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EDITORIAL

Speckle tracking echocardiography in cirrhosis: is it ready for prime time?

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Cirrhotic cardiomyopathy is a form of myocardial dysfunction specific to patients with cirrhosis, consisting of normal systolic function at rest, systolic incompetence under conditions of stress, increased thickness of the left ventricle, associated with impaired relaxation during diastole, and electrophysiological abnormalities [1]. All these changes occur independently of the underlying etiology of cirrhosis and in the absence of any known causes of cardiac disease [2]. Although first thought to be an academic novelty, the condition is now increasingly recognized as an important issue in cirrhosis, contributing to many complications of cirrhosis and negatively impacting survival. For example, systolic incompetence in cirrhotic patients with ascites and spontaneous bacterial peritonitis has been implicated in the development of renal dysfunction [3], the presence of diastolic dysfunction is associated with slow clearance of ascites following the insertion of a transjugular intrahepatic portosystemic stent shunt for the treatment of refractory ascites [4], while increasing severity of diastolic dysfunction in cirrhosis is linked to worse survival [5].

Of the various aspects of cirrhotic cardiomyopathy, diastolic dysfunction is the most commonly investigated entity, as it has a prevalence of up to 64 % [5–7], and it is present at rest in affected patients and can be diagnosed with well-defined diagnostic criteria [8] and fairly standardized techniques. Diastolic dysfunction is said to be present when there is a failure of the left ventricle to relax during diastole, thereby impeding the filling of the left ventricle. The first indication of diastolic dysfunction is demonstrated by a decreased early filling of the left ventricle (*E* wave), slower deceleration of the jet stream of blood as it enters the left ventricle, and a greater dependence on the atrial systole to contribute to the final filling of the left ventricle (*A* wave). The echocardiographic findings that correspond to these changes include a reduced *E/A* ratio of <1 and a prolonged deceleration time when pulsed Doppler analysis of the transmitral flow pattern is used. Supportive findings include a prolonged isovolumic relaxation time (the time interval in the cardiac cycle from the closure of the aortic valve, to onset of filling by opening of the mitral valve), and/or thickened myocardium. As the diastolic dysfunction progresses, left ventricular compliance is reduced, which increases left atrial pressure and, in turn, increases early left ventricular filling despite impaired relaxation. This paradoxical normalization of the *E/A* ratio is called pseudonormalization. Further reduction in left ventricular compliance will lead to a stiffer ventricle. Left atrial pressure is markedly elevated and compensates with vigorous early diastolic filling. This 'restrictive' filling pattern is associated with an abrupt deceleration of flow with little additional filling during mid-diastole and atrial contraction, thus providing a markedly elevated *E/A* ratio [9] (Fig. 1). The left ventricular filling pressure is also markedly elevated. These various findings are graded according to the degree of severity [10] (Fig. 1) and have prognostic significance.

The use of Doppler assessment of the mitral inflow on echocardiography has its limitations. The mitral *E* velocity and *E/A* ratio decrease with age, whereas isovolumic relaxation time, deceleration time, and the *A* velocity increase with age [11]. Other factors that affect mitral inflow include heart rate, heart rhythm, PR interval, cardiac output, mitral annular size, left atrial function, and left

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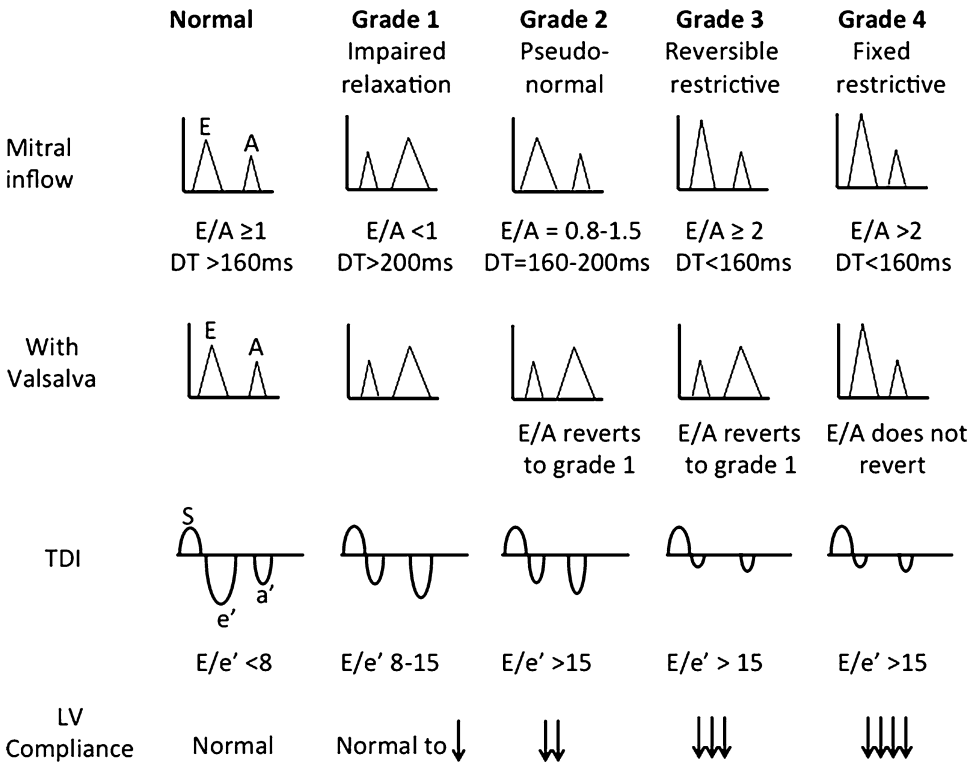

Fig. 1 Echocardiographic assessment and grading of diastolic dysfunction, with typical findings using different modalities of echocardiography. *LV* left ventricle, *TDI* tissue Doppler imaging

ventricular end-systolic or end-diastolic volumes [12]. Other methods of assessing diastolic function that are independent of these confounding factors include the use of tissue Doppler imaging (TDI). This particular technique uses frequency shifts of ultrasound waves to calculate myocardial velocity, that is, it is the movement of the myocardial tissue rather than the mitral inflow velocity that is being measured. When placed over the apex of the heart, the ultrasound beam is best suited to measure the longitudinal motion of the left ventricle. The mitral annular motion is used as a surrogate measure of overall longitudinal left ventricular contraction (systolic function) and relaxation (diastolic function) [13]. Three wave forms are usually obtained: (1) s wave above the baseline, which represents systolic myocardial velocity as the annulus descends toward the apex; (2) an e wave below the baseline, which represents early diastolic myocardial relaxation velocity as the annulus ascends from the apex; and (3) an a wave below the baseline, which represents myocardial velocity associated with atrial contraction (Fig. 1). TDI parameters are designated with a superscripted prime symbol ($'$) to differentiate them from Doppler velocities measured from mitral inflow. An e' velocity of >8 cm/s is generally considered to be consistent with normal diastolic function. Furthermore, simultaneous cardiac catheterization and echocardiographic studies have shown that left ventricular filling pressures are correlated with the ratio of the mitral inflow E wave to the tissue Doppler e' wave (E/e') [14]. Therefore, the additional measurement of TDI following conventional echocardiography will allow an estimation of left ventricular filling pressure, thus providing further information regarding the severity of diastolic dysfunction [15]. An E/e' ratio of <8 is generally accepted as being indicative of normal left ventricular filling pressure, and a value of >15 usually correlates with increased filling pressure and hence more severe diastolic dysfunction.

It appears that TDI also has its own limitations. For example, the echo beam has to be perfectly aligned to the vector of contraction before tissue velocity measurements is feasible. Therefore, the technique is angle-dependent. In addition, the images are complex to analyze and to interpret. An improvement on the TDI technique is the use of speckle tracking echocardiography (STE). Speckle tracking evaluates myocardial deformation and quantifies left ventricular rotation, twists, and untwists. Therefore, STE allows for easy assessment of segmental and global longitudinal, radial, and circumferential strain (shortening of muscle fibers or contraction) and strain rate, as well as left ventricular rotation, and torsion [16]. STE is usually used to assess systolic function, but characteristic changes during diastole also lend its use in the evaluation of diastolic dysfunction. A decrease of early diastolic apical untwisting rate as well as a shortening of the time from peak apical diastolic untwist to mitral valve opening can be observed in patients with diastolic dysfunction [17].

Since atrial function is an integral part of ventricular function, cardiovascular investigations frequently involve the assessment of atrial hemodynamics and mechanical

characteristics in addition to assessment of left ventricular function. The left atrium primarily modulates left ventricular filling through changes of its three functions: a reservoir function during ventricular systole when it collects and stores pulmonary venous blood; a conduit function during early ventricular diastole when it allows blood to directly flow through from the pulmonary vein into the ventricle; and a booster pump function during late ventricular diastole when it actively contracts and pumps 15–30 % of the total ventricular filling into the ventricle. Alterations in any of these different functions can be assessed non-invasively using TDI and STE. In this issue of the journal, Sampaio et al. [18] report on the use of STE to assess atrial function in a cohort of cirrhotic patients; in particular, they wanted to know whether the presence of diastolic dysfunction affected left atrial function. In a total of 111 patients with cirrhosis of all etiologies and various severities of liver dysfunction, the authors report that the prevalence of diastolic dysfunction to be 16.2 % using the diagnostic criteria of the American Association of Echocardiography [8], with the majority of these patients having grade 1 diastolic dysfunction. Patients with diastolic dysfunction had significantly higher left atrial volume index [18]. In addition, the peak longitudinal strain at the end of ventricular systole (PALS), or the maximum atrial reservoir function, showed a significant negative correlation with E/e', that is, the higher the E/e' ratio (which represents diastolic dysfunction), the less the atrium is able to perform its reservoir function, with less distension, as indicated by a smaller positive strain value. The authors, therefore, have suggested that the same pathological process might be responsible for causing reduced atrial and ventricular compliance. In addition, a PALS value of 47.1 was able to predict elevated left ventricular filling pressure (another sign of significant diastolic dysfunction) with 97 % sensitivity and 55 % specificity. In contrast, the left ventricular volume index did not correlate significantly with E/e', suggesting that other factors may also be responsible for the increased left atrial volume observed in patients with diastolic dysfunction. The corollary from this observation is that an increased left atrial volume index cannot be regarded as an indication for the presence of diastolic dysfunction. Finally, the peak atrial strain just before atrial contraction (PACS) was the same between cirrhotic patients and control subjects. The authors have therefore concluded that atrial contraction was not affected in cirrhosis. However, we are not provided with the information as to whether the PACS was different between patients with or without diastolic dysfunction.

Despite identifying atrial compliance abnormalities in patients with cirrhosis, there is absolutely no correlation between PALS and any of the clinical parameters measured. Because this paper does not provide follow-up data, we are not sure whether this atrial abnormality will be able to predict prognosis in these patients. Since severe diastolic dysfunction is not typically seen in cirrhosis, and mild diastolic dysfunction is not associated with significant atrial abnormalities, it is not clear how much more information STE will add to the other parameters of diastolic dysfunction that we already have, especially when applied to the management of the cirrhotic population. Therefore, for now, an abnormal PALS can be regarded at best as an academic curiosity. Furthermore, in order for the information to be useful, the hepatology community will need to be educated in echocardiography, and this is not going to happen any time soon. So, while this new technique is an advance over the traditional pulsed Doppler 2D echocardiography, and even TDI, STE may not be all that applicable in patients with cirrhosis. Perhaps in those patients showing significant diastolic dysfunction who are about to undergo a stressful procedure such as the insertion of a transjugular intrahepatic portosystemic stent shunt, STE can supplement TDI in the assessment of left ventricular filling pressure, thereby helping to determine which patients will be able to successfully negotiate the procedure without getting into diastolic heart failure.

Compliance with ethical requirements and Conflict of interest This article does not contain any studies with human or animal subjects. Florence Wong declares that she has no conflict of interest.

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