

REVIEW



CARDIOLOGY // IMAGING

# New Imaging-based Tools for the Assessment of Ventricular Function in Ischemic Heart Diseases

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#### ABSTRACT

Ischemic heart disease morbidity and mortality are closely related to global and regional left ventricular function. The evaluation of left ventricular global function is a relevant part in the evolution of ischemic heart disease because it plays a significant role in prognosis prediction and patient management after revascularization. Regional function is also a critical part of the evolution, offering a possible and reliable mode for the assessment of myocardial disease. Currently several techniques for the evaluation of left ventricular parameters and function are in use. In this review we will discuss and compare currently available methods for the evaluation of global and regional left ventricular function such as 2D and 3D echocardiography, 3D speckle-tracking echocardiography, multi-slice computed tomography, and cardiac magnetic resonance imaging.

**Keywords:** ischemic heart disease, echocardiography, 3D speckle-tracking echocardiography, multi-slice computed tomography, cardiac magnetic resonance imaging

Ischemic heart disease is the leading cause of death around the world. The morbidity and mortality rates are closely associated to regional and global left ventricular function in these patients.<sup>1,2</sup>

The evaluation of global left ventricular (LV) function with noninvasive imaging tools has an important role in the therapeutic management and prognosis of patients with ischemic cardiac diseases. Several parameters have been proposed as illustrative for global left ventricular function such as volumes, ejection fraction, dimensions, end-diastolic pressure, contractility, and deformation parameters. Global systolic function is most often evaluated by measuring the difference in the end-diastolic and end-systolic volumes, determined in one, two and three dimensions, divided by the adequate end-diastolic volume.<sup>3</sup> Echocardiography is the most frequently used noninvasive technique for the analysis of LV parameters and function because of its accessibility, portability, and widely validated scale.

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LV regional function has the benefit of offering a feasible and valid mode for the evaluation of myocardial disease. Regional function parameters can give a prognostic value regarding common LV efficiency parameters.<sup>4,5</sup> Imagingbased tools like 2D and 3D echocardiography, 3D speckletracking echocardiography, multi-detector computed tomography and cardiac magnetic resonance are constantly evolving. The aim of this review is to provide an overview regarding the usefulness of these imaging tools for the assessment of ventricular function in ischemic heart disease.

# ECHOCARDIOGRAPHY FOR THE EVALUATION OF LV FUNCTION

### 2D and 3D echocardiography

Transthoracic echocardiography (TTE) is the most commonly used noninvasive cardiac imaging method for assessing the global and regional function of the left ventricle.4 Global LV function can be evaluated on the basis of LV dimensions, volumes, or ejection fraction (EF). Several studies evaluated the reliability of 3D TTE measurements of LV volumes and EF, using cardiovascular magnetic resonance (CMR) as a reference. Most studies showed that 3D TTE slightly underestimates both end-diastolic and endsystolic volumes.<sup>6,7</sup> Evaluating the regional function using 3D TTE has important benefits because, unlike 2D TTE, it can illustrate all ventricular walls in a single echocardiographic loop. For these reasons, 3D TTE is well adaptable to discover the location and extension of segmental wall motion abnormalities. The determination of regional LV volumes by 3D TTE shows a good correlation with CMR data.<sup>8,9</sup> Thorstensen et al. have shown in their study that wall motion score index by 3D TTE presents a significant correlation with the extent of delayed gadolinium enhancement by CMR.10

# 3D speckle-tracking echocardiography

3D speckle-tracking echocardiography represents an innovative technique used for the quantitative estimation of LV volumes and function, and regional wall motility disturbances with superior accuracy and reproducibility. 3D speckle-tracking echocardiography (3D-STE) provides information on the motility of the myocardium by tracking speckle echoes that are uniformly spread in the myocardial muscle and are moving with myocardial movement. Helle-Valle *et al.* showed that regional left ventricular rotation and torsion can be precisely evaluated by 3D-STE; hence, it is a new method for quantifying LV contractility.<sup>11</sup> Thebault *et al.* established, in another study, that 3D-STE offers a rapid strategy for measuring global LV mechanical asynchronism in subjects undergoing cardiac resynchronization.<sup>12</sup> While this method has numerous benefits, it also has some restrictions such as its dependence on image quality or a relatively low temporal resolution.<sup>13</sup>

# CARDIAC COMPUTED TOMOGRAPHY IN THE ASSESSMENT OF LV FUNCTION

Cardiac computed tomography is an accepted tool for the evaluation of ischemic heart disease and global cardiac function. The analysis of LV function after an acute coronary syndrome has treatment and prognostic implications.<sup>14,15</sup> This technique is especially useful in subjects with severe claustrophobia or implanted devices such as cerebral vascular clips, because these devices can cause large image artifacts on CMR.<sup>16</sup> Currently accessible multidetector computed tomography (MDCT) and dual-source computed tomography (DSCT) scanners offer a high spatial and temporal resolution with faster gantry rotation, enabling the 3D reconstruction of the heart.<sup>17</sup>

Several studies were performed comparing global function parameters determined by MDCT with other investigation techniques results. Sarwar et al. compared the LV global analysis of contrast-enhanced 64-slice MDCT with CMR in ST-elevation myocardial infarction following primary PCI treatment. MDCT had demonstrated a good correlation with CMR for the estimation of EF and LV volumes including end-systolic volume (ESV) and end-diastolic volume (EDV). The mean deviation between MDCT and CMR values were 3 ml for ESV, -0,2 ml for EDV and 1% for EF.18 The use of DSCT for the determination of ventricular volumes and EF in comparison to CMR showed similarly good results: EDV was underestimated by 3.7 ml, while ESV and EF were overestimated by 2.6 ml and 3.8%, respectively.<sup>19</sup> In another publication by Greupner et al., MDCT was compared with CMR, 2D echocardiography, and 3D echocardiography for the analysis of LV global function after coronary angiography. The study showed comparable limits of agreement for both MDCT and 2D echocardiography in the evaluation of EF vs. CMR. MDCT also showed better agreement for stroke volume than 2D or 3D echocardiography and CMR, while EDV and ESV were significantly underestimated by 2D and 3D echocardiography, but not by MDCT.20

The utility of MDCT in the assessment of regional function has not been proven yet. The limitations of MDCT in the evaluation of LV regional function are the low temporal resolution and the absence of markers for identifying myocardial strain. A study using a floating axis system, which means a different LV geometric center in end-systolic and end-diastolic images, showed that regional EF assessed by MDCT is comparable to single-photon emission computed tomography (SPECT) for predicting ischemia; moreover, it is a better predictor of significant lesions compared to SPECT.<sup>21</sup>

# CARDIAC MAGNETIC RESONANCE IMAGING IN LV FUNCTION ASSESSMENT

Cardiac magnetic resonance imaging is the gold standard method for evaluating the global function of the left ventricle.<sup>22</sup> The most frequently used quantification technique for LV volumetric analysis is ECG-gated, segmental balanced steady-state free precession cinegraphic imaging, which gives excellent blood-tissue differentiation without any contrast.<sup>23,24</sup> LV volumes are evaluated by applying the Simpson rule, using a series of shortacting images obtained with a slice thickness of 6-8 mm. Although the absolute and indexed LV volumes, as well as the absolute and indexed myocardial mass are important quantitative indices, left ventricle EF is the most frequently reported measurement when assessing systolic function. The accuracy and reproducibility of the quantification of LV systolic function by CMR was analyzed in multiple studies.

Bellenger et al. demonstrated a wide range of agreement between EF assessment with Simpson's technique using echocardiography and CMR in patients with ischemic heart disease (IHD) and systolic heart failure.<sup>25</sup> Gardner et al. evaluated 47 patients with recent infarction analyzing the EF and LV volumes with the use of echocardiography and CMR. Modest correlations were found for LV volumes, but significant differences were discovered in absolute volumes and EF between the two methods.<sup>26</sup> Gruszcynska et al. found similar results when evaluating 67 patients with IHD by CMR and transthoracic echocardiography. Significant differences were noted between the techniques, with LV volume underestimation by echocardiography.<sup>27</sup> Recent data evidenced better correlations between 3D echocardiography and CMR for the quantification of EF, with similar values between the two methods  $(50\% \pm 14\% \text{ vs. } 50\% \pm 16\%).^{28}$ 

Regarding the data collected on the clinical utility of global function evaluation with EF as a marker, it is relatively insensitive to the early manifestations of ischemic heart disease. A good example is non-transmural myocardial infarction or small transmural infarctions, which do not reduce LVEF significantly. Quantifying regional function using quantitative imaging parameters such as myocardial velocities and strain has shown promising results in the occurrence of LV dysfunction with normal EF.<sup>29</sup>

To understand regional function better, it is necessary to understand the myocardial structure and muscle fiber orientation. The LV has three different fiber orientations with circumferential, oblique and longitudinal layers, arranged in two helical geometries.<sup>30</sup> These orientations are essential for the development of the shearing and torsion mechanics of the LV.<sup>31</sup> The right-handed helix in the subendocardium contributes to the longitudinal mechanism, while the lefthanded helix in the subendocardium mostly generates the circumferential mechanism.<sup>30</sup> Myocardial strain refers to a change in the length of the myocardium compared to its original length and is an extensively studied marker for the assessment of regional dysfunction.32 The attenuation of subendocardial function is reflected by abnormalities in the longitudinal strain, while the mid-myocardial and epicardial attenuation is reflected by circumferential and radial strain. In early IHD, subendocardial modifications appear first, and abnormalities in longitudinal strain can predict early myocardial dysfunction, before global dysfunction occurs.<sup>32</sup>

Various CMR techniques are available for the assessment of regional LV function such as myocardial thickening, balanced steady-state free precession imaging (bSSFP), tissue phase mapping (TPM), myocardial tagging, displacement encoding with stimulated echoes (DENSE), strain encoding (SENC), and feature-tracking MRI (FT-MRI).<sup>29</sup>

The bSSFP technique is most commonly used for the quantitative or qualitative segmental analysis of the wall motion, which is more sensitive than global function in IHD. The image recording in bSSFP can be segmented or ECG-triggered real-time cine. Both of these two methods can be used in the evaluation of qualitative regional function, however real-time cine images are not adequate for the quantitative assessment of function. Qualitatively the segmental wall motility is categorized as normal, hypokinetic, akinetic, or dyskinetic. The quantitative interpretation can be performed by measuring regional myocardium thickening between the diastole and systole from the epicardial and endocardial contours.<sup>30</sup>

Myocardial tagging is probably the most studied CMR method for regional function analysis. Tagging consists in a preparatory pulse, which generates grids or parallel lines on the myocardium over the cardiac cycle at the start of the R wave. The advantage of tagging over other techniques is represented by the intuitive, visually appealing images. Grid tagging is preferred over line tagging because it allows analysis of the perpendicular components of myocardial deformation. Tags can be qualitatively interpreted

visually, but quantitative tag evaluation is laborious and time-consuming.<sup>33</sup>

TPM uses a bipolar gradient to encode velocity vector fields into the phase.<sup>34</sup> This method proposes a higher spatial resolution of functional information compared to the tagging method. Regional function is assessed by using myocardial velocities. Studies have demonstrated altered myocardial velocities in patients with IHD. Long axis velocities were reduced in patients with IHD and were further reduced in subjects with infarction. The radial velocities were significantly reduced in subjects with myocardial infarctions.<sup>35,36</sup>

DENSE is a phase-based method that encodes tissue velocity into image phase in three directions. Due to T1 recovery, the encoding does not last for an entire cardiac cycle, limiting the interpretation of diastolic tissue displacement. DENSE has an inherently low signal-to-noise ratio.<sup>30,37</sup> This technique has been shown to be useful in the assessment of subjects with acute myocardial infarction and ventricular dyssynchrony.<sup>38</sup>

SENC is a relatively new method in which the tag planes are oriented parallel to the imaging plane.<sup>34</sup> Because of the orientation, the circumferential strain is measured on a long axis plane and the longitudinal strain on a short axis plane.<sup>37</sup> In this technique, tag fading with T1 recovery is limited to late diastolic function evaluation. SENCE strain rate reserves, at full dobutamine stress, reveal the presence of a significant coronary artery stenosis.<sup>39</sup> The strain rate reserve at intermediate dobutamine stress, when evaluating regional wall motion abnormalities, has an increased diagnostic accuracy for significant CAD. Similarly, peak systolic circumferential and longitudinal strains are useful for identifying chronic myocardial infarctions and identifying myocardial scar transmurality.<sup>40</sup>

FT-CMR is a newer optical flow technique analogue to STE, which allows the quantification of myocardial motion such as strain, strain rate, displacement, and tissue velocities.<sup>41</sup> This imaging method is not limited to tracking the blood myocardium junction, it can also be used to track midmyocardium features. Currently, the use of FT-CMR for segmental strain assessment is not supported due to its inherent strain heterogeneity.<sup>30</sup> The clinical utility of FT-CMR has been evaluated in a limited number of studies. Schuster *et al.* demonstrated valuable results on the quantification strategy for reversible myocardium dysfunction with low dose dobutamine stress in subjects with IHD.<sup>42</sup> The results showed that the assessment of regional function using FT-CMR seems to be useful in analyzing viability and ischemia in patients with IHD.

# CONCLUSION

The assessment of global cardiac function is a basic step in evaluating left ventricular performance. Ejection fraction and LV volumes have an important role in guiding the clinical decision and providing a main prognostic value. Advanced techniques such as 3D echocardiography, MDCT, and CMR, allow a more precise analysis of the EF and LV volumes. The assessment of regional function is a feasible approach for the subclinical identification of myocardial disease and gives incremental prognostic value. The previously listed techniques are quickly evolving as noninvasive methods that extend our knowledge about the remarkable sides of myocardial fiber architecture. Cardiac magnetic resonance offers possibilities for acquiring the best parameters for left ventricular regional function such as torsion, twisting, shearing, strain, and strain rate. These parameters are of great aid in the management of ischemic heart disease by offering sensitive subclinical signs of the disease progression.

# **CONFLICT OF INTEREST**

Nothing to declare.

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