Int J Cardiovasc Imaging (2010) 26:199–202
DOI 10.1007/s10554-009-9560-0

EDITORIAL COMMENT

Cardiac resynchronization therapy; evaluation by advanced imaging techniques

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Received: 7 December 2009 / Accepted: 14 December 2009 / Published online: 29 December 2009

Cardiac resynchronisation therapy (CRT) is an effective treatment for patients with advanced heart failure (HF), New York Heart Association class (NYHA) III or IV, a reduced left ventricular ejection fraction (LVEF <35%), and wide QRS complexes (>120 ms) [1, 2]. The beneficial effects include improvement in HF symptoms, exercise capacity, and LV function, as well as less HF hospitalizations and lower mortality rates. Despite these impressive results around 30% of patients show no benefit after CRT, being the so-called 'non-responders' [3–5]. The presence of LV dyssynchrony prior to implantation and its subsequent reduction after implantation are proposed the key mechanism for response to CRT. Initially, QRS duration was used as a marker of LV dyssynchrony. Recently, various studies have demonstrated that patients with extensive baseline LV dyssynchrony have a high likelihood of responding after CRT implantation, whereas patients without baseline LV dyssynchrony fail to benefit [6–8].

A variety of techniques has been proposed to quantify LV dyssynchrony in HF patients, ranging from simple M-mode echocardiography to more sophisticated techniques such as tissue Doppler imaging (TDI), real time three-dimensional echocardiography (RT3DE), and strain imaging techniques including speckle tracking [9]. Recent research using advanced echocardiographic modalities have provided new insight on the proper patient selection, lead implantation, optimization and reasons for non-response [10, 11].

In the current issue of the *International Journal of Cardiovascular Imaging*, Pavlopoulos and Nihoyannopoulos [12] discuss the recent advances of echocardiography in the evaluation of patients eligible for CRT. The authors nicely describe the various parameters that can be used for optimal patient selection and for evaluation of the response to therapy. Advanced echocardiographic modalities do provide new insights on proper patient selection, lead implantation, optimization and reasons for non-response. Several echocardiographic parameters can be used in order to define the acute or long-term CRT responses. These parameters are changes in LVEF ≥15%, reverse LV remodeling (LV end-systolic dimensions/volumes ≥15%); degree of mitral regurgitation, dp/dt, and cardiac output. Interestingly, the authors point out that overall assessment of echocardiographic parameters appears to contribute significantly to the outcome of CRT beyond electrical or mechanical dyssynchrony.

In addition to the described echocardiographic parameters, several non-echocardiographic imaging techniques such as magnetic resonance imaging (MRI), nuclear imaging, and computed tomography

Editorial comment on the article of Pavlopoulos and Nihoyannopoulos (doi: 10.1007/s10554-009-9523-5).

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(CT) have also been advocated to evaluate patients with LV dyssynchrony. The use of MRI has been proven for patients with a variety of cardiac diseases [13–20] and is rapidly expanding for selecting patients for CRT [21–24]. Cardiac MRI does not only provide information on size, shape and function of the LV (which is of interest in patients with a suboptimal acoustic window), but also on LV dyssynchrony. In particular the identification of scar tissue is of paramount interest in patients eligible for CRT in selecting the optimal positioning of the pacing lead. Westenberg et al. [23] compared LV dyssynchrony assessed by TDI with LV dyssynchrony assessed by velocity-encoded MRI in 20 HF patients and found an excellent agreement between both modalities ($r = 0.97$, $P < 0.01$). With contrast-enhancement MRI accurate visualization of scar tissue was possible. Bleeker et al. [24] applied this technique in 40 patients with ischemic HF and investigated the relationship between response to CRT and the presence of scar tissue in the posterolateral wall, being the preferred region for the LV pacing lead. After 6 months of CRT, 21 of the 26 (81%) patients without transmural scar tissue in the posterolateral region responded to CRT compared with only two of the 14 (14%) patients with transmural scar tissue in the posterolateral area ($P < 0.01$). Moreover, patients with transmural posterolateral scarring exhibited no significant reduction in LV dyssynchrony the day after CRT implantation, suggesting absence of LV resynchronization, thereby explaining the lack of response.

Similar to MRI, nuclear imaging is well suited for the assessment of viability, scar tissue [25–31], and LV dyssynchrony [32–35]. Only a few studies used radionuclide angiography with phase image analysis for the assessment of LV and interventricular dyssynchrony in CRT candidates [35, 36]. However, these studies demonstrate greatest benefit of CRT in patients with LV rather than interventricular dyssynchrony. This finding is in contrast with larger TDI studies, and further studies including comparisons with TDI are therefore required. Recent studies showed that gated SPECT imaging can be used for the assessment of LV dyssynchrony [37, 38]. Henneman et al. [37] analyzed four quantitative indices of phase analysis in 75 HF patients and compared them with conventional TDI. The variables histogram bandwidth and phase standard deviation showed a good correlation with TDI. In addition, cut-off values of 135° for histogram bandwidth and 43° for phase standard deviation were proposed to predict an improvement in NYHA class after CRT. In addition, nuclear imaging is well suited for assessment of viability and scar tissue. Sciagra et al. [38] were the first to demonstrate that patients with severe resting defects at 99mTc-sestamibi SPECT imaging at baseline showed lack of response after CRT.

Computed tomography (CT) techniques can not yet be used to determine LV dyssynchrony itself, but CT does allow noninvasive visualization of the coronary anatomy and the coronary venous system [39–52]. Van de Veire et al. [53] investigated the cardiac venous anatomy in 34 patients with a previous myocardial infarction, 38 patients with significant coronary artery disease and 28 control patients using a 64-slice MSCT. The coronary sinus, anterior interventricular vein, and posterior interventricular vein could be visualized in nearly all these patients. However, in patients with a history of myocardial infarction, the left marginal vein was detected significantly less often (27%). At present, MSCT is not routinely used prior to CRT implantation, mainly because of the radiation dose and lack of information on LV dyssynchrony and site of latest activation [54]. However, these findings suggest that patients with previous infarction may have less suitable venous anatomy for LV lead placement, and surgical (epicardial) LV lead positioning may be considered.

To summarize, several noninvasive imaging modalities have been proposed for the quantification of LV dyssynchrony but there is currently no agreement on which technique best predicts response to CRT. For now, most experience is gained with echocardiographic TDI and it remains the technique of choice, as also mentioned by Pavlopoulos and Nihoyannopoulos [12]. Major consensus is 'the more LV dyssynchrony prior to implantation, the higher the likelihood of significant LV reverse remodeling during follow-up'. At present, substantial evidence is growing for non-echocardiographic imaging methods to assess LV dyssynchrony such as MRI, nuclear imaging and CT. These techniques may provide valuable additional information that is potentially important for the selection of CRT candidates.

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