

# A pilot randomized controlled trial to evaluate the benefit of the cardiac rehabilitation paradigm for the non-acute ischaemic stroke population

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Received 22nd December 2006; returned for revisions 25th February 2007; revised manuscript accepted 18th April 2007.

**Objective:** To evaluate risk factor reduction and health-related quality of life following a 10-week cardiac rehabilitation programme in non-acute ischaemic stroke subjects.

**Design:** Single-blinded randomized control trial.

**Setting:** Outpatient rehabilitation.

**Subjects:** Forty-eight community-dwelling ischaemic stroke patients (38 independently mobile, 9 requiring assistance, 1 non-ambulatory) were randomly assigned to intervention or control groups by concealed allocation.

**Intervention:** The trial consisted of a 10-week schedule with measures taken at weeks 1 and 10. Both groups continued usual care (excluding aerobic exercise); intervention subjects attended 16 cycle ergometry sessions of aerobic-training intensity and two stress-management classes.

**Main outcome measures:** Cardiac risk score (CRS);  $\text{VO}_2$  (mL  $\text{O}_2$ /kg per minute) and Borg Rate of Perceived Exertion (RPE) assessed during a standardized ergometry test; Hospital Anxiety and Depression Scale (HADS); Frenchay Activity Index; Fasting Lipid Profiles and Resting Blood Pressure.

**Results:** Group comparison with independent *t*-tests showed significantly greater improvement at follow-up by intervention subjects than controls in  $\text{VO}_2$  (intervention  $10.6 \pm 1.6$  to  $12.0 \pm 2.2$ , control  $11.1 \pm 1.8$  to  $11.1 \pm 1.9$   $t = 4.734$ ,  $P < 0.001$ ) and CRS (intervention  $13.4 \pm 10.1$  to  $12.4 \pm 10.5$ , control  $9.4 \pm 6.7$  to  $15.0 \pm 6.1$   $t = -2.537$ ,  $P < 0.05$ ). RPE rating decreased in intervention subjects ( $13.4 \pm 12.2$  to  $12.4 \pm 2.0$ ) and increased in controls ( $13.8 \pm 1.8$  to  $14.4 \pm 1.6$ ); Mann-Whitney *U* ( $U = 173.5$ ,  $P < 0.05$ ). Within-group comparison showed significant decrease in the HADS depression subscale in the intervention group alone ( $5.1 \pm 3.4$  to  $3.0 \pm 2.8$ ) (Wilcoxon signed ranks test  $Z = -3.278$ ,  $P < 0.001$ ).

**Conclusion:** Preliminary findings suggest non-acute ischaemic stroke patients can improve their cardiovascular fitness and reduce their CRS with a cardiac rehabilitation programme. The intervention was associated with improvement in self-reported depression.

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## Introduction

Cardiovascular disease and ischaemic stroke are both vascular diseases sharing many predisposing, potentially modifiable risk factors (hypertension, abnormal blood lipids and lipoproteins, cigarette smoking, physical inactivity, obesity and diabetes mellitus).<sup>1,2</sup> Their association is not benign, with the risk of death in the stroke population, in part due to cardiac disease, at least twice that of age-matched controls.<sup>3</sup> Modification of multiple risk factors through lifestyle interventions and pharmacological therapy is recognized as the cornerstone of prevention of recurrent events.<sup>3-5</sup>

Regular physical activity and cardiac rehabilitation have proven benefits in the general population and post cardiac event,<sup>6-9</sup> however, adoption of the cardiac rehabilitation paradigm to the ischaemic stroke population has remained untested. Stroke patients are known to have low endurance to exercise and decreased activity levels<sup>10</sup> and few can avail themselves of cardiovascular training through exercise counselling alone due to acquired disability.<sup>11</sup> A Cochrane review and the American Stroke Association have highlighted as a priority the need for research into the efficacy and feasibility of aerobic exercises post stroke.<sup>2,12</sup>

As adapted cycle ergometers allow aerobic fitness training post stroke<sup>10,13,14</sup> this pilot study aims to establish the feasibility of a 10-week cardiac rehabilitation programme including 16 cycle ergometry sessions. Of interest is whether the programme improves:

- Cardiovascular fitness using estimated  $\dot{V}O_2$  and Borg's Rate of Perceived Exertion<sup>15</sup> (RPE), at a given workload and resting heart rate (HR).
- Multivariate cardiac risk score<sup>16</sup> (CRS) measured by a coronary disease prediction algorithm.
- Cardiovascular-metabolic risk factor profile using fasting lipid profiles and resting blood pressure.
- Health-related function and quality of life as measured by the Frenchay Activity Index<sup>17</sup> and the Hospital Anxiety and Depression Scale.<sup>18</sup>

## Methods

### Study design

A randomized, controlled, single-blind trial was conducted, approved by University College Dublin Human Research Ethics Committee. Measurements were made by an independent assessor blinded to allocation.

### Patients

Subjects were recruited from the Stroke Rehabilitation Database, Baggot Street Community Hospital, Dublin. Information leaflets were posted and volunteers contacted the research team for initial telephone screening, including the PAR-Q Questionnaire.<sup>19</sup>

Informed consent was obtained. Participants' general practitioners were asked to notify contraindications to exercise or medication changes. All participants received a medical screening by a physician in the stroke unit prior to participation.

Sample size calculations with 80% power and  $P < 0.05$  were conducted on the following outcome measures:

- Borg's RPE<sup>15</sup> scale to detect a 2-point change between groups indicated that a minimum of 16 subjects would be required per group (mean 17 (SD 2)).<sup>20</sup>
- Hospital Anxiety and Depression Scale (HADS) depression subscale to detect a 2.5-point change between groups indicated a minimum of 24 per group (mean 6.2 (SD 3.1)).<sup>21</sup>
- Systolic blood pressure reduction of 5 mmHg indicated a minimum of 170 subjects in each group<sup>22</sup> which was not feasible for this pilot study. Data for CRS in stroke patients was not available for sample size calculation.

Inclusion criteria: >1 year post ischaemic stroke (confirmed by CT or MRI scan) and over 18 years of age. Patients were included irrespective of their ability to ambulate independently.

Exclusion criteria:  $O_2$  dependence, angina, unstable cardiac conditions, uncontrolled diabetes mellitus, major medical conditions, claudication, febrile illness, cognitive impairment or beta

blocker medication (RPE, a primary outcome measure, was shown to be unreliable in subjects taking beta blocker medication).<sup>22,23</sup>

### Random allocation

Participants were assigned an ID number, stratified by age and sex into four blocks of six and randomly assigned using a sequence generator (SPSS version 12.0), to either intervention or control groups, by an independent party. Following initial testing, participants were handed an opaque envelope which contained details of their group assignment, by clerical staff unrelated to the trial.

### Programme

Both control and intervention subjects who were in receipt of physiotherapy and occupational therapy services continued with usual care. Occupational and physiotherapy received focused on functional activities, balance and gait. No therapy contained an aerobic exercise component.

Control subjects had a baseline assessment on week 1 and re-assessment on week 10 with no additional intervention in the interim.

The Cardiac Rehabilitation Programme consisted of a 10-week schedule with baseline measures in week 1 and reassessment in week 10. Intervention subjects attended twice weekly for 30-minute cycle ergometry exercise (Motomed Viva 2) using either the upper or lower limbs. They exercised through biofeedback alarms set at 50–60% of their maximal heart rate, calculated sessionally (Karvonen formula  $THR = (HR_{max} - HR_{rest})(50-60\%) + HR_{rest}$ ). Resistance and speed were adjusted daily to ensure tailored progression. As participants did not exceed 60% max HR, the programme posed very low risk of adverse events.<sup>2</sup> Participants attended two life skills classes addressing stress management, relaxation and life balance.

Two participants exercised concurrently in a controlled environment and all sessions were supervised by a physiotherapist. Staff had cardiac resuscitation and defibrillation certification. Indications to stop exercise included: chest pain,

dizziness, malaise, heart rate in excess of 60% maximal heart rate, oxygen saturation levels lower than 90% or participant request to stop in accordance with American Heart Association (AHA) guidelines.<sup>24</sup>

### Measurements

- Baseline descriptives including Oxfordshire Stroke Subtype Classification,<sup>25</sup> medical history including stroke, previous cardiac events and Functional Ambulation Category<sup>26</sup> were noted from each participant's medical chart.
- Fitness testing<sup>19</sup> was conducted with a standardized 3-minute submaximal exercise test using a cycle ergometer (Reck, Motomed Viva 2) at resistance setting 8 (5.6 Nm). Participants were fasting overnight for 12 hours at the time of testing, they were instructed to wear loose, comfortable clothing and room temperature was maintained at 20°C. The machine passively moved for 1 minute at 50 rpm, allowing a warm-up and assuring no joint discomfort. Participants took over pedalling for 3 minutes at a steady state of 50 rpm with a workload of 5.6 Nm. A metronome was present to assist with pacing.
- $\dot{V}O_2$  (mL  $O_2$ /kg/min) was calculated  $(10.8 \times W \times M^{-1}) + 7$ , using average wattage output during the test.
- RPE was rated at the end of the test, in accordance with the recommended guidelines.<sup>15</sup>
- Peak wattage was recorded at the end of the 3-minute exercise test.
- Cardiac risk score<sup>16</sup> (CRS) was calculated for each participant. This is an algorithmic score based on age, resting blood pressure, smoking status, diabetic status, total cholesterol and high-density lipoprotein (HDL) scores.
- Resting heart rate and  $SaO_2$  were measured following a 5-minute seated rest period (Nanox 2 oximeter, Medlab).
- Resting brachial artery blood pressure (unaffected limb) was measured with a calibrated mercury sphygmomanometer in accordance with the Joint National Committee VI.<sup>27</sup>
- Body mass index (BMI) was calculated using a calibrated weighing scales and metre rule.

- Fasting lipids were measured from blood samples obtained by venipuncture following overnight fasting by the subjects. Serum was analysed for total cholesterol and triglycerides. HDL cholesterol was determined from plasma. Low-density lipoprotein (LDL) cholesterol calculated using the Friedewald equation.<sup>28</sup>
- Frenchay Activity Index<sup>17</sup> and HADS<sup>18</sup> forms were filled in by all participants.
- Spirometry testing was performed with the participant in upright sitting using the Microlab 3300 (Micro Medical Limited). Routine use of respiratory medications including inhalers was permitted.

#### Data analysis

Data were entered onto the Statistical Package for the Social Sciences (SPSS) version 12. Analysis performed was on an intention to treat basis and

as such final scores are included on patients who failed to complete the intervention.<sup>29</sup> Change scores were compared between groups using independent *t*-tests where data were interval or ratio level and conformed to the assumptions of normality. Mann-Whitney non-parametric tests were otherwise used. Ancillary analysis included single-group analysis using paired *t*-tests and Wilcoxon signed ranks test.

#### Results

Demographic and clinical characteristics of the intervention and control groups are presented in Table 1. Forty-eight subjects entered the trial with participant flow represented in Figure 1.

No change in cholesterol lowering medication was reported in either group. Three control subjects had blood pressure medication changes during the trial: subject 4, from hypertension

**Table 1** Baseline and clinical descriptives

Baseline descriptives	Control ( <i>n</i> = 24) Mean (SD)	Active ( <i>n</i> = 24) Mean (SD)
Age (years)	60.5 (10.0)	59.0 (10.3)
Time since cerebrovascular accident (CVA) (weeks)	245.3 (169.8)	237.3 (110.7)
	<i>n</i> (%)	<i>n</i> (%)
Male	14 (58%)	14 (58%)
Female	10 (42%)	10 (42%)
Right CVA	11 (45%)	13 (54%)
Left CVA	13 (54%)	11 (45%)
Oxfordshire Stroke Subtype Classification		
Total anterior circulation infarct (TACI)	1 (4.2%)	3 (12.5%)
Partial anterior circulation infarct (PACI)	12 (50%)	9 (37.5%)
Lacunar infarct (LACI)	5 (20.8%)	7 (29.2%)
Posterior circulation infarct (POCI)	3 (12.5%)	2 (8.3%)
Unknown	3 (12.5%)	3 (12.5%)
Functional Ambulation Category		
0	1 (4.2%)	0 (0%)
1	2 (8.3%)	3 (12.5%)
2	1 (4.2%)	1 (4.2%)
3	1 (4.2%)	1 (4.2%)
4	6 (25%)	4 (16.7%)
5	13 (54.2%)	15 (62.5%)
Known cardiac history		
Ischaemic heart disease	1 (4.2%)	3 (12.5%)
Myocardial infarct	1 (4.2%)	0 (0%)
Coronary artery bypass graft	0 (0%)	1 (4.2%)
Atrial fibrillation	2 (8.3%)	2 (8.3%)
Recurrent stroke	3 (12.5%)	4 (16.7%)