Diastolic dysfunction: improved understanding using emerging imaging techniques

Frank Lloyd Dini, Cardiac, Thoracic and Vascular Department, Division of Cardiology, University Hospital, Pisa, Italy

Correspondence: Frank Lloyd Dini, Cardiac, Thoracic and Vascular Department, Division of Cardiology, University Hospital, Pisa, Italy
Tel: +39 (050) 995307; fax: +39 (050) 995308
e-mail: f.dini@ao-pisa.toscana.it

Abstract

New echo-Doppler imaging techniques enable detailed evaluation of left ventricular (LV) diastolic function and an estimate of LV filling pressure, since they are less load sensitive that traditional mitral flow variables. In recent years, tissue Doppler imaging (TDI) has emerged as a reliable tool to assess LV diastolic function noninvasively. An averaged mitral-to-TDI early velocities (E/e') ratio ≥ 13 is considered the stand alone evidence of LV diastolic dysfunction. In the presence of an E/e' ratio between 8 and 13, the so called "grey zone", additional investigations are deemed necessary to diagnose diastolic dysfunction. A multiparametric approach, including measurements of left atrial volume, pulmonary venous flow, colour M-mode flow propagation velocity showed to have a superior sensitivity and specificity compared with standard approach in identifying an increased LV filling pressure in patients with a wide range of LV ejection fractions. Strain analysis has been used to evaluate myocardial relaxation in a variety of cardiac diseases associated with diastolic dysfunction. Since myocardial mechanical events precede LV filling, these ultrasound modalities may be less dependent on extrinsic variables and therefore more accurate in characterizing intrinsic myocardial properties. The ratio of mitral E to 2D global longitudinal diastolic strain has been found to be a better predictor of LV filling pressure than E/e'.

Keywords: Diastolic function; left ventricular filling pressure; tissue Doppler imaging; strain analysis

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Introduction

Diastole allows left ventricular (LV) filling to ensure the forward movement of blood while maintaining a normal LV filling pressure at rest, during exercise, and through a wide range of heart rates. LV filling is determined by the active relaxation of the myocardium, the LV compliance, left atrial (LA) contraction, and the return of blood from the pulmonary circulation (Table 1). Patients with diastolic dysfunction have concomitant alterations in LV relaxation, filling, and compliance [1]. Diagnostic evidence of LV diastolic dysfunction can be obtained invasively by left or right cardiac catheterization: LV end-diastolic pressure greater than 16 mmHg or mean pulmonary capillary wedge pressure (PCWP) greater than 12 mmHg, or noninvasively by Doppler echocardiography [2].

• LA pressure • LV relaxation • LV compliance • LV suction • Diastolic restoring forces • Ventricular interaction • LA systolic function • Pericardial restraint • Coronary artery turgor • Viscoelastic properties • Loading conditions • Nonuniformity • Heart rate • Age
LA = left atrial, LV = left ventricular.

Table 1 *Determinants of LV filling.*

The interpretation of Doppler echocardiographic information has increased our understanding of LV diastolic function. Spectral Doppler ultrasound is ideally suited to the evaluation of the instantaneous velocities of blood flow. The importance of Doppler echocardiography for non-invasive assessment of LV filling pressure is mainly dependent on the close relationship between LV flow velocities and LA–LV diastolic pressure differences. The Doppler patterns of mitral flow velocity curves are determined by changes in the LA–LV driving pressures throughout the diastolic filling period. The early flow velocity (E) is related to rapid filling, while the latter (A) is due to atrial contraction.

When a compromised relaxation is the dominant LV diastolic alteration, the reduction in the initial LA–LV pressure gradient and the accompanying compensatory flow at atrial contraction are considered responsible for low E velocity, prolonged deceleration time (EDT) and high A velocity with an E/A ratio less than 1. This type of abnormality has usually been considered to be associated with normal or nearly normal LV filling pressure. In patients with an abnormal relaxation filling pattern, increased loading conditions – especially in the presence of decreased LV compliance – may be responsible for an elevation in LA pressure or PCWP, that is necessary to maintain the early LA–LV driving pressure, and this is followed by changes in LV filling dynamics. This accounts for increased mitral E velocity, E/A ratio of 1.0 to 1.5 and normalized EDT. As diastolic dysfunction progresses, there is a further reduction in LV compliance and this results in early cessation of filling due to rapid equalization of LA and LV pressures. Therefore, faster and more pronounced increases in LA pressure are necessary to maintain the driving pressure to a degree that allows LV filling to accommodate in a stiffer ventricle. The resulting mitral flow velocity profile – characterized by marked elevation of E velocity, shortened EDT with an increased E/A ratio – is referred to as restrictive pattern, i.e., similar to that associated with restrictive cardiomyopathy [3–6].

Analyzing the Doppler mitral velocity curve and PCWP recorded at catheterization, a strong correlation was found between EDT and LV filling pressure [7, 8], but only in patients with reduced LV ejection fraction [9]. Additional diagnostic flow information – beyond that contained in mitral flow velocity recordings – may be attained from the study of pulmonary venous flow velocities and combined analysis of mitral and pulmonary venous flow tracings [10-12].

Tissue Doppler imaging

In recent years, tissue Doppler imaging (TDI) has emerged as a reliable tool to assess LV diastolic function noninvasively (Fig. 1). TDI is obtained in the apical view by placing the sample volume at the junction between the LV wall and the mitral annulus. Lateral annulus velocity is usually higher than the velocity from the medial annulus. Values can be averaged for medial and lateral walls. In patients with normal diastolic function, the early diastolic TDI velocity (e′) is higher than the late TDI (a′) velocity. Although e′ has been suggested as being less load sensitive than mitral flow variables, this issue remains controversial [13].

Similar to mitral flow, with mild diastolic dysfunction the early TDI diastolic velocity decreases below the late diastolic velocity (ie, e′/a′ became less than 1.0). However, in contrast to mitral flow, with worsening diastolic dysfunction e′ continues to decrease. As mitral flow E velocity is determined equally by both LA pressure and LV relaxation, whereas e′ is related primarily to LV relaxation, when LV filling pressure rises, e′ remains decreased (ie, persistent underlying relaxation abnormality), while E velocity increases.

The ratio E/e′ may be used to predict LV filling pressure [14,15]. In individuals with normal LV relaxation and normal LV filling pressure, both E and e′ are elevated. In patients with impaired relaxation and normal

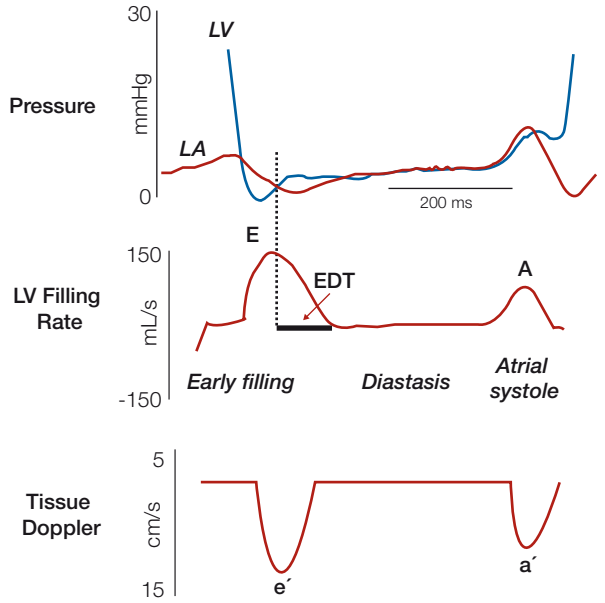

Fig. 1 Doppler-derived mitral flow and tissue Doppler pattern changes during diastole. A = mitral atrial velocity, a′ = atrial tissue Doppler velocity, E = mitral velocity, e′ = early tissue Doppler velocity, EDT = E velocity deceleration time, LA = left atrial, LV = left ventricular.

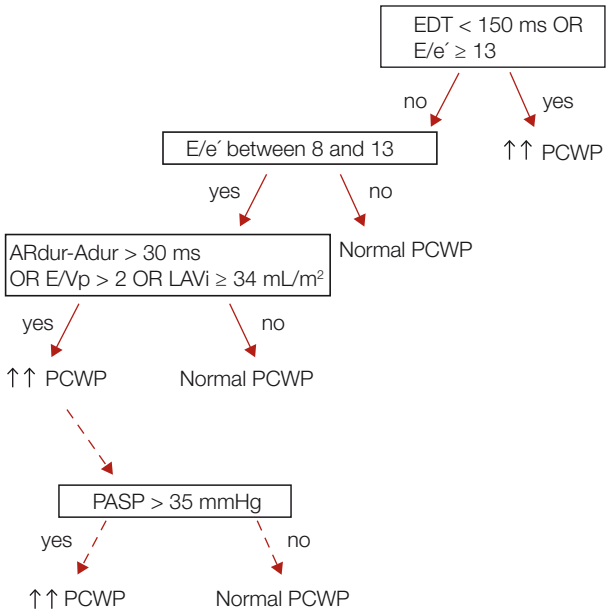

Fig. 2 Classification and regression tree-based predictive model of elevated pulmonary capillary wedge pressure constructed with Doppler and echocardiographic variables. Variables are connected by OR Boolean operators, so that the whole box response is positive if at least one criterion is satisfied, and negative if all criteria are not satisfied. ARdur–Adur = difference in duration of pulmonary venous and mitral flow at atrial contraction, EDT = E-wave deceleration time, E/e′ = ratio of mitral to myocardial early velocities, E/Vp = ratio of mitral E-wave and color M-mode flow propagation velocity, LAVi = left atrial volume index, PASP = pulmonary artery systolic pressure, PCWP = pulmonary capillary wedge pressure.

LV pressure, both E and e′ are decreased. In patients with impaired relaxation and elevated LV filling pressure, E is elevated but e′ is reduced.

An averaged E/e′ ratio of 13 or greater is considered the stand-alone evidence of LV diastolic dysfunction. In the presence of an E/e′ ratio between 8 and 13, the so called "grey zone", additional investigations are deemed necessary to diagnose diastolic dysfunction. These consist of mitral flow E/A ratio, its reduction with the Valsalva maneuver, EDT less than 150ms, LA volume index of 34 mL/m^2 or greater, pulmonary venous reversal flow duration greater than mitral A duration plus 30ms, E/color M-mode velocity of propagation greater than 1.5 [16–18]. The noninvasive identification of elevated LV filling pressure may be particularly challenging in patients with heart failure and preserved LV ejection fraction, hypertrophic and restrictive cardiomyopathy. In these cases, different methods, including specific diagnostic flow charts, have been proposed for the prediction of LV filling pressure [19, 20]. A multiparametric approach, including measurements of LA volume, pulmonary venous flow, color M-mode flow propagation velocity, with a sequential testing based on the classification and regression tree analysis (Fig. 2) was shown to have a superior sensitivity and specificity compared with the standard approach in identifying an increased LV filling pressure in patients with a wide range of LV ejection fractions [21].

Early echo-Doppler indexes of LV diastolic function have proved to be useful in patients with diastolic dysfunction or mixed systolic and diastolic dysfunction. A reduced e′ has been associated with decreased survival in patients with cardiac disease [22]. An increased E/e′ ratio velocity exhibited an additional predictive power with respect to demographic, clinical and echocardiographic variables both in myocardial infarction and heart failure [23, 24]. However, TDI parameters have limited accuracy in predicting intrinsic parameters of diastolic function due to the confounding effects of extrinsic loading conditions and therefore are less reliable in patients with preserved LV ejection fraction.

Myocardial strain imaging

Myocardial strain imaging may be applied to study LV myocardial mechanics [25]. Myocardial strain is a measure of regional deformation defined as the percentage change in length of a segment of the

myocardium in comparison to its original length (end-diastolic length minus end-systolic length/end-diastolic length). Strain rate (Sr) can be defined as the speed at which deformation occurs [26]. According to the direction of different myocardial strain vectors, myocardial strain can be divided into longitudinal, radial and circumferential strain (Fig. 3). Myocardial strain may be quantified using TDI or high-frame rate two-dimensional echocardiography with Speckle tracking. TDI-derived strain quantifies tissue deformation based on Doppler velocity shifts, but it is considerably affected by tissue tethering and translational motion. Speckle tracking echocardiography (STE) is a novel non-Doppler-based method for the objective quantification of myocardial deformation. In contrast to Doppler flow-derived indexes, STE has the advantage of being angle independent, and to be less affected by reverberations, and dropout artefacts.

Strain analysis has been used to evaluate myocardial relaxation in a variety of cardiac diseases associated with diastolic dysfunction. As myocardial mechanical events precede LV filling, these ultrasound modalities may be less dependent on extrinsic variables and therefore more accurate in characterizing intrinsic myocardial properties.

In order to assess the usefulness of STE parameters for the evaluation of diastolic dysfunction in patients with cardiac disease and preserved LV systolic function, a study was carried out in 50 patients with a mean LV ejection fraction of 49 ± 18% [27]. Two-dimensional global longitudinal diastolic strain (ε) and Sr were measured during peak mitral filling, and combined with E (E/ε and E/10DSr). These indexes were compared with simultaneously invasively measured LV pre-atrial (pre-A) contraction pressure and E/e′. The correlations between E/ε and E/10DSr with LV pre-A pressure were closer (R = 0.81; $P < 0.001$ and R = 0.80; $P < 0.001$) compared with that of E/e′ with LV pre-A pressure (R = 0.63; $P < 0.001$). Therefore, both E/ε and E/10DSr were better predictors of LV filling pressure than E/e′.

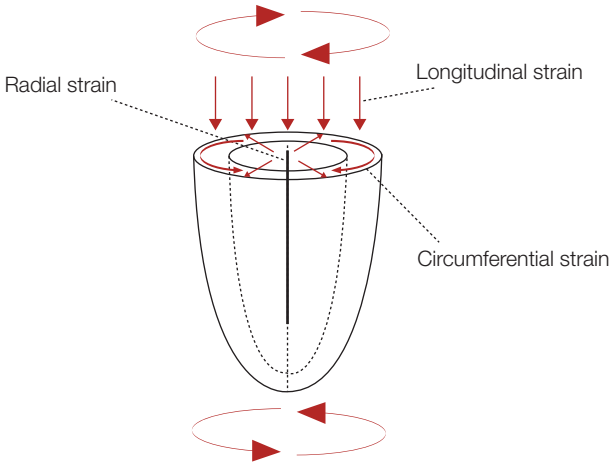

Fig. 3 *The diagram indicates the direction of different myocardial strain vectors. The basal clockwise twist and the apical counter-clockwise twist are also indicated; torsion is the sum of both components.*

STE has recently evolved enabling the quantification of longitudinal myocardial LA deformation dynamics [28]. LA deformation analysis by STE was recently proposed as an alternative approach to estimate LV filling pressure. A close negative correlation between global peak atrial longitudinal strain and PCWP was found. The potential mechanism of this inverse correlation could be explained by the principle that PCWP is the afterload of LA function; if PCWP is high, the left atrium should be chronically stressed, resulting in a decrease of LA reservoir function and finally in remodeling with LA chamber dilation, as demonstrated in patients with heart failure. In a recent study performed in 54 patients with normal LV ejection fraction, the assessment of LA strain indexes was useful at identifying the presence of LA dysfunction among patients with preserved LV systolic function and an E/e′ ratio between 8 and 13 [29].

In addition to myocardial strain, there is torsional deformation of the left ventricle during the cardiac cycle due to the helical orientation of the myocardial fibers [30]. LV torsion, defined as the instantaneous net difference of the basal and apical rotation, and subsequent untwisting, plays an important role in diastolic filling [31]. There is, however, limited information about how LV torsion and untwisting are related to the severity of diastolic dysfunction. The results of this study showed that systolic torsion and diastolic untwisting were significantly increased in patients with mild diastolic dysfunction. In patients with advanced diastolic dysfunction with increased filling pressure, they were normalized or reduced. •

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