“Value” of improved treadmill exercise capacity: lessons from a study of rate responsive pacing

A D Staniforth, R Andrews, M Harrison, A Perry, A J Cowley

Abstract

Objectives—To compare the value of a series of cardiovascular measurements in patients with symptomatic disease receiving an effective treatment (rate responsive pacing).

Patients—12 pacemaker dependent patients with VVIR units.

Interventions—Single blind crossover between VVI and VVIR.

Outcome measures—Exercise capacity was assessed by treadmill tests (modified Bruce protocol and a fixed workload protocol) with respiratory gas analysis. Self paced corridor walk tests were also undertaken. Quality of life (QOL) was assessed by questionnaire. Daily activity was measured in the patients’ homes using shoe and belt pedometers.

Results—Treadmill tests and QOL questionnaires correctly identified the clinical benefit associated with VVIR. The modified Bruce protocol was superior to the fixed workload protocol as it was better tailored to the fairly well preserved exercise capacity of the patients. Symptom scores, but not walking times, were improved with VVIR during corridor walk tests. VVIR did not improve daily activity measured using either the belt or shoe pedometers.

Conclusions—VVIR pacing improved some but not all measures of exercise capacity. This finding illustrates the difficulty of selecting an instrument to measure symptomatic improvement in clinical research; and raises the question, what is the best way of measuring exercise capacity?

(Heart 1998;80:383–386)

Keywords: rate responsive pacing; exercise capacity; quality of life

The evidence in favour of rate responsive pacing is indisputable. Rate responsive pacing can be used as a tool to compare the usefulness of cardiovascular tests for detecting improvements in clinical status.

Exercise capacity (treadmill exercise duration,1–3 maximal oxygen consumption (VO₂),45 and cardiac output67) and subjective assessment of symptoms by patients1–4 are significantly improved by rate responsive pacing. Laboratory based exercise tests are, however, highly artificial and their clinical relevance has been questioned.89 This has led to the development of corridor walk tests, which are considered to be a more natural way of assessing exercise capacity. Unsurprisingly, rate responsive pacing also improves exercise capacity using six10 and 1211 minute corridor walk tests. In spite of the fact that these tests are self paced their results correlate well with maximal VO₂ and they probably tell us little about patients’ daily activity in their own homes.

Rate responsive pacing is assumed to improve daily activity in the home environment. In this study we investigate this assumption and compare the value of cardiovascular tests in patients receiving an established pacing technique of proven benefit.

Methods

Patients

Twelve patients (mean (SD) age 59 (15) years) with VVIR units were recruited from the pacemaker clinic of a university hospital. All patients were pacemaker dependent. Table 1 lists their baseline characteristics and pacemaker details. Six had had therapeutic AV nodal ablation for drug resistant atrial dysrhythmia. The mean (SD) time interval between pacemaker implantation and the study date was 22 (22.4) months. Pacemakers were

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*Activity sensor; †minute ventilation sensor.

RR, rate response; SR, sinus rhythm; PAF, paroxysmal atrial fibrillation; AF, atrial fibrillation; CHB, complete heart block; IHHD, ischaemic heart disease; Ablate, nodal ablation.
MEASUREMENTS OF EXERCISE CAPACITY

Treadmill tests
There was an initial three week run in period during which symptom limited treadmill tests were performed in VVIR mode according to a modified Bruce protocol (table 2).

Patients breathed through a mouthpiece connected through a flow meter to a mixing box. Mass spectrometry (ESS Ltd, Cheshire, UK) was used to analyse the composition of inspired air from the inlet valve and mixed expired air from the mixing box for determination of oxygen uptake and carbon dioxide (CO₂) production. Subjective assessment of exercise difficulty was made at the end of each stage using Borg scores.¹² Randomisation occurred when modified Bruce exercise times stabilised to within 5% of the previous test. Two additional treadmill tests were performed at randomisation: a submaximal (80%) modified Bruce test with measurements of cardiac output (see later) and a symptom limited fixed workload test (slope 4.3%, speed 2.7 km/h).

The fixed workload test was terminated either at the patient's request on symptom limited exercise or after 30 minutes (whichever was sooner).

Estimation of cardiac output
Cardiac output was measured non-invasively by the indirect Fick method using CO₂ as an indicator gas. Mass spectrometry was used to measure CO₂ production, mean end tidal CO₂ (equivalent to pulmonary venous CO₂), and the plateau phase CO₂ concentration following re-breathing into an anaesthetic bag (equivalent to pulmonary artery CO₂). Measurements were made at rest and at 80% of the predetermined peak modified Bruce exercise time. We have previously validated this method against direct measurements of cardiac output by thermodilution.¹³

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PACEMAKER PROGRAMMING AND STUDY DESIGN
Patients were randomly programmed to either predetermined VVIR or default VVI modes (table 1) for successive periods of one week in a single blind, crossover fashion. Programming was performed by a cardiac technician who was not involved in the study. Seven patients were initially programmed to VVI, and the remaining five to VVIR. The investigator could not be blinded as all exercise tests were performed with electrocardiogram monitoring. Early crossover to the next arm of the study was permitted at the patient's request.

DAILY ACTIVITY

Daily activity was measured using Digi-walker hip pedometers (Yamax, Yokohama, Japan) and electronic shoe pedometers contained within the sole of an everyday pair of shoes (Medical Physics Department, Queen's Medical Centre, Nottingham). Both have previously been validated as methods of step counting.¹⁴ The hip pedometers were calibrated before and after every use to permit total foot fall to be estimated. Patients were instructed to wear the hip pedometers all day, every day for the seven days of each study arm.

Shoe pedometers were available only for male patients. Each pedometer consists of a transducer, a battery, and circuitry containing a memory chip and clock. The transducer is a flexible strip switch that exhibits decreasing resistance when a force is applied to its surface. The weight required to activate the transducer is about 2 kg. Pulses from the transducer are accepted or rejected according to a preset frequency window to eliminate false activation. The memory chip records the number of foot falls in every 20 second period for a total of 25 minutes on the treadmill at zero incline. Steps were counted manually by an observer and using the shoe pedometers. The memory chip records the number of foot falls in every 20 second period for a total of 25 minutes on the treadmill at zero incline. Steps were counted manually by an observer and using the shoe pedometers. The accuracy of these pedometers is within 3% of the true total number of steps.

The memory chip records the number of foot falls in every 20 second period for a total of 25 minutes on the treadmill at zero incline. Steps were counted manually by an observer and using the shoe pedometers. The memory chip records the number of foot falls in every 20 second period for a total of 25 minutes on the treadmill at zero incline. Steps were counted manually by an observer and using the shoe pedometers. The accuracy of these pedometers is within 3% of the true total number of steps.
Scores at peak exercise were equivalent for VVI and VVIR during both the modified Bruce and fixed workload exercise protocols, indicating that the patients consistently exercised to equivalent levels of symptom limitation.

Mean (SEM) improvements in peak VO$_2$ (2.9 (0.8) vs 0.3 (0.4) ml/min/kg, $p < 0.05$) and rate pressure product (6656 (1011) vs 3159 (836), $p < 0.005$) were greater with the modified Bruce protocol than with the fixed workload protocol. There were no significant differences between the protocols according to improvements in either exercise time or work done.

**CORRIDOR WALK TESTS**

Clinical improvement between VVI and VVIR was not detected by corridor walk times at slow, normal, or fast speeds (table 4). However, measurement of self rated symptomatic impairment during exercise with Borg scores indicated that patients exercised with greater ease at their normal and fast speeds in VVIR ($p < 0.05$).

**QUALITY OF LIFE SCORES**

There was a mean overall improvement in QOL scores of 13% in VVIR ($p < 0.05$, table 4). There was no significant difference in QOL between baseline and VVIR.

**DAILY ACTIVITY**

Table 4 shows that switching from VVI to VVIR was not associated with improved daily activity measured using either belt or shoe pedometers.

**Discussion**

Treadmill based exercise tests and self administered QOL questionnaires were effective tools for assessing the beneficial effect of VVIR pacing on exercise performance and patient symptoms. The modified Bruce protocol was marginally superior to the fixed workload protocol as seen in the significantly greater improvements in peak VO$_2$ and rate pressure product. This finding shows that it is important to match the design of an exercise protocol to the expected abilities of the study patients. The fixed workload protocol was too easy for our relatively fit and active patients; VO$_2$ reached a plateau during exercise in six patients in VVI, all of whom continued to exercise for the full 30 minute schedule.

Surprisingly, large improvements in treadmill based exercise capacity and patients’ symptoms did not translate to improvements in daily activity. In this study, using shoe pedometers, 85% (steps/hour) and 90% (% of time active) power led to the detection of a 25% change in daily activity at a significance level of $p < 0.05$. These negative findings are unlikely to have arisen as a result of a type II error. Contrary to what was expected, an effective treatment (rate responsive pacing) failed to improve daily activity. This observation is similar to one that we have already made concerning vasodilator treatment in patients with mild to moderate heart failure. The explanation for these observations is unclear, but may be related to patient selection. It is important to
realise that our patients were relatively fit and active. In spite of their underlying cardiovascular disease (as reflected by their reduced peak VO\textsubscript{2}) their level of daily activity was comparable to that for medically fit, young adults (70 000 steps/week). 17 Most people live their daily lives to ordered routines during which they rarely exercise maximally. It may be that unless a disease state severely limits exercise capacity, we should not expect a treatment to result in an improvement in daily activity. Furthermore, the results of the corridor walk test support the interpretation that although the addition of VVIR did not influence the level of daily activity, it did permit patients to exercise at the same level with fewer symptoms (as shown by the lower Borg scores in VVIR at normal and fast walking speeds).

Daily activity is an important measurement as it tells us something about what patients do in their real lives, as opposed to what they can do when they are “flogged” on a treadmill. Furthermore, in heart failure, reduced daily activity has been identified as an independent marker of poor prognosis. 19 Step counting is a sensible and easy method of assessing daily activity. Shoe pedometers are superior to belt pedometers as they directly measure foot fall rather than the tilting motion of the pelvis associated with walking, and incorporation of a timing device permits analysis of activity levels over the study period.

CONCLUSIONS
This study highlights the difficulties of selecting a test to measure clinical improvement in patients with symptomatic disease. The best way of evaluating exercise capacity is still unclear, possibly because it may vary according to aetiology and severity of the disease.

8 Francis GS, Rector TS. Maximum exercise tolerance as a therapeutic end point in heart failure—are we relying on the right measure? Am J Cardiol 1994;73:304–6.
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