Int J Cardiovasc Imaging (2011) 27:59–63
DOI 10.1007/s10554-010-9664-6

EDITORIAL COMMENT

Evidence of scar tissue: contra-indication to cardiac resynchronization therapy?

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Received: 21 June 2010 / Accepted: 25 June 2010 / Published online: 8 July 2010

Cardiac resynchronization therapy (CRT) has shown to be an effective treatment for patients with advanced heart failure (HF) (NYHA Class III or IV), reduced left ventricular ejection fraction (LVEF $< 35\%$) and wide QRS complexes (>120 ms) [1, 2]. The beneficial effects include improvement in heart failure symptoms, exercise capacity, and left ventricular function, as well as less heart failure hospitalizations and lower mortality rates. Despite these remarkable results, 30–40% of patients show no benefit after CRT, the so-called 'non-responders' [3–5]. It remains, however, difficult to distinguish responders from non-responders in the early period after CRT. The presence of LV dyssynchrony prior to implantation and its subsequent reduction after implantation have been proposed as the key mechanisms for a positive response to CRT [6].

A variety of imaging modalities has already been applied to identify dyssynchrony and to evaluate the effects of CRT [7–10]. The use of echocardiography [11–17], magnetic resonance imaging (MRI) [18–29], and multi-slice computed tomography (MSCT) [30–43] has recently been proven for patients eligible for CRT. In addition, nuclear imaging techniques have become suited for the evaluation of LV dyssynchrony [44–51]. Until now, scintigraphic studies in CRT mainly concerned radionuclide angiography with phase image analysis [52–56]. In recent years positron emission tomography (PET) has emerged as a suitable modality to study the metabolic mechanisms of left ventricular dyssynchrony and the effects of CRT. Several studies did already report that 11C-acetate PET performed in the chronic phase after CRT showed improvement of oxygen metabolism and cardiac efficiency by CRT [57, 58].

In the current issue in the *International Journal of Cardiovascular Imaging*, Zacá et al. [59] provide an interesting analysis about the selection of candidates to CRT beyond responders and non-responders with the perspective of the potential identification of patients who will not respond to CRT. The authors clearly state that of all evaluated indices of mechanical dyssynchrony only a QRS duration of >120 ms is recommended in current treatment guidelines for the selection of candidates to CRT. No conclusive evidence is currently available about which of the many variables can predict individual response and should be included in selection criteria. The disappointing results of the PROSPECT trial may be due to high variability in tissue Doppler imaging (TDI) measurements and pathophysiological issues potentially affecting response to CRT mainly in ischemic

Editorial comment to the article by Zacá et al. doi:10.1007/s10554-010-9651-y.

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patients [60]. Zacá et al. [59] challenge the view that patients with ischemic cardiomyopathy and extensive scar tissue should be withheld CRT. Several studies by the group of Bax [29, 61, 62] have shown that the presence of postero-lateral scar tissue diagnosed by contrast-enhanced MRI resulted in ineffective CRT in 30–40% of patients with ischemic heart failure. Using biventricular pacing, left ventricular dyssynchrony remained unchanged, and there were no functional improvements at 6 months follow-up. The results of these studies have been confirmed by many other studies that showed a clear negative association between scar burden and the response to CRT [63–68]. Notwithstanding, it is the belief of Zacá et al. [59] that these observations and the ensuing implications not to treat with CRT are too preliminary. The value of CRT in this subset of ischemic heart failure patients would mandate larger multi-center studies. In their vision, even non-responders should receive a CRT device whereby the certain risk of withholding the treatment might be more consistent than the potential risk of being a non-responder. This point of view is in line with the recent study by Riedlbauchová et al. [69], who showed that the response to CRT was independent of the presence of extensive myocardial scarring. It was shown that left ventricular pacing at sites with ischemia, hibernation, or non-transmural scar did not appear to modify the effect of CRT as compared to viable tissue. It follows that incorporation in the standard selection criteria of algorithms to predict the response to CRT is yet not ready for clinical use. To this purpose, appropriate application of sophisticated imaging techniques may improve efficacy of resynchronization in the subset of ischemic patients who might respond to CRT. Therefore, identification of these individuals by means of echocardiography, nuclear cardiology, MSCT or MRI potentially has substantial implications in defining the optimal strategy for device implantation. In this respect, consistent data are likely to be expected from echocardiographic studies using advanced measures of mechanical dyssynchrony such as two-dimensional strain imaging, speckle tracking, and real-time three-dimensional echocardiography [15, 17, 70–76]. Although it appears legitimate to withhold CRT in patients with ischemic cardiomyopathy who show extensive scar tissue, a definite treatment policy in these patients can only be fully embraced after supportive data from large multi-center studies.

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