Search for non-invasive load-independent indices of left ventricular relaxation

ABSTRACT

Echocardiography is an invaluable tool for the routine evaluation of patients with congestive heart failure. A number of Doppler modalities are now available. In this comment, the haemodynamic determinants and the clinical application of the more recent indices of left ventricular relaxation, namely tissue Doppler imaging of the mitral annulus and the flow propagation velocity by colour M-mode, and the importance of the study by Graham et al. in this issue of Clinical Science are discussed.

It is estimated that up to 40–60 % of patients with congestive heart failure have their symptoms despite a normal ejection fraction [1]. This group of patients are frequently referred to as having ‘diastolic heart failure’. Recent guidelines [2,3] have emphasized the need (invasive or non-invasive) for the estimation of left ventricular (LV) filling pressures and/or relaxation in establishing this diagnosis, along with the standard clinical criteria of congestive heart failure and a normal ejection fraction (EF). Given the risks and costs of invasive assessments of LV diastolic function, the use of a reliable non-invasive parameter is the most practical approach. An ideal non-invasive index of LV relaxation is one that is acquired with a high feasibility, has a reasonable reproducibility with respect to acquisition and measurement, is strongly related to invasive parameters of LV relaxation and is load-independent. Early on, echocardiography emerged as an important test in this field.

Since echocardiography can determine LVEF, regional function, the presence of valvular and/or pericardial disease as well as cardiomyopathies, it is not surprising that it is frequently the single test needed to reach a reliable determination of the absence or presence of a cardiac aetiology for dyspnea as well as to monitor therapy in cardiac patients. Specifically, it offers several indices that can be utilized to determine the status of LV relaxation and filling pressures [4]. Among the conventional indices that have stood the test of time, mitral inflow and pulmonary venous flow velocities are currently utilized in most laboratories [5]. They are highly reproducible and are generally acquired with a high feasibility.

Although mitral inflow and pulmonary venous flow velocities can provide invaluable information in many clinical circumstances, they have their shortcomings. Specifically, they are most useful in patients with a depressed EF; however, when the EF is normal (> 50 %), these parameters are much less reliable [6,7]. In addition, the strong influence of loading conditions on these velocities precludes their application to drawing inferences about LV relaxation in situations where filling pressures are increased.

These limitations, along with the recent developments in ultrasound technology, have fuelled the search for other indices of LV diastolic function. Novel indices of regional and global LV diastolic function were thus identified and now include tissue Doppler imaging (TD) of the mitral annulus [8–12] and the different myocardial segments as well as the flow propagation velocity (FPV) of LV early diastolic filling by colour M-mode [13–16]. Furthermore, since mitral inflow peak early diastolic transmitral velocity (E) is dependent on both left atrial pressure and LV relaxation and the more novel indices are believed to be primarily relaxation-dependent, the ratio of E/FPV and E/E’ (where E’ is the mitral annular early diastolic velocity) are used to estimate LV filling pressures [7,11,12,15]. In this comment, we discuss the clinical application of both techniques to the study of LV diastolic function in light of the recently published studies.

FPV has been reported to have a strong relationship with invasive indices of LV relaxation in animals and humans [13,14,16], to be load independent [16] and accurate in estimating LV filling pressures in conjunction with E [15]. FPV thus appeared to fill the existing gap.

Key words: diastolic function, early diastole, echocardiography, long-axis function, mitral annulus.
in the Doppler methodology. Recently, however, studies [7,17] have shown its stronger dependence on LV systolic function than on LV relaxation. Consequently, it was observed to be normal or increased in patients with a normal EF, but impaired LV relaxation [7,17]. In fact, a recent study from our laboratory [7] noted that FPV added no incremental information to mitral inflow peak E in the prediction of wedge pressure in patients with a normal EF. Reproducibility is also a problem for this index. Again a number of studies have shown a high inter- and intra-observer variability and, depending on the methodology of measurement, which needs to be standardized, widely different conclusions about LV relaxation could be reached [18].

In this issue of Clinical Science, Graham et al. [19] provide important new insights into the load-dependency of FPV. The investigators noted that FPV decreased significantly with decreased intravascular volume in patients with a normal fractional shortening, but with abnormal LV diastolic function (as inferred from the mitral inflow pattern, TD velocities and the presence of LV hypertrophy). Their findings also confirm previous reports of lower reproducibility (variability 12.3 ° 12.6 %) and normal velocity values (55 ° 12 cm/s), despite abnormal LV relaxation when LVEF is preserved.

In comparison, E′ acquired by two different techniques, namely spectral pulse-Doppler and M-mode recordings of mitral annulus motion, was not altered by the 1.6 kg decrease in body weight [19]. The validity of the authors’ conclusion with respect to E′ is well supported by the consistency of results using two different methodologies. This is a particularly important finding in the study by Graham et al. [19], since a previous report [20], which used dialysate to achieve a large decrement in LV diastolic pressures, suggested the existence of load dependency of the annular velocities, but did not address the effect of a more physiological reduction of filling pressures on these indices. Although there are a number of reasons, as discussed by the authors for the different results, two important factors stand out: (i) the amount of fluid loss, which was much more in the study by Agmon et al. [20], and (ii) the aggressive fluid loss in the latter study led to a significant decrease in arterial pressure as well as an increase in heart rate. Although these haemodynamic changes can induce ischaemia and thereby alter annular velocities, tachycardia in and of itself is capable of decreasing E′ [21]. Therefore the changes induced by dialysis in the study by Graham et al. [19] allowed the authors to examine, as much as possible clinically, the pure effects of preload reduction on these novel indices of LV relaxation. The observations by Graham et al. [19] in patients with impaired LV relaxation parallel animal studies showing the minimal impact of preload on E′ in the setting of prolonged relaxation [22]. This investigation also confirms the higher reproducibility and the strong dependence of E′ on age and LV mass, variables which are known to adversely influence LV relaxation. Another interesting observation is the successful detection of the decrease in LV filling pressures using both septal and lateral E/E′ ratios.

Putting the study by Graham et al. [19] in the context of existing literature and considering the totality of evidence, it is reasonable to conclude that TD velocities meet many of the requirements of an ideal non-invasive index of LV relaxation: the significant correlation with invasive indices of LV relaxation [9,10,12,22], the minimal impact of preload in the setting of impaired relaxation [11,19,22] as well as the practical aspects of high feasibility and reproducibility [11,12]. As for the FPV, it is most accurate in the setting of a depressed LVEF [7] and is most vulnerable to the effects of ventricular volumes and preload in patients with a normal EF.

Finally, detecting the presence of abnormal LV diastolic function by these non-invasive tests is not a banality in this day and age as these very same measurements are capable of providing important prognostic information [23,24], the ultimate test of clinical relevance.

SHERIF F. NAGUEH
Section of Cardiology, Department of Medicine, Baylor College of Medicine, 6550 Fannin Street, SM-1246, Houston, TX 77030-2717, U.S.A.

(ON BEHALF OF THE EDITORIAL BOARD)

REFERENCES

© 2003 The Biochemical Society

Received 24 June 2003; accepted 9 July 2003
Published as Immediate Publication 9 July 2003. DOI 10.1042/CS20030214

© 2003 The Biochemical Society