Cardiovascular disease (CVD) is the leading cause of death after stroke [1]. Cardiovascular abnormalities can be causal, consequential, or coincidental in stroke. Since the presence of CVD can adversely affect maximal oxygen uptake (VO\textsubscript{2max}), the most widely used index of exercise capacity [2], limited exercise capacity (i.e. the ability to respond to physiologic stresses induced by prolonged physical effort) is likely to further disable stroke patients in their ability to carry out routine functional tasks and extended activities of daily living. Hence, cardiovascular and neuromuscular impairments, together with physical inactivity resulting from stroke, adversely affect exercise capacity.

Patients in the chronic post stroke period (>6 months) were reported to have abnormally low peak oxygen uptake (VO\textsubscript{2peak}) levels, approximately 25–45% below that of age- and sex-adjusted normative values for sedentary individuals [3,4]. Similarly, the mean VO\textsubscript{2peak} about 1 month post stroke was 60% of the normative values for sedentary healthy individuals [5]. Although survivors of stroke often have poor VO\textsubscript{2peak}, fitness training has not been a standard component of stroke rehabilitation. Instead, strengthening, coordination, and self-care abilities have been the focus of rehabilitation after neurologic status becomes stable. Therefore, exercise testing is critical for the safe design of fitness exercise prescription. However, there are serious barriers to the assessment and treatment of limited aerobic capacity after stroke. Treadmill exercise testing can be used to diagnose exercise-induced cardiac risk and to devise an exercise prescription. However, standard treadmill testing can be very difficult in post-stroke survivors because of impairments in leg and trunk strength and in coordination. Cycle ergometry is
generally preferred to the treadmill because it can more precisely estimate the work rate (i.e. oxygen uptake of work performance and work efficiency) and oxygen utilization by the muscle cells in relation to the quantity of external work [6]. More importantly, cycle ergometry provides advantages over treadmill for post stroke survivors with impairments in walking and balance [3].

Despite the high risk for limited aerobic capacity, exercise testing has not been documented during the post-acute stage after stroke. During this period of time, stroke rehabilitation takes place and the potential for functional improvement would be much greater if an effective and appropriate exercise program can be established after exercise testing. Therefore, the purposes of this study were to investigate the feasibility of cycle ergometry exercise testing, and to evaluate exercise performance in patients with post-acute stroke.

**MATERIALS AND METHODS**

**Subjects**

All patients with their first primary diagnosis of stroke, as confirmed by clinical and radiographic means, and who were admitted to the acute stroke service of Kaohsiung Medical University Medical Center, were consecutively screened for eligibility. Eligible patients included those aged ≥18 years of age within 2 weeks post stroke, with no evidence of dementia (as indicated by a score ≥24 of 30 on the Mini-Mental State Examination) [7] or coronary artery disease (as indicated by the presence of at least 1 of the following: myocardial infarction by history or electrocardiogram, angina pectoris, percutaneous coronary intervention, or coronary artery bypass graft surgery) [8], Brunnstrom recovery scales of greater than stage 2 for the lower limb (where active voluntary movement is present without facilitation) [9], and who had no contraindications for exercise testing as outlined by the American College of Sports Medicine [10].

The clinical history and medical examination were recorded for each subject enrolled, including smoking habits and comorbidities (such as hypertension, diabetes mellitus, and chronic obstructive pulmonary disease). Spasticity of the hemiparetic lower limb was evaluated by the modified Ashworth Scale [11]. None of the subjects had any significant physical training prior to stroke. None were trained cyclists. The prospective subjects were informed of the procedures, the known risks and benefits, and gave signed informed consent. The study was approved by the Human Experiment and Ethical Committee at Kaohsiung Medical University Hospital. Remuneration was not offered.

**Anthropometry and respiratory function**

Body height and weight were measured following standard techniques with the subjects in light clothes without shoes. Body height was measured to the nearest 0.5 cm and body weight was measured with a precision of ±0.1 kg.

Forced spirometry was assessed using a digital computer-based spirometer (microQuark; COSMED; Rome, Italy). Vital capacity and forced expired volume in 1 second were calculated from the flow-volume curves. Maximal voluntary ventilation (MVV) was directly estimated. The highest values of at least three measurements were used.

**Exercise tests**

All testing was performed on a calibrated electromagnetically braked cycle ergometer (Corival V2; Lode BV, Groningen, the Netherlands). During the testing, the subjects were seated in an upright position on the cycle with their hands in a relaxed position on the handlebars. The exercise testing was performed according to the 5-W ramp-incremental protocol for stroke patients to either voluntary exhaustion or the inability to maintain a pedaling rate of 50 rpm [12]. The subjects were required to maintain a constant pedaling rate at 60 rpm at all power outputs. Tests were terminated in accordance with American College of Sports Medicine guidelines [10]. Expired gas was analyzed by open-circuit spirometry using a gas analyzer (Meta-Max 3B; CORTEX Biophysik GmbH, Leipzig, Germany) to determine VO2, carbon dioxide production, minute ventilation (MV) and respiratory exchange ratio (RER). Volume and gas calibration using standard gases were done before each test. The patient wore a mask and breathed through a two-way directional valve system. An electrocardiogram provided continuous monitoring of heart rate (HR) and cardiac electrical activity. Left brachial artery systolic and diastolic blood pressure (BP) was measured using a calibrated mercury sphygmomanometer after a 4-minute rest, every 3 minutes during exercise, and every minute during recovery until BP returned to baseline.

Tests were stopped when abnormal BP responses were observed [10], including hypertensive responses
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(systolic BP > 210 mmHg or diastolic BP > 115 mmHg) when exercising at high work rate, or hypotensive responses (decrease in BP > 10 mmHg) despite an increase in work rate.

Resting measurements were determined during the 4th minute of the rest period. Peak values were the averages of values recorded during the last 30 seconds of the test. Oxygen pulse (O2 pulse) in milliliters of oxygen per beat (VO2/HR) and ventilatory reserve as a percentage (VEpeak/MVV) were calculated. We selected VO2peak as the measure of exercise capacity. Anaerobic threshold (AT) was determined using the V-slope method [13]. Age-predicted maximal heart rate (HRmax) was determined as 220 – age (years). The criteria for attainment of VO2max included: (1) an increase in VO2 of < 150 mL in the final minute of exercise, (2) RER > 1.0, and (3) HRpeak within 15 beats/min of age-predicted HRmax [14].

Statistical analysis
Descriptive analyses were initially performed to evaluate the distributions of the variables. Means and standard deviations were calculated for continuous variables. Frequencies and percentages were calculated for categorical variables.

RESULTS

Subjects characteristics
Of the 21 subjects enrolled in the study, two did not perform a steady rate of cycling at zero load, and were subsequently withdrawn from the study. The 19 subjects’ demographic and clinical characteristics are summarized in Tables 1 and 2. Brunnstrom recovery scale for the leg was stage 3 for four subjects (21.1%), stage 4 for eight subjects (42.1%) and stage 5 for seven subjects (36.8%). The modified Ashworth Scale score for the leg was 0 for 17 subjects (89.5%) and 1 for two subjects (10.5%). Resting systolic and diastolic BP was 130±14 mmHg and 85±11 mmHg, respectively. All of the subjects were tested within 2 weeks post stroke. Of the 12 subjects with a history of smoking, none had quit prior to the time of their stroke.

Measures of exercise testing
No adverse events occurred during or after the tests. All subjects terminated testing of their own volition, the most common reasons for termination being leg fatigue and a drop in pedaling rate (< 50 rpm). All subjects were closely monitored after the tests. There were no other symptoms, electrocardiographic abnormalities, or adverse effects during or after the tests. Post-exercise systolic and diastolic BP was 164±26 mmHg and 98±10 mmHg, respectively.

Measurements of respiratory function and peak exercise intensity are summarized in Tables 3 and 4, respectively. Left and right hemiplegic stroke subjects demonstrated no significant difference in any measured variable. Similarly, there was no difference between subjects with and without diabetes, hypertension, and hyperlipidemia, or between smokers and nonsmokers. Only two subjects achieved both RER and HRpeak criteria. Fifteen (78.9%) subjects reached RER > 1.0. The HRpeak criteria was attained by two subjects, whereas

Table 1. Stroke characteristics of subjects with post-acute stroke* (n = 19)

<table>
<thead>
<tr>
<th>Type of stroke</th>
<th>Ischemic 17 (89.5)</th>
<th>Hemorrhagic 2 (10.5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemiparetic side</td>
<td>Right 11 (57.9)</td>
<td>Left 8 (42.1)</td>
</tr>
<tr>
<td></td>
<td>Bilateral 0 (0)</td>
<td></td>
</tr>
<tr>
<td>Brunnstrom recovery scales for leg</td>
<td>4.2±0.8 (3–5)</td>
<td></td>
</tr>
<tr>
<td>MAS for leg (score)</td>
<td>0.2±0.4 (0–1)</td>
<td></td>
</tr>
<tr>
<td>Time post stroke (d)</td>
<td>9.9±2.0 (8–14)</td>
<td></td>
</tr>
</tbody>
</table>

*Data presented as n (%) or mean±standard deviation (range). MAS = modified Ashworth Scale.

Table 2. Demographic and clinical characteristics of subjects with post-acute stroke* (n = 19)

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>62.7±9.2 (47–81)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height (cm)</td>
<td>166.7±1.2</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>70.0±2.0</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>24.1±0.6</td>
</tr>
<tr>
<td>Medications</td>
<td></td>
</tr>
<tr>
<td>Calcium-channel blockers</td>
<td>8 (42.1)</td>
</tr>
<tr>
<td>Angiotensin II receptor blockers</td>
<td>10 (52.6)</td>
</tr>
<tr>
<td>Antiplatelets</td>
<td>16 (84.2)</td>
</tr>
<tr>
<td>Anticoagulants</td>
<td>1 (5.3)</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>13 (68.4)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>17 (89.5)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>8 (42.1)</td>
</tr>
<tr>
<td>History of smoking</td>
<td>12 (63.2)</td>
</tr>
</tbody>
</table>

*Data presented as n (%) or mean±standard deviation (range).
AT relative to VO2peak (AT of VO2peak) was 73.4%.

**DISCUSSION**

This study has demonstrated the response of patients in the post-acute stroke period to maximal cycling ergometry testing. As early as 1 week after a stroke, cycle ergometry exercise testing is feasible and safe in post-acute stroke survivors who have been thoroughly screened.

Stroke and CVD represent forms of atherosclerotic vascular disease and occur in patients with similar risk profiles [1]. Therefore, patients with stroke are expected to have increased risk for coexistent CVD and for coronary events such as death and nonfatal myocardial infarction.

Before fitness training can be started as part of stroke rehabilitation, its safety must be addressed in this high-risk population. Cycle ergometry exercise testing provides an opportunity for safety screening before fitness training. Indeed, based on our findings, cycle ergometry is feasible during the post-acute stage after stroke. Almost all of our subjects (90.5%) completed the testing. Most subjects in previous studies terminated the test because of exhaustion without reaching the predicted HRmax or because of hypertensive or hypotensive responses [15,16], whereas most of the subjects in our study (78.9%) reached RER > 1.0. Exhaustion is a realistic indicator of functional capacity [12]. The rigorous criteria for VO2max are seldom met by deconditioned or elderly individuals [14], which would include most patients with stroke. The exercise testing in the present study allows for the assessment of symptoms, signs, and electrocardiographic abnormalities. The exaggerated BP response to exercise also predicts future adverse cardiovascular events and mortality [15,17]. Accordingly, this testing is feasible for assessing the safety of exercise before commencing a training program in post-acute stroke patients. It should be noted that none of the subjects had ischemic exercise responses in this study. This might be considered an exclusion criterion and subjects with recent cardiac events or symptoms of angina should be deemed ineligible.

With VO2peak of 11.8 mL/kg/min, aerobic capacity is significantly compromised in the post-acute period after stroke and is lower than the 15 mL/kg/min required for independent living [18]. For patients in the sub-acute period after stroke despite using semirecumbent cycle ergometry and wider post stroke intervals, Tang et al [19] documented VO2peak values of 10–11 mL/kg/min, which is comparable with the mean VO2peak in our study. In a study of patients at 2.5 months post stroke [20], the VO2peak was 11.4 mL/kg/min, again consistent with our observation. In the body weight suspension treadmill exercise study by MacKay-Lyons et al [5], VO2peak was 14.4 mL/kg/min in patients at 1 month post stroke. The cycle ergometry exercise testing typically yields lower VO2peak values than treadmill testing. Aerobic capacity was previously shown to be limited in chronic stroke patients using cycle ergometry [3]. Mean VO2peak values ranging from 13.3 mL/kg/min to 17.3 mL/kg/min have been reported, higher than in our study. In contrast to the possible increase in aerobic capacity over time post stroke [4], it seems there is increase from the post-acute to the sub-acute period post stroke.

| Table 3. Respiratory function measurements of subjects with post-acute stroke* (n = 19) |
| Parameters | VC (L) 3.0 ± 0.1 | FEV1 (L) 2.5 ± 0.1 | FEV1/VC (%) 84.4 ± 1.8 | MVV (L/min) 63.9 ± 5.1 |
| *Data presented as mean ± standard deviation. VC = Vital capacity; FEV1 = forced expired volume in one second; MVV = maximal voluntary ventilation. |

| Table 4. Peak exercise testing measurements of subjects with post-acute stroke* (n = 19) |
| Parameters | VO2peak (mL/min) 792.0 ± 69.4 | VO2peak (mL/kg/min) 11.8 ± 0.8 | MEpeak (L/min) 29.2 ± 2.5 | VR (%) 48.1 ± 16.8 |
| | HRpeak (beats/min) 107.7 ± 5.3 | HRpeak of predicted HRmax (%) 67.9 ± 3.4 | O2 pulsepeak (mL/beat) 7.5 ± 0.5 | RER 1.1 ± 0.1 |
| | AT (mL/min) 569.0 ± 50.8 | AT (mL/kg/min) 8.4 ± 1.8 | AT of VO2peak (%) 73.4 ± 3.2 | Peak workload (W) 46.5 ± 6.7 |
| *Data presented as mean ± standard deviation. VO2 = Oxygen uptake; MV = minute ventilation; VR = ventilatory reserve; HR = heart rate; RER = respiratory exchange ratio; AT = anaerobic threshold. |
However, the extent to which early fitness training contributes to rehabilitation outcomes after stroke still needs to be evaluated.

The mean AT value in our study (569.0 mL/min or 8.4 mL/kg/min) is substantially lower than $1 \times 10^3$ mL/min [21]. As an effort-independent measurement, the AT might aid clinical decisions in terms of fitness training [22]. Tang et al reported AT values of 8.7–9.3 mL/kg/min and 86.8–87.4% of VO$_{2\text{peak}}$ [19], which is higher than those of our subjects. This might be partly due to the different methods of determining the AT and the wider age range of the subjects in the study by Tang et al. Indeed, comparisons between our results and previously published results are limited because earlier studies included patients with longer and wider post-stroke intervals, and there are marked differences in the distributions of age and sex. However, the consistent finding of low exercise capacity is clinically meaningful. Post-acute stroke survivors have such severe exercise limitations that they reach aerobic capacity and AT at low work rates that would interfere with self-care activities and daily function.

The decreased exercise capacity found here is supported by other indices of cardiopulmonary exercise response. The HR$_{\text{peak}}$ percent of the predicted HR$_{\text{max}}$ (67.9±3.4%), as a marker for the relative level of physical exertion, is substantially compromised and is <90% of the age-predicted HR$_{\text{max}}$ [22]. Yates et al reported HR$_{\text{peak}}$ of 116 beats/min and an HR$_{\text{peak}}$ percent of predicted HR$_{\text{max}}$ of 77%, which are similar to those in our study. Also, the peak O$_2$ pulse decreases, indicating worsening of tissue extraction of oxygen from the blood ejected with each heart beat [23]. As indirect evidence of cardiac abnormalities or peripheral muscle impairment for oxygen utilization, the mechanism underlying the reduction in exercise capacity post-stroke remains to be investigated.

The reduction in MV$_{\text{peak}}$ and MVV, representing ventilatory capacity, is significant in the post-acute stroke period. MacKay-Lyons et al [5] documented a much higher mean MV$_{\text{peak}}$ (42.1 L/min) despite using the treadmill, a method that typically yields similar MV$_{\text{peak}}$ values to the cycling ergometer [24]. In addition, the MVV was less than the indirect MVV (forced expired volume in 1 second × 40) (93.8 L/min) in our subjects. It was previously recommended that respiratory function after stroke is often only modestly affected, notwithstanding the relatively high occurrence of acute respiratory complications [25]. Although poor cooperation or effort in the performance of the MVV maneuver, extreme obesity, or inspiratory obstruction may be possible causes [26], it is likely that the decreased MVV is very dependent on the subject’s poor effort and technique of performance due to neurologic deficits post stroke. Moreover, the ventilatory reserve values in the current study are equal to the low end of the reported values for normal subjects (50%) [27]. This suggests that respiratory impairments do not substantially contribute to the reduced exercise capacity post-stroke.

Our present results must be interpreted with caution because we used a small sample of males, and we used an uncontrolled study design. Further studies are needed to establish valid measures of cardiopulmonary response over a wider age range in males and females in the post-acute stroke period to accurately evaluate exercise capacity. This will be important in future research to establish valid measures of BP response to exercise, with respect to the optimal BP management during the post-acute phase of stroke. In addition, although the findings of ventilatory capacity suggest that respiratory impairments modestly affect exercise capacity post stroke, the relative contributions of neuromuscular, cardiovascular, and respiratory impairments to the reduction in exercise capacity also need to be clarified. Future research is needed to establish the relationship between exercise capacity and varying levels of motor control impairment and different stages of recovery to effectively establish appropriate rehabilitation programs in patients post stroke.

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REFERENCES

急性期後腦中風患者的心肺運動功能的初步研究

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本文的目的在探討踏車式心肺功能運動測試對於急性期後腦中風患者的應用及腦中風
患者在急性期後的心肺運動功能的評估分析。19 位平均年齡為 62.7 ± 9.2 歲的腦中
風患者，在平均腦中風後 9.9 ± 2.0 天，進行漸增式心肺運動功能測試。以開放式肺
量計量測標準直立式踏車運動的尖峰心肺運動能力。平均尖峰攝氧量為 11.8 mL/
kg/min，尖峰心跳率為年齡決定預測最大心跳率的 67.9 ± 3.4%，尖峰氧氣心搏量
為 7.5 mL/beat。無氧閾值為尖峰攝氧量的 73.4%。平均尖峰每分鐘換氣量為 42.1
L/min，呼吸儲備值為 48.1 ± 16.8%。本研究顯示在腦中風後 2 週內即可用踏車式
運動測試評估患者的心肺運動功能，及患者的心肺運動能力是受損的。而肺功能障礙
可能並不是造成急性期後腦中風患者心肺運動能力障礙的成因。

關鍵詞：有氧運動能力，運動測試，急性期後腦中風
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