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TEACHING CORNER: REVIEW

Non-invasive Estimation of Left Ventricular Filling Pressures by Doppler Echocardiography

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Besides being complicated reality,
in my experience, is odd . . ..
Of course anyone can be simple
if he has no facts to bother about
C. S. Lewis

Heart failure is haemodynamically characterized by elevated left ventricular filling pressure. Its determination is important in order to optimize unloading therapy, interpret equivocal symptoms, predict prognosis and the follow-up of treatments[1]. Invasive techniques are impractical for repeated measurements. Therefore there is a need for more comfortable and less expensive methods of measurement.

Over the past 10 years, pulsed-wave Doppler echocardiography has emerged as a practical tool for the non-invasive estimation of left ventricular filling pressures and several indices derived from transmitral and pulmonary venous flow velocity recordings have been validated for estimating left ventricular filling pressures in various subsets of patients with both systolic and diastolic left ventricular dysfunction, excluding those in whom left ventricular filling is affected by extrinsic factors such as mitral stenosis or pericardial constraint. The basic principle of all these methods is that blood flow is driven from the left atrium into the left ventricle by the instantaneous pressure gradient across the mitral valve and that mitral flow velocity therefore reflects the level of left atrial pressure[2,3]. However, since the transmitral pressure gradient (and flow velocity) is determined not only by left atrial pressure, but depends also on ventricular factors such as relaxation rate and compliance, the correlations between Doppler variables and left atrial pressure are too weak for an accurate estimation and may vary between different subsets of patients. In fact, the rate of left ventricular relaxation affects left ventricular pressure fall in early diastole and consequently plays an important role in determining the E wave velocity. Thus, when the rate of left ventricular relaxation is high (such as in normal young subjects and in hyperthyroid patients) the early diastolic wave velocity (E) and its deceleration may be increased even if the left atrial pressure is low. Conversely, when relaxation is markedly impaired (such as in patients with severe left ventricular hypertrophy and diastolic heart failure) E wave velocity and its deceleration rate may be relatively low even in the presence of elevated left atrial pressure. The opposite effects of left atrial pressure and impaired left ventricular relaxation may make it difficult to estimate left ventricular filling pressure in a given patients on the basis of transmitral flow velocity wave alone.

To overcome the confounding effects of the multiple interacting factors that affect transmitral flow velocities, several strategies are followed. First of all Doppler indices should be considered in the context of the clinical picture (age, heart rate, etiology of the disease, etc.) and the M-mode and two-dimensional echocardiographic findings (left atrium and left ventricular dimensions and systolic function). For example, in a patient with a dilated left ventricle and poor systolic function we know that left ventricular relaxation is impaired. Consequently, a high amplitude E wave with rapid deceleration must be due to high left atrial pressure and a non-compliant left ventricle. On the other hand, in a patient with poor systolic function and a delayed or reduced E wave followed by a slow deceleration and an increased late diastolic A wave velocity left ventricular filling pressures are normal or mildly elevated. Consequently, several studies have shown that in patients with severe systolic dysfunction and normal sinus rhythm the correlation between simple variables,

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such as E/A and deceleration time, and left ventricular filling pressure are excellent[4–7].

The estimation of left ventricular filling pressures in conditions where left ventricular dysfunction is less apparent can be improved by the analysis of the pulmonary vein flow velocity pattern. The pulmonary vein flow velocity pattern mirrors the changes of the left atrial pressure. When the left atrium pressure is elevated and, particularly, when there is a high V-wave because of a non-compliant left atrium, the systolic forward flow velocity (S wave) decreases while the diastolic velocity (D wave) increases. Although systolic pulmonary venous flow velocity is determined by multiple factors (including left ventricular systolic function, left atrium relaxation, right ventricular *vis a tergo* and mitral regurgitation), the systolic forward flow velocity in patients with left ventricular systolic dysfunction is strongly and inversely related to the left ventricular filling pressures. In particular, a systolic fraction <40% is a reliable index of a pulmonary artery wedge pressure >18 mmHg[8–10]. However, in young normal subjects, in patients with eccentric mitral regurgitation and in those with a cardiac allograft a blunted S wave may be present even when left ventricular filling pressures are low. Conversely, in patients with good left ventricular systolic function and vigorous displacement of the mitral annulus, the S wave can be relatively high in spite of high filling pressures.

Another useful index for estimating left ventricular filling pressure is the difference between the duration of the reverse pulmonary vein flow wave (Ar) and of the mitral forward A wave (Fig. 1). In normal subjects the duration of these two waves is almost equal. When the left atrium contracts against a stiff ventricle, the forward flow across the mitral valve stops early while the reversed flow into the pulmonary veins increases. Thus, an Ar wave duration longer than that of the transmitral A wave is an accurate sign of a left ventricular end-diastolic pressure >15 mmHg[11]. This index has the additional advantage of being independent of age, mitral regurgitation and left ventricular systolic function. It should be noted that although this index is strongly correlated with left ventricular end-diastolic pressure, its correlation with pulmonary wedge pressure is rather poor. The fact that patients with a high left ventricular end-diastolic pressure may occasionally have mildly elevated or even normal early diastolic left atrium pressures accounts for this discrepancy. Other limitations of this index are: the difficulty of recording Ar wave duration in patients with dilated left atrium and pulmonary veins; its dependence on atrial systolic function and its merge with the diastolic forward flow when the heart rate is high and/or the PR interval is long. Technical details on how to obtain and correctly measure this and other transmitral and pulmonary venous flow vardiables can be found in a comprehensive review published by Appleton [12].

Despite these limitations, the analysis of pulmonary vein flow in combination of transmitral flow in order to differentiate normal from pseudonormal velocity patterns improves the estimation of left ventricular filling pressures in patients with moderately impaired function and dilated left ventricles.

There remains, however, a sizeable number of patients in whom even this method is not reliable enough: patients with a single transmitral flow wave due to tachycardia and /or a prolonged PR interval; patients in atrial fibrillation, those who have isolated diastolic dysfunction; those with a cardiac allograft and those with inadequate Doppler recordings of pulmonary vein flow. Two methods have been recently proposed to estimate left ventricular filling pressures. The first method combines transmitral E wave velocity with its propagation velocity (Pv) into the left ventricular recorded by colour M-mode Doppler. The second method combines transmitral E wave velocity with the early diastolic velocity of the mitral annulus motion recorded by pulse-wave tissue Doppler. Both of these methods are based on the concept that normalizing transmitral E wave velocity by an index that reflects the rate of left ventricular relaxation which is independent from pre-load reduces the confounding effect of the relaxation rate and improves the correlation with left atrial pressure. It has been shown by several studies that the wavefront of the early diastolic inflow velocity reaches the left ventricular apex almost instantaneously when the relaxation rate is high, while it takes longer when relaxation is impaired[13,14]. The Pv of this wavefront can be assessed by color M-mode in the apical four-chamber view with the beam aligned with the centre of the left ventricular inflow. The slope of the first colour aliasing (set at 45 cm/s) from the mitral annulus to 4 cm into the left ventricular is then identified, either visually or by isovelocity maps[14]. This measurement is strongly related to the time constant (tau) of the left ventricular pressure decay and the E /Pv ratio with pulmonary wedge pressure. Recent observations, however, suggest that this method is more reliable in patients with dilated ventricles while its accuracy is limited in patients with normal systolic function and small left ventricles[13,14].

Like Pv, the velocity of early diastolic mitral annulus motion (E′) has also been found to be related to tau and to be relatively independent of left atrial pressure[15,16]. Again the E/E′ ratio has been successfully applied to estimate left ventricular filling pressures in subsets of patients, including those with atrial fibrillation, sinus tachycardia, cardiac allograft and normal systolic function[17–20]. An early study indicated that a E/E′ ratio >10 is a reliable index to estimate a pulmonary wedge pressure >12 mmHg[15]. A more recent study showed that an E/E′ ratio <8 accurately identifies patients with a normal pressure and a ratio >15 those with an elevated pulmonary wedge pressure[21]. In patients with intermediate values (>8 and <15) pulmonary wedge pressures may vary widely and the other Doppler flow methods can be used. It remains unresolved whether better results can be obtained using the lateral or the septal E′. In patients with ischaemic heart disease it is probably best to average the values obtained from the lateral, septal, anterior and inferior mitral annulus. The

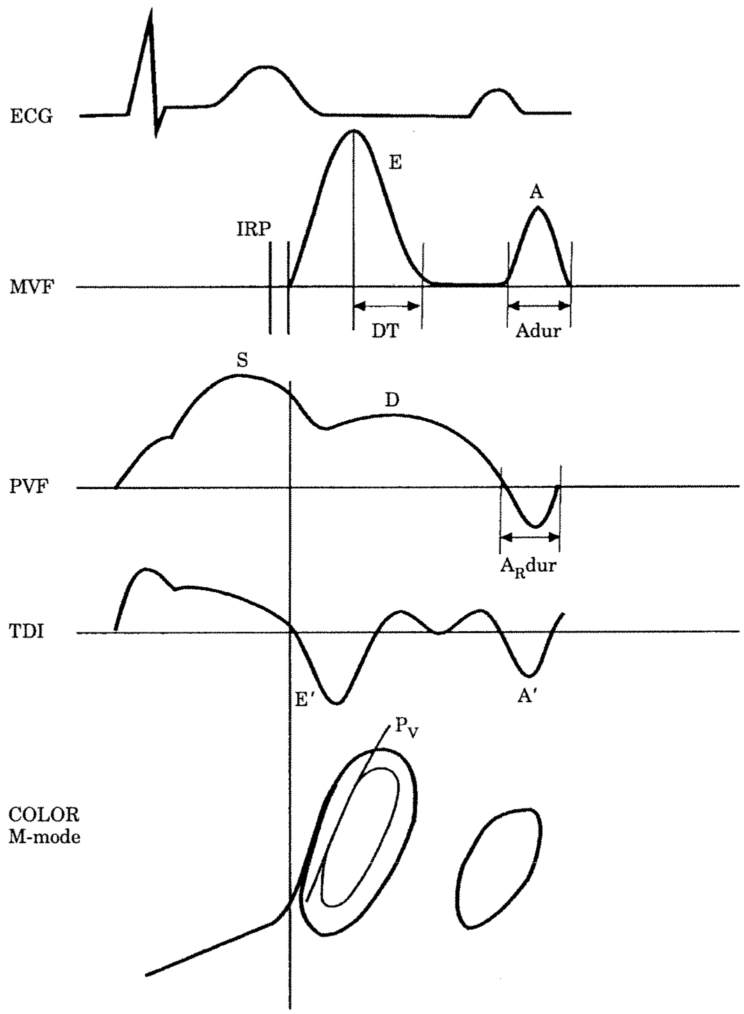

Figure 1. Parameters used for the estimation of left ventricular filling pressures.
Pulsed Doppler of transmitral flow (MVF): isovolumic relaxation period (IRP); early diastolic (E) and late diastolic (A) wave amplitude; deceleration time (DT); late diastolic wave duration (Adur). Derived measurements: ratio between early diastolic and late diastolic wave amplitude (E/A); deceleration rate (E/DT). Pulsed Doppler of pulmonary vein flow (PVF): systolic forward flow wave amplitude (S) ; diastolic forward flow wave amplitude (D); diastolic reverse flow duration (Ardur). Derived measurements: systolic fraction (S/S+D); difference between diastolic reverse flow duration of pulmonary venous flow and late diastolic wave duration of mitral flow (Ar-A duration). Tissue Doppler of mitral annulus (TDI): amplitude of early diastolic wave (E′); amplitude of late diastolic wave (A′); Derived measurements: ratio between early diastolic wave amplitude of transmitral flow and early diastolic wave amplitude of mitral annulus (E/E′). Colour M-mode Doppler of transmitral inflow: propagation velocity of early diastolic flow (Pv) calculated as the slope of the first aliasing (45 cm /s) from the mitral valve plain to 4 cm into the left ventricle. Derived measurements: ratio between early diastolic wave amplitude of transmitral flow and its propagation velocity into the left ventricule (E/Pv).

Table 1. Parameters for identification of patients with an elevated left ventricular filling pressure.

• Enlarged left atrium size
• E/A ratio >2
• DT <150 msec
• SF of pulmonary vein flow <40%
• E/E′ ratio >15
• E/Pv >2

DT: deceleration time of early diastolic wave of transmitral flow; E/A: ratio between early diastolic and late diastolic wave amplitude of transmitral flow; E/E′: ratio ratio between early diastolic wave amplitude of transmitral flow and early diastolic wave amplitude of mitral annulus; E/Pv: ratio between early diastolic wave amplitude of transmitral flow and its propagation velocity into the left ventricular. LA: left atrium. SF: systolic fraction.

Table 2. Proposed formulas for the estimation of left ventricular filling pressure.

MFV and PVF (for patients in sinus rhythm+left ventricular systolic dysfunction)
$PCWP=1{\cdot}85 \times \text{deceleration rate} - 0{\cdot}1 \times SF + 10{\cdot}9$[10]
MFV and colour M-mode (for patients in sinus rhythm and various cardiac conditions)
$PCWP=5{\cdot}27 \times (E/Pv)+4{\cdot}66$[13]
MFV and TDI mitral annulus (for patients in sinus rhythm and various cardiac conditions)
$PCWP=1{\cdot}9+1{\cdot}24 \times (E/E')$[16]
MFV and TDI mitral annulus (for patients with single transmitral flow wave due to tachycardia)
$PCWP=1{\cdot}55+1{\cdot}47 \times (E/E')$[17]
MFV and TDI mitral annulus (for patients in atrial fibrillation)
$PCWP=6{\cdot}489+0{\cdot}821 \times (E/E')$[20]

MFV: mitral flow velocity; PVF: pulmonary vein flow; PCWP: pulmonary artery wedge pressure; TDI: tissue Doppler. See Table 1 for the other abbreviations.

parameters used for the estimation of left ventricular filling pressure are summarized in Fig. 1. Table 1 shows parameters that can be used to identify patients with an elevated left ventricular filling pressure. The next step in the analysis of patients is to use formulas which provide an estimate of the actual filling pressure (Table 2).

Two questions arise: (1) should left ventricular filling pressures be routinely estimated during the echocardiographic examination of patients with known or suspected heart failure? and (2), what indices should be used in a given patient? To answer the first question additional studies specifically designed to assess the practical impact of this non-invasive measurement on treatment and outcome are needed. We should realize, however, that in everyday practice we try to assess the haemodynamic status on the basis of symptoms and clinical signs despite the fact that the sensitivity of these indices in identifying patients with a high filling pressure is, at best, 60%[22]. Doppler echocardiography is far more accurate and reproducible, provided that an appropriate methodology is applied.

As far as the method and the indices are concerned, we think that two concepts should be kept in mind. The first is that because of the complex pathophysiologic mechanisms that govern the relation between Doppler echocardiographic variables and left atrial pressures, no single variable can be used to assess left ventricular filling pressures in a given patient. Second, different methods should be applied in different subsets of patients, taking into consideration factors such as the etiology of the disease, heart rate and rhythm, and systolic function. We suggest beginning the evaluation of left ventricular filling pressure by looking at dimensions and function of the left ventricular by standard M- and B-mode echo. As stated above, if the left ventricle is dilated and its systolic function depressed the transmitral flow velocity parameters alone[6] or in combination with pulmonary venous flow parameters[10] (Table 2, first equation) are usually sufficient for estimating left ventricular filling pressure. If there are still doubts, or the pulmonary venous flow recording is technically inadequate, E/Pv or E/E′ ratios can also be caclulated. If the left ventricular systolic function is normal or mildly depressed, the E/E′ ratio is the measurement of choice. It allows differentiation of patients with normal (low left ventricular filling pressure) from those with pseudonormal (high left ventricular filling pressure) mitral flow velocity pattern, those in whom an impaired filling is due to ‘restriction’ from those in whom this is due to ‘constriction’[23]. In addition, E/E′ ratio incorporated in different equations (Table 2) can be used to quantitatively estimate left ventricular filling pressure in various subsets of patients such as those with a single transmitral flow due to sinus tachycardia, hypertrophic cardiomyopathy, cardiac allograft and atrial fibrillation[17–20]. The concepts presented will be exemplified by several patients who underwent simultaneous invasive and Doppler echocardiographic assessment.

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