

## SCIENTIFIC LETTER

# Influence of conduction time intervals on symptoms and exercise tolerance in patients with heart failure with left ventricular systolic dysfunction

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Conduction disturbances are commonly observed in patients with heart failure with left ventricular systolic dysfunction (LVSD).<sup>1–3</sup> Conduction disturbances increase in prevalence and severity as disease progresses. Several controlled studies have shown that correcting for conduction disturbance related electromechanical asynchrony by atrio-biventricular pacing may significantly improve symptoms and exercise tolerance in patients with drug refractory heart failure and a wide QRS complex or prolonged PR interval.<sup>4,5</sup> This suggests that conduction disturbances and electromechanical correlates contribute to increased symptoms and exercise intolerance regardless of baseline LVSD severity.

In such a context, between September 1999 and January 2001 we conducted a prospective, observational study of 103 consecutive patients with heart failure (mean age 60 (13) years) with chronic LVSD to determine whether conduction time intervals as simply measured on surface ECG may independently influence symptoms and exercise tolerance. Patients with an echocardiographically determined left ventricular ejection fraction (LVEF) of < 40% and left ventricular end diastolic diameter (LVEDD) > 60 mm and who were in stable sinus rhythm were considered for participation in the study. Eighteen patients were in New York Heart Association (NYHA) functional class I, 47 in class II, 27 in class III, and eight in class IV. LVSD was of non-ischæmic origin in 87%. The study population was characterised by a high prevalence of conduction abnormalities: PR was > 200 ms in 36% of patients and QRS duration was ≥ 120 ms in 60% (including 54% with left bundle branch block). The mean (SD) LVEF was 26 (9)% and mean (SD) LVEDD was 71 (8) mm. Baseline exercise capacity was moderately reduced with a mean (SD) exercise time of 480 (180) seconds and mean (SD) peak oxygen consumption ( $\text{VO}_2$ ) of 17 (5) ml/kg/min (that is, 64 (15)% of the maximum predicted  $\text{VO}_2$ ).

Correlations of ECG conduction intervals (PR and QRS duration) with symptoms (NYHA classification), exercise tolerance by cardiopulmonary exercise testing (total exercise time, peak  $\text{VO}_2$ ), LVEF by radionuclide imaging, and left ventricular dimensions by echocardiography were studied by univariate and multivariate analysis.

## RESULTS

In univariate analysis (analysis of variance or  $\chi^2$  tests), symptom grade (NYHA class) increased and exercise tolerance decreased as conduction times increased. PR interval were 166 (31) ms, 185 (36) ms, 209 (45) ms, and 228 (56) ms in patients in NYHA classes I, II, III, and IV, respectively ( $p = 0.0003$ ). Exercise time ( $r = -0.34$ ,  $p = 0.0007$ ), maximum heart rate at peak exercise ( $r = -0.29$ ,  $p = 0.004$ ), and peak  $\text{VO}_2$  ( $r = -0.29$ ,  $p = 0.004$ ) decreased as the PR interval increased. Likewise, QRS duration was 117 (35) ms, 135 (36) ms, 145

(38) ms, and 166 (28) ms in patients in NYHA classes I, II, III, and IV, respectively ( $p = 0.01$ ). QRS widening was also associated with decreased exercise time ( $p = 0.02$ ). A non-significant trend was observed towards a lower peak  $\text{VO}_2$  ( $r = -0.19$ ,  $p = 0.07$ ). LVEF was 30 (10)%, 28 (9)%, 22 (6)%, and 17 (5)% in patients in NYHA classes I, II, III, and IV, respectively ( $p = 0.0001$ ). Decreased LVEF was also associated with shorter exercise time ( $r = 0.33$ ,  $p = 0.0009$ ) and lower peak  $\text{VO}_2$  ( $r = 0.29$ ,  $p = 0.004$ ). No significant correlations were found between LVEDD and the various parameters that assessed exercise capacity.

In multivariate analysis (regression and logistical models), a prolonged PR interval was an independent predictor of increased NYHA class (odds ratio 1.36, 95% confidence interval 1.12 to 1.65,  $p = 0.002$ ) and decreased exercise capacity (exercise time ( $p = 0.004$ ) and peak  $\text{VO}_2$  ( $p = 0.007$ )) independently of LVEF and left ventricular dimensions. In contrast, prolonged QRS duration did not appear as an independent factor in functional deterioration and exercise intolerance. Lastly, LVEF was confirmed as an independent factor in symptom deterioration and decreased exercise time.

## DISCUSSION

Although the correlations were relatively weak, the study results suggest that PR interval prolongation, but not QRS widening, contribute to increased symptoms and exercise intolerance regardless of baseline LVSD severity in patients with chronic heart failure. Not only does PR interval measured at rest reflect advanced LVSD but its prolongation also constitutes a major functional parameter that, after optimisation, potentially contributes to improving symptoms and exercise tolerance. Such was the rationale of the first attempts at pacing for heart failure in the early 1990s, but controlled trials did not show any sustained benefit with short atrioventricular delay DDD pacing. Failure may be related to increased ventricular asynchrony resulting from right ventricular apical pacing that counterbalances the relative benefit of correcting atrioventricular asynchrony in the left heart.

In contrast, in this study QRS widening did not appear to be related to LVEF and left ventricular dimensions as an independent factor in symptom deterioration and exercise capacity impairment.

Lastly, in our study LVEF reduction at rest was another independent factor in exercise capacity impairment, contrary to what is generally reported in the literature; however, most studies were of very small patient series.

In conclusion, symptoms and exercise tolerance were independently affected by both the baseline severity of LVSD and the intracardiac conduction status. Although the

**Abbreviations:** LVEDD, left ventricular end diastolic diameter; LVEF, left ventricular ejection fraction; LVSD, left ventricular systolic dysfunction; NYHA, New York Heart Association;  $\text{VO}_2$ , oxygen consumption

present study essentially addressed the effect of spontaneous electrical asynchrony on exercise tolerance, some conclusions regarding cardiac resynchronisation<sup>4,5</sup> can be drawn from our results. Firstly, the pathophysiological bases of electrical treatment for heart failure are valid. Secondly, atrioventricular asynchrony as a result of a prolonged PR interval may be sufficient to propose pacing for treating heart failure. Lastly, QRS duration should not be regarded as the only criterion for selecting patients for this new treatment.

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## IMAGES IN CARDIOLOGY

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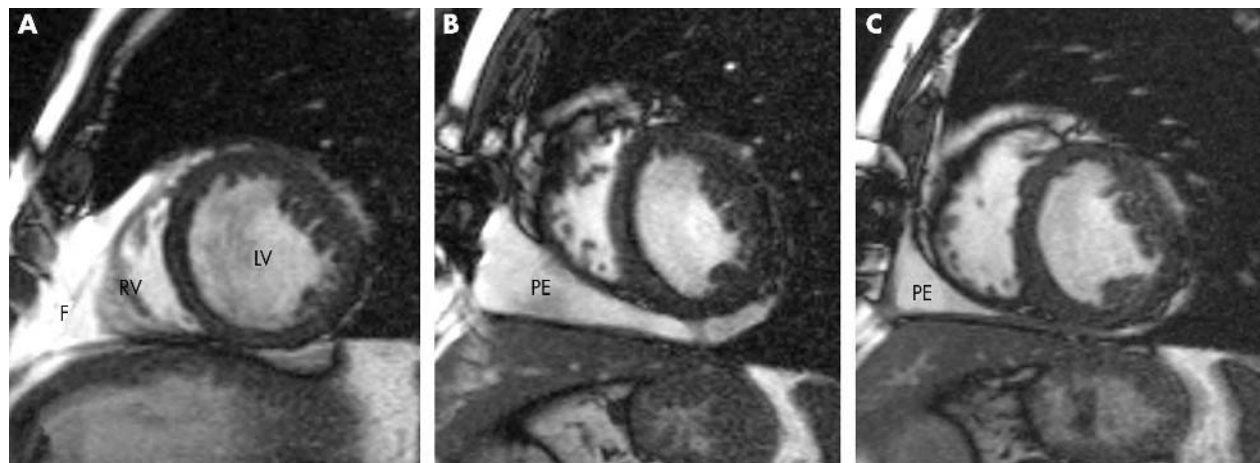
### Transient pericardial effusion after cardiac surgery: often unrecognised

A 52 year old man with ischaemic heart failure was evaluated with cardiovascular magnetic resonance imaging (CMR) before coronary artery bypass surgery (CABG), demonstrating a dilated left ventricle with depressed ejection fraction (panel A). Surgery was performed without complications and the patient recovered well. CMR was repeated three months after the procedure for routine evaluation of cardiac function. Besides recovery of left ventricular function, approximately 350 ml of pericardial effusion was observed located posterior to the left and right ventricle (panel B). There were, however, no signs of tamponade from a clinical point of view and the patient was asymptomatic. Follow up CMR six months after CABG revealed notable resolution of the pericardial effusion (panel C).

The presence of pericardial effusion shortly after cardiac surgery is mainly detected clinically when a patient develops

right and/or left sided heart failure, usually accompanied by chest discomfort, a pericardial rub, fever, and leucocytosis. This condition is often referred to as post-pericardiotomy syndrome. The vast majority of patients recover from cardiac surgery without these symptoms, and therefore no diagnostic effort is being made to detect pericardial effusion. However, postoperative pericardial effusion is considerably more common than clinically apparent, and occurs in as many as 85% of patients. Although anti-inflammatory agents may be useful to facilitate resolution, postoperative pericardial effusion is usually transient and the clinical course benign.

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True fast imaging with steady state precession (FISP) cine end diastolic short axis images. F, fat; LV, left ventricle; PE, pericardial effusion; RV, right ventricle.