Echocardiographic Evaluation of Left Ventricular Diastolic Function

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1. Introduction

The mortality, hospitalization, and prevalence rates of heart failure (HF) are increasing, in spite of decrease in coronary artery and cerebrovascular disease mortality.[1]

Approximately half of patients with a diagnosis of heart failure have a normal left ventricular (LV) ejection fraction (EF) without valve disease which is defined as diastolic heart failure (DHF), because it is attributed to LV diastolic dysfunction.[2] Studies examining prevalence of diastolic heart failure in hospitalized patients or in patients undergoing outpatient diagnostic screening and prospective community based studies have shown that the prevalence of diastolic heart failure approaches 50%.[3-5]

They tend to be older and female, and their condition is likely to be associated with hypertension, diabetes mellitus and ischemic heart disease. Many reports show that the mortality and morbidity of DHF is minimal differences from that of HF with a reduced EF. Moreover, although the mortality and morbidity have improved for patients with HF with a reduced EF, it has not changed for patients with DHF. So, the Evaluation of LV diastolic function is important.

LV diastolic function is related to myocardial relaxation and passive LV properties and is modulated myocardial tone. Myocardial relaxation is an active process, while stiffness is on the contrary a mechanical property of the myocardial wall.

Echocardiography is useful for the evaluation of LV diastolic function. The points of diastolic function to be estimated with echocardiography are propagation velocities, pulmonary vein Doppler, mitral inflow pattern and tissue Doppler imaging. We discuss the estimation of LV diastolic function with echocardiography.

2. The mechanism of DHF

Heart failure is a clinical syndrome characterized by symptoms and signs of increased tissue water and decreased tissue perfusion. Definition of the mechanisms that cause this clinical syndrome requires measurement of both systolic and diastolic function. When heart failure is accompanied by a predominant or isolated abnormality in diastolic function, this clinical syndrome is called diastolic heart failure. The pathophysiology is attributed to LV diastolic dysfunction, in which LV diastolic chamber size is normal or reduced despite elevated filling pressures resulting in decreased cardiac output. DHF occurs when the ventricular chamber is unable to accept an adequate volume of blood during diastole, because of a decrease in ventricular relaxation and/or an increase in ventricular stiffness,[2] and increased circulating blood volume is present. Hypertension, ischemia, aging and diabetes mellitus are the major risk factor of a decrease in ventricular relaxation and/or an increase in ventricular stiffness. Endocardial biopsies from HF patients without coronary artery disease (CAD) showed structural and functional differences in cardiomyocytes from patients with diastolic HF compared to cardiomyocytes from patients with abnormal systolic ejection fraction.[6] Myocytes from patients with diastolic HF had increased diameter and higher myofibrillar density and developed greater passive force and had greater calcium sensitivity. Myocardial collagen volume fraction was equally elevated.

Patients with DHF were shown to have similar pathophysiological characteristics, compared with HF patients with a reduced EF including reduced exercise capacity and impaired quality of life. DHF will be present in heart failure with preserved ejection fraction. When it is difficult with diagnosing HF, it is important to use echocardiography. [7,8]

2.1. The diagnosis of DHF

The diagnosis of heart failure with preserved left ventricular (LV) ejection fraction (HFpEF) requires the following conditions to be satisfied: (1) signs or symptoms of heart failure; (2) normal or mildly abnormal systolic LV function; (3) evidence of diastolic LV dysfunction. Normal or mildly abnormal systolic LV function implies both an LVEF > 50% and an LV end-diastolic volume index (LVEDVI) < 97 mL/m². Diagnostic evidence of diastolic LV dysfunction can be obtained invasively (LV end-diastolic pressure >16 mmHg or mean pulmonary capillary wedge pressure >12 mmHg) or non-invasively by tissue Doppler imaging (TDI) (E/E' >15) with an echocardiography. If TDI yields an E/E' ratio suggestive of diastolic LV dysfunction (8 < E/E' < 15), additional non-invasive investigations are required for diagnostic evidence of diastolic LV dysfunction. These can consist of blood flow Doppler of mitral valve or pulmonary veins, echocardiographic measures of LV mass index or left atrial volume index, electrocardiographic evidence of atrial fibrillation, or plasma levels of natriuretic peptides. If plasma BNP is more than 200 pg/mL, diagnostic evidence of diastolic LV dysfunction also requires additional non-invasive investigations.

A similar strategy with focus on a high negative predictive value of successive investigations is proposed for the exclusion of HFpEF in patients with breathlessness and no signs of congestion. If a patient with breathlessness and no signs of fluid overload has a BNP of less

than 100 pg/mL, any form of heart failure is virtually ruled out because of the high negative predictive value of the natriuretic peptides, and pulmonary disease becomes the most likely cause of breathlessness. [9, 10]

As far as diastolic dysfunction, in decompensated patients with advanced systolic heart failure (LVEF≦30%, New York Heart Association class III to IV symptoms), tissue Doppler-derived with E/E' ratio may not be as reliable in predicting intracardiac filling pressures, particularly in those with larger LV volumes, more impaired cardiac indices, and the presence of cardiac resynchronization therapy. [11]

2.2. Echocardiography in LV diastolic dysfunction

2.2.1. Doppler echocardiographic assessment of diastolic function and filling pressures

Comprehensive Doppler echocardiography is invaluable in the evaluation of HF patients. It is established that the mitral E wave velocity reflects the LA-LV pressure gradient during early diastole and is therefore affected by preload and alterations in LV relaxation. Assessment of diastolic function begins with the transmitral flow velocity profile. Decreases in the ratio of early to late diastolic filling (E/A), increases in the deceleration time, increases in the isovolumic relaxation time, or increases in tissue Doppler imagings (E/E') indicate impaired relaxation. However, in the presence of impaired relaxation, increases in filling pressure progressively modify the transmitral gradient and mitral inflow pattern. A comprehensive Doppler assessment must be used to determine diastolic function from filling pressures and tissue Doppler imagings. [10] Patients studied at various times during their presentation will display a spectrum of filling patterns, including abnormal relaxation and psuedonormal or restrictive patterns. Such a spectrum has also been reported in patients with HF with a depressed EF and reflects the potent effect of filling pressures and blood pressure and their interaction with underlying diastolic dysfunction on the Doppler patterns. Thus, depending on their level of compensation and their filling pressures and whether they have exertional or rest symptoms, patients with HFpEF may display any of the filling patterns.[12]

2.2.2. Tissue Doppler imaging

Tissue Doppler imaging (TDI) is performed in the apical views to acquire mitral annular velocities with pulse wave. The sample volume should be positioned at 1 cm within the septal and lateral insertion sites of the mitral leaflets. It is recommended that spectral recordings be obtained at a sweep speed of 50 to 100 mm/s at end-expiration and that measurements should reflect the average of more than 3 consecutive cardiac cycles. Primary measurements include the systolic and early (e') and late (a') diastolic velocities. For the assessment of global LV diastolic function, it is recommended to acquire and measure tissue Doppler signals at least at the septal and lateral sides of the mitral annulus and their average. In patients with cardiac disease, e' can be used to correct for the effect of LV relaxation on mitral E velocity, and the E/e' ratio can be applied for the prediction of LV filling pressures. The E/e' ratio is not accurate as an index of filling pressures in normal subjects or in patients with heavy annular calcification, mitral valve disease, and constrictive pericarditis.

Strain and strain rate can be derived from either tissue Doppler or speckle tracking 2-dimensional echocardiography. Using tissue Doppler, which is a form of pulsed Doppler, specific points within the myocardium can be identified. Tracking these Doppler points enables measurement of strain rate. Because Doppler is velocity or distance divided by time, the initial measurement is strain rate. Integrating the strain rate gives strain. The estimation of strain in the global left ventricular wall is called as global longitudinal strain (GLS).
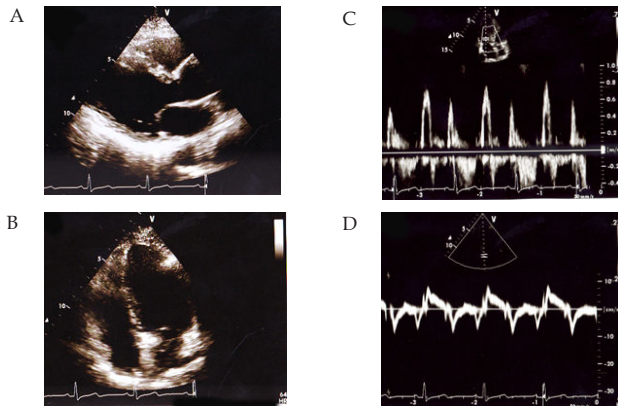

Figure 1. Normal pattern in LV inflow: Panel A shows long axis view. Panel B shows 4 chamber view. Panel C shows LV inflow. Panel D shows tissue Doppler imaging.
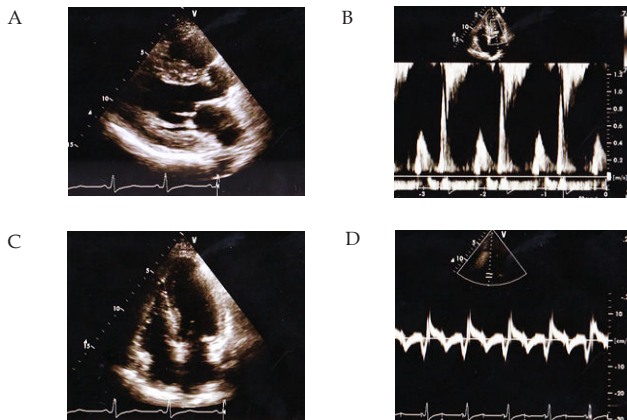

Figure 2. Abnormal relaxation pattern in LV inflow: Panel A shows long axis view. Panel B shows 4 chamber view. Panel C shows LV inflow. Panel D shows tissue Doppler imaging.
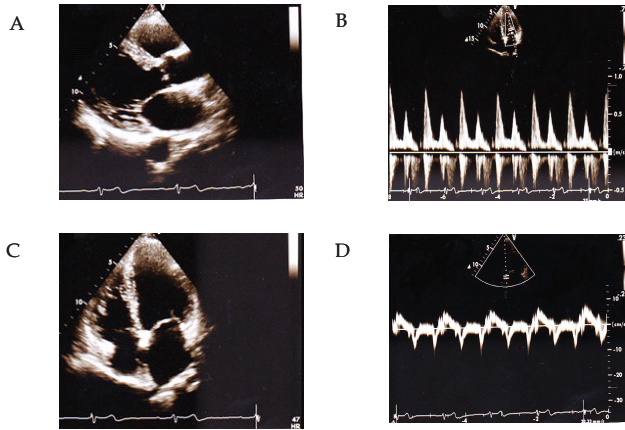
Figure 3. Pseudonormalized pattern in LV inflow: Panel A shows long axis view. Panel B shows 4 chamber view. Panel C shows LV inflow. Panel D shows tissue Doppler imaging.
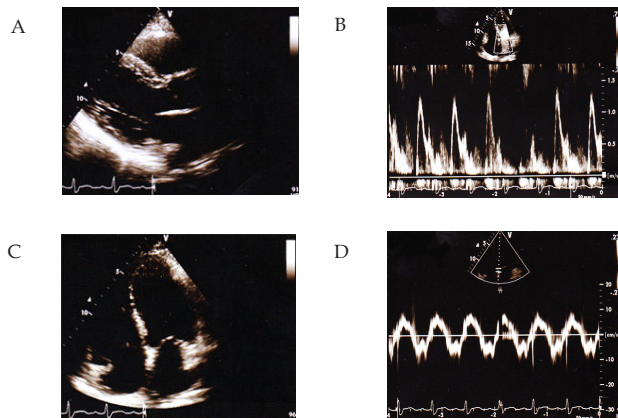

Figure 4. Restrictive pattern in LV inflow: Panel A shows long axis view. Panel B shows 4 chamber view. Panel C shows LV inflow. Panel D shows tissue Doppler imaging.

2.2.3. Left ventricle in diastolic heart failure

Most patients with HFpEF have normal chamber dimensions, although a small subset may have variable degrees of LV enlargement.

Although HF preserved EF has been thought to occur primarily patients with left ventricular hypertrophy (LVH), studies that have carefully quantified LV mass report that echocardiographic criteria for LVH are met in less than 50% of patients. [13-16]

2.2.4. Left atrium in diastolic heart failure

Increases in the left atrial dimension or volume are commonly present in patients with HF preserved EF. [17-19] The left atrium modulates ventricular filling through its reservoir, conduit, and pump functions. During ventricular systole and isovolumic relaxation, when the atrioventricular (AV) valves are closed, atrial chambers work as distensible reservoirs accommodating blood flow from the venous circulation. The atrium is also a pumping chamber, which contributes to maintaining adequate LV end-diastolic volume by actively emptying at end-diastole. Finally, the atrium behaves as a conduit that starts with AV valve opening and terminates before atrial contraction and can be defined as LV stroke volume minus the sum of LA passive and active emptying volumes.

The measurement of left atrial (LA) volume is highly feasible and reliable in most echocardiographic studies, with the most accurate measurements obtained using the apical 4-chamber and 2-chamber views. This assessment is clinically important, because there is a significant relation between LA remodeling and echocardiographic indices of diastolic function. In the previous observational studies, patients without baseline histories of atrial fibrillation and significant valvular heart disease have shown that more than 34 mL/m^2 LA volume index is an independent predictor of death, heart failure, atrial fibrillation, and ischemic stroke.

The dilated left atria may be seen in patients with bradycardia and 4-chamber enlargement, anemia and other high-output states, atrial flutter or fibrillation, and significant mitral valve disease, in the absence of diastolic dysfunction. Likewise, it is often present in elite athletes in the absence of cardiovascular disease. Therefore, it is important to consider LA volume measurements in conjunction with a patient's clinical status, other chambers' volumes, and Doppler parameters of LV relaxation.

2.2.5. Pulmonary hypertension in diastolic heart failure

Symptomatic patients with diastolic dysfunction usually have increased pulmonary artery (PA) pressures. [17,20] Therefore, in the absence of pulmonary disease, increased PA pressures may be used to infer the presence of elevated LV filling pressures. Indeed, a significant correlation was noted between PA systolic pressure and noninvasively derived LV filling pressures. The peak velocity of the tricuspid regurgitation (TR) jet by continuous-wave (CW) Doppler together with systolic right atrial (RA) pressure are used to derive PA systolic pressure. In patients with severe TR and low systolic right ventricular–RA pressure gradients, the accuracy of the PA systolic pressure calculation is dependent on the reliable estimation of systolic RA pressure. Likewise, the end-diastolic velocity of the pulmonary regurgitation (PR) jet can be applied to derive PA diastolic pressure. Both signals can be enhanced, if necessary, using agitated saline or intravenous contrast agents, with care to avoid overestimation caused by excessive noise in the signal. The estimation of RA pressure is needed for both calculations

and can be derived using inferior vena caval diameter and its change with respiration, as well as the ratio of systolic to diastolic flow signals in the hepatic veins.

2.2.6. Pulmonary venous flow

Pulse wave (PW) Doppler of pulmonary venous flow is performed in the apical 4-chamber view and aids in the assessment of LV diastolic function. A 2-mm to 3-mm sample volume is placed more than 0.5 cm into the pulmonary vein for optimal recording of the spectral waveforms. Measurements include peak S and D velocities, the S/D ratio, systolic filling fraction, and peak Ar velocity in late diastole. Another measurement is the time difference between Ar duration and mitral A-wave duration (Ar - A). With increased LV end-diastolic pressure, Ar velocity and duration increase, as well as the Ar - A duration. In patients with depressed EFs, reduced systolic filling fractions (less than 40%) are related to decreased LA compliance and increased mean LA pressure. Atrial fibrillation results in a blunted S wave and absence of Ar velocity.

2.2.7. Other echocardiographic findings in diastolic heart failure

Regional wall motion abnormalities with preserved EF and right ventricular dilatation, either from ischemic disease or secondary to chronic pressure overload from chronic pulmonary venous hypertension, can also be present at echocardiography in patients with HFpEF. Additional negative findings at echocardiography include the absence of valvular disease, pericardial tamponade, pericardial constriction, the presence of congenital heart diseases such as atrial septal defect, other more extensive structural abnormalities are important enough to cause the HF symptoms.

3. Conclusions

HFpEF currently accounts for more than 50% of all heart failure patients. The updated strategies for the diagnosis and exclusion of HFpEF are useful not only for individual patient management but also for patient recruitment in future clinical trials exploring therapies for HFpEF. Echocardiography is useful for the diagnosis of HFpEF, noninvasively.

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