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Heart failure diagnosis: the role of echocardiography and magnetic resonance imaging

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1. ABSTRACT

Heart failure (HF) is the final common pathway of any heart disease, being a major cause of cardiovascular morbidity and mortality. Echocardiography is the most useful tool in the diagnosis of HF: echocardiographic evidence of left ventricular (LV) systolic dysfunction is generally associated with a dilated left ventricle (LV) and a reduced LV ejection fraction (EF). In many patients (pts) with symptoms of HF, however, EF and LV volumes are normal. Quantitative assessment of global and/or regional LV and right ventricle (RV) function is, therefore, necessary, and some emerging techniques, as Tissue Doppler Imaging (TDI) and Strain Imaging (SI), can provide such information. Moreover, cardiac magnetic resonance imaging (MRI) has emerged as an extremely useful technique in the investigation of pts with HF. Cardiac MRI permits calculation of myocardial mass, volumes and EF with Simpson's algorithm from three-dimensional data and with no geometric assumptions. The integration of conventional echocardiographic measurements, new echocardiographic parameters, and cardiac MRI is a very promising approach for an accurate evaluation of pts with HF.

2. INTRODUCTION

Heart failure (HF) is a major public health problem in the developed countries. The prevalence of HF in the general populations ranges between 0.4 and 2%, and increases with age (1,2). In the United States, approximately 5 million pts suffer from HF, and more than 550.000 pts every year are diagnosed with HF for the first time (3). In Italy, about 190.000 pts with HF per year seek hospital care and about 65.000 of them are admitted (4).

According to the ESC guidelines (5), HF is defined as "a complex clinical syndrome that can result from any structural or functional cardiac disorder which impairs the ability of ventricles to fill with or eject blood"; this includes diastolic as well as systolic HF. Both ESC and ACC/AHA guidelines (5,6) point out that echocardiography is the most useful test to diagnose HF, since structural abnormality, functional abnormality, systolic dysfunction and/or diastolic dysfunction need to be documented in pts who present clinical signs of HF, in order to establish a final diagnosis.

Nowadays, cardiac MRI has shown to be an extremely useful technique, associated with

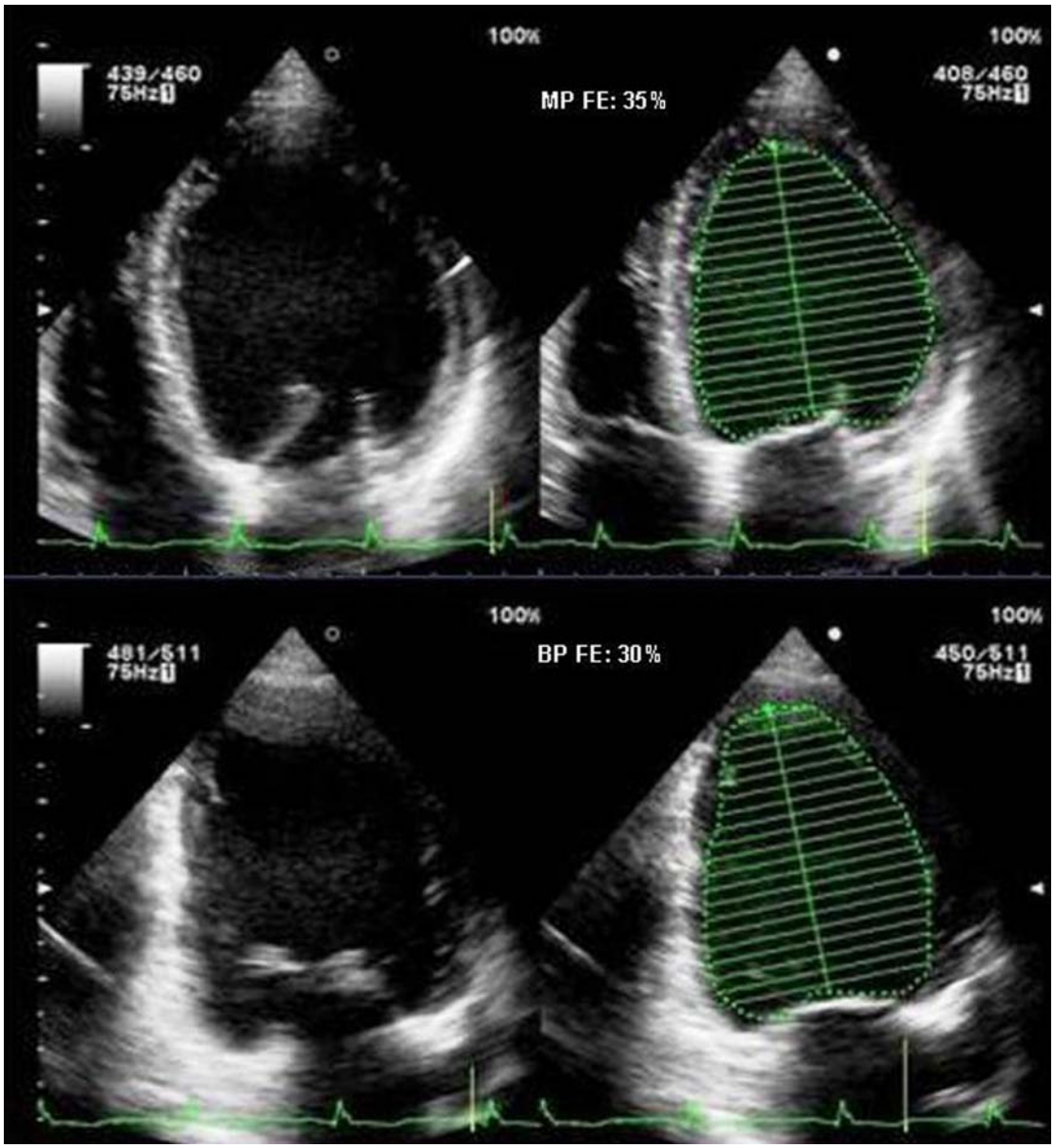

Figure 1. Evaluation of left ventricular volumes and ejection fraction (EF) by Biplane Sympson's rule. In this patient, with previous inferior and lateral myocardial infarction, the monoplane Sympson's rule (top) overestimates the ejection fraction. MP EF: monoplane ejection fractio; BP EF: biplane ejection fraction.

echocardiography, in investigation of cardiovascular disease (7).

A definite and complete diagnosis of HF needs an integration between echocardiography and cardiac MRI, taking different advantages from each of them.

3. NON INVASIVE EVALUATION OF LV SYSTOLIC DYSFUNCTION

Two-dimensional (2D) transthoracic echocardiography (TTE) is the most used technique to document systolic or diastolic cardiac dysfunction. Left ventricular (LV) systolic function is traditionally evaluated by parameters of global function such as LV end-diastolic and end-systolic volumes, ejection fraction (EF), etc. "Figure 1". Many pts with symptoms of HF, however, have normal EF and LV volumes. This condition has traditionally been classified as diastolic HF and, more recently, as HF with normal EF (HFNEF) (8). Growing evidence suggests that the use of new echocardiographic technologies and cardiac MRI can reveal the coexistence of an abnormal systolic function in these patients (9,10).

3.1. Role of echocardiography

LV systolic dysfunction is generally associated with dilated LV and reduced EF. It has been documented that LV volume and EF are important prognostic indicators for pts with ischemic or dilated cardiomyopathy (11-12). With LV remodelling and progressive heart dilatation, the

ventricle becomes more spherical, and the mitral annulus is dilated with apical displacement of papillary muscles and mitral leaflets, causing functional mitral valve regurgitation (13-15) (MVR). Grayburn et al. (12) have demonstrated that LV end-diastolic volume, deceleration time (DT) of early diastolic mitral inflow velocity and severity of MVR are the strongest predictors of survival in pts with EF 35% or less.

Non-invasive diagnosis of LV dysfunction by 2D TTE, based on the assessment of volumes and EF, however, is often unsatisfactory. The planimetrical measurement of LV end-diastolic and end-systolic areas is the most used method, but its reproducibility is weak, due to the high inter- and intra-observer variability. EF, end-diastolic volume, end-systolic volume, stroke volume and fractional shortening are also limited by both preload and after load dependence.

The myocardial performance index (MPI) is a combined systolic and diastolic Doppler-derived index for the assessment of global LV performance, and is well related with invasive measurements of LV systolic and diastolic function (16). In pts with normal LV function, MPI is less than 0.5: values above 0.8 suggest significantly depressed LV performance. The prognostic MPI value has also been demonstrated in pts with acute myocardial infarction (AMI): MPI is significantly higher in pts who develop congestive HF or die, than in survivors free of congestive HF. MPI, therefore reflects the severity of LV dysfunction and has a prognostic value in pts with AMI (17).

Non invasive estimation of LV dP/dt from the Doppler spectrum of MVR correlates well with invasive methods, and is used as an index of LV contractility (18). A reduced value, less than 1000 mmHg/sec, suggests a depressed dP/dt.

Another important tool for assessment of HF is the evaluation of LV contractile reserve. Dobutamine echocardiography is useful to explore the myocardial contractile reserve in pts with chronic HF and non ischemic dilated cardiomyopathy. The changes in echo-parameters during dobutamine infusion are related with VO2 max, and reliably evaluate the functional status of pts with non ischemic dilated cardiomyopathy and HF (19). The echo Dobutamine International Cooperative (EDIC) study (20) has shown that, in medically treated pts with severe ischemic global LV dysfunction occurring early after AMI, the presence of myocardial viability, identified as inotropic reserve after low-dose dobutamine, is associated with a good survival. The higher the number of segments showing improvement of function, the better is the impact of myocardial viability on survival. The presence of inducible ischemia in these pts is the best predictor of cardiac death.

A well known limitation of traditional 2D echocardiography is the difficulty to accurately quantify the global right ventricular (RV) function and the regional myocardial function of both ventricles. The measure of tricuspid annular plane systolic excursion (TAPSE) is a simple echocardiographic method for evaluating RVEF, although this index may be affected by co-existent chronic obstructive pulmonary disease. Despite this limitation, a decreased TAPSE is associated with increased mortality in pts admitted for HF, and is independent of other risk factors including LV function (21).

Quantitative assessment of global and/or regional LV myocardial function can be obtained by emerging techniques, the most widely accepted and validated technique so far used being TDI, which provides an assessment of regional and global LV and RV function (22,23). Mitral annular systolic velocity (MASV) “Figure 2” can be used as an index of global longitudinal LV function (22). Several investigators have shown a positive correlation between EF and the peak of MASV (24,25). A cut-off mean systolic velocity greater than 7.5 cm/sec has a sensitivity of 79% and a specificity of 88% in predicting an EF equal or greater than 50%. Values less than 7.5 cm/sec correlate with an EF of less than 50%. Furthermore, MASV can detect abnormal systolic function in pts with HF and normal EF (HFNEF) (26). In pts with HF, MASV has recently been demonstrated to be a powerful predictor of cardiac death, and to provide significant incremental prognostic information when compared with clinical data and mitral DT (27).

Furthermore, TDI permits calculation of the systolic and diastolic velocities at each LV segment, but this process is time consuming and analysis is possible only in LV walls along the ultrasound beam (see below).

Tricuspid annular systolic velocity (TASV) can also be used as an index of RV global function in pts with HF. A good correlation between TASV and RVEF assessed by radionuclide ventriculography has been demonstrated. A TASV less of 11.5 cm/sec predicts RVEF less than 45% with a sensitivity of 90% and a specificity of 85% (23). TASV has also a prognostic role in pts with HF (28).

In order to overcome TDI limitations (angle dependence, lack of discrimination between active contraction and passive motion), “strain” (S) and “strain rate” (SR) have been proposed as parameters to quantify regional contractility (23). Greenberg et al. (29) demonstrated that peak and mean systolic SR are powerful, non-invasive LV contractility parameters that are more reliable than peak systolic TDI velocities. Sutherland et al. (30) have studied the clinical applicability of strain imaging (SI) for the assessment of regional LV function in pts with chronic transmural infarction. Not only is SR able to accurately identify infarct-involved segments, but this parameter is also significantly altered in normokinetic segments supplied by a coronary artery with a significant stenosis (>70%). Furthermore, in pts with HF and ischemic cardiomyopathy SR can be used to detect myocardial viability. A dobutamine induced increase in peak systolic SR by more than 0.23 s^{-1} allows accurate

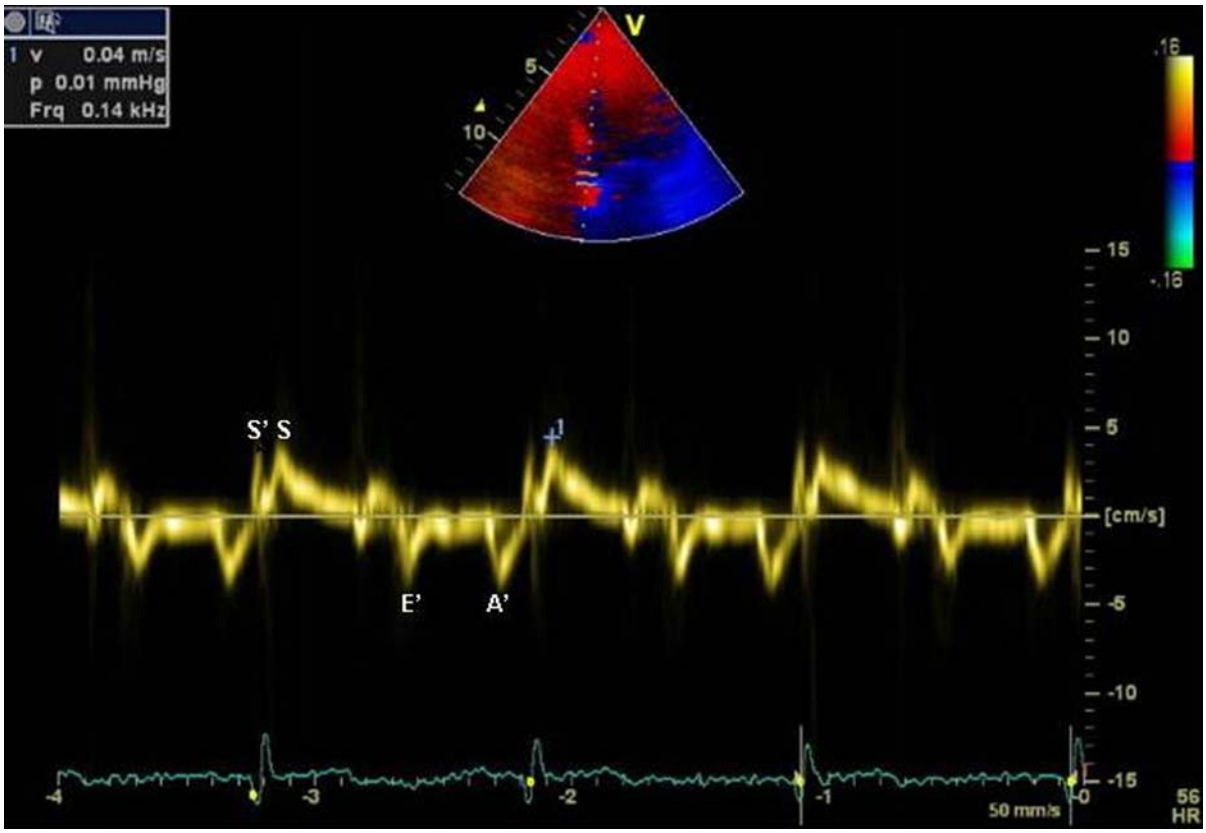

Figure 2. Mitral annular systolic velocity (MASV), evaluated by Pulsed-Wave Tissue Doppler Imaging (PW-TDI). MASV measures 4 cm/sec, expression of a severe left ventricular (LV) longitudinal dysfunction. It is also shown a reduction of E' wave velocity due to a diastolic dysfunction. S': peak velocity during isovolumic LV contraction; S: peak velocity during systolic LV contraction; E': peak velocity during early-diastolic LV relaxation; A': peak velocity during end-diastolic phase.

discrimination of viable from nonviable myocardium, with sensitivity of 83% and specificity of 84% (30).

Nevertheless, TDI is only able to estimate S and SR along the ultrasound beam, and these parameters cannot be reliably measured in the azimuth or perpendicular plane. In order to overcome these limitations, Speckle Tracking Echocardiography (STE) has been proposed. This is a new technique based on comparison of the image texture (i.e., pattern of individual speckle elements) from frame to frame. These speckles, ultrasound reflectors within tissue, behave like magnetic resonance tags. Several studies have investigated the possibility of assessing regional LV function using 2D strain measurements, not only for longitudinal function but also for radial and circumferential strains (31-33) "Figures 3-4". An excellent correlation between cardiac MRI tagging and STE, both for radial and circumferential strain has been shown, with good inter- and intra-observer agreement (31). STE provides accurate and angle-independent measurements of LV strain and is, therefore, in the future likely to become a clinical bedside tool for quantifying myocardial function. Other researchers (34,35) have focused on the ability of STE to measure LV rotation: during systole, a twisting of the LV is produced by an anti-clockwise rotation of the apex and a clockwise rotation of the base of the heart. The LV torsion (or twist) plays an important role in determining LV ejection and filling, and is sensitive to changes in both regional and global LV function. An impaired LV torsion has been suggested to have an impact on LV suction. Moreover, as tagged cardiac MRI revealed, the torsion is a relatively load-independent index of contractility and relaxation, useful to non-invasively understand the mechanism of HF. In ischemic cardiomyopathy, it has been observed that apical ischemia does not cause any significant change in basal rotation, suggesting that there is no impairment of LV function between equator and base. Furthermore, in pts with chronic HF, after six months of treatment resulting in clinical improvement, an increase in basal rotation occurs, whereas apical rotation is unchanged, indicating that measurement of basal rotation is clinically relevant (36).

Finally, STE is very useful for identifying stunned myocardium and non-transmural infarction, which are associated with both reduction of S and SR, and post-systolic thickening (PST). Low dose of dobutamine increases S and SR and reduces PST in stunned myocardium, whereas non-transmural infarcts only show a transient increase of SR, without any S change or PST increase (9).

3.2. Role of MRI

MRI is a non invasive and non ionising radiation technique that provides, with high spatial and temporal

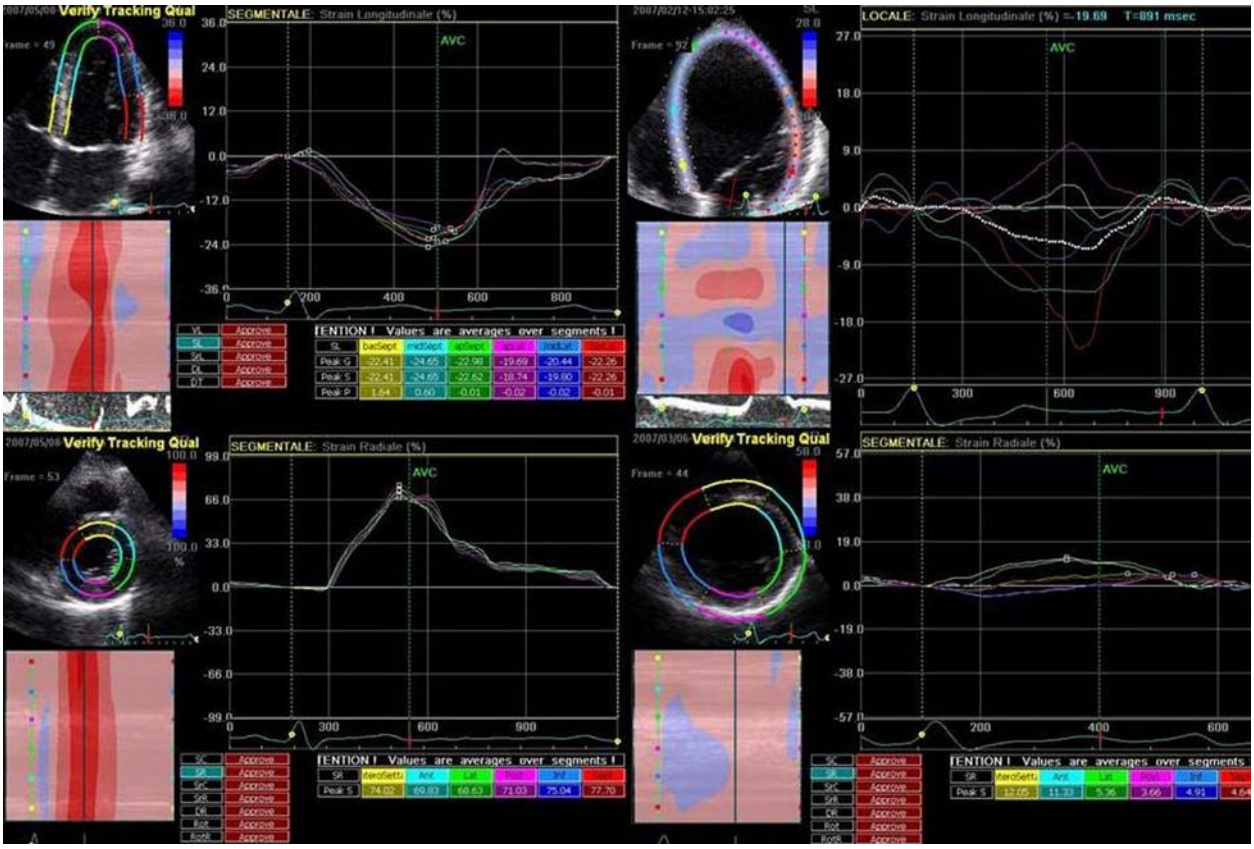

Figure 3. Top: longitudinal 2D strain in a healthy subject (left panel) and in a patient with dilated cardiomyopathy and HF (right panel). Bottom: radial 2D strain in a healthy subject (left panel) and in a patient with dilated cardiomyopathy and HF (right panel). A reduction of both radial and longitudinal strain is present in the patient with cardiomyopathy.

resolution, both morphological and functional parameters of the heart. Due to a topographic approach, the whole heart system can be acquired to obtain anatomical and functional information and tissue characterization data (7).

The method, strongly validated *in vivo* and *ex-vivo*, has shown high accuracy, as well as good inter and intra-observer reproducibility, in quantifying global and regional ventricular function. It is, therefore, considered as the gold standard for assessing mass and volume of both ventricles in normal subjects and in pts with ventricular dysfunction (7,37). Two-dimensional (2D) echocardiography, using a limited 2D rule (i.e: 2D Simpson's algorithm), does not permit an accurate quantification of LV volume and mass in all pts, particularly in those with abnormal LV shape. Conversely, cardiac MRI obtains myocardial mass, volumes and EF with Simpson's algorithm from three-dimensional (3D) data and with no geometric assumptions by using 9 to 12 cine short-axis views, from the atrio-ventricular ring to the LV apex, through a Steady-State-Free-Procession (SSFP) sequence. Similar considerations can be applied to evaluate the function of the RV, whose anatomical geometry does not permit application of echocardiographic algorithms.

It has been recently suggested that 3D echocardiography has a similar accuracy in measuring right and left ventricular volume and mass, when compared with cardiac MRI (38). Despite the emergent role of 3D echocardiography, MRI has significant advantages as easy standardization of acquisition, high quality images and good spatial resolution.

Moreover, cardiac MRI can obtain a very accurate quantitative assessment of LV wall motion, S and SR, through the myocardial tagging technique (39). Relevant clinical applications include quantification of remodelling and viability following myocardial infarction, and assessment of the effects of therapeutic interventions.

Cardiac MRI cine-sequences enable wall motion analysis at rest, detection of viable myocardium with low dose-dobutamine, and detection of ischemia with high-dose dobutamine (40).

Myocardial perfusion can be studied with cardiac MRI to determine whether coronary artery disease contributes to the development of HF. After contrast injection, ischemic myocardium regions appear as areas with little or no signal intensity change in comparison with well-perfused myocardium (7).

A further application of cardiac MRI in HF is the identification of aetiology of cardiomyopathies; in this

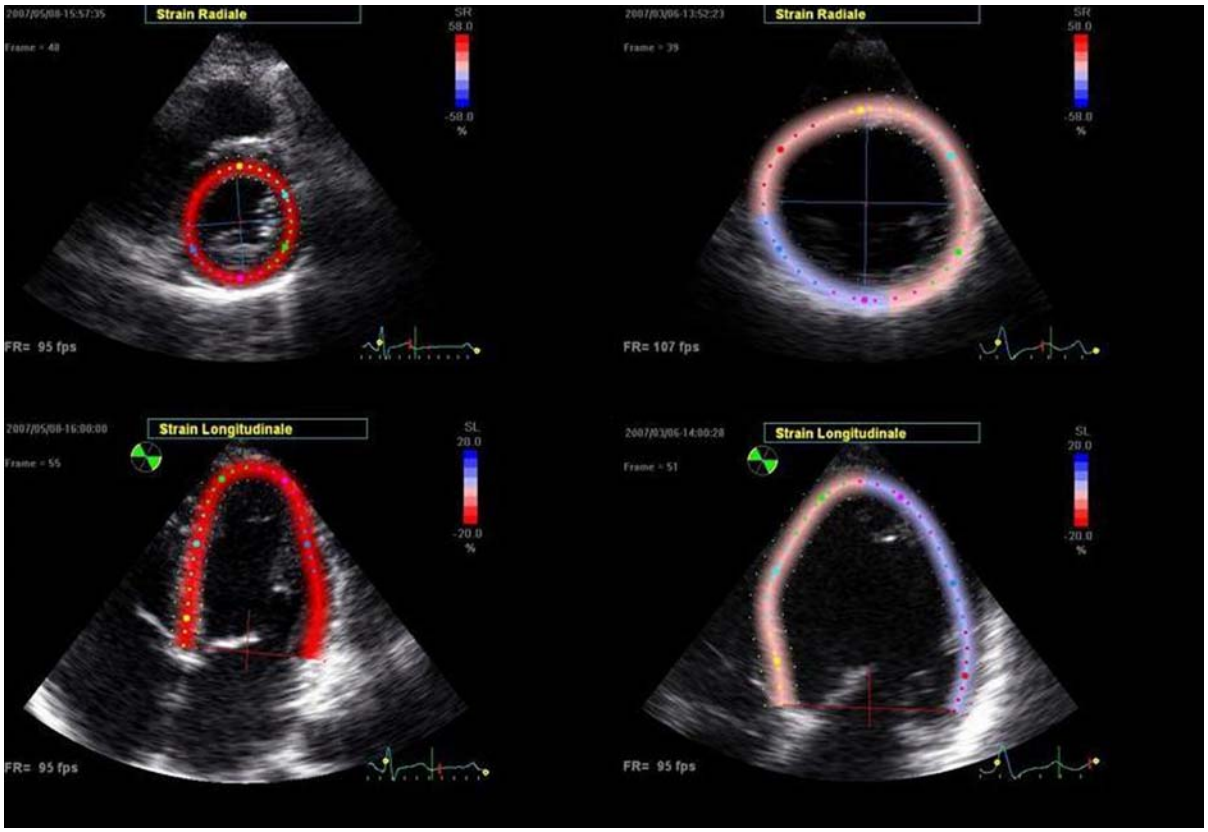

Figure 4. Left panel: radial (top) and longitudinal (bottom) 2D strain in a healthy subject, at the end-systolic phase. Right panel: radial (top) and longitudinal (bottom) 2D strain in a patient with HF, at the end-systolic phase. The amplitude of radial and longitudinal strain is measured by the colour of the walls (red in normal LV; pink and blue in dysfunctioning LV). A dyssynchrony between septum and infero-lateral wall is also present in the HF patient.

setting, the role of cardiac MRI is crucial, especially for the management of pts with LV dysfunction and new-onset HF. The LV wall motion abnormalities detected by echocardiography do not permit distinction between dilated ischemic and non ischemic cardiomyopathy, whereas delayed contrast enhancement (DCE) differentiates non-ischemic from ischemic cardiomyopathy, and in the latter permits identification of myocardial viability (41). DCE can detect myocardial areas of hyper-enhancement due to necrosis and fibrosis both in animal models and in humans (42). This technique is based on delayed images acquisition after administration of a paramagnetic contrast agent, selectively accumulated in areas of myocardial fibrosis or scar tissue. Due to high spatial resolution, DCE can identify and accurately localize even a very small fibrotic area due to subendocardial infarct, permitting distinction of dilated ischemic from non ischemic cardiomyopathy (41-43) "Figure 5". In ischemic cardiomyopathy, DCE shows that the ischemic wave of cellular death is directed from the endocardium to the epicardium ("ischemic" pattern of DCE). The presence of dysfunctioning myocardial regions without DCE or with DCE less than 50% suggests a good chance of functional recovery after coronary revascularization (44).

On the contrary, in non ischemic cardiomyopathy, DCE is absent or shows a "non ischemic" pattern, characterized by patchy or linear midwall striae prevalently located in the interventricular septum. Bello et al (45) have recently published results suggesting that the extent of DCE can also predict the response to beta-blocker therapy.

Another important role of cardiac MRI is the study of myocarditis. The metanalysis of Liu et al. (46) on the diagnostic role of cardiac MRI in myocarditis has showed 86% of sensitivity and 95% of specificity. Moreover, DCE is an important tool for evaluating the efficacy of therapy and for selecting pts needing myocardial biopsy (47,48). DCE can also identify myocardial damage in pts with myocarditis and normal systolic function: in such condition, the integration between echocardiographic new technologies, such as SI and SRI, and cardiac MRI, is useful to identify LV wall oedema "Figure 6" (49).

4. EVALUATION OF LV DIASTOLIC DYSFUNCTION

About 50% of pts with new onset of HF has normal EF (50,51). This condition, defined as HF with normal EF (HFNEF), includes many situations other than a myocardial disease, such as constrictive pericarditis, severe valvular heart disease, congenital heart disease and

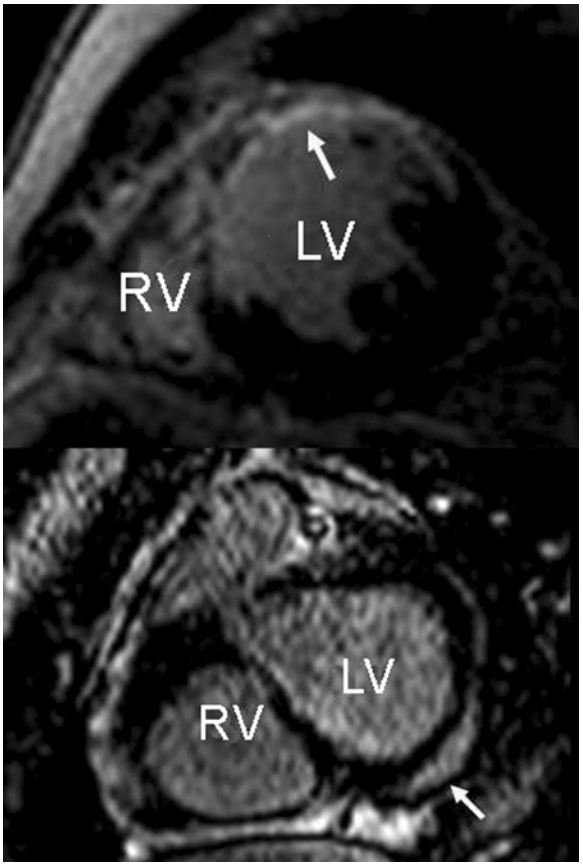

Figure 5. Top: midventricular short-axis view by delayed contrast enhancement (DCE)-Cardiac Magnetic Resonance (CMR), showing the ischemic pattern of DCE (scar tissue located from subendocardial to epicardial layer) in the anterior and anteroseptal wall (white arrow). Bottom: non-ischemic pattern of DCE (epicardial localization) in the basal inferolateral segment of the left ventricle.

intracardiac tumour. The most common aetiology for HFNEF and no other structural abnormalities, however, is diastolic dysfunction, so that diastolic HF appears the better term to describe this entity.

4.1. Role of echocardiography

Doppler techniques play a crucial role in evaluating diastolic function by means of the following parameters: early (E) and late (A) diastolic velocity of the mitral inflow, E/A ratio, mitral inflow velocity at peak Valsalva manoeuvre, Deceleration Time (DT) of mitral E velocity, pulmonary vein velocity, (Systolic, Diastolic, atrial reversal wave), mitral inflow propagation velocity obtained by colour M-mode, early diastolic mitral annulus velocity (Ea), and E/Ea ratio (52-53). Impaired myocardial relaxation, which is usually the earliest diastolic abnormality (Grade I), decreases E velocity, increases A velocity, and lengthens DT. As filling pressure increases with worsening of diastolic function, mitral E velocity increases with shortening DT, and A velocity decreases with shorter flow duration (Grade II-IV) (54) "Figure 7". DT less than 150 msec is a strong predictor of cardiac events in pts with ischemic or non ischemic cardiomyopathy (55). TDI allows measurement of myocardial tissue velocity at the mitral annulus (Ea), which is well related with myocardial stiffness (tau) and with LV myocardial relaxation (56-57). In all phases of diastolic dysfunction, early diastolic velocity of the mitral annulus (Ea) is reduced and does not show any increase at high filling pressure. The ratio of mitral E velocity and mitral annulus Ea velocity (E/Ea) has a good correlation with both pulmonary capillary wedge pressure (PCWP) and LV filling pressure. E/Ea more than 15 suggests a PCWP greater than 20 mmHg (56). Numerous studies have demonstrated that E/Ea more than 15 is one of the strongest predictors for reduction of survival after AMI, independent of LVEF (58-61)**.**

Left atrium volume appears to reflect the duration of LA pressure increase due to LV diastolic dysfunction; in several clinical settings, it has a diagnostic and prognostic potential higher than that of conventional Doppler parameters. It has been suggested that the combination of parameters reflecting acute LV diastolic dysfunction (Doppler indexes), and chronic LV diastolic dysfunction (LA volume) is the best prognostic tool (62). Tsang et al. (63) have shown in 1.160 elderly pts (older than 65 years) in sinus rhythm and without valvular or congenital heart disease, that a LA maximal volume greater than 32 ml/mq, obtained by biplane area-length method, is a powerful and independent predictor of a first cardiovascular event including myocardial infarction, HF, atrial fibrillation (AF), stroke, transient ischemic attack (TIA), and cardiovascular death.

Unfortunately, approximately 20% of pts with chronic HF has AF, and the relationship between Doppler variables and LV filling pressure becomes less reliable (64). A relatively accurate estimation of PCWP, however, can be achieved in HF pts with AF. Temporelli et al. (65-66) have found that a value of 120 msec in mitral DT time is the best cut-off in predicting elevated PCWP in pts with HF and AF, sensitivity and specificity of a mitral DT below 120 msec in predicting PCWP above 20 mmHg being 100% and 96%, respectively. Naguegh et al. (67) have found that E wave peak acceleration, isovolumic relaxation time, DT, and the ratio of E velocity to propagation velocity (E/Vp) are strongly related with LV filling pressure. E/Ea appears to be a useful parameter for assessing the risk of complications even in pts with AF (68).

4.2. Role of MRI

MRI provides both functional and anatomical data to assess diastolic dysfunction. The cine-sequences are able to quantify diastolic function from the derivative of the time/volume curve, expressed as peak filling rate (PFR); similarly, like echocardiography, early and active peak filling rates (EPFR and APFR) can be obtained, and their ratio calculated (7). The phase-contrast technique permits quantifying the flow velocity (cm/sec) and thereby deriving the flow (ml/sec) by the average velocity (cm/sec) × area (cm2), in many sections of the

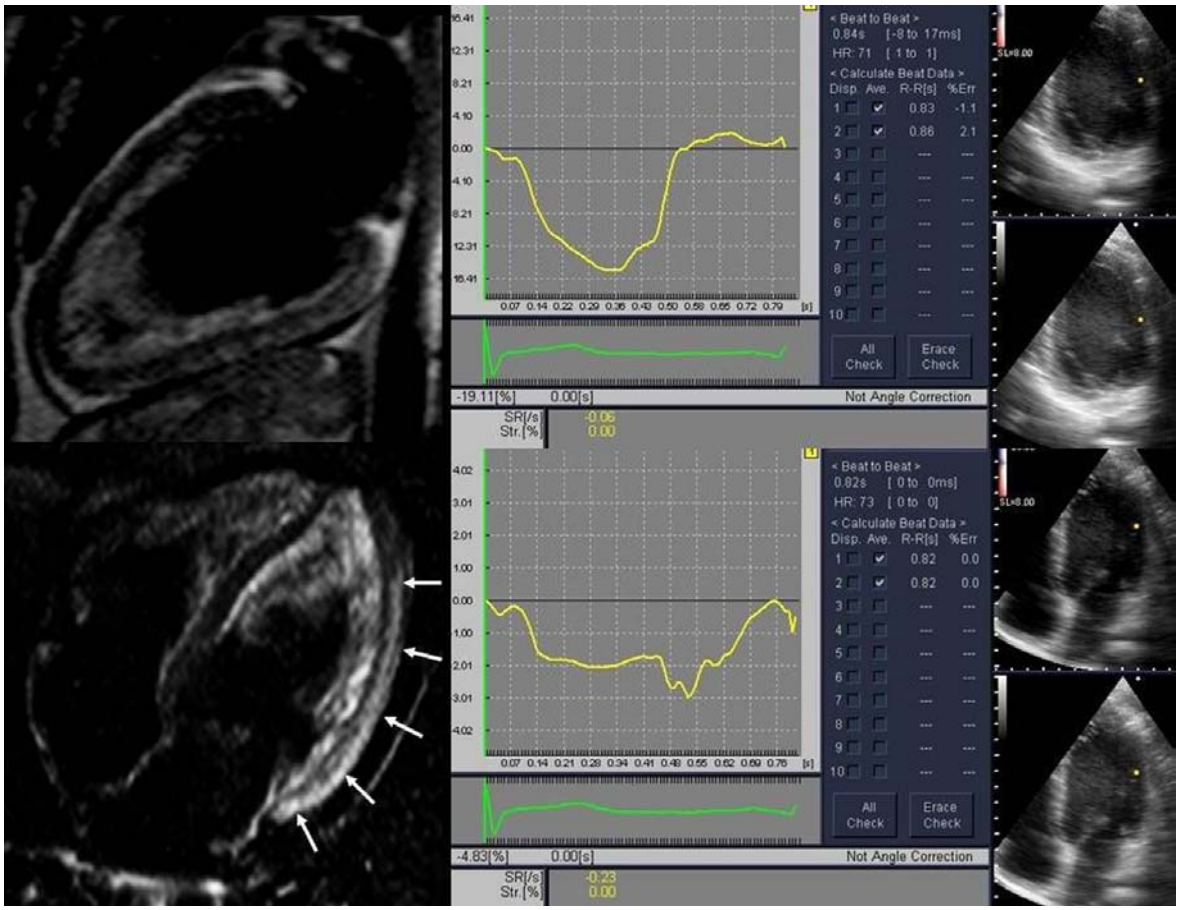

Figure 6. Cardiac magnetic resonance images and echocardiography strain curves in myocarditis and normal systolic LV function. Strain Doppler echocardiography identifies longitudinal segmental myocardial dysfunction derived from edema in the acute phase of myocarditis. (reproduced with permission from Di Bella G et al (49): Strain Doppler echocardiography can identify longitudinal myocardial dysfunction derived from edema in acute myocarditis. Intern J of Cardiol 2007, e-pub ahead of print).

cardiovascular system (vessels and atrio-ventricular valves). As with echocardiography, these measurements can be applied to mitral and pulmonary vein flow to detect the presence of diastolic dysfunction (7). In this respect, an adjunctive role of MRI is the assessment of the substrate underlying LV filling impairment: MRI can easily differentiate restrictive cardiomyopathy from chronic constrictive pericarditis, as well as cardiac amyloidosis from hypertrophic cardiomyopathy, and identifies other infiltrative myocardial diseases associated with LV stiffening (7, 42). Cardiac MRI can identify the increased thickness of pericardium (more than 4mm) that represents the typical pathological substrate of constrictive pericarditis "Figure 8". Furthermore, in pts with constrictive pericarditis and normal or minimally thickened pericardium, and in pts with inflammatory pericarditis, real-time cine-MRI can easily depict increased ventricular coupling. This may be helpful to distinguish constrictive pericarditis from restrictive cardiomyopathy (69).

As with 2D echo, a differential diagnosis between hypertrophic cardiomyopathy and cardiac amyloidosis is, at times, difficult. Using DCE-MRI, cardiac amyloidosis shows a characteristic decreased contrast between blood and myocardium and a pattern of enhancement usually located in the subendocardial layer (70).

5. IDENTIFICATION OF RESPONDERS TO CARDIAC RESYNCHRONIZATION THERAPY

In the failing heart, impairment of LV performance may also be due to a conduction disturbance: P-R interval prolongation and left bundle branch block (LBBB) result in an uncoordinated contraction sequence and delayed LV ejection at the expense of diastolic filling.

5.1. Role of Echocardiography

LV reverse remodelling is an end point of cardiac resynchronization therapy (CRT) and may herald improved survival (71-75). Approximately one third of pts submitted to CRT, however, does not benefit from this therapy from a clinical point of view, or fail to show reverse remodelling. This might be explained by the fact that direct assessment of asynchrony rather than QRS

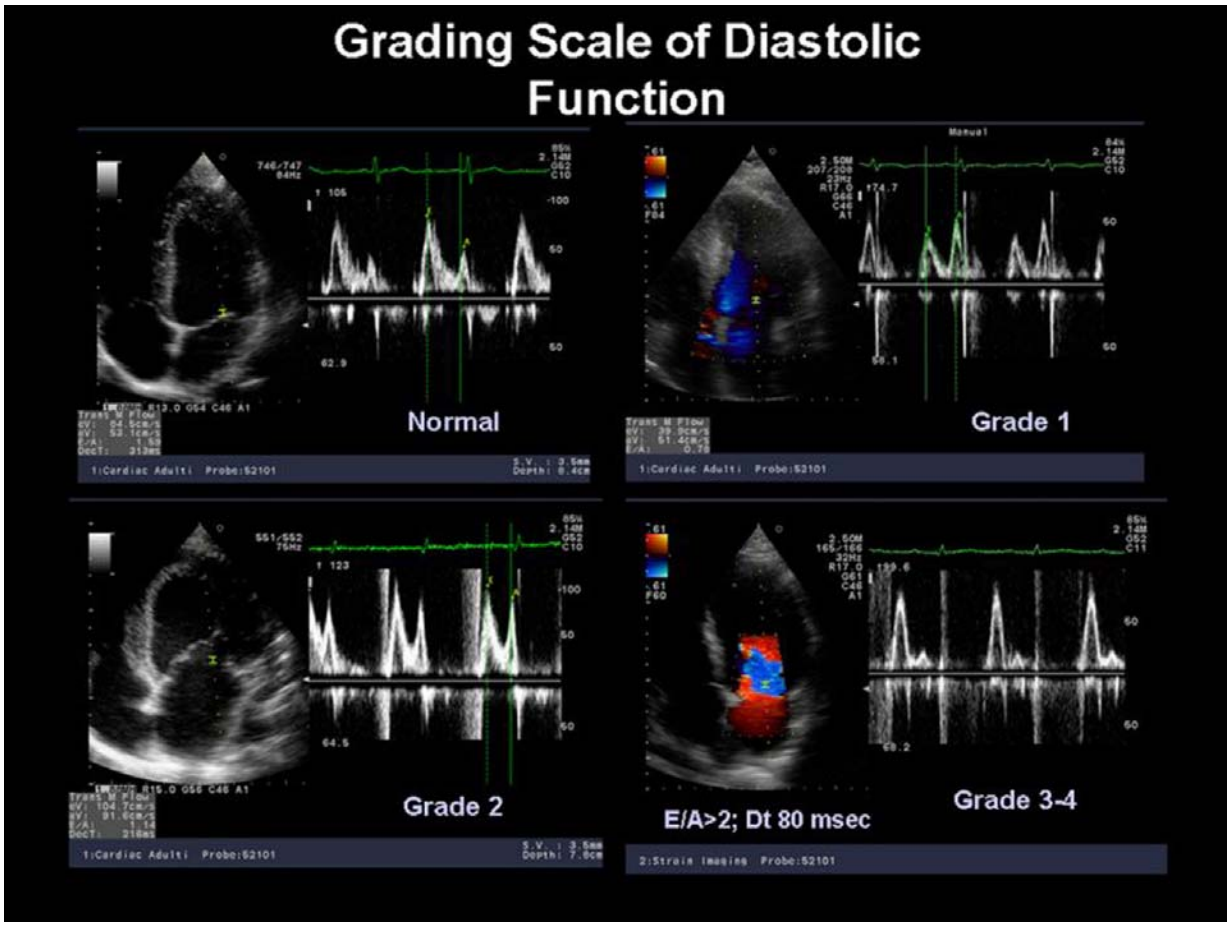

Figure 7. Grading of diastolic dysfunction from normal to severe dysfunction (grade 3-4), evaluated by Pulse Wave (PW) Doppler of mitral inflow. Normal: DT 140-240 msec; E/A 0.75-1.5. Grade 1: DT> 240 msec, E/A <0.75. Grade 2: DT 140-240 msec, E/A 0.75-1.5. Grade 3-4: DT < 140 msec, E/A > 1.5; in grade 3, the E/A ratio is reversible, when compared to grade 4, with the pre-load changes.

duration measurement should be the key for selecting appropriate candidates to CRT and predicting a favourable response (74,76).

Echocardiography plays a key role in CRT. Through this technique, three different levels of dyssynchrony (atrio-ventricular, inter-ventricular, intra-ventricular) can be distinguished, the first two being easily identified by conventional Doppler echocardiography. Intra-ventricular dyssynchrony, probably the most important level of dyssynchrony, can be assessed by TDI, although M-mode echocardiography has been proposed as an alternative diagnostic tool. It has recently been shown that LV dyssynchrony assessment is feasible in 59% of patients with M-mode echocardiography compared with 96% when TDI was used (77).

A number of indices of mechanical dyssynchrony have been proposed, and the list is continuously growing. The most widely used ones are: a difference greater than 65 msec between time to peak myocardial systolic velocity (T_s) recorded at the basal septum and the velocity recorded at the basal lateral wall, proposed by Bax et al. (78); T_s - standard deviation (SD) of six basal, six mid LV segments greater than 32.6 msec, proposed by Yu et al (79); sum of intra-ventricular (Ts-onset), and inter-ventricular delay greater than 102 msec, proposed by Penicka et al. (80).

The quantitative parameters derived from TDI measure the difference or variation in time to peak regional contraction between 2 or more LV segments, the presence of post-systolic shortening (PSS) and possibly strain rate imaging (75).

In addition, the pattern of systolic asynchrony may be different in ischemic, with respect to non-ischemic HF pts. This may affect the predictive value of the echocardiographic tool chosen. It has been demonstrated that the time to peak myocardial contraction (Ts-SD more than 32.6 msec) is the most powerful predictor of LV reverse remodelling and is consistently useful for ischemic and non ischemic HF (75).

Another potential reason for non-response to CRT may be the presence of scar tissue in the region of the

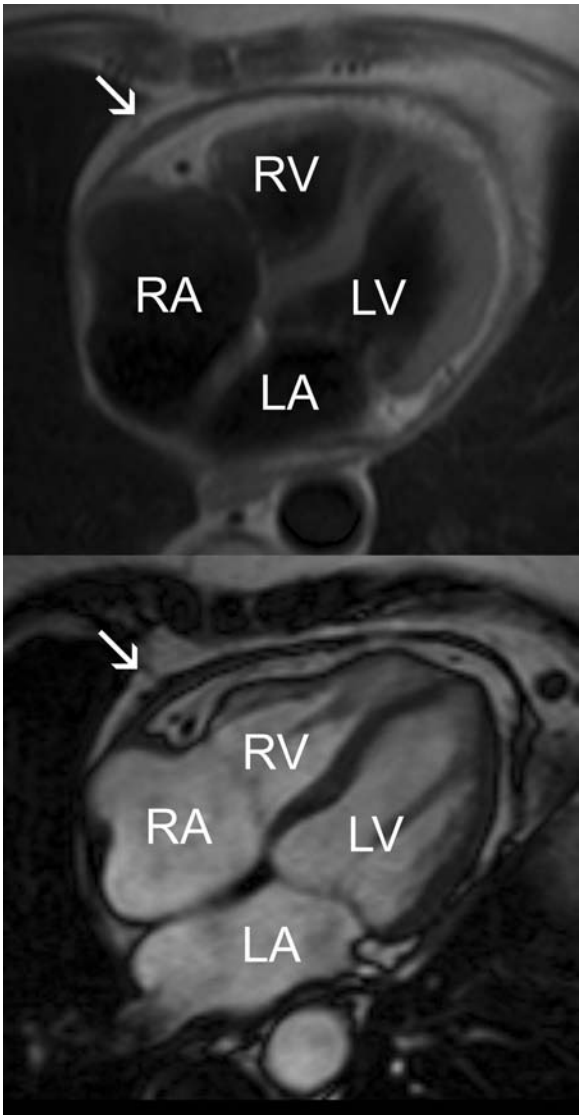

Figure 8. Constrictive pericarditis and CMR. A T1-weighted (top) and a Steady-State-Free-Procession (bottom) axial CMR images show diffuse pericardial thickening (white arrows).

tip of the LV pacing lead (usually the postero-lateral LV region). CRT does not reduce LV dyssynchrony in pts with transmural scar; on the other hand, pts without transmural scar but with severe baseline LV dyssynchrony have an excellent response (95%) to CRT (81). Recently, Chan et al. (82) have shown that, although cardiac MRI can be considered the gold standard for identification of transmural extension of infarction, 2D strain permits recognition of transmurality in chronic infarctions and overcomes the limitations of conventional TDI and SRI. Furthermore, in pts with ischemic heart disease, the degree of improvement in systolic and diastolic performance after CRT is influenced by the extent of myocardial viability (83). Penicka et al. (80) have reported that pts with poor viability did not show any significant remodelling regardless of baseline dyssynchrony.

With respect to the long-term outcome, after biventricular pacing, 2D radial strain derived values are able to predict clinical response to CRT. It has been shown that radial dyssynchrony evaluated by 2D strain is higher in pts that show an acute response, defined as an increase in stroke volume greater than 15%. A pre-determined dyssynchrony value more than 130 ms predicts an acute response with 91% sensitivity and 75% specificity. At long term follow-up, this parameter shows a sensitivity of 89% and specificity of 83% (84).

Based on these data, the new echocardiographic methods such as TDI and real time 3D echocardiography are probably sensitive and precise enough for a quantitative evaluation of dyssynchrony; it should be pointed out, however, that important information about both the presence and severity of dyssynchrony can also be obtained by conventional echocardiographic techniques. For example, a Doppler derived cut-off dP/dt of under 700 mmHg/sec can discriminate pts with an asynchrony index (calculated by SRI) of 55 msec with high sensitivity and specificity. Non-invasive dP/dt assessment can be therefore used, in addition to advanced imaging techniques, to identify pts suitable for CRT (85).

5.2. Role of MRI

In addition to echocardiographic data, mainly detected by TDI, recent studies have suggested an additional role of cardiac MRI for assessment of cardiac dyssynchrony, despite only a few data being available so far (86).

In pts with dilated cardiomyopathy, intra-ventricular dyssynchrony has been detected by tagged cardiac MRI, assessing the circumferential strain in about 80 sites throughout the LV. Strain variance at the time of maximal shortening is used as a marker of systolic dyssynchrony; this is correlated with acute post-CRT improvement of hemodynamics, as reflected by the percentage change in $+dP/dt_{max}$ (87). Leclercq et al. (88) have used tagged cardiac MRI to demonstrate that acute improvement in LV dyssynchrony after biventricular pacing is dissociated from electrical dyssynchrony, which remains abnormal after LV pacing. The same Authors suggested that cardiac dyssynchrony should be analysed by means of circumferential rather than longitudinal strain maps.

The main limitations of cardiac MRI techniques are time-consuming data acquisition and analysis, and the fact that repeated analysis after CRT is not possible, due to the presence of a pacemaker.

As previously described, cardiac MRI is well-suited for the assessment of viability and scar tissue. This approach is likely to further optimize selection of pts for CRT by excluding pts with a large scar in the region targeted for LV lead placement.

In a recent clinical study, Bleeker et al. (81) have reported that among pts with end-stage HF (NYHA class III/IV), LV ejection fraction less than 35%, left bundle

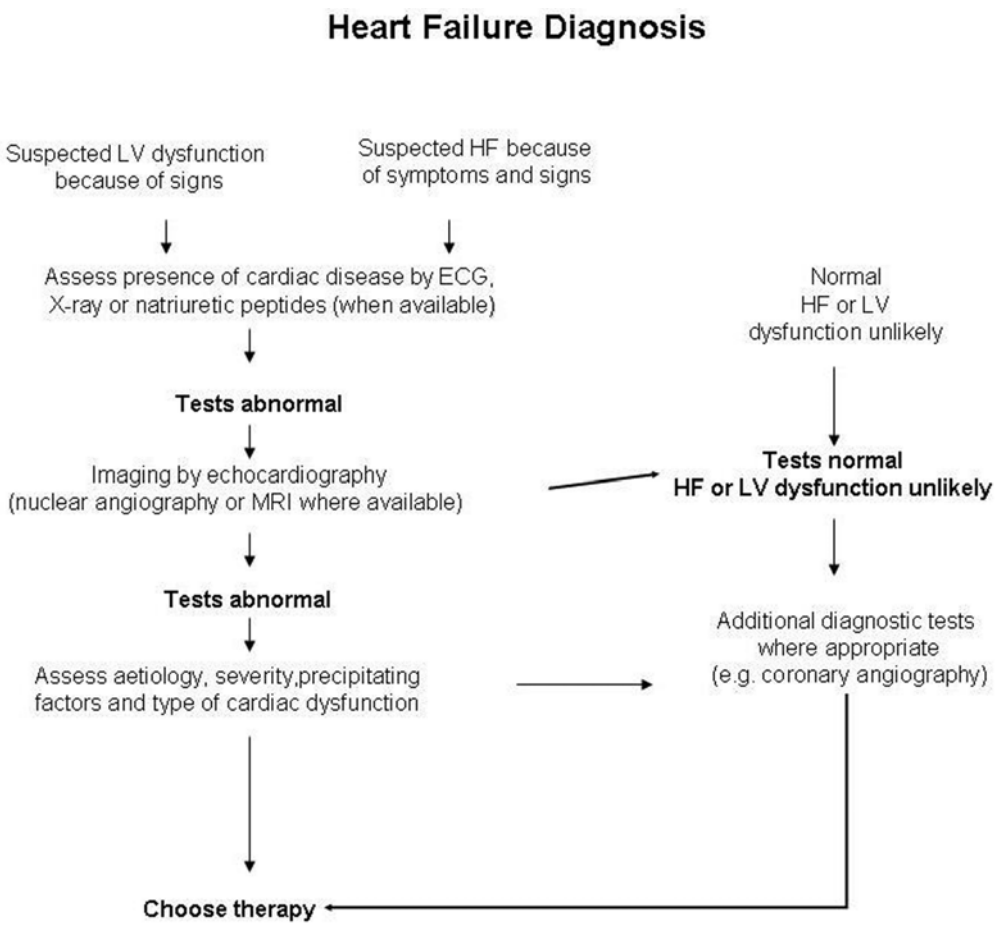

Figure 9. Diagnosis of heart failure by European Society Cardiology Guidelines (5) for the diagnosis and treatment of chronic heart failure.

branch block with QRS duration greater than 120 ms and severe baseline LV dyssynchrony on TDI, a reduction of LV dyssynchrony at 6 months follow-up only occurred in pts without postero-lateral scar tissue.

Moreover, it has also been demonstrated that responders to CRT at 3 months follow-up have less global extent of scar tissue. In particular, a cut-off value of 15% of total scar provides a sensitivity and specificity of 85% and 90%; on the other hand, a scar tissue less than 40% but strictly limited to the septal wall provides a sensitivity and specificity of 100% for response to CRT (89).

6. PERSPECTIVES

ESC guidelines as well as ACC/AHA guidelines (5-6) state that echocardiography is the most useful test for recognizing HF in pts with resting or/and exertion symptoms suggesting this condition, since structural abnormalities, as well as systolic or diastolic dysfunction, need to be documented to establish a definite diagnosis "Figure 9". Echocardiography is extremely useful in HF pts to monitor LV function during follow-up and to guide the optimal choice of treatment (medical or surgical). Recent technologies (i.e. TDI, SRI, STE) have led to the development of new concepts in the pathophysiology of HF. Cardiac MRI is a very interesting technique to assess LV function in pts with suspected LV systolic and/or diastolic dysfunction or with clinically manifest HF. Cardiac MRI allows an accurate analysis of LV functional parameters and provides accurate morphological and structural information on myocardial walls and pericardium. This kind of evaluation, integrated with the echocardiographic data, permits a precise diagnosis in a very high percentage of cases.

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Abbreviations: HF: heart failure, ESC: European Society of Cardiology, ACC: American College of Cardiology, AHA: American Heart Association, MRI: magnetic resonance, 2D: two-dimensional, 3D: three-dimensional, TTE: transthoracic echocardiography, LV: left ventricle; EF: ejection fraction, DT: deceleration time, AMI: acute myocardial infarction, MPI: myocardial performance index, TAPSE: tricuspid annular plane systolic excursion, RV: right ventricle, TDI: Tissue Doppler Imaging, MASV: mitral annular systolic velocity, TASV: tricuspid annular systolic velocity, MVR: mitral valve regurgitation, S: strain, SR: strain rate, STE: Speckle Tracking Echocardiography SI: strain imaging, PST: post-systolic thickening, SSFP: steady-state-free-procession, DCE: delayed contrast enhancement, PCWP: pulmonary capillary wedge pressure, TIA: transient ischemic attack, AF: atrial fibrillation, PFR: peak filling rate, EPFR: early peak filling rate, APFR: active peak filling rate, CRT: cardiac resynchronization therapy, SI: strain imaging, SRI: strain rate imaging, SD: standard deviation

Key Words Heart Failure, Left Ventricular Function, Echocardiography, Cardiac Magnetic Resonance, Review

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