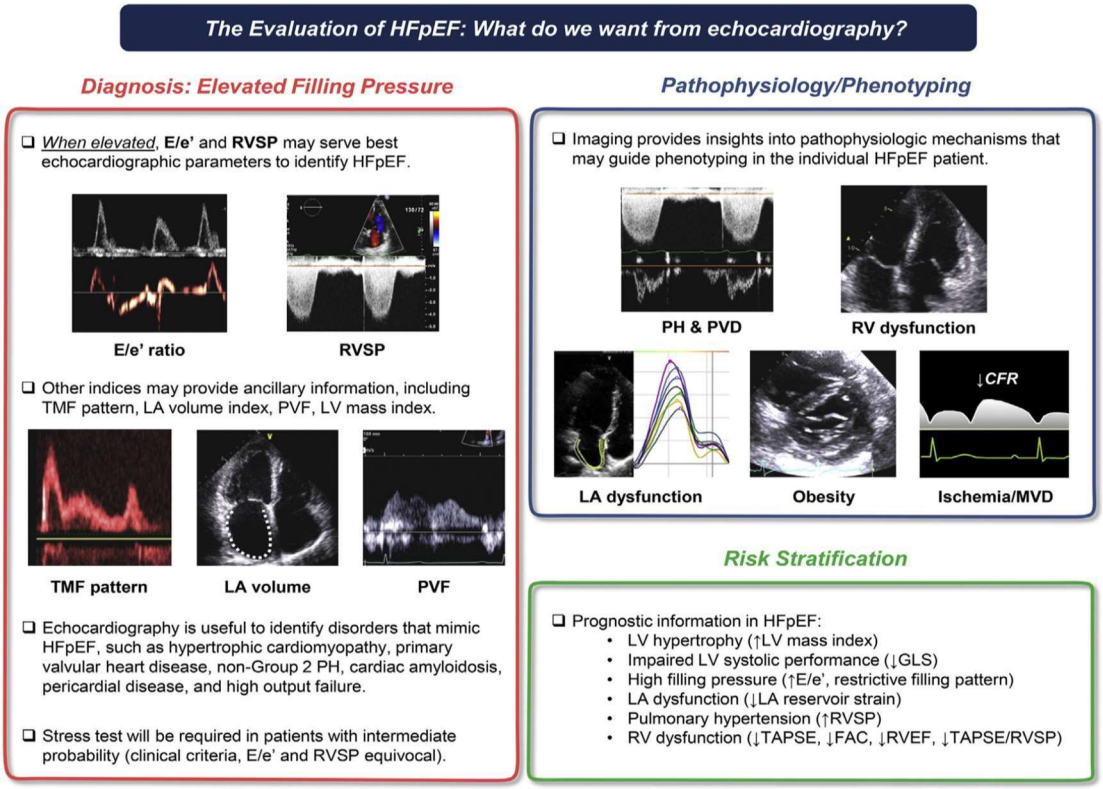


**Figure (1):** An overview of noninvasive imaging's function in HFpEF assessment. TAPSE stands for tricuspid annular plane systolic excursion; MVD for microvascular dysfunction; PH for pulmonary hypertension; PVD for pulmonary vascular disease; PVF for pulmonary venous flow; and FAC for RV fractional area change.

**Diastolic stress echocardiography for the diagnosis of HFpEF:**

The difficulty in detecting HFpEF is exacerbated by the fact that filling pressures are often normal at rest but only increase under the stress of exercise. As a result, the gold standard for conclusively identifying or ruling out HFpEF as the cause of dyspnea is invasive cardiopulmonary exercise testing. Recent research has assessed whether diastolic stress echocardiography can provide comparable information noninvasively. (**Fig. 2**) **(11)**.

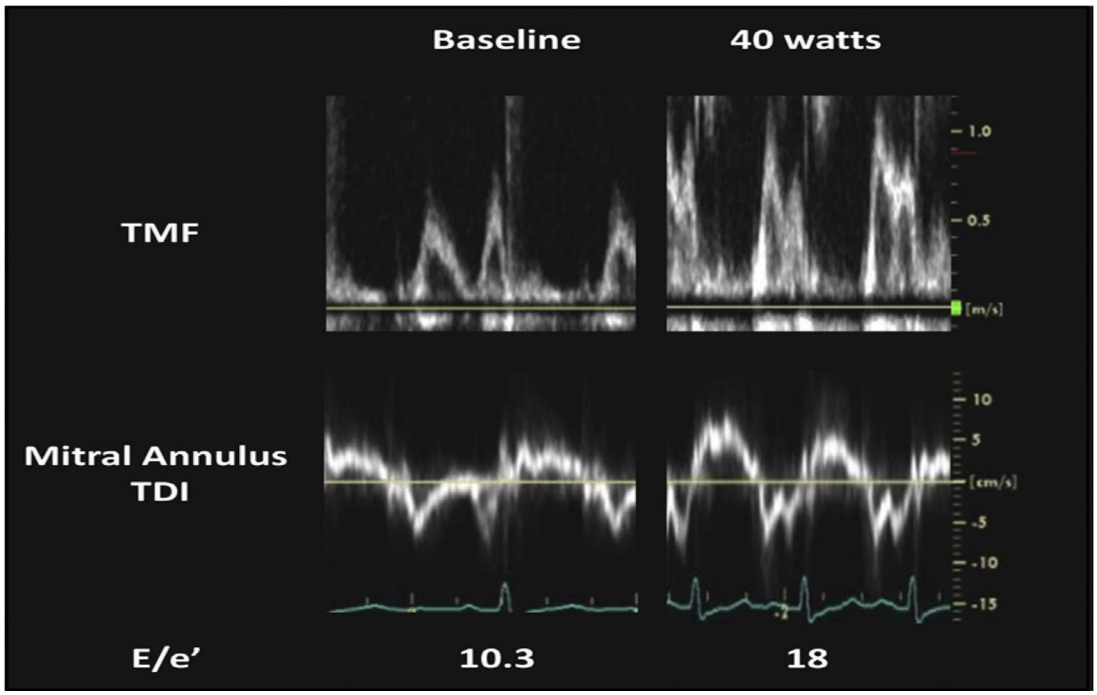


**Figure (2):** Diastolic stress echocardiography in a typical scenario. TMF and mitral annular tissue Doppler velocities were measured at rest and during 40 W supine ergometer exercise in a patient with invasively proven HFpEF (PCWP during exercise, 27 mm Hg). At baseline, transthoracic echocardiogram shows normal E/e' (average 10.3), normal EF (70%), normal LA volume index (30 mL/m2), and an estimated RVSP of 28 mm Hg. The E/e' ratio rises when exercise up to 40 W generates a significant increase in mitral E without a noticeable change in e'. The tricuspid regurgitant velocity increases from 2.5 to 3.5 m/s during exercise. TDI stands for tissue Doppler imaging.

A recent study that used simultaneous catheterization-echocardiographic evaluation at rest and during exercise found that adding E/e' during exercise increased sensitivity for diagnosing HFpEF when compared to resting assessment alone, but at the expense of decreased specificity, in patients being evaluated for exertional dyspnea (EF ≥ 50%). However, only 74 patients were enrolled in this single-center experiment, and other organizations have not shown favorable results in HFpEF using exercise echocardiography. Some studies have questioned E/e's ability to track changes in filling pressure during exercise because it increases significantly less than directly measured filling pressures. Given the conflicting results in all published studies to date and the lack of reproducibility, more validation is required to elucidate the value of noninvasive diastolic stress echocardiography in the evaluation of HFpEF, ideally using multicenter designs(25).

It has been demonstrated that aberrant LV systolic and diastolic responses to exercise, as determined by LV longitudinal strain or strain rate and E/e', increase risk prediction when compared to clinical and resting measures in HFpEF; however, further validation in larger, multicenter studies is also necessary for this use (26).

**Echocardiography to Identify HFpEF Phenotypes:**

It was recently acknowledged that HFpEF is a heterogeneous condition, and clinical trials have consistently shown that treatments that take a one-size-fits-all approach have not worked. 83 Cardiovascular imaging may be a very helpful technique to facilitate this categorization, because there is an unmet need to group different phenotypes into pathophysiologically homogenous groups within the broader spectrum of HFpEF. Potential phenotypes that might be used for further in-depth echocardiography characterization in HFpEF are described below **(27)**.

**Left Atrial Dysfunction Phenotype:**

Poorer dyspnea symptoms, more pulmonary vascular disease, greater RV dysfunction, less exercise capacity, and adverse HFpEF outcomes are all associated with increased LV filling pressure-induced LA remodeling and dysfunction. Therefore, one possible subphenotype of HFpEF could be LA hypertension/dysfunction. Numerous recent studies have demonstrated the value of using speckletracking echocardiography to measure LA reservoir strain in order to detect LA dysfunction, aid in diagnosis, and forecast outcomes in HFpEF **(28)**.

**Pulmonary Hypertension and Pulmonary Vascular Disease Phenotype:**

Pulmonary hypertension (PH), which is associated with poorer clinical outcomes and exercise capacity, is common in patients with HFpEF. Although PH is mostly linked to LA hypertension in most HFpEF patients, some people develop pulmonary vascular disease, which is defined by a decrease in pulmonary arterial compliance and an increase in pulmonary vascular resistance. In pulmonary vascular disease, HFpEF is associated with reduced exercise capacity, inadequate RV systolic reserve, and worse outcomes, suggesting a unique HFpEF spectrum profile. Pulmonary vascular disease is indicated by midsystolic notching in the RV outflow Doppler profile and a short acceleration time caused by increased pulmonary artery impedance with enhanced early wave reflection. An increasing number of people are realizing the importance of the RV-PA coupling. A recent study found that RV-PA coupling, as determined by tricuspid annular plane systolic excursion (TAPSE) to RVSP (<0.36 mm/mm Hg), predicts pulmonary vascular disease in HFpEF **(29)**.

**Right Ventricular Dysfunction Phenotype:**

RV systolic dysfunction in HFpEF is caused by PH, However, recent studies suggest that RV-PA coupling is considerably more important. TAPSE, RV fractional area change, free wall strain, tricuspid annular s' velocity, and RV index of myocardial performance are all markers of RV systolic function. Therefore, RV-PA coupling can be assessed by the ratio of RV function to RVSP, and a lower TAPSE/RVSP ratio (<0.36 mm/mm Hg) is associated with poorer HFpEF outcomes (30).

RV remodeling is linked to RV dysfunction. Echocardiography can be used to assess right atrial (RA) dilatation, RV hypertrophy, and RV dilatation (basal, mid, and longitudinal dimensions and areas). It has been shown that increasing RV diameter, area, and wall thickness predict adverse outcomes in HFpEF. Tricuspid annular dilatation and tricuspid insufficiency are brought on by RV and RA dilatation, especially during activity. These conditions can exacerbate left heart filling and promote systemic venous congestion. Therefore, the severity of tricuspid insufficiency should be assessed in all patients with HFpEF (31).

**Obesity Phenotype:**

Nowadays, obesity is acknowledged as a significant HFpEF characteristic. When compared to patients with nonobese HFpEF, patients with the obesity phenotype show some notable changes. These include lower exercise capacity, ventricular remodeling, deleterious hemodynamics, higher pericardial constraint, changed RV-pulmonary artery coupling, and stronger correlations between cardiac filling pressures and body weight. Noninvasive measures of the degree of relative pericardial constraint, which increases PCWP in patients with HFpEF obesity, pulmonary vascular phenotype, and severe tricuspid insufficiency, can be obtained from assessments of the septal configuration of the short axis (**Fig. 3**) **(23)**.

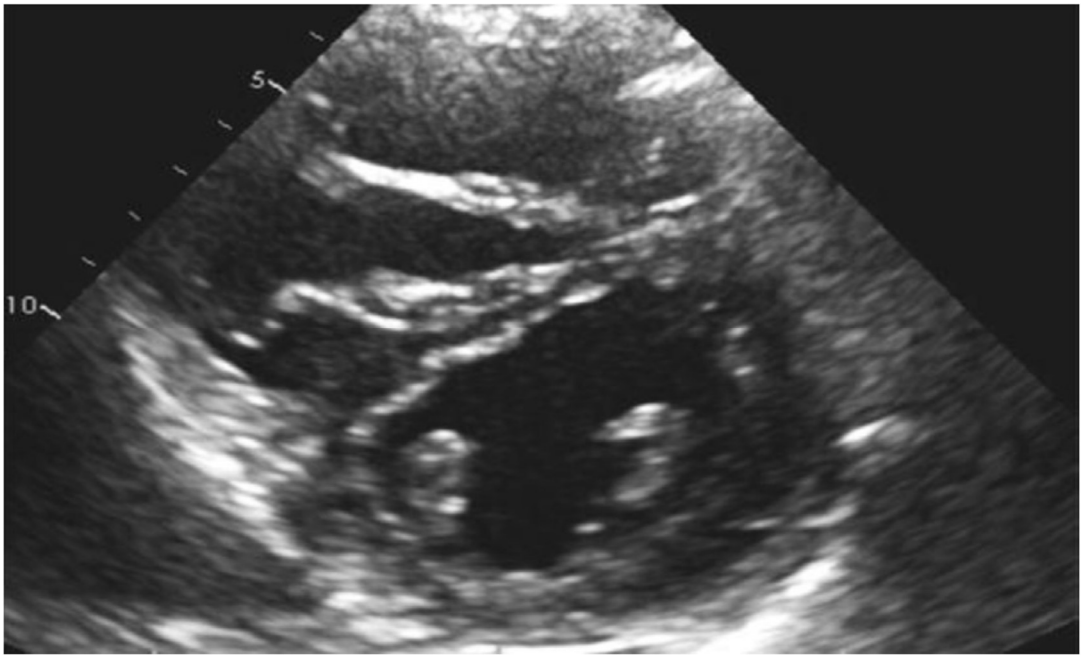


**Figure (3):** An example of obese HFpEF. The D-shaped septum is seen in an echocardiographic parasternal short-axis image at end-diastole in a patient with obese HFpEF (BMI, 44 kg/m2). After cardiac catheterization, the RA pressure (17 mm Hg) is significantly higher than the PCWP (21 mm Hg).

Because they change hemodynamics, generate ectopic fat deposits, visceral adiposity, and systemic and local inflammation. They can also result in mechanical compression that exacerbates pericardial constriction. It has recently been discovered that abdominal obesity is linked to higher mortality in HFpEF and is also connected with epicardial fat. Echocardiography can be used to measure epicardial thickness (Fig. 4), but other modalities including computed tomography and MRI provide more reliable results. **(32)**.

**Ischemia/microvascular dysfunction phenotype:**

Given its high incidence, poor prognosis, and most importantly the potential for revascularization to improve outcomes, the presence of epicardial coronary artery disease characterizes a unique HFpEF profile. Patients with HFpEF have been shown to have large rates of false-positive and false-negative testing, as well as reduced accuracy rates for stress imaging, including echocardiography. This study would suggest that even in the absence of epicardial coronary stenosis, HFpEF can result in subendocardial ischemia, which is caused by a combination of coronary microvascular dysfunction and hemodynamic abnormalities that limit subendocardial perfusion. **(33)**.

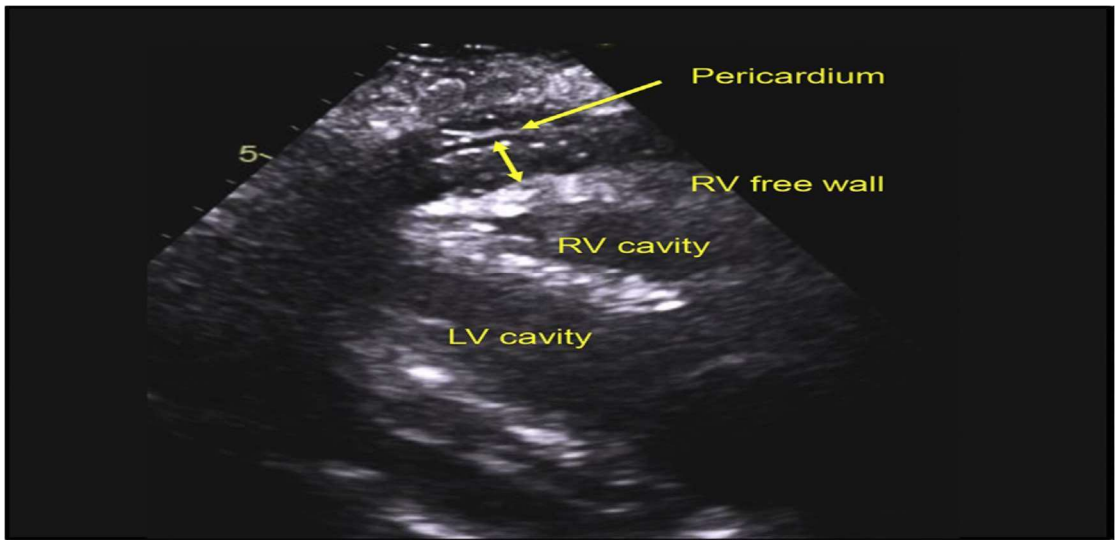


**Figure (4):** In obese HFpEF, there is noticeable epicardial fat. End-systole parasternal long-axis image of a patient with HFpEF who is obese (BMI: 38 kg/m2). Take note of the 14 mm increase in epicardial fat thickness between the pericardium and the RV free wall.

Patients with HFpEF who also have more myocardial damage during exercise in addition to myocardial supply-demand mismatch exhibit the most notable losses in left ventricular systolic and diastolic reserve, elevated filling pressures during exercise, and more reduced exercise capacity (33).

According to a recent study, coronary flow reserve in these patients can be evaluated using adenosine stress echocardiography. This could be a useful noninvasive phenotyping tool, especially if novel therapies are created that target microvascular function. With the help of the many imaging modalities, it is hoped that new treatments for microvascular dysfunction will be properly directed to the suitable individuals. Other teams have used nuclear and MRI-based imaging to assess coronary microvascular dysfunction in HFpEF (34).

**Future Perspectives:**

Echocardiography is unquestionably crucial to the assessment of HFpEF and offers useful data for estimating left ventricular filling pressure, comprehending pathogenesis, and enhancing diagnosis and prognostic evaluation. Echocardiography, when combined with clinical features, can assist in assessing the probability of HFpEF and enable better decision-making on the necessity of further sophisticated testing. However, invasive hemodynamic exercise testing is frequently necessary to confirm or deny the diagnosis of HFpEF, as echocardiography alone is frequently insufficient in this regard. Although the best approaches to classify individuals are yet uncertain, echocardiography is essential in helping to provide customized treatment by classifying patients with HFpEF according to underlying pathophysiologic characteristics. Furthermore, prognostic data indicating certain pathophysiologic anomalies in HFpEF are provided by echocardiographic measures. Further study is necessary to determine the optimum uses of noninvasive imaging in combination with other clinical markers for HFpEF phenotyping, the roles of different modalities in its assessment, the potential utility of diastolic stress echocardiography, and standardized diagnostic criteria for HFpEF.

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