NON-INVASIVE ASSESSMENT OF LEFT VENTRICULAR DIASTOLIC FUNCTION: FOCUS ON TISSUE DOPPLER IMAGING AND B-TYPE NATRIURETIC PEPTIDE

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INTRODUCTION

Tissue Doppler (TD) imaging is a novel echocardiographic technique that directly measures myocardial velocities. Systolic TD measurements assess left and right ventricular (RV) myocardial contractile function. Diastolic TD values reflect myocardial relaxation, and in combination with conventional Doppler measurements, ratios (E/Ea) have been developed to non-invasively estimate left ventricular (LV) filling pressures. These TD-derived ratios have been helpful in diagnosing elevated LV filling pressures, clinical congestive heart failure (CHF), and the prognosis of patients with cardiac disease and CHF. B-type natriuretic peptide reflects myocardial stretch and has been correlated to LV filling pressures and cardiac morphological abnormalities (depressed EF, RV dysfunction). TD echocardiography is being used in an ever-widening group of patients to assess LV diastolic function, and researchers are actively investigating its correlation and comparison with B-type natriuretic peptide.

DEVELOPMENT OF TISSUE DOPPLER IMAGING

Tissue Doppler imaging of the heart was first described in 1989 by lsaaz et al., who demonstrated that low myocardial velocities at the posterior mitral annulus correlated with abnormal posterior wall motion on left ventricular (LV) angiography.[1] Thereafter, regional variation of myocardial velocity gradients proved valuable in assessing regional myocardial function.2 TD systolic mitral annular velocities also were shown to correlate with global LV myocardial function as assessed by radionuclide ventriculography.3 Sohn et al. demonstrated that early diastolic mitral annular velocity (Ea) correlated with Tau measured invasively,4 and Nagueh et al. demonstrated that the peak pulsed Doppler transmittal early diastolic inflow velocity (E) divided by Ea resulted in a ratio {E/Ea) that correlated well with pulmonary capillary wedge pressure (PCWP).5 Figure 1 shows the typical appearance of TD velocities at the mitral annulus in a patient with cardiac disease but normal LV ejection fraction.

TISSUE DOPPLER FOR DIASTOLIC ASSESSMENT AND ESTIMATING LV FILLING PRESSURES

As a single measurement, Ea is a relatively preload-independent measure of myocardial relaxation in patients with cardiac disease., Our laboratory generally uses an average from the mitral lateral and sepcal annuli (apical four-chamber view), which is particularly useful in patients

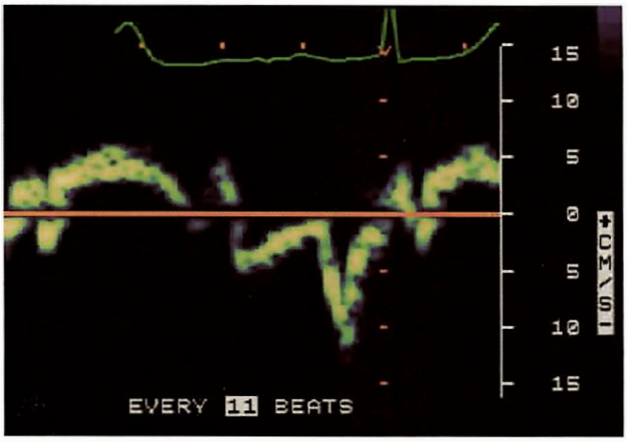

Figure 1.
Tissue Doppler Velocities in a patient with cardiac disease. Aa = late diastolic tissue Doppler (TD) myocardial velocity; Ea= early diastolic TO myocardial velocity; MC = isovolumic contraction TD myocardial velocity; MR = isovolumic relaxation TD myocardial velocity; Sa = systolic TD myocardial velocity. Note that both the Sa and Ea velocities are ~5 cm/s, indicating depressed myocardial velocities (normal > 10 cm/s). This patient had a left ventricular ejection fraction of 64%, demonstrating myocardial disease in the presence of a normal ejection fraction.

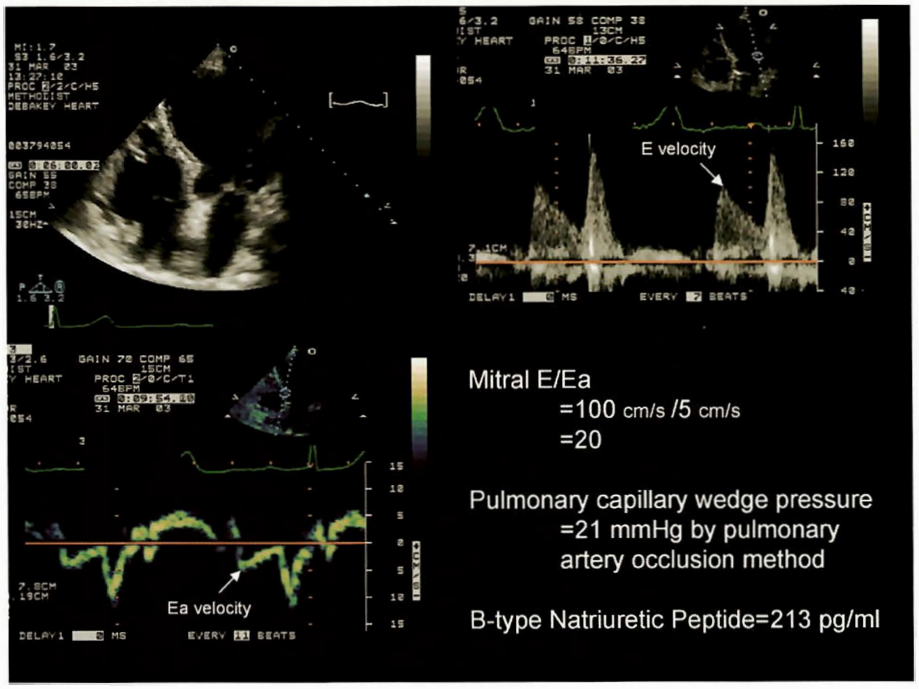

Figure 2(a).
Tissue Doppler imaging in the prediction of LV filling pressures: normal LV ejection fraction. E = early diastolic pulsed Doppler transmitral inflow velocity; Ea = early diastolic mitral annular tissue Doppler myocardial velocity. This patient had a left ventricular ejection fraction of 67% and clinical congestive heart failure. The mitral E/Ea ratio was 20, indicating elevated left ventricular filling pressures. Simultaneous pulmonary capillary wedge pressure by Swan-Ganz catheterization was 21 mmHg. Given the elevated filling pressures, BNP was elevated (213 pg/ml).

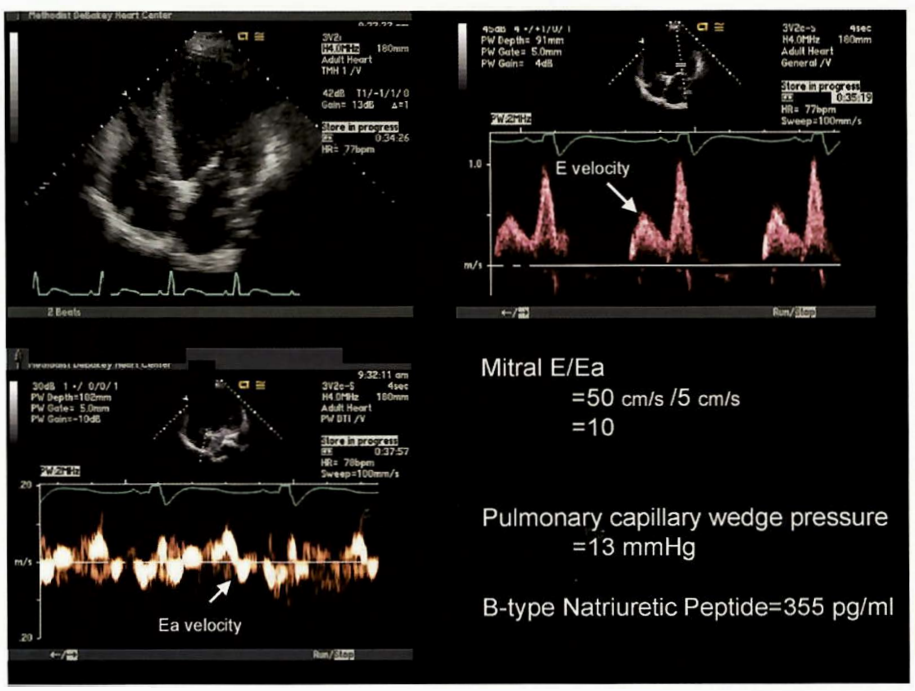

Figure 2(b).
Tissue Doppler imaging in the prediction of LV filling pressures: depressed LV ejection fraction. E = early diastolic pulsed Doppler transmitral inflow velocity; Ea = early diastolic mitral annular tissue Oqppler myocardial velocity. This patient had known depressed left ventricular function with an ejection fraction of 29% but was not in clinical congestive heart failure. The mitral E/Ea ratio was 10, indicating normal left ventricular filling pressures. Simultaneous pulmonary capillary wedge pressure by Swan-Ganz catheterization was 13 mmHg. Despite the normal filling pressures, BNP was elevated (355 pg/ml) owing to LV dilatation and depressed EF.

with regional wall abnormalities.[6] Generally speaking, for patients over 60 years of age, impaired myocardial relaxation is present when average Ea < 8 cm/s and severely impaired when Ea < 5 *emfs*. Adding E to Ea forms an index of volume load, corrected to myocardial relaxation; thus, the F/Ea ratio can be used to non-invasively assess LV filling pressures. As both E and Ea are affected by the presence of severe micral annular calcification, mitral stenosis, prosthetic mitral valve, severe micral regurgitation and paced rhythm, patients with these conditions are generally excluded from the Doppler assessment of LV diastolic function. For situations such as atrial fibrillation, we find that shortened micral E acceleration and deceleration times are more useful than TD assessment in predicting elevated filling pressures?

TISSUE DOPPLER IN PATIENTS WITH PRESERVED LV EJECTION FRACTION

Recent investigations have used tissue Doppler to identify myocardial disease in the presence of preserved ejection fraction. Yu er al. demonstrated a continuum of increasing TD systolic annular velocities (Sa): Patients with systolic heart failure had the lowest Sa, those with diastolic heart failure had the second lowest, those with diastolic dysfunction but no heart failure had the highest, and all three groups had depressed Sa velocities compared to healthy controls.[8] Given chat LVEF may be preserved in a patient with cardiac disease, it is important to determine whether the E/Ea ratio can be employed to estimate LV filling pressures in these patients. Rivas-Gorz et al. demonstrated that in patients with EF > 50%, E/Ea can provide a reasonably accurate estimate of PCWP.[6] Furthermore, in patients with regional wall motion abnormalities, rhe average of the septa! and lateral mirral annuli is particularly useful in estimating LV filling pressure.

USE OF B-TYPE NATRIURETIC PEPTIDE AND TISSUE DOPPLER IMAGING IN ASSESSING LEFT VENTRICULAR DIASTOLIC FUNCTION

B-type natriuretic peptide (BNP) is a protein released from rhe cardiac ventricles in response to myocyte stretch.[9] Since cardiac myocytes are strained in patients with elevated LV filling pressures, BNP release from the myocyres, coupled with subsequent plasma levels, are useful in detecting elevated LV filling pressures. BNP is also helpful in diagnosing clinical CHF in patients presenting to the Emergency Department with dyspnea[10] and in predicting outcomes in patients withCHF.[11]

Given that both BNP and E/Ea correlate with LV filling pressures, recent work has sought to define the relationship between BNP and E/Ea. Troughton er al. demonstrated that BNP had a significant correlation (r = 0.51) with mitral E/Ea.[12] However, strong correlations of BNP to LVEF and RV systolic function highlight one of its limitations in assessing LV filling pressures: While BNP is extremely sensitive (thus having an excellent negative predictive value) to elevated filling pressures, it is less specific due to BNP elevations in cardiac morphologic abnormalities, independent of filling pressures.13 Other investigations have demonstrated that BNP and mitral E/Ea are comparably accurate in diagnosing clinical CHF in patients hospitalized with d_{y_s} pnea.[14] In patients with indwelling pulmonary artery catheters, E/Ea and BNP were highly and comparably sensitive for PCWP > 15 mmHg, but E/Ea was more specific than BNP since E/Ea is not elevated by cardiac structural abnormalities alone. Figure 2(a) demonstrates that patients with preserved EF and elevated filling pressures have eievared E/Ea and BNP, while Figure 2(6) illustrates that patients with depressed EF yet normal filling pressures have normal E/Ea but elevated BNP. Figure 3 provides an algorithm for using BNP and E/Ea to assess LV filling pressures.

TISSUE DOPPLER, B-TYPE NATRIURETIC PEPTIDE AND PROGNOSIS

As most work in TD imaging has been diagnostic in nature, there has been great interest in the prognostic implications of TD variables. Redfield et al. have shown

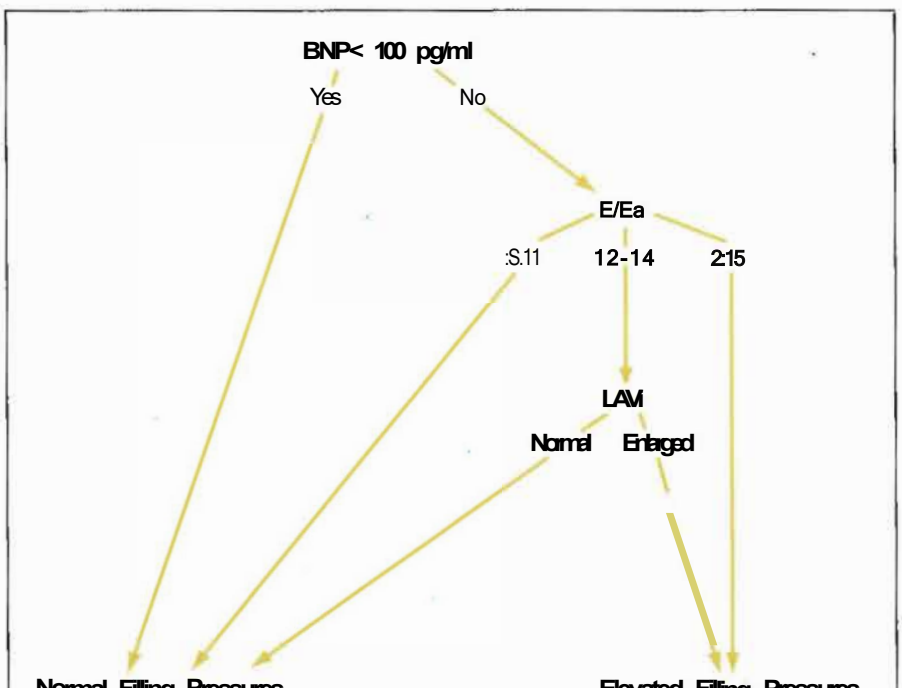

Figure 3.

BNP and E/Ea to predict LV filling pressures. BNP = b-type natriuretic peptide; E/Ea = transmitral pulsed Doppler early diastolic velocity/tissue Doppler early diastolic mitral annular velocity; LAVi = left atrial volume indexed to body surface area (LAVi > 34 ml/m2 is enlarged; LAVi < 34 ml/m2 is normal); LV = left ventricular

in a population-based study that patients wich increasing degrees of diastolic dysfunction-from impaired relaxation alone to elevated filling pressures to restrictive filling-have increasingly worse outcomes.15 Another study demonstrated that E/Ea is a strong multivariate predicror of patient outcome after acute myocardial infarction.[16] Recent work also has shown that both pre-discharge BNP and E/Ea predict cardiac death or re-hospitalization in patients hospitalized with CHF and that conventional echocardiographic variables do not significantly add to the prognosis.17

SUMMARY

TD imaging directly measures myocardial velocities and is an important variable in assessing LV diastolic function. TD-derived ratios (E/Ea) are being employed to non-invasively estimate LV filling pressures and predict outcomes in a widening group of patients. Recent studies evaluating the relationship between E/Ea and BNP have demonstrated char both parameters are useful in diagnosing clinical CHF. However, E/Ea is more specific than BNP for elevated filling pressures since BNP is elevated by cardiac structural abnormalities alone. Finally, an algorithm combining BNP and E/Ea can be used to estimate LV filling pressures.

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