Seeing is believing: acute haemodynamic response to predict long-term outcome in cardiac resynchronization therapy

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This editorial refers to "Echocardiographic measures of acute haemodynamic response after cardiac resynchronization therapy predict long-term clinical outcome"¹ by F.B. Tournoux et al., on page 1143

"An acute hemodynamic study ... was performed prior to the implant, which demonstrated a significant increase in cardiac output and decrease of pulmonary capillary wedge pressure" (1)

Many heart failure specialists still believe that the pathophysiology of cardiac resynchronization therapy (CRT) is incompletely understood; however, it must be emphasized that the main effects of biventricular pacing have already been described more than a decade ago.¹ In 1994, Cazeau et al.¹ reported how biventricular pacing improves clinical signs and symptoms of heart failure, acutely increases cardiac output and decreases pulmonary capillary wedge pressure and that those effects were likely mediated by better synchronization of left ventricular (LV) mechanical contraction. However, despite the obvious clinical success of this novel therapeutic approach, the authors were very modest with speculations on the impact on mortality:

"We doubt that this technique will have an impact on long-term survival, but it could be of major importance to improve the patients well-being and control heart failure." (1)

Fortunately, this was the only false estimation at that time. The doubts with regard to the potential survival benefit were later refuted by the results of well controlled, randomized clinical trials which clearly demonstrated a reduced overall mortality in the CRT treatment arm² and which paved the way for a class I indication in symptomatic heart failure patients with a prolonged QRS complex of 120 ms or above. However, despite the undisputed success of CRT for this selected population, many questions remain. The non-responder rate of more than 30–40% is relatively high for such a costly and invasive therapy and has pushed investigators to search for new strategies to better identify CRT responders and to improve optimization of the device settings. However, there are many reasons that might explain CRT failure.

First, heart failure is a multifactorial disease with dysynchrony representing only one aspect. Thus, a single therapy strategy might not 'cure' the entire disease process, in particular, not in patients who already have reached a 'point of no return'.

Secondly, important implantation criteria are often not met, above all, the presence of correctable mechanical dysynchrony. In general, patients with a lesser degree of QRS widening (QRS < 150 ms) tend to respond less favourably in terms of LV systolic function (estimated by peak positive LV dP/dt) and pulse pressure improvement during acute haemodynamic testing when compared with patients with more severe electrical dyssynchrony (QRS > 150 ms).³ We also learned that patients with a non-correctable cause for mechanical dyssynchrony (such as a myocardial scar) will benefit less from CRT.⁴

Thirdly, even if the pre-implant assessment indicates that a patient is a perfect candidate for resynchronization, he might still not respond favourably if the LV stimulation site does not correspond to a delayed activated site or if the stimulation settings are suboptimal for his individual situation. Butter et al.⁵ demonstrated that the haemodynamic response is lower during LV anterior and anterolateral pacing than during posterolateral pacing. But in many patients, the choice of an optimal stimulation site is limited by the anatomic variations of the cardiac veins with frequent ineffective or intolerable LV stimulation. Furthermore, there is still controversy about the optimal stimulation mode, i.e., single-site LV pacing vs. biventricular pacing and simultaneous vs. sequential biventricular pacing. Invasive studies have suggested that univentricular LV pacing may increase LV peak positive dP/dt even more than simultaneous biventricular pacing⁴ and that sequential pacing may further increase haemodynamic function by additional 5–10% from baseline values.⁶ However, it must also be noted that the impact of single-site LV pacing and of CRT ‘fine-tuning’ with sequential biventricular pacing on long-term outcome is still unclear and it seems that...
only a minority of patients benefit significantly.\textsuperscript{7,8} But for some individuals with a poor response to standard biventricular pacing, a device optimization procedure might be essential to improve the outcome. Furthermore, although biventricular pacing is usually better than the intrinsic left bundle branch block or right ventricular pacing, it is still far from optimal and it is important to remember that CRT also has the potential to worsen the haemodynamic situation compared with no pacing in some patients.\textsuperscript{3}

Therefore, the positive as well as the potential negative effects of biventricular pacing define our responsibilities in patient selection and follow-up. Most clinicians and, in particular, the affected patients would probably favour a non-invasive approach to improve the selection of CRT candidates and their follow-up assessment. After implantation of such a complex device, it is not sufficient to confirm the technical operability, but it is also mandatory to assure that the programmed settings have improved cardiac function. Patients with no evidence of mechanical and haemodynamic improvement might be candidates for a optimization procedure. Particular attention must be given when the follow-up assessment indicates deterioration of cardiac function.

In this context, the study by Tournoux \textit{et al.}\textsuperscript{9} reminds us that we should not blindly rely on the implanted CRT device without scrutinizing its impact on haemodynamics. The authors measured the acute increase in LV $dP/dt$ ($\Delta dP/dt$) by Doppler echocardiography as a relatively simple non-invasive test for the acute haemodynamic response after CRT implantation. Patients were classified as non-responders ($\Delta dP/dt < 0\%$), poor responders ($\Delta dP/dt 0–25\%$) and high responders ($\Delta dP/dt > 0\%$). Over a period of 12 months, a combined endpoint of hospitalization due to heart failure and all-cause mortality was followed. The study demonstrated in a small patient cohort that $\Delta dP/dt$ was the most powerful parameter to predict long-term outcomes in CRT patients. In addition, the authors were able to confirm the previously established link between the haemodynamic response and mechanical synchronization\textsuperscript{10} in this study by tissue Doppler imaging (TDI).

What are the implications from this study? First, a simple, non-invasive acute haemodynamic assessment within 24 h after implantation allows to predict the long-term CRT response. Such a test might also be performed even earlier within the operating theatre as an approach to predict long-term outcome before final device implantation. As a result, the implantation of a CRT system in a predicted non-correctable situation best manifested by a circulatory improvement with pacing ventricular segments suffering from delayed activation.' (1)

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\textbf{Reference}


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Multiple myocardial abscesses successfully treated with medical management in an immunosuppressed patient

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Myocardial abscess is usually resulted from the septicemia of various microorganisms such as Candida, Staphylococcus, Aspergillus, Streptococcus, and Salmonella species. Since it is a potentially fatal complication which can cause myocardial rupture and death, surgical treatment is sometimes warranted. A 59-year-old man had a second cadaveric liver transplantation because of previous graft failure and received immunosuppressive therapy including FK506 and prednisolone. Twenty-four days after the surgery, chest X-ray showed rapidly progressive multiple nodular infiltrations in both lung fields. On chest computed tomography, the nodular infiltrations appeared to be cavity-forming lesions with central necrosis suggestive of fungal pneumonia, and multiple low-density round lesions were detected within the myocardium (upper panel). Transthoracic echocardiography showed echo-free spaces within the interventricular septum and mid-posterolateral wall (middle panel). Although no microorganism was identified by repeated microbiologic studies, empirical antibiotics and antifungal therapies were implemented. The myocardial abscesses were found to be decreased in size on the follow-up echocardiography after 20 days of medical management (lower panel), and he was uneventfully discharged from hospital 8 days after the echocardiography.

**Upper panel.** Chest computed tomography showed a cavity-forming lesion in the right upper lobe suggestive of fungal pneumonia (arrow head) and multiple low-density round lesions within the myocardium (arrows).

**Middle panel.** Transthoracic echocardiography demonstrated multiple echo-free spaces suggesting abscesses within the myocardium of the interventricular septum and posterolateral wall (arrow heads).

**Lower panel.** On the follow-up echocardiography performed after 20 days of medical management, the myocardial abscesses were found to be decreased in size (arrow heads).