Echocardiography in left ventricular dysfunction

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Left ventricular (LV) function is an important predictor of cardiac morbidity and mortality. The role of echocardiography in the assessment of LV function is well established and has been expanded over the last few years with the development of new methodologies. Echocardiography can assess LV global and regional function, as well as systolic and diastolic function. It has the ability to measure volumes, including cardiac output, pressures, LV mass, dP/dt. It can also assess regional dysfunction using the wall motion score. However quantitation by standard echo can be limited, due to poor endocardial definition, time-consuming, and reproducibility, lack of accuracy, particularly considering it takes a lot of geometric assumptions.

Therefore, new methodologies have been recently developed to increase echo accuracy. These include the introduction of second harmonics, which is becoming a standard in most equipments; the use of contrast echo to improve LV opacification and endocardial border definition; color kinesis, which allows automated segmental motion analysis; tissue Doppler imaging, which can help in the assessment of regional and diastolic function; and more recently the ability to assess strain and strain rate. This last technology has the ability to quantify local myocardial deformation and it has shown to be a potential strong marker of ischemia, as well as a predictor of LV myocardial recovery post-revascularization.

In conclusion, echocardiography is widely used to assess LV function. The recent developments of new ultrasound-related technologies have further increased the interest and importance of echocardiography in the assessment of LV function.

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Left ventricular (LV) function is the most important prognostic indicator in patients with cardiac disease[1,2]. Several methods have been developed over the years to assess both qualitatively and quantitatively different parameters of LV function. Echocardiography has been the most popular since it is a non-invasive technique that can provide information on the structure of the heart as well as on its function. In addition it can help assessing the etiology of the heart condition and improve the understanding of the underlying pathophysiology, and at the same time it can be repeated as many times as needed with no discomfort for the patient. Its role in the prognostic stratification of patients with poor LV function is well established[2].

Echocardiography and systolic function

There are several aspects related to the assessment of systolic function that echocardiography can provide, such as: global and regional function, degree of ventricular remodeling, contractile reserve, ischemia and viability, particularly in patients post-acute coronary syndromes or post-revascularization, and the concomitant presence of valvular lesions, which may significantly impact on the assessment of LV function (particularly the presence of mitral and/or aortic regurgitation).

Resting systolic dysfunction can be classified into global and segmental dysfunction. Although the presence of segmental dysfunction has been usually related to ischemic nature and global to idiopathic dilated cardiomyopathy, it is clear today that several patients with ischemic heart disease as well as with other end-stage heart conditions can present with globally dilated ventricles. In addition patients with cardiomyopathies, myocarditis, etc., can also present with segmental dysfunction. Since the prevalence of coronary artery disease is very high in the western population, this diagnosis should always be excluded in the presence of global LV dysfunction.

The use of M-mode, two-dimensional and Doppler flow assessment can provide an array of anatomical and functional information very useful in the assessment of patients with heart failure (Fig. 1). From the M-mode several parameters can be obtained, such as the E-point septal separation or the presence of a b-bump at end diastole, which relate to increased LV end-diastolic pressures and LV impaired systolic function.

There are several other measurements that can be done, including internal diameters, areas, volumes (end-diastolic and end-systolic volumes, therefore ejection fraction), cardiac output, LV mass, dP/dt (from the mitral regurgitation jet). However, some of these measurements have to be taken with great caution, since there are several limitations in the way they are obtained. Just as an example, the calculation of LV volumes by any method (area-length, Simpson, etc.) is based upon several geometric assumptions that may not fit the different geometries the left ventricle can assume according to the different pathologic substrates.

Echocardiography and diastolic function

Echocardiography has the ability to study the filling phase of the cardiac cycle, providing substantial information on both components of diastole, myocardial relaxation, and ventricular compliance (Fig. 2)[3]. Diastolic dysfunction can be simply summarized as the presence of an abnormal filling of the left ventricle together with increased filling pressures. The main causes for diastolic dysfunction are ischemic heart disease, hypertensive heart disease, cardiomyopathies, systemic diseases, such as amyloidosis, hemochromatosis or Fabry's disease, among others, and valvular heart disease. The introduction of Doppler flow assessment in clinical practice helped to improve our ability of studying and understanding LV filling, despite some of the pitfalls and limitations that have been described. The mitral valve inflow, together with the pulmonary venous flow and the size of the left atrium provide important information with real clinical applications. The most useful parameters to observe and measure are: deceleration time, duration of *a* wave in the mitral and pulmonary venous flow, *e/a* ratio. A Valsalva maneuver should be routinely performed to differentiate the pseudo-normalization patterns from the normal.

With mildly reduced compliance an increase in pressure may occur only at end diastole or with atrial contraction, which is shown as an increased duration of flow reversal into the pulmonary or hepatic veins during atrial contraction, while duration of forward flow may be abbreviated[4]. As compliance is gradually impairing, the abnormal pressure increase is progressively occurring more early in diastole, resulting in abbreviated early diastolic filling (shortened deceleration time) and reduced filling with atrial contraction[5]. With

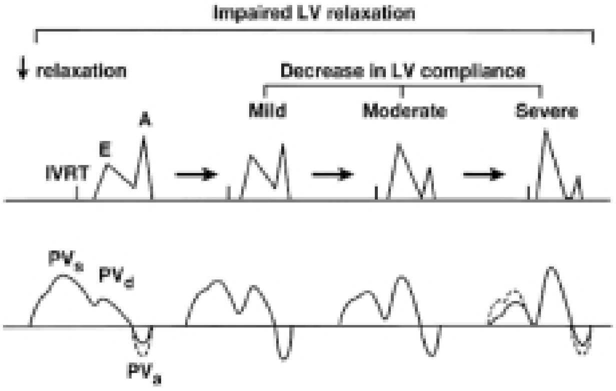

Figure 2. *Diagram showing the impact of impaired left ventricular (LV) relaxation and decrease in LV compliance in the mitral flow and pulmonary venous (PV) flow. IVRT = isovolumic relaxation time. Adapted from Appleton and Hatle[3].*

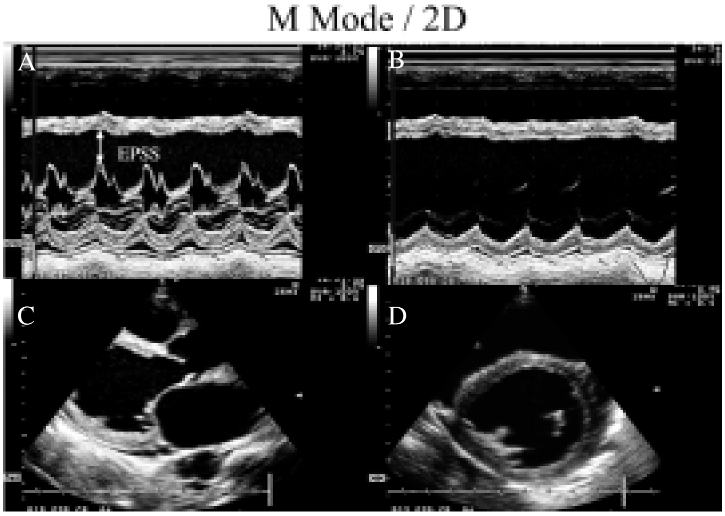

Figure 1. A *and* B *are an example of an M-mode of a patient with left ventricular dilation and impaired systolic function, showing increased E-point septal separation (EPSS) and a b-bump representing high end-diastolic pressure.* C *and* D *are two-dimensional (2D) images of the same patient.*

abnormal pressure rise prior to atrial contraction, left and right atrial pressure will also be elevated, resulting in shortening of isovolumic relaxation time and atrial enlargement[5]. The presence of mainly early diastolic filling can be shown in regular M-mode as a lack of enlargement in mid and late diastole or by color flow M-mode as early cessation of filling.

The presence of abnormal relaxation can be easily detected by mitral valve flow velocity recording. It shows prolonged isovolumic relaxation time due to delayed mitral valve opening and impaired early diastolic velocity with an inverse e/a ratio, due to more filling during atrial contraction (Fig. 2).

The use of tissue Doppler added a new dimension to the understanding of diastolic function or, to be more precise, of the filling phase of the cardiac cycle. The main advantage regards the direct measurement of myocardial function, by sampling directly the myocardium with fewer limitations than blood flow velocity analysis. It also allows assessment of both global and regional function, as we will see later in this paper.

Limitations in quantification: role of the new technologies

Despite the ability of echocardiography to measure several parameters, there are several limitations that have to be known and understood before the technique can be properly used. Some of these limitations are related to the technique itself, others to some simplifications that have been done in order to make it easier to use it. One of the most important limitations has to do with the poor endocardial definition that can be observed in some patients. This is more often seen in the presence of obesity, chronic obstructive pulmonary disease or other pulmonary problems, chest abnormalities, etc., that result in poor ultrasound windows. It is obvious that this will limit significantly our ability to assess, for instance, regional contractility. Other limitations include: geometric assumptions used in some of the formulae (for instance in the Simpson's or the area-length methods), reproducibility (there is some degree of intra- and interobserver variability as well as in the acquisition of images; it still is in some way an operator-dependent technique), it can be sometimes complicated and time-consuming.

The need to overcome some of these limitations led to the development of new technological refinements and methodologies, which appeared over the last few years. One of the first ones to appear was automated border detection, which was based on the ability to define an acoustic interface between the blood and the endocardium by using the integrated backscatter information from the blood pool and tissues. This method has the advantage of representing the cardiac cycle over time mimicking the volume curves, but it is very much operator-dependent as well as image quality-dependent[6,7]. Some data have been published on its use to assess diastolic function and also to improve border detection, such as in the continuous estimation of cardiac output for hemodynamic monitoring of patients in the operating room and intensive care settings[7]. With further development, this method may measure cardiac output in selected patient care settings. This technique may also be regarded as complementary to Doppler echocardiography. The combined use of the methods may improve the diagnosis of LV relaxation abnormalities[8]. The waveform of LV area obtained by the automated border detection technique identifies the phases of the cardiac cycle and correlates with Doppler values of LV diastolic function. Therefore, this new method of automated border detection has potential uses in the assessment of LV diastolic function[9].

Another method that has also been developed to facilitate the evaluation of regional wall motion is color kinesis[10]. It is based on acoustic quantification and it tracks the motion of the endocardium in real time throughout systole and results in color-encoded images reflecting the magnitude and timing of endocardial motion. One of its developments is called automatic segmental motion analysis and it allows assessing regional LV function, including the display of a histogram bar graphic. Again, one of the major limitations with this method regards its operator dependence as well as on image quality and border definition.

One of the main technical refinements over the last few years has been the introduction of second harmonic imaging into the ultrasound systems[11]. With this method we have the possibility of sending an ultrasound beam at a certain frequency and receive it at doubled frequency. This allows improving dramatically the image quality without losing penetration and it improves significantly the ability to detect endocardial borders (Fig. 3). The use of second harmonic imaging also allowed the development of contrast ultrasound, since it improved the ability to detect the ultrasound bubbles in the blood pool, as well as in the myocardium. The use of contrast echo to improve endocardial border definition, particularly in some instances, such as during stress echocardiography, is supported by several studies[12,13].

The use of Doppler to obtain information on heart motion was first introduced by Yoshida et al.[14] in 1961, but it was in 1970 that Sonnenblick et al.[15] proposed that recording the velocity of myocardial contraction could be a way to assess myocardial function. However it was only in 1989 that Isaaz et al.[16] reported for the first time the use of pulsed Doppler to record LV posterior wall motion both in normal subjects and in patients with regional function abnormalities. Despite these initial reports it was only in the 1990s that the use of myocardial velocities to assess regional LV function had its major expression[17]. It is based on the ability to sample myocardium and obtain myocardial velocities at a specific site. The rationale to use it is based on the fact that my-

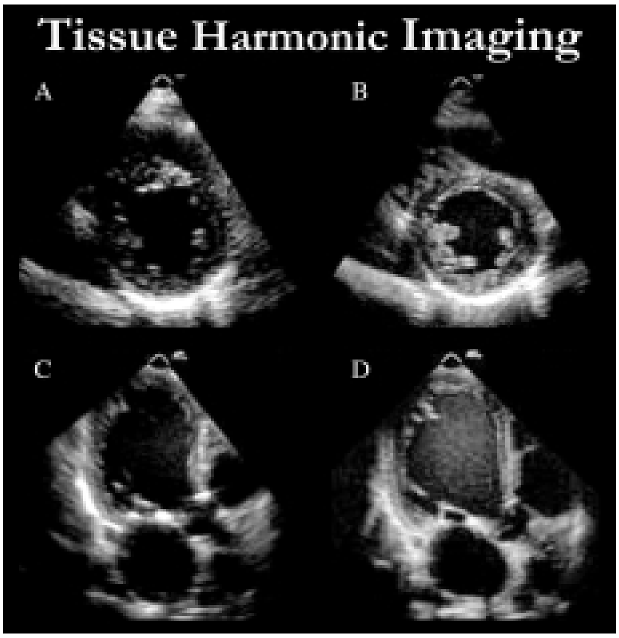

Figure 3. *Comparison of fundamental imaging* (A *and* C) *and tissue harmonic imaging* (B *and* D)*, showing a better endocardial definition with tissue harmonic imaging.*

ocardial velocities are less dependent than blood pool velocities, therefore representing more precisely the different set of events that occur throughout the cardiac cycle. Some important uses of this method have been on differentiating a pseudo-normal from a normal pattern[18], constriction vs restriction[19], in patients with hypertrophic cardiomyopathy[20], more recently in cardiac resynchronization, where it has been used for selection, monitoring and follow-up of these patients[21,22]. Another important application has been on the study of the so-called subclinical disease, such as, in cardiomyopathies (hypertrophic, Friedreich's ataxia, Duchenne, etc.), diabetes, ageing, drugs, and athlete's heart[22-26].

Despite all these potential applications the use of pure tissue velocities still has some limitations, with angle dependency and load dependence being the more significant, as well as the fact that it represents motion and not deformation. This was the rationale to develop a method that could be more accurate and better assess the sequence of events that occur at a very fast rate in the myocardium, for which the human eye has no ability to differentiate (our eye can only detect motion that takes > 80 ms and some phenomena occur much faster than this). In the recent years the use of strain and strain rate has been adopted as a new modality[27]. With this method local myocardial deformation is assessed as opposed to motion. Strain is basically the amount of deformation of a certain segment of myocardium, while strain rate is the rate at which this deformation occurs throughout a certain period, such as the cardiac cycle. This seems to be a more direct and accurate surrogate of regional LV function. There are already some data showing its use in assessing, for instance, myocardial ischemia. Kukulski et al.[28] showed that during coronary occlusion there is a significant decrease in absolute strain, but also a displacement of peak strain to end systole or even early diastole, in what is called post-systolic thickening (Fig. 4). This has also been shown as a marker of myocardial viability. More recently, Voigt et al.[29] showed the added value of using strain in dobutamine stress echo, increasing its sensitivity and specificity in the detection of myocardial ischemia. Other studies have demonstrated the potential benefits of this methodology in other clinical settings, including cardiomyopathies, right ventricular function abnormalities, cardiac transplantation, and congenital heart disease[30,31].

Chronic left ventricular dysfunction

In assessing patients with chronic LV dysfunction there are two important questions to ask:

1. How to distinguish ischemic from non-ischemic cardiomyopathy?
2. How to identify the candidates that will benefit most from revascularization?

The importance of myocardial viability has been shown in several studies. A summary is presented in figure 5 from Afridi et al.[32] where it shows clearly that patients who demonstrated viability and were revascularized had a much better prognosis. However it also shows that revascularization in the absence of viability can be highly deleterious. This highlights the need for proper investigation of these patients. There are several methods to assess viability, including echocardiography, nuclear magnetic resonance imaging and positron emission tomography, which have similar accuracies[33]. The use of stress echo has been shown to predict survival. It is also important to understand that the worse the LV function in the presence of viability the better are the results of revascularization. In addition Bax et al.[34] showed that there is a direct correlation between the degree of myocardial viability and functional recovery. These authors showed that only when more than four segments had evidence of myocardial viability a significant improvement in functional recovery was observed. This is very important since it means that it is equally important to demonstrate not only the presence of myocardial viability but also that a significant amount of viable myocardium has to be present to predict functional recovery. More recently the same authors also showed that once the patients with significant viability are identified the sooner they are revascularized the better is the outcome and prognosis in these patients[35].

In conclusion, echocardiography is the method more used to assess LV function due to its instantaneous diagnostic capacity, high-quality images, portability, safety, and accuracy. Recent developments have further expanded its indications and the potential to assess more refined parameters of LV function.

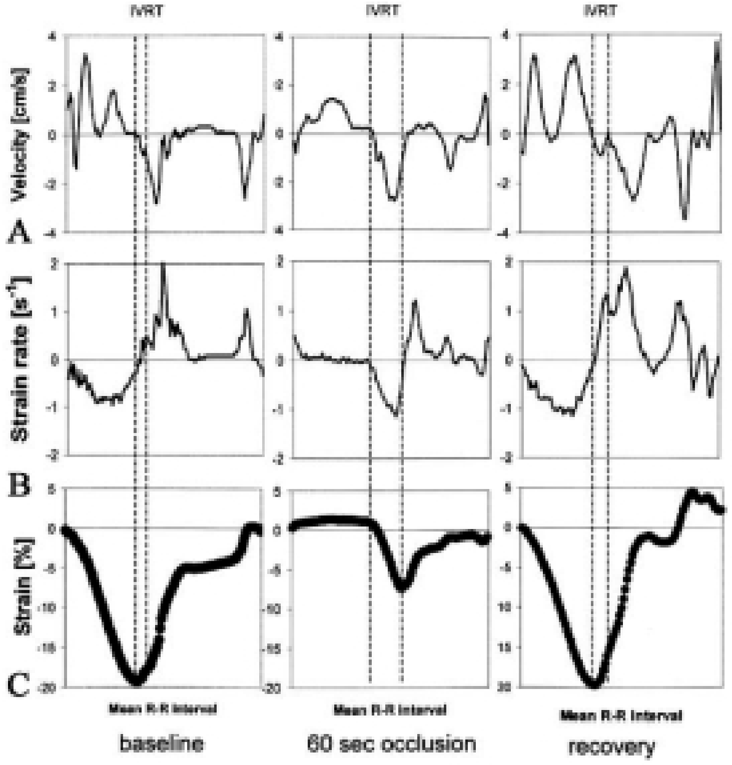

Figure 4. *Post-processed velocity* (A)*, strain rate* (B)*, and strain curves* (C) *obtained at baseline, during 30 to 60 s balloon occlusion of the left anterior descending coronary artery, and immediately after balloon deflation, showing decreased systolic deformation during occlusion by nearly 50% compared with baseline values. At the same time, post-systolic deformation increased in absolute values. IVRT = isovolumic relaxation time. Adapted from Kukulski et al.*[28].

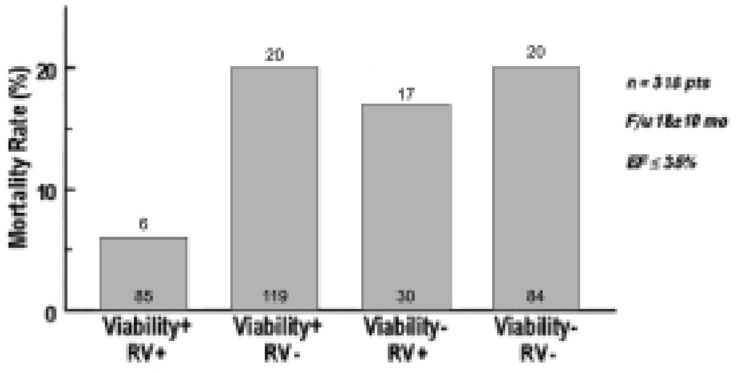

Figure 5. *Impact of revascularization (RV) in mortality rates in patients with coronary artery disease according with the presence or absence of myocardial viability. EF = ejection fraction. Adapted from Afridi et al.*[32].

Riassunto

La funzione ventricolare sinistra è un importante fattore predittivo per la mortalità e la morbilità cardiovascolare. Il ruolo dell'ecocardiografia nella valutazione della funzione ventricolare sinistra è ben consolidato e si è notevolmente ampliato negli ultimi anni con lo sviluppo di nuove metodiche ecocardiografiche. L'ecocardiografia è in grado di valutare la funzione ventricolare sinistra globale, sia come funzione sistolica che diastolica. È infatti in grado di misurare i volumi, inclusa la gittata cardiaca, le pressioni, la massa ventricolare sinistra, e il rapporto dP/dt. È anche possibile valutare la disfunzione cardiaca regionale mediante lo studio del punteggio di cinetica regionale. Tuttavia le misurazioni di tipo quantitativo con l'ecocardiografia tradizionale mostrano notevoli limiti, a causa della scarsa definizione dell'endocardio, del molto tempo necessario e della scarsa riproducibilità ed accuratezza, soprattutto considerando che esse utilizzano numerose assunzioni di tipo geometrico.

Pertanto lo sviluppo di nuove tecnologie ecocardiografiche ha permesso di migliorarne l'accuratezza. Fra queste nuove tecnologie ricordiamo la seconda armonica, che è diventata lo standard nella maggior parte delle apparecchiature; l'uso dell'ecocontrasto per migliorare l'opacizzazione ventricolare sinistra e la definizione del bordo endocardico; la color chinesi, che permette l'analisi automatica della cinetica segmentaria; il Doppler tissutale, che è di aiuto nella valutazione della funzione sistolica e diastolica regionale e, più di recente, la valutazione dello "strain" e dello "strain rate". Quest'ultima tecnologia permette di quantizzare la deformazione miocardica regionale ed ha dimostrato di essere un forte segno di potenziale ischemia, ed un fattore predittivo per il recupero della funzione ventricolare sinistra dopo rivascolarizzazione coronarica.

In conclusione, l'ecocardiografia è estesamente utilizzata per valutare la funzione ventricolare sinistra. Accanto a ciò, i recenti sviluppi delle nuove tecnologie applicate agli ultrasuoni hanno ulteriormente ampliato l'interesse e l'importanza di tale tecnica nella diagnosi della disfunzione ventricolare sinistra.

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