Cardiac resynchronization therapy: relevance of right ventricular function evaluation

Victoria Delgado and Jeroen J. Bax*

Department of Cardiology, Leiden University Medical Center, Albinusdreef 2, 2333 ZA Leiden, The Netherlands

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This editorial refers to ‘Right ventricular systolic function and cardiac resynchronization therapy’ by H. Burri et al., on page 389.

Heart failure constitutes one of the major public health problems with an incidence that approaches 10 per 1000 population after 65 years of age.1 The majority of clinical trials have focused mostly on left ventricular (LV) failure and have led to established therapeutic approaches that are included in the current guidelines.2,3 In contrast, right ventricular (RV) failure is poorly understood and its therapeutic management is largely empirical. Chronic LV failure is the most frequent cause of RV dysfunction.4 Importantly, the presence of RV dysfunction is a strong and independent predictor of mortality in patients with chronic LV heart failure.5,6 Therefore, routine evaluation of RV performance in patients with LV heart failure is mandatory in order to refine the therapeutic management of these patients.

Cardiac resynchronization therapy (CRT) is an established treatment for patients with chronic LV heart failure. By restoring the atrio-, inter-, and intra-ventricular synchronicity, CRT improves LV diastolic filling, increases LV stroke volume, decreases mitral regurgitation, and induces favourable LV reverse remodelling.7,8 In addition, several studies have shown a significant improvement in RV dimensions and function after CRT.9,10 Finally, this improvement in both LV and RV performance leads to improved survival of heart failure patients treated with CRT.8,11 The mid- and long-term response to CRT is influenced by several pathophysiological factors. Left ventricular dyssynchrony, extent and localization of the myocardial scar, and optimal LV lead position are known independent determinants of LV response to CRT.9,11,12 In addition, several studies have recently shown that baseline RV function may determine the LV response to CRT.13–15 Indeed, the beneficial effects that CRT exerts on LV performance may be less significant if baseline RV function is impaired.13–15 The interaction between the LV and the RV may explain these findings. However, the effects of CRT on this ventricular interdependence remain poorly understood.

Burri et al.16 extend the results of previous studies of the effects of CRT on RV performance. With the use of radionuclide angiography, 44 heart failure patients were evaluated at baseline (within 3 days of CRT device implantation) and at follow-up (9 ± 5 months). Right ventricular and LV ejection fraction was measured and ventricular mechanical dyssynchrony was evaluated by radionuclide phase analysis. In the overall population, a slight but significant improvement in RV ejection fraction was observed at mid- and long-term follow-up after CRT. However, LV function improved to a larger extent than RV function. In addition, a poor correlation between changes in RV ejection fraction and those in LV ejection fraction was noted. The different response of the RV and the LV to CRT remains unclear and further studies addressing this issue are warranted.

The study of the effects of CRT on RV performance may be challenged by the complex geometry of the RV. In the evaluation of RV function in patients treated with CRT, radionuclide angiography may constitute a useful tool that overcomes the limitations of two-dimensional echocardiography and magnetic resonance imaging. Radionuclide angiography does not rely on geometrical assumptions and is feasible in patients with implanted devices. Nevertheless, beyond the assessment of RV dimensions and function, the study of different pathophysiological factors involved in RV dysfunction secondary to chronic LV failure may provide meaningful information for better understanding the effects of CRT on RV performance. These pathophysiological factors include: pulmonary venous hypertension, intrinsic myocardial involvement, ventricular interdependence, neurohormonal interactions, or myocardial ischaemia.4 Particularly, there is growing interest in the effects of CRT on ventricular interdependence.

Ventricular interdependence is one of the factors that contribute to the low cardiac output of patients with RV dysfunction. Right ventricular dilatation and pressure overload determine a change of LV geometry with a leftward shift and dyskinesia of the inter-ventricular septum. In addition, RV volume overload leads to increased pericardial constraint. Consequently, LV compliance and preload are reduced contributing to the 'low cardiac

* Corresponding author. Tel: +31 71 526 2020; fax: +31 71 526 6809. Email: j.j.bax@lumc.nl

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output state’. CRT may favourably influence this ventricular interdependence by inducing a more synchronous contraction and improving the mechanics of the inter-ventricular septum. In addition, CRT reduces mitral regurgitation and pulmonary vein hypertension leading to LV and RV reverse remodelling. In their turn, these changes lead to improved LV and RV performance. Recently, Parsai et al.17 demonstrated that the group of heart failure patients with pronounced ventricular interdependence (exaggerated dysfunctional septum) showed a favourable clinical response to CRT with significant improvement in LV ejection fraction, and reduction in pulmonary artery pressure and natriuretic peptides. However, this series included only a small number of patients and additional studies are warranted to elucidate the effects of CRT on ventricular interdependence.

Finally, the study by Burri et al.16 demonstrated that patients with RV ejection fraction <35% were less likely to show clinical or echocardiographic improvement after CRT than those with RV ejection fraction ≥35%. Several observational studies have pointed out the importance of baseline RV function for mid- and long-term CRT response.13,14 In 44 heart failure patients treated with CRT, Scuteri et al.14 have recently demonstrated that patients with more advanced RV failure, according to tricuspid annulus peak systolic excursion (TAPSE) value <1.4 cm, showed less significant LV reverse remodelling than those with better preserved RV function (TAPSE ≥1.4 cm). Furthermore, Field et al.13 evaluated the prognostic value of several measures of RV performance in 77 consecutive heart failure patients undergoing CRT implantation. A reduced RV myocardial performance index was strongly related to poor outcome and, in particular, each 0.1 U increase in RV myocardial performance index was associated with a 16% increased risk in all-cause mortality, heart transplantation, or ventricular assist device placement.13 A more comprehensive assessment of RV performance, probably including the study of ventricular interdependence, may refine the evaluation of heart failure patients who are candidates for CRT. In addition, in order to optimize CRT response, the indications for CRT may well be established before overt RV dysfunction is observed. Indeed, recent results of the MADIT-CRT and the REVERSE trials, demonstrating the beneficial effects of CRT in patients with mild heart failure, may support this theory and promote an earlier indication for CRT.18,19 In contrast, the presence of severely reduced RV function may not contraindicate CRT since the potential of recovery of the RV has been demonstrated in several studies.4

In conclusion, the study by Burri et al. confirms the findings of previous studies evaluating the effects of CRT on RV function. In addition, the present study points out important questions of the effects of CRT on RV performance and of the influence of RV dysfunction severity on CRT response that will need further study.

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References