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HOW TO

# How to assess left ventricular filling pressures by echocardiography in clinical practice

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## Introduction

Left ventricular diastolic dysfunction (LVDD) plays a key role in the pathophysiology of heart failure (HF). It is caused by impaired left ventricular (LV) relaxation with or without reduced restoring forces and increased LV chamber stiffness leading to the inability of the ventricle to fill adequately and to provide a normal stroke volume at normal filling pressure (LVFP), at rest and/or during exercise.

## What is LVFP and why is it important?

Left ventricular filling pressure is the pressure that fills the ventricle in diastole and determines stroke volume according to the Frank-Starling mechanism. In patients with HF, there is typically elevated LVFP at rest, and in some cases only during exercise. Elevated LVFP is a hallmark of HF and therefore has great importance in HF diagnostics.

During left heart catheterization, LVFP is measured as LV end-diastolic pressure (LVEDP). Alternatively, LVFP is measured as LV pressure prior to onset of left atrial (LA) contraction (LV pre-A pressure), which approximates LA mean pressure. During right heart catheterization, LVFP is assessed as pulmonary capillary wedge pressure (PCWP), which is an indirect measure of LA mean pressure. During sinus rhythm, LVEDP is higher than PCWP and LV Pre-A pressure.

Left ventricular filling pressure is considered elevated when LVEDP ≥16 mmHg and PCWP or LV pre-A pressure ≥15 mmHg.[1,2]

## Echocardiographic indices of LVFP

A number of echocardiographic parameters may be used to differentiate between normal and elevated LVFP. All the recommended parameters can be acquired during a routine echocardiographic study (*Figure 1*).

These parameters may also be used for grading diastolic dysfunction.[2] Importantly, not all individuals with diastolic dysfunction have structural heart disease as grade 1 diastolic dysfunction, which implies normal LVFP, may be seen in many conditions.[2]

A combination of transmitral flow velocities, mitral annular velocities, LA volume and strain, and estimated systolic pulmonary pressures is recommended to assess LVFP in clinical practice. Importantly, none of these parameters is accurate enough to be used as a single diagnostic marker. Mitral flow velocities are largely determined by the transmitral pressure gradient. Thus, peak mitral E wave velocity and the ratio between early (E) and late (atrial - A) ventricular filling velocity (E/A ratio) are valuable parameters in the estimation of LA pressure, particularly in patients with myocardial disease or LV systolic dysfunction, in whom diastolic dysfunction is ascertained. However, elevated mitral E velocity cannot be used alone to confirm elevated LAP in normal hearts where a tall mitral E is normally expected due to a brisk LV untwist leading to rapid decrease in early diastolic LV pressure.

The combination of mitral E velocity (which increases with LVDD severity) with PW Tissue Doppler Imaging-derived e′ velocity (which decreases with LVDD severity) provides the E/e′ ratio, a parameter directly related to LVFP. The correlation between E/e′ and LVFP has been confirmed in patients with both reduced and preserved LVEF, using different cut-off values according to the site of e′ measurement. An E/e′ ratio <8 (calculated using the average of septal and lateral e′ velocities) is associated with normal LVFP, whilst a ratio >14 is associated with elevated LVFP.[1] The E/e′ ratio has the advantage of being less age-dependent compared to mitral flow velocities and e′. Moreover, the ratio can be used to assess LVFP in patients with atrial fibrillation or LA dysfunction.

LA size and function measured by echocardiography can be used in combination with other indices as additional markers of chronic

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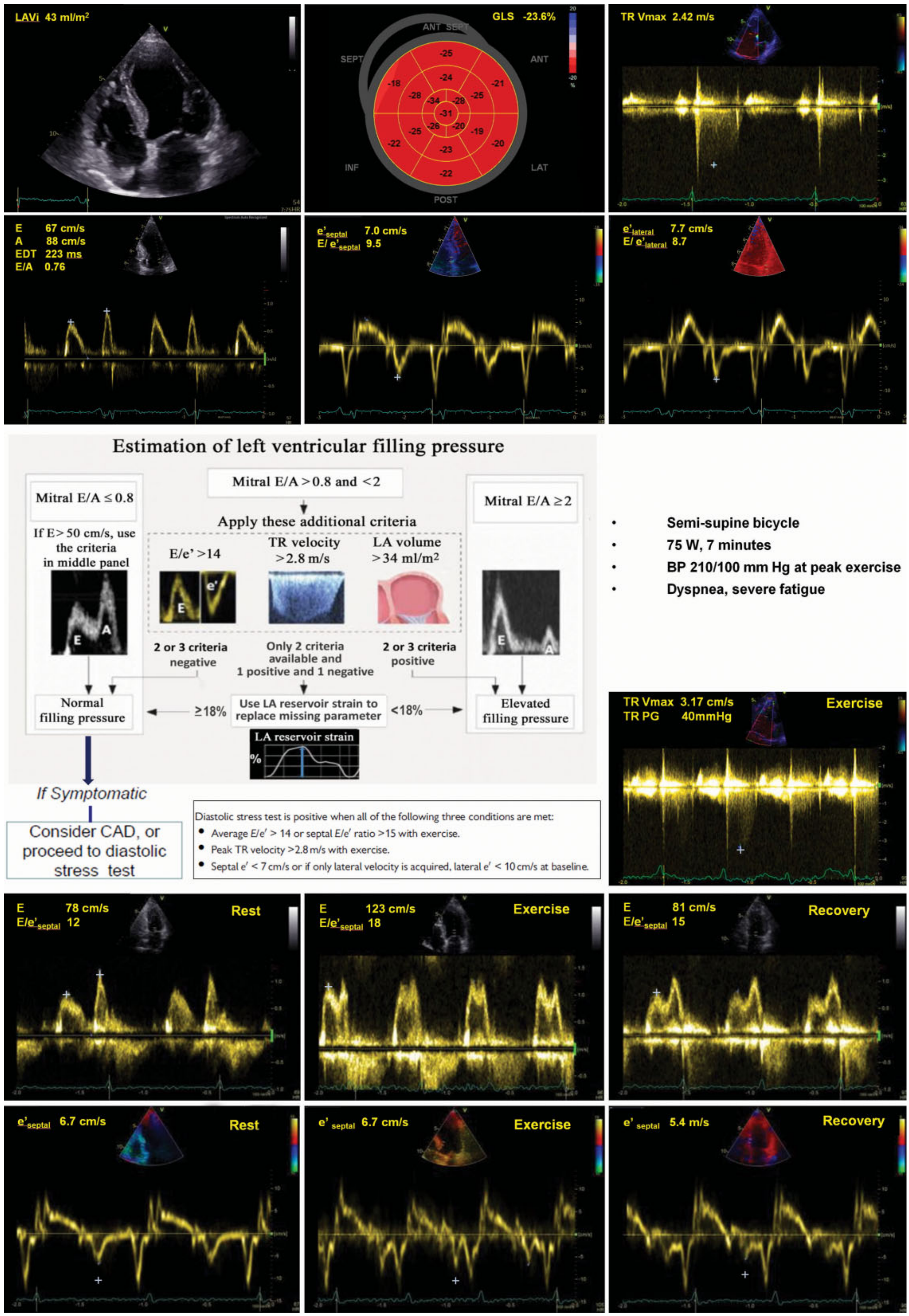


**Figure 1** Diastolic stress echocardiographic data acquired at rest, at symptom limited peak exercise and during recovery in a 66-year-old woman with hypertension and exertional dyspnoea. Echocardiographic assessment of left ventricular diastolic function at rest indicates normal left ventricular filling pressure. However, during exercise, there is a significant increase in the E/e′ ratio and the tricuspid regurgitation peak velocity, suggestive of elevated left ventricular filling pressure with exercise.

elevation of LAP. Thus, an enlarged LA [maximum LA volume index (LAVi) ≥ 34 mL/m$^2$] is a marker of elevated LAP in subjects without alternative causes for LA dilation (e.g. athletes, mitral valve disease, atrial fibrillation/flutter, high output states—anaemia, hyperthyroidism, bradycardia).[1] LA volume is measured using the biplane disk summation technique and is indexed to body surface area (LAVi).[1] Underestimation of LAV with 2D echocardiography can be avoided by using dedicated apical views, avoiding foreshortening to maximize LA size. However, LAVi should not be used as a stand-alone parameter of elevated LVFP since it is insensitive to early raises of LVFP and, on the other hand, LA enlargement may persist after normalization of LAP (e.g. patients with congestive HF treated with diuretics).[2]

LA reservoir strain by 2D-speckle tracking echocardiography is measured during ventricular systole as the average of peak positive longitudinal strain values from all LA segments in the apical four-chamber view. The lower limit of normality of LA reservoir strain is vendor and age-dependent, but values <19–23% are considered abnormal.[2] LA reservoir strain <18% predicted elevated LVFP better than LA volume and conventional Doppler parameters in a population with cardiovascular disease of different aetiologies and median LV EF of 55%.[3] It should be noted though that the ability of LA strain to differentiate between normal and elevated LVFP is better in patients with LVEF < 50%. Another important parameter to evaluate LVFP is systolic pulmonary artery pressure calculated as the sum of the systolic tricuspid pressure gradient and the estimated right atrial pressure. In the absence of pulmonary arterial hypertension or other suspected cause of non-cardiac pulmonary hypertension, a tricuspid regurgitation peak velocity >2.8 m/s supports the presence of elevated LVFP.[2] This method is limited by the absence of suitable tricuspid regurgitation recordings in many patients, particularly in those with normal LVEF. Intravenous saline may be used to enhance the tricuspid velocity signal and obtain reliable measurements of its peak velocity in these patients.

# Algorithm for evaluation of LVFP

*Figure 1* shows the algorithm recommended by the European Association of Cardiovascular Imaging (EACVI) to evaluate LVFP.[2]

Importantly, the recommendations advocate careful consideration of all available clinical, 2D, and Doppler data to conclude about diastolic function. Thus, the evaluation of LV diastolic function should always start by assessing the presence of clinical risk factors associated with LVDD (e.g. hypertension, coronary artery disease, diabetes), by looking for structural cardiac abnormalities (e.g. pathological LV hypertrophy, LA dilation), or by detecting LV systolic dysfunction (e.g. reduced EF, mitral annulus systolic velocities, and LV global longitudinal strain). In patients with ascertained LVDD based on this preliminary evaluation (i.e. patients with reduced LVEF, patients with normal LVEF and myocardial disease), evaluation of LVFP should follow based on the algorithm illustrated in Figure 1. In subjects with normal ejection fraction and absent clinical/2D/Doppler data of myocardial disease, the guidelines advocate an additional algorithm based on the four variables mentioned above to diagnose LVDD and only if LVDD is confirmed the assessment of LVFP should follow. LA reservoir strain is recommended as a parameter for LVFP assessment when one of the three key criteria is missing, and the remaining two are conflicting.[2]

Because LVFP may be elevated only during exercise, a diastolic stress test should be added in the setting of suspected heart failure with preserved ejection fraction (HFpEF) and normal resting LVFP. The most appropriate population for diastolic exercise testing are patients with delayed myocardial relaxation and normal LAP at rest. Measurements of E/e′ ratio and peak TR velocity during exercise are feasible and have been invasively validated for the estimation of LVFP during exercise (*Figure 1*). An important limitation of the algorithm is that it cannot be applied in patients with atrial fibrillation. Alternative approaches in these patients are presented in detail in the 2016 American Society of Echocardiography/EACVI recommendation document.[1] The accuracy of this algorithm shown in *Figure 1* has been validated against invasive gold-standard measurement of LVFP in several studies.[2–5]

# Clinical implications

Identification of elevated LVFP at rest or during exercise is pivotal for the diagnosis of HFpEF, which gained additional interest since medical treatment options have recently expanded. The algorithm shown in *Figure 1* can identify patients with preserved LVEF and elevated LVFP with high feasibility and fairly good accuracy. Moreover, excellent interobserver accuracy and reproducibility have been reported.[2,5] Information about LVFP is important not only to diagnose HF but also to better appreciate its severity, response to treatment and prognosis. The prognostic significance of diastolic function grading regardless of EF has recently been recognized in several patient populations. A low event rate has been reported in patients classified with normal diastolic function.

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