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Left ventricular (LV) diastolic function can be evaluated invasively and noninvasively. Invasive measures of diastolic function include the peak instantaneous rate of LV pressure decline (-dP/dt), the time constant of LV relaxation (tau), and the stiffness modulus(1). Although echocardiography does not directly measure these parameters, echocardiography is the most practical routine clinical approach for evaluating LV diastolic function given clinical and experimental evidence supporting its use as well as its safety, versatility, and portability(1,2). During this lecture we will discuss two advanced metrics of diastolic function: transmitral color m-mode flow propagation velocity (Vp) and tissue Doppler annular early and late diastolic velocities.

Color M-Mode Flow Propagation Velocity (Vp)

In the perioperative setting the Vp slope method(1,3,4) appears to have the least variability(5). Acquisition via transesophageal echocardiography (TEE) is performed with the ME 4-chamber view and with transthoracic echocardiography (TTE) it is performed with the apical 4-chamber view. In both, color flow Doppler with a narrow sector angle and gain adjusted to avoid noise is utilized with an M-mode scan line placed through the center of the LV inflow column from the mitral valve to the LV apex(1). The color scale baseline is adjusted so that the central highest velocity jet is blue. Vp is measured as the slope of the first aliasing velocity during early transmitral filling as measured from the mitral valve plane to 4 cm distally into the LV cavity(1,4). Alternatively the slope of the transition from no color to color can be measured(3). Normal Vp is 45-50 cm/sec (1,4,6). Similar to the pulse-wave Doppler transmitral inflow
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velocities, there is an early wave and a late atrial contraction wave (1). With normal
diastolic function, the early filling wave propagates rapidly toward the apex and is driven
by the pressure gradient from the LV base to apex (1,7). This suction force results from
energy-dependant active LV relaxation. With diastolic dysfunction, from ischemia or
heart failure, there is slowing of mitral-to-apical flow propagation consistent with a
reduction of apical suction (1,3,8,9). However, in clinical practice evaluation and
interpretation of intraventricular filling is complicated by the multitude of variables that
determine intraventricular flow (1). Despite the multiple variables affecting flow, the
slowing of mitral-to-apical flow propagation by color M-mode Doppler has proved to be
a semiquantitative marker of LV diastolic dysfunction (1). In addition, the ratio of the
peak early transmitral inflow velocity (E) to Vp (E/Vp) can be used to predict LV filling
pressures (1,4). In patients with decreased systolic function (decreased LVEF) an E/Vp ≥
2.5 predicts a PCWP ≥ 15 (1,10). However, in patients with normal systolic function
(normal LVEF) LV filling pressures can not be predicted by E/Vp (10). Also patients
with elevated filling pressures but a normal LVEF, and normal LV volumes can have an
erroneously normal Vp (11) (10,12,13). In addition, preload has been shown to have a
positive influence on Vp in patients with normal and depressed LVEF (1,12,14).

Key Points regarding Vp according to the EAE/ASE (1)

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1. Acquisition is performed in the 4-chamber view, using color flow Doppler imaging.
2. The M-mode scan line is placed through the center of the LV inflow blood column from the mitral valve to the apex, with baseline shift to the color scale so the central highest velocity jet is blue.
3. Vp is measured as the slope of the first aliasing velocity during early filling, measured from the mitral valve plane to 4 cm distally into the LV cavity, or the slope of the transition from no color to color.
4. Vp ≥ 45-50 cm/s is considered normal.
5. In most patients with depressed EFs, Vp is reduced, and should other Doppler indices appear inconclusive, an E/Vp ratio ≥ 2.5 predicts PCWP ≥15 mm Hg with reasonable accuracy.
6. Patients with normal LV volumes and EFs but elevated filling pressures can have misleadingly normal Vp.

Mitral Annular Tissue Doppler Early (Em) and Late (Am) Diastolic Velocities (1,15):

Pulse wave (PW) Doppler tissue imaging (DTI) is performed with TEE in the ME-4-chamber view and with TTE in the apical views, which allow acquisition of mitral annular velocities (1,16). The sample volume should be placed at or 1 cm within the septal and lateral insertion sites of the mitral leaflets and adjusted as necessary (usually 5-10 mm) to cover the longitudinal excursion of the mitral annulus in both systole and diastole (1). DTI velocities have higher amplitude and lower peak velocities when compared with transmural inflow velocities. Spectral gain settings can be manually optimized for DTI, but most current ultrasound systems have tissue Doppler presets for the proper velocity scale and Doppler wall filter settings (1). Usually the velocity scale

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should be set at about 10-20 cm/s above the zero-velocity baseline (1). Given the angle
dependance of all Doppler measurements, minimal angulation (< 20 degrees) should be
present between the ultrasound beam and the place of cardiac motion (15). Regardless of
the 2D image quality, DTI waveforms can be obtained in nearly all patients (>95%). The
recommended sweep speed is 50-100 mm/s at end expiration and measurements should
reflect the average of ≥ 3 cardiac cycles (1). Primary measurements included systolic (S),
early diastolic (e’), and late diastolic velocities (a’) (17). Early diastolic annular tissue
velocity has been expressed as Ea, Em, E’ and e’, in this syllabus we will use e’ and E’
(1). Peak velocities alone are all that needs to be measured, as E’ deceleration time,
acceleration rates and deceleration rates, do not contain incremental information and need
not be performed (1,18).

E’ has been shown to have a significant association with LV relaxation in human
and animal studies (1,19-23). E’ is related to LV diastolic properties, such as elastic recoil
and relaxation, regardless of filling pressures or systolic function but E’ is also influenced
by systolic function, preload, and LV minimal pressure (1,15,24). E’ changes in the same
direction as preload in patients with normal diastolic function(15). This effect is less
pronounced in ventricles with impaired relaxation where E’ remains decreased regardless
of changes in preload (15,20,25,26). Thus E’ is relatively preload independent in sick
patients, (those with significant diastolic dysfunction) including most of the patients
presenting for cardiac surgery.

The time interval between the QRS complex and the E’ onset is prolonged with
impaired LV relaxation and can provide incremental information in special patient
populations (1). Given the influence of regional function on tissue velocities and
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intervals, it is recommended to acquire and measure tissue Doppler signals at least at the septal and lateral sides of the mitral annulus and calculate their average, for assessment of global LV diastolic function (1,2,10,27).

Once transmitral inflow PW flow, annular velocities and time intervals are acquired, it is possible to compute additional time intervals and ratios (1,15). Important ratios include: E/e’, E’/A’ and IVRT/T\textsubscript{E-e’}. The ratio E/e’, has been shown to help estimate LV filling pressures in patients with LV diastolic dysfunction (17). An E/e’ > 12-15 is consistent with elevated LV filling pressures (2,17). In addition, E/e’ has been shown to be a marker of severe cardiac disease. In a recent study of 205 patients an E/e’ ratio ≥8 was shown to be associated with increased intensive care unit length of stay (ICU-LOS) P = 0.037) and need for inotropic support (P = 0.002) (28). These results were seen after making adjustments to account for other predictors (female gender, hypotension, diabetes, history of myocardial infarction, emergency surgery, renal failure, procedure type, and length of aortic cross-clamp time) thereby implicating E/e’ as a serious prognostic indicator (28,29). The T\textsubscript{E-e’} interval is the time interval between the QRS complex and the onset of the mitral E velocity subtracted from the time interval between the QRS complex and the e’ onset (1). The T\textsubscript{E-e’} interval is prolonged with diastolic dysfunction, and animal and human studies have shown it to be strongly dependent on the time constant of LV relaxation (tau) and minimal LV pressure (1,30,31). Technically, it is essential to match the RR intervals for measuring both time intervals (time to E and time to e’) and to optimize the Doppler gain and filter settings, because higher gain and filter settings interfere with correct identification of the onset of e’(1).
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The main hemodynamic determinants of a’ include: LA systolic function and LVEDP. An increase in LA contractility leads to an increase in a’, and an increase in LVEDP leads to a decrease in a’(1,18). Normal values for DTI-derived velocities are influenced by age, similar to other indices of LV diastolic function, but an e’ <8 cm/sec is generally considered low(1,2). With age e’ decreases, a’ increases and E/e’ increases(1,32).

Clinical Application of DTI(1,15):

DTI mitral annular velocities assist in the evaluation of LV relaxation, and E/e’ can be used to estimate LV filling pressures (1,2). Reliable conclusions require consideration of multiple factors such as patient age, coexisting cardiovascular disease and other echocardiographic abnormalities. Thus e’ and E/e’ should not be used in isolation. It is also important to use the average of e’ obtained from the septal and lateral sides of the mitral annulus over several cardiac cycles. Skubas et al. (15) suggest utilizing the lateral mitral annulus e’ in the E/e’ ratio for estimating filling pressures because the lateral mitral annulus is rarely involved in ischemic disease and e’ measurements at this location will usually reflect LV relaxation. An E/e’ < 8 indicates normal filling pressures and E/e’ > 12-15 indicates elevated filling pressures. The mean pulmonary capillary wedge pressure can be estimated by the following formula: mean PCWP = (1.3 x E/e’) + 2 (1,15).

Technical limitations to DTI include factors such as angle dependence, proper sample size, gain, and Doppler filter settings. In addition, there are a number of clinical settings in which e’ and E/e’ are misleading. In normal subjects e’ velocity is positively related to preload and E/e’ can not be used to estimate filling pressures (1). E’ is also significantly...
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reduced in patients with significant mitral annular calcification, surgical rings, mitral stenosis and prosthetic mitral valves(1). E’ is increased in patients with moderate to severe MR and normal LV relaxation due to increased flow across the MV. E/e’ should not be used in these patients, but the isovolumetric relaxation time to T_E-e’ ratio (IVRT/T_E-e’) can be applied (an IVRT/ T_E-e’ <2 is consistent with increased filling pressures) (1,30,33). Patients with constrictive pericarditis usually have elevated e’ due to preserved LV longitudinal expansion compensating for limited lateral and anteroposterior diastolic excursion. Lateral e’ may be less than septal e’ in theis condition and the E/e' should not be used to estimate filling pressures(1). However, a normal e’ in the setting of restrictive transmitral inflow velocities can help distinguish constrictive pericarditis from restrictive diastolic dysfunction due to an infiltrative restrictive cardiomyopathy (34).

**Key Points regarding DTI according to the EAE/ASE (1)**

1. PW DTI is performed in the ME-4 Chamber view
2. The sample volume should be positioned at or 1 cm within the septal and lateral insertion sites of the mitral leaflets.
3. 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 ≥3 consecutive cardiac cycles.
4. Primary measurements include the systolic and early (e´) and late (a´) diastolic velocities.
5. 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.
6. In patients with cardiac disease, e’ can be used to correct
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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.

(7) 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.

Addendum regarding perioperative TEE and diastolic function(35). Recently Swaminathan M, et. al. found that a simplified perioperative approach using the lateral mitral annular tissue Doppler e´ measurement and the ratio of the transmitral pulsed-wave Doppler E peak velocity to the lateral mitral annular tissue Doppler peak early velocity ratio (E and E/ e´) can be used to predict survival. In summary: an e´<10 cm/sec + E/e´ > 13 predicted a significantly lower survival vs patients with an e´ > 10 cm/sec in 905 patients undergoing CABG.


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