A COMPARISON OF FUNCTIONAL AND ECHOCARDIOGRAPHIC OUTCOMES IN NICE COMPLIANT AND NON-COMPLIANT PATIENTS UNDERGOING CRT IN THE REAL WORLD

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Introduction The National Institute for Clinical Excellence (NICE) define a population of patients that are most likely to respond to cardiac resynchronisation therapy (CRT) and have a favourable health economic profile. Current NICE criteria (technology appraisal, TA120) for CRT include: NYHA class III or IV symptoms despite optimal medical therapy, sinus rhythm, ejection fraction ≤35%, and either QRS duration >150 mS alone or 120–149 mS together with echocardiographic (echo) evidence of mechanical dyssynchrony. Several randomised clinical trials however have consistently reported beneficial effects of CRT in patients outside current NICE guidelines. In our centre, potential CRT patients are discussed at a multi-disciplinary team (MDT) meeting attended by a heart failure specialist, electrophysiologist, interventional cardiologist, cardiac surgeon and hospital manager. CRT is offered where there is consensus agreement that the individual patient is likely to benefit. This individualised and evidence based approach provides for a comparison of outcomes in NICE compliant (NICE:+ve) and NICE:−ve patients (patients with a clinical need and evidence base supporting CRT, but who do not meet NICE criteria).

Methods Our unit operates an integrated CRT service with pre-assessment, implantation, and follow-up components. Pre-assessment includes clinical evaluation and baseline echo (EF: ejection fraction, and ESV: left ventricular end-systolic volume) and functional characterisation: a) Minnesota quality of life score (QoL), b) 6 min walk test (6MWT), and c) peak oxygen consumption on cardiopulmonary exercise test (VO2).

Follow-up at 3 and 6 months post CRT includes clinical evaluation, device/medical optimisation, and reassessment of echo and functional outcomes. This study involves a retrospective analysis of our CRT database and compares outcomes in NICE:+ve and NICE:−ve patients.

Results Between January 2007 and December 2009, 253 patients received CRT. Complete paired data comparing baseline and 6 month functional and echo data are available for 139 patients; 89 NICE:+ve and 80 NICE:−ve (Abstract 94 table 1). Exclusions for the NICE:−ve patients included: atrial fibrillation (n=19), QRS 120–149 mS without mechanical dyssynchrony (n=12); QRS <120 mS (n=5); pacemaker upgrades (n=9). An additional 5 patients with right bundle branch block and otherwise NICE CRT compliance are analysed as NICE:−ve in this study. Compared to baseline, 6-month outcomes were similar and significantly improved in both NICE:+ve and NICE:−ve groups (Abstract 94 table 2).

Conclusions We observed significantly favourable and similar functional and echocardiographic responses to CRT in patients meeting and not meeting current NICE criteria for CRT. Guidelines should guide therapy but ultimately each therapy should be individualised and evidence based.

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Cardiopulmonary exercise testing for peak oxygen uptake (VO₂peak) is widely used to evaluate severity, pathophysiology and prognosis in patients with chronic heart failure (CHF). A VO₂peak ≤14 (or 12 with β-blocker) ml/kg/min is associated with increased mortality and is a key criterion for cardiac transplant listing. A symptom-limited exercise test, however, may elicit a VO₂peak lower than the maximum physiological limit (VO₂max); the latter commonly “confirmed” using the secondary criterion of respiratory exchange ratio (RER) >1.05. RER, however, is sensitive to the test format. We, therefore, determined if a ramp-incremental (RI) step-exercise (SE) (or RISE) test could determine VO₂max in CHF patients without using RER, by satisfying the criterion that two different work rates are terminated at the same VO₂peak. Twenty-one male CHF patients (NYHA class I: n=5, II: n=16, and III: n=1) initially performed a modified Bruce treadmill test. Patients then completed a symptom-limited RISE95 cycle ergometer test in the format: RI (4–18 W/min; ~10 min); 5-min recovery (10 W); SE (95% of peak RI work rate). Thirteen of these patients also performed RISE95 tests using slow (RI 3–8 W/ min; ~15 min) and fast (RI 10–30 W/min; ~6 min) ramp rates. VO₂ and RER were measured breath-by-breath by a mass spectrometer and turbine (MSX, NSpire, UK). Peak VO₂ and RER were compared within-subjects, between RI and SE, by unpaired t test of the final 12 breaths of exercise. This approach allowed VO₂max and its associated 95% confidence limits to be estimated. VO₂peak was similar (p>0.05) in treadmill and cycle exercise (mean±SD: 16.2±2.7 vs 15.0±3.2 ml/kg/min, n=20, respectively), despite RER being greater in cycling (1.08±0.12 vs 1.15±0.09; p<0.05). As a group, VO₂peak was similar (p>0.05) between RI and SE (mean±SD: 14.6±5.2 vs 14.9±3.2 ml/kg/min, n=21). A within-subject comparison, however, revealed that the VO₂max criterion was met in 14 of 21 patients (measurement sensitivity range 0.6–3.8 ml/kg/min), despite RER being >1.05 in the remaining 7 (1.16±0.09). There was no effect of ramp rate on VO₂peak (p>0.05), however RER was greater (p<0.05) in the fast ramp (1.24±0.09) compared to the slow (1.12±0.06). The single-visit RISE95 test incorporating incremental- and step- exercise phases, each to the volitional limit, was well tolerated by CHF patients: The SE phase was contraindicated in only 3 of the 47 tests. The RISE95 detected VO₂max in 14 of 21 patients with a sensitivity of ~10% (ie, similar to healthy subjects), and without the need for secondary criteria or incidence of false-positive.

In contrast, the end-exercise RER was sensitive to both modality and ramp rate and provided a false-positive for VO₂max attainment in every incidence. Therefore, the RISE95 protocol provides a robust measure of VO₂max in CHF patients, to within an individually-defined CI without dependence on secondary criteria.

Rapid adaptation of pulmonary oxygen uptake (VO₂) at exercise onset reduces the reliance on limited anaerobic energy stores and is associated with increased exercise tolerance. These VO₂ kinetics, however, are slow in patients with chronic heart failure (CHF). This could be due to limitations in the control of muscle O₂ consumption and/or O₂ delivery. Recent evidence in CHF of a transient overshoot in microvascular deoxygenation at exercise onset supports the latter. As prior exercise is known to increase muscle blood flow in healthy individuals, we examined whether it could attenuate the fall in microvascular deoxygenation and speed VO₂ kinetics on transition to moderate exercise in CHF patients. Thirteen CHF patients (NYHA class I: n=3, II: n=9, and III: n=1) performed a ramp test on a cycle ergometer for estimation of lactate threshold (LT) and VO₂max. Patients subsequently repeated two 6-min moderate-intensity exercise transitions (bout 1, bout 2) from rest to 90%LT, separated by 6-min of rest. Measurements included breath-by-breath VO₂ using a turbine and mass spectrometer (MSX, NSpire, UK), and tissue oxygenation index (TOI) of the vastus lateralis by spatially resolved near-infrared spectroscopy (NIR200, Hamamatsu, Japan). The exponential time-constant (τ) for TOI and phase II VO₂ were estimated using nonlinear least-squares regression. The τVO₂/TOI, or “kinetic index”, was taken to reflect the relative matching of muscle oxygenation to its instantaneous requirement. LT and VO₂max were 9.7±1.7 (mean±SD) and 15.0±5.2 ml/kg/min, respectively. Prior exercise increased resting TOI by 10±3% (p<0.05), attenuated the transient overshoot in muscle deoxygenation by ~50% (p<0.05) and slowed the rate of deoxygenation in the transient (τTOI: 10±1 vs 21±3 s; p<0.05). Both τVO₂ (46±20 vs 39±18 s; p<0.05) and the kinetic index (4.5±1.8 vs 2.7±0.9; p<0.05) were reduced following prior exercise. VO₂ was well correlated to the kinetic index (R²=0.92) in bout 1. However, although a lower τVO₂ was typically reflected in a reduced kinetic index in bout 2, VO₂ kinetics remained slowed in 4 patients. These patients had a higher NYHA class (2.3±0.5 vs 1.6±0.5; p=0.06) and greater initial τVO₂ (62±17 vs 33±9 s; p<0.05) than the others. In CHF prior moderate-intensity exercise improved the dynamic matching of muscle oxygenation to its instantaneous requirement and speeded VO₂ kinetics in all patients. This suggests that slow VO₂ kinetics in CHF are due, at least in part, to a dynamic limitation in O₂ delivery. However, this approach revealed an apparent limitation in the control of muscle O₂ consumption in the most severe patients, which was only partly ameliorated by improving O₂ delivery. Nevertheless, these findings suggest that an acute intervention to improve muscle oxygenation can increase aerobic energy provision on transition to exercise in CHF patients.