





# The safety and feasibility of early cardiorespiratory fitness testing after stroke

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## Abstract

**Background:** Cardiorespiratory fitness testing is recommended as part of a pre-exercise evaluation to aid the programming of safe, tailored cardiorespiratory fitness training after stroke. But there is limited evidence for its safety and feasibility in people with stroke with varying impairment levels in the early subacute phase of stroke recovery.

**Objective:** To assess the safety and feasibility of cardiorespiratory fitness testing in the early subacute phase after stroke.

**Design:** A sub-study of a larger single service, multi-site, prospective cohort feasibility study (Cardiac Rehabilitation in Stroke Survivors to Improve Survivorship [CRiSSIS]).

**Setting:** Private subacute inpatient rehabilitation facilities.

**Participants:** Consecutive admissions of people with ischemic stroke admitted to subacute rehabilitation facilities.

**Intervention:** Not applicable.

**Main Outcome(s):** Safety was determined by the occurrence of adverse or serious adverse events. Feasibility was determined by assessing the (1) number of participants recruited and (2) number of participants able to complete the fitness test.

**Results:** Between April 2018 and December 2019, a total of 165 people with stroke were screened to participate; 109 were eligible and 65 were recruited. Of the 62 who completed testing, 41 participants were able to complete a submaximal fitness test at a median of 12 days post-stroke. One minor adverse event was recorded. Of the 21 participants unable to complete the fitness test; 4 declined to complete the test, 9 were unable to commence the test, and 8 were unable to complete the first stage of the protocol due to stroke-related impairments. Participants with mild stroke, greater motor and cognitive function, and fewer depressive symptoms were more likely to be able to complete the cardiorespiratory fitness test.

**Conclusion:** Cardiorespiratory fitness testing was safe for most people with mild-to-moderately severe ischemic stroke and transient ischemic attack in the early subacute phase, but only two-thirds of the participants could complete the test.

## INTRODUCTION

Clinical stroke guidelines recommend that all people with stroke or people who have experienced a transient ischemic attack should undergo a pre-exercise evaluation,

including a graded cardiorespiratory fitness test, prior to commencing cardiorespiratory fitness training.<sup>1,2</sup> Cardiorespiratory fitness testing is utilized to evaluate an individual's aerobic capacity, monitor exertional symptoms such as heart rate and blood pressure during exercise, and

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support the prescription of individualized cardiorespiratory fitness training.<sup>3</sup> However, cardiorespiratory fitness testing after stroke or transient ischemic attack is not commonplace,<sup>4,5</sup> resulting in therapists lacking the necessary information to deliver safe, individualized cardiorespiratory fitness training.<sup>3</sup> This suggests a possible knowledge gap in the current literature, and may contribute to clinician hesitancy to implement early-initiated cardiorespiratory fitness testing in people with stroke.

The gold standard in cardiorespiratory fitness testing is an assessment of the maximal volume of oxygen consumption ( $VO_{2max}$ ) during a graded cardiorespiratory fitness test. However, maximal fitness testing is often impractical in clinical practice as it requires expensive, laboratory-based equipment and trained personnel to administer the test. It can also be costly and time consuming to complete. In people with stroke, stroke-specific impairments, including muscle weakness, contractures, and spasticity, can limit the ability to achieve maximum capacity using standard maximal fitness tests.<sup>6</sup> The risk of an abnormal response is also increased (ie, exaggerated hypertensive response) at or near maximal exercise intensity.<sup>7,8</sup> Sub-maximal cardiorespiratory fitness testing is an alternative method of measuring cardiorespiratory fitness. It is recommended when exercising at moderate intensity,<sup>7</sup> and may be more tolerated by people with stroke.<sup>6</sup>

Despite barriers to the uptake of cardiorespiratory fitness testing (ie, stroke-related impairments, testing being costly and time consuming), the safety and feasibility of fitness testing in chronic stroke has been well documented.<sup>9-12</sup> Less is known in early subacute stroke. Few studies have tested the safety and feasibility of cardiorespiratory fitness testing in the early subacute phase of stroke recovery.<sup>13-15</sup> However, these studies recruited people with predominantly mild stroke or transient ischemic attack with minimal stroke deficits.<sup>13-15</sup> Further studies are required to determine if cardiorespiratory fitness testing in the early subacute phase of stroke recovery is safe and feasible for people with a broader range of impairments. There is also a need to identify the specific characteristics of people with stroke that may influence their capacity to participate in and complete a cardiorespiratory fitness test. The sex of a person, for example, can have a direct impact on cardiorespiratory fitness indicators<sup>16</sup> and reduce the likelihood of participation in structured exercise programs.<sup>17</sup> This, in combination with other characteristics such as level of disability and mood, may impact the likelihood of people with stroke initiating or engaging in physical exercise.<sup>18-20</sup> Identifying the characteristics that influence engagement and participation in cardiorespiratory fitness testing may improve a clinician's understanding of which people with stroke to target for cardiorespiratory fitness interventions in the early subacute phase of stroke recovery.<sup>18-20</sup>

The aim of this study was to assess the safety and feasibility of cardiorespiratory fitness testing in the early subacute phase of stroke recovery. The secondary aim of this study was to describe the characteristics of people with stroke that can complete a cardiorespiratory fitness test in this study population. We hypothesized that (1) submaximal cardiorespiratory fitness testing would be safe and feasible for the majority of people in the early subacute phase of stroke recovery; and (2) participant characteristics, such as lesser stroke severity, lower levels of impairment, and greater mood state and quality of life (QoL) would be associated with a greater capacity to complete a cardiorespiratory fitness test in the early subacute phase of stroke recovery.

## METHODS

### Study design

This was a sub-study of a larger single service, multi-site, prospective cohort feasibility study (Cardiac Rehabilitation in Stroke Survivors to Improve Survivorship [CRiSSIS]). CRiSSIS had ethical approval from Epworth HealthCare Human Research Ethics Committee (ID: EH2017-282), and the University of Melbourne Psychology Health and Applied Sciences Human Ethics Sub-Committee (ID: 1954294).

### Participants

We screened all consecutive rehabilitation inpatient ischemic stroke admissions to two private inpatient rehabilitation sites at Epworth HealthCare in Melbourne, Australia, from April 2018 to December 2019. All participants provided informed written consent, or if unable to physically sign for themselves due to stroke-related impairments, had a person responsible sign by proxy before inclusion in the study. Participants were eligible to participate if they were: (1) >18 years of age, (2) diagnosed with an acute ischemic stroke or transient ischemic attack, (3) able to provide consent, and (4) able to comprehend verbal and/or written commands. Participants were excluded from the study if they (1) sustained a hemorrhagic stroke, (2) were pregnant, (3) had significant musculoskeletal or pain issues that precluded completion of the fitness test, or (4) had contraindications to cardiorespiratory fitness testing as per the American College of Sports Medicine (ACSM).<sup>21</sup> Participants completed testing as soon as possible once eligibility was determined.

### Procedure

Demographic data (ie, participant's age and stroke diagnostics) were extracted from each participant's

on-site medical record. All participants completed the testing session, which took ~1 hour, while inpatients at an Epworth HealthCare rehabilitation facility. All baseline outcome measures were collected by two investigators (N.M. and L.J.) and a research assistant. All were certified to conduct the National Institute of Health Stroke Scale (NIHSS) and the Modified Rankin Scale (mRS).

## Outcome measures

### Cardiorespiratory fitness

Participants completed a symptom-limited, sub-maximal, graded cardiorespiratory fitness test utilizing the YMCA protocol<sup>22</sup> on an upright cycle ergometer (Monark 928E and 828E; Sweden). Where feasible, participants were instructed to limit food or drink within 2 to 3 hours of the cardiorespiratory fitness test and to avoid caffeine for 6 hours prior to the test. Resting heart rate, blood oxygen saturation (Nonin Onyx Vantage 9590; Plymouth, MN) and blood pressure (Omron HEM-7121/HEM-7322; Kyoto, Japan) were obtained prior to testing. Participants were positioned on the cycle ergometer and seat height was adjusted so that the participant's knee was slightly bent (~5°) at the bottom of the revolution with a neutral ankle. Participants were instructed to pedal at a rate of 60 rpm, commencing at a resistance of 30 watts and increased every 3 minutes as per test protocol (Table 1).<sup>23</sup> The test was terminated if: (1) the test was completed, (2) participants reached volitional fatigue, (3) participants achieved 85% of their age-predicted maximal heart rate ( $HR_{max}$ ) ( $0.85 \times [220 - \text{age}]$  or  $[164 - 0.7 \times \text{age}] \times 0.85$  for those on beta blockers)<sup>24</sup>, or (4) participants experienced signs/symptoms necessitating cessation of the test (ie, feeling faint). A participant was required to complete at a minimum the first stage (ie, 3 minutes at 30 watts) of the test, for it to be considered valid.

### Anthropometric measures

Height and weight were used to determine body mass index (BMI). Participants' weight was assessed using

either digital (A&D Medical Australasia HV-150KA1; Adelaide, Australia) or analogue (Proper Speedmeter, McGloins Supertex; New South Wales, Australia) scales and height was assessed utilizing a fixed stadiometer (Seca 206, Seca GMBH & Co.kg; Hamburg, Germany). The participants stood bare foot for the height and weight measurement and wore light clothing where possible.

### Fatigue

Fatigue was assessed using the 10-item Fatigue Assessment Scale (FAS),<sup>25</sup> with scores ranging from 0 to 50. Items are scored from 1 to 5 (1 = never to 5 = always affected by fatigue) with items four and 10 reverse scored. The total FAS score is the sum of all 10 items. Fatigue is rated as no fatigue (FAS 10 to 21), fatigue (FAS 22 to 34), and extreme fatigue (FAS  $\geq 35$ ).<sup>25</sup> This scale has been validated in people with stroke.<sup>26</sup>

### Stroke severity

The NIHSS is a measure of stroke severity that is recommended by the Stroke Recovery and Rehabilitation Roundtable (SRRR).<sup>27</sup> Scores range from 0 to 42, with the total NIHSS score being the sum of all items. Stroke severity is rated as no symptoms (NIHSS 0), mild (NIHSS 1 to 4), mild-to-moderately severe (NIHSS 5 to 14), severe (NIHSS 15 to 24), and very severe (NIHSS  $\geq 25$ ).<sup>28</sup>

### Degree of disability

The mRS is an assessment of post-stroke level of disability recommended by the SRRR.<sup>27</sup> Scores range from 0 (no symptoms) to 6 (death), with higher scores signifying greater disability. Functional status is rated as independent (mRS 0 to 2) or dependent (mRS  $> 2$ ).<sup>29</sup>

### Motor and cognitive function

The Functional Independence Measure (FIM) assesses an individual's capacity to perform activities of daily

**TABLE 1** Submaximal cardiorespiratory fitness test protocol stages based on heart rate

Stage 1 begins at 30 W				
	If HR <80 bpm	If HR 80-89 bpm	If HR 90-100 bpm	If HR >100 bpm
Stage 2	125 W	100 W	75 W	50 W
Stage 3	150 W	125 W	100 W	75 W
Stage 4	175 W	150 W	125 W	100 W

Abbreviation: bpm, beats per minute; HR, heart rate; W, watts. Reprinted with permission from Billinger, et al. (2012).<sup>23</sup>

living. Each item is scored on a 7-point ordinal scale with the total score being the sum of 18 items. Scores range from 18 (total assistance in all areas) to 126 (independence in all areas) and can be broken down into motor (scores ranging from 13 to 91) and cognitive (scores ranging from 5 to 35) components. Lower scores indicate lower motor and cognitive function. The FIM has been validated in people with stroke.<sup>30</sup>

## Mood

The Patient Health Questionnaire-9 (PHQ-9) is a 9-item depression screening tool with scores ranging from 0 to 27, with higher scores indicating a greater impact of depressive symptoms more frequently. Depression was rated as no depressive symptoms (PHQ-9, 0), minimal depression (PHQ-9, 1 to 4), mild depression (PHQ-9, 5 to 9), moderate depression (PHQ-9, 10 to 14), and moderately-severe depression (PHQ-9, 15 to 19).<sup>31</sup> This scale is a reliable measure of depression in people with stroke.<sup>32</sup>

## Health-related quality of life (QoL)

The EuroQoL-5D-5L (EQ-5D-5L) is a self-report questionnaire of health status that has been validated in stroke<sup>33</sup> and is recommended by the SRRR.<sup>27</sup> Participants rate their overall health status in five domains; mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Participants record level of difficulty on a five-point scale for each domain, where 1 is no problem; 2 is slight problem; 3 is moderate problem; 4 is severe problem; and 5 is unable to perform/extreme problem.<sup>34</sup> Health status was converted to a utility index value using the crosswalk methodology, with the United Kingdom value set, where 1.0 indicates best health status and -0.111 indicates worst health status.<sup>34</sup> Participants also recorded their subjective global health rating on a visual analogue scale of 0 to 100, with higher scores indicating greater health-related QoL.

## Primary outcomes

### Safety

Safety was assessed by recording all adverse events during testing. An adverse event was defined as any untoward medical occurrence (ie, exacerbation of a pre-existing condition or a new condition or diagnosed after participation in the study) experienced by participants during or immediately following the cardiorespiratory fitness test. A serious adverse event was defined as an event resulting in death, was life-

threatening, required hospitalization or prolonged existing hospitalization, or resulted in disability (substantial disruption to a person's ability to function) or incapacity.<sup>35</sup>

## Feasibility

Study feasibility was determined by assessing process and resources feasibility,<sup>36</sup> including:

- The number of participants recruited.
- The number of participants able to complete the cardiorespiratory fitness test.
- The reasons for participants being unable to commence or complete the cardiorespiratory fitness test.

Inability to complete cardiorespiratory fitness testing was determined if: (1) participants declined to participate in the test before an attempt was made, (2) participant impairments precluded commencement of the test (ie, participants were not able to mount the bike even with assistance), or (3) participants were unable to complete the first stage of the testing protocol (pedal at 60 rpm against 30 watts resistance for 3 minutes).

## Demographic variables

Age, sex, stroke severity, and time post-stroke were assessed to demographically characterize the participants enrolled into the study.

## Sample size and statistical analysis

This was a safety and feasibility study; therefore, estimation of sample size and assessment of treatment effect was not completed.<sup>37</sup> Descriptive statistics, including mean and standard deviation (SD) for normative data, and median and interquartile range (IQR) for nonparametric data, were used to report demographic and stroke characteristics of the participants as well as secondary outcome measures such as mood state (ie, depression), fatigue, and QoL. Normality was assessed using the Kolmogorov-Smirnov calculation. Differences in secondary outcome measures between participants who were able and unable to complete the test were assessed using the Mann-Whitney *U* test. Male and female participants were assessed separately, as there are known sex differences in cardiorespiratory fitness parameters,<sup>9,16</sup> using the Mann-Whitney *U* test. Statistical analysis was completed using Microsoft Excel and IBM SPSS Statistics for Windows, Version 26 (IBM Corp., Armonk, New York, USA).

## RESULTS

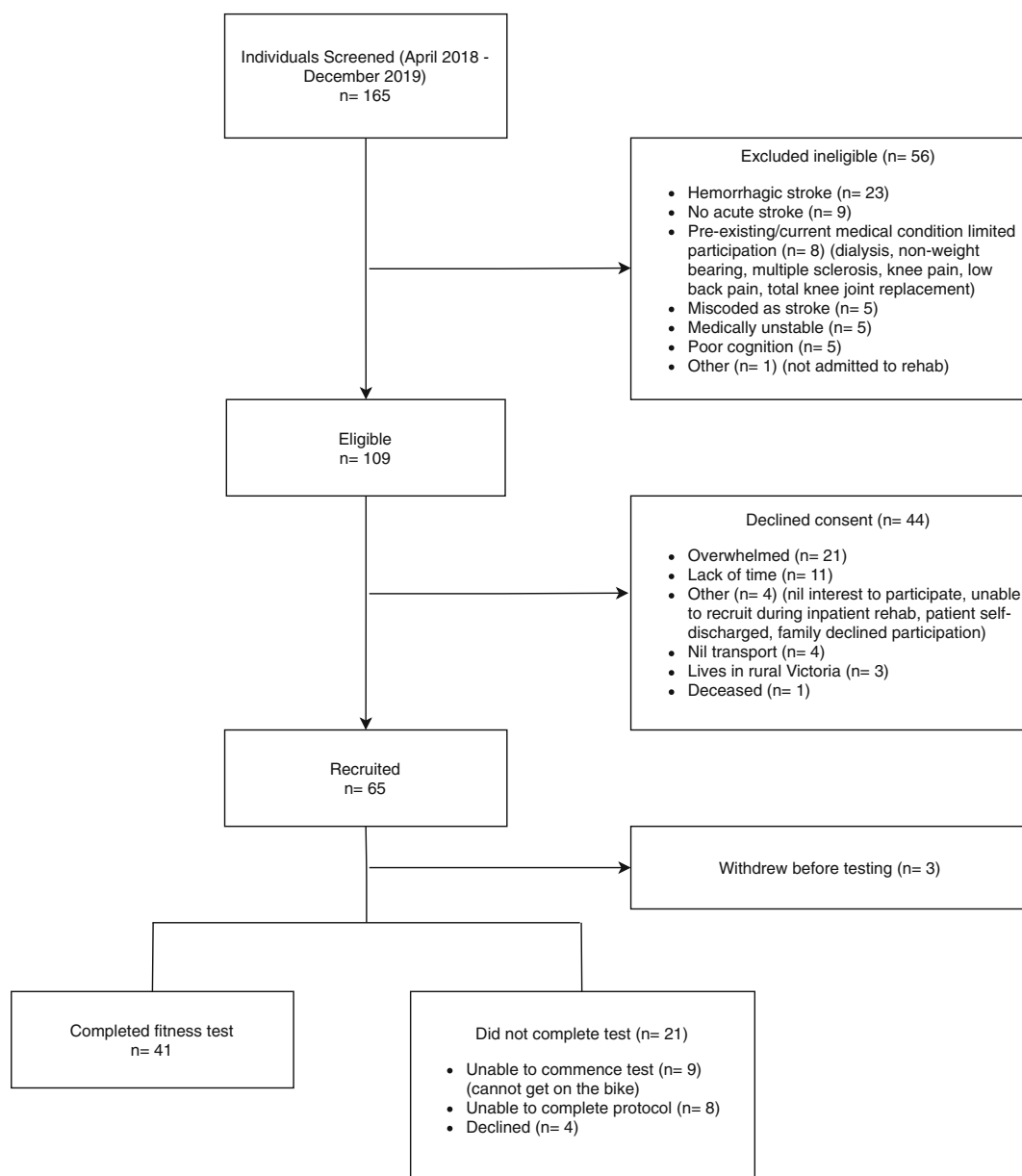
We screened 165 individuals admitted to two Epworth HealthCare subacute rehabilitation facilities, from April 2018 to December 2019. Of those screened, 109 people with stroke (66%) were eligible to participate; 56 people with stroke (34%) were ineligible (Figure 1). Of those who were eligible, 44 (40%) declined consent, mostly due to being overwhelmed at the time of consent (see Figure 1). A total of 65 people with stroke (60%) provided written consent; however, 3 withdrew consent prior to commencing testing. The remaining 62 participants completed this study.

## Safety

There was one minor adverse event (exacerbation of pre-existing knee pain) recorded during fitness testing. However, the participant was still able to continue rehabilitation. There were no cardiovascular adverse events or serious adverse events during or immediately following the cardiorespiratory fitness test.

## Feasibility

Of the 62 recruited participants, 41 completed the fitness test. Of the 21 participants who did not complete



**FIGURE 1** Study recruitment flow diagram



**TABLE 2** Demographic characteristics of study participants

Demographic Characteristics	All participants (n = 62)	Participants able to complete CRF test (n = 41)	Participants not able to complete CRF test (n = 21)	p value
Age (years), mean (SD)	77.2 (9.7)	76.3 (10.1)	78.9 (8.7)	.376
Male, n (%)	32 (51.6)	23 (56.1)	9 (42.9)	
Time post-stroke (days), median (IQR)	13.5 (11-20)	12 (10-18)	16 (11.5-26.5)	.080
Stroke type, n (%)				
Ischemic	60 (96.8)	40 (97.6)	20 (95.2)	
TIA	2 (3.2)	1 (2.4)	1 (4.8)	
BMI, mean (SD)	26.1 (4.9)	26.8 (4.9)	24.7 (4.8)	.086
Cardiovascular risk factors, n (%)				
Hypertension	42 (67.7)	25 (70.0)	17 (81.0)	
Atrial fibrillation	17 (27.4)	11 (26.8)	6 (28.6)	
Hyperlipidemia	16 (25.8)	13 (31.7)	3 (14.3)	
TIA	7 (11.3)	5 (12.2)	2 (9.5)	
Previous stroke	8 (12.9)	3 (7.3)	5 (23.8)	
Type 2 DM	10 (16.1)	6 (14.6)	4 (19.0)	
Ischemic heart disease	11 (17.7)	7 (17.1)	4 (19.0)	
Previous smoker/smoker	3 (4.8)	2 (4.9)	1 (4.8)	
Medications, n (%)				
Beta-blockers	15 (24.2)	9 (22.0)	6 (28.6)	
Hypertensive medication	41 (66.1)	27 (65.9)	14 (66.7)	
Statins	48 (77.4)	34 (82.9)	14 (66.7)	
Blood modifiers	59 (95.2)	39 (95.1)	20 (95.2)	
Diuretics	11 (17.7)	9 (22.0)	2 (9.5)	

Abbreviations: BMI, body mass index; CRF, cardiorespiratory fitness; IQR, interquartile range; SD, standard deviation; TIA, transient ischemic attack; Type 2 DM, type 2 diabetes mellitus.

the test, 4 declined prior to attempting the fitness test (declined with no reason provided  $n = 3$ , anxious  $n = 1$ ), 9 participants were unable to safely mount the bike with assistance, and 8 could not complete the test. Of these eight, six were able to mount the bike but unable to start the test protocol (ie, cycle at 60 rpm or against 30 watts as per protocol) and two participants were able to commence the test but were unable to complete the first stage (ie, 3 minutes) as they were unable to maintain the required 60 rpm cadence (Figure 1).

Of the 41 completed tests, 18 tests were stopped because participants reached 85% of  $HR_{max}$ , 17 were stopped because participants were unable to maintain cycling cadence or cycle against indicated resistance, and 3 tests were ceased due to volitional fatigue. A further 3 tests were stopped without a reason being specified.

There was no significant difference in age ( $p = .376$ ) or time post-stroke between participants who were ( $n = 41$ ) or were not able ( $n = 21$ ) to complete cardiorespiratory fitness testing. The median time post-stroke for completion of the fitness test was 12 days, while the median time post-stroke for those unable to complete the fitness test but complete all other testing (ie, NIHSS) was 16 days (Table 2). Of the

62 enrolled participants, on average each participant had at least two cardiovascular comorbidities, none of which were contraindications to exercise as per the ACSM guidelines.<sup>21</sup> One or more hypertensive medications were prescribed to 41 participants (66%); 48 (77%) were prescribed statins and 59 (95%) were prescribed blood modifiers (Table 2).

There were no significant differences between those able and unable to complete cardiorespiratory fitness testing for levels of fatigue ( $p = .359$ ), BMI ( $p = .086$ ), systolic ( $p = .766$ ) and diastolic ( $p = .876$ ) blood pressure, and health-related QoL (EQ-5D-5L index value  $p = .157$  or subjective health rating  $p = .231$ ). However, people with stroke who were not able to complete the fitness test experienced significantly greater stroke severity, disability, functional impairment (motor and cognitive), and depressive symptoms (Table 3).

### Gender differences in cardiorespiratory fitness indicators

There was no significant difference between male and female participants for final heart rate ( $p = .350$ ) and

**TABLE 3** Outcome measures of study participants able to and unable to complete fitness testing

Outcome measures	All participants (n = 62)	Participants able to complete CRF test (n = 41)	Participants not able to complete CRF test (n = 21)	p value
NIHSS total, median (IQR)	3 (1–5)	2 (1–4)	4 (3–7)	.004
Stroke severity, n (%)				
Nil (NIHSS 0)	4 (6.5)	4 (9.8)	0 (0)	
Mild (NIHSS 1–4)	41 (66.1)	29 (70.7)	12 (57.1)	
Mild-Moderately Severe (NIHSS 5–14)	17 (27.4)	8 (19.5)	9 (42.9)	
Severe (NIHSS 15–24)	0 (0)	0 (0)	0 (0)	
Very Severe (NIHSS ≥25)	0 (0)	0 (0)	0 (0)	
mRS total, median (IQR)	2 (1–3)	2 (1–2)	3 (2–4)	.002
Disability, n (%)				
Independent (mRS 0–2)	41 (66.1)	33 (80.5)	8 (38.1)	
Dependent (mRS >2)	21 (33.9)	8 (19.5)	13 (61.9)	
FIM	<sup>a</sup> n = 61	<sup>a</sup> n = 40		
Motor function, mean (SD)	62.4 (13.7)	67.9 (10.9)	52.1 (12.6)	.000
Cognitive function, median (IQR)	32.0 (28.0–35.0)	35.0 (30.0–35.0)	29.0 (28.0–31.5)	.002
Blood Pressure, mean (SD)				
Systolic	134.2 (19.2)	134.5 (17.4)	133.7 (22.9)	.766
Diastolic	74.5 (10.9)	74.5 (9.6)	74.3 (13.4)	.876
FAS total, median (IQR)	20.5 (16.0–26.0)	20.0 (15.0–26.0)	22.0 (17.0–26.0)	.359
Fatigue, n (%)				
No fatigue (FAS 10–21)	33 (53.2)	23 (56.1)	10 (47.6)	
Fatigue (FAS 22–34)	27 (43.6)	17 (41.5)	10 (47.6)	
Extreme fatigue (FAS ≥35)	2 (3.2)	1 (2.44)	1 (4.8)	
PHQ-9 total, median (IQR)	<sup>a</sup> n = 61 6 (3–9)	<sup>a</sup> n = 41 4.5 (2–9)	7.5 (4.5–9.5)	.042
EQ-5D-5L				
Utility index value, median (IQR)	.735 (.582–.836)	.735 (.632–.837)	.709 (.360–.842)	.157
Subjective health rating (VAS 0–100), mean (SD)	<sup>a</sup> n = 61 62.4 (19.5)	64.9 (19.3)	<sup>a</sup> n = 20 57.3 (19.4)	.231

Abbreviations: CRF, cardiorespiratory fitness; EQ-5D5L, Five-level version of the EuroQol five-dimensional quality of life questionnaire; FIM, Functional Independence Measure; FAS, Fatigue Assessment Scale; IQR, interquartile range; mRS, Modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale; SD, standard deviation; PHQ-9, Patient Health Questionnaire-9; VAS, visual analogue scale.

<sup>a</sup>Missing data: FIM, n = 1; PHQ-9, n = 1; EQ-5D-5L subjective health rating, n = 1.

**TABLE 4** Gender differences for cardiorespiratory indicators

Cardiorespiratory fitness indicators	All participants completing fitness test n = 41	Male n = 23 (56.1%)	Female n = 18 (43.9%)	p value
Age (years), mean (SD)	76.3 (10.1)	74.9 (11.1)	78.1 (7.3)	.486
Final HR (bpm), mean (SD)	106.3 (22.1)	109.4 (20.5)	101.9 (23.8)	.350
Final W, median (IQR)	75.0 (30.0–110.0)	100.0 (50.0–150.0)	50.0 (30.0–75.0)	.005
Test duration (min), median (IQR)	4.5 (3.5–6.8)	6.0 (4.0–8.0)	4.2 (3.2–5.0)	.023
%HR <sub>max</sub> , median (IQR)	82.6 (68.2–85.1)	84.2 (75.9–85.1)	78.9 (62.8–85.2)	.599

Abbreviations: bpm, beats per minute; HR, heart rate; IQR, interquartile range; SD, standard deviation; %HR<sub>max</sub>, percentage of heart rate max; W, watts.

the percentage of HR<sub>max</sub> ( $p = .599$ ) achieved at the completion of the test. However, male participants achieved significantly greater final watts ( $p = .005$ ) and greater total test duration ( $p = .023$ ) (see Table 4).

## DISCUSSION

The results of this study demonstrate that submaximal cardiorespiratory fitness testing was safe for most people

with mild and mild-to-moderately severe ischemic stroke in the early subacute phase of stroke recovery. This further extends the evidence for cardiorespiratory fitness testing for those with mild-to-moderately severe stroke from previous studies reporting the safety of fitness testing early after stroke in non-disabling and very mild stroke participants.<sup>13,14</sup> The results of this study should provide clinicians with confidence that a submaximal cardiorespiratory fitness test using equipment routinely available in the hospital setting, such as a bike ergometer and heart rate monitor, can be completed in the early subacute phase post-stroke.<sup>38</sup> This work may improve a clinician's knowledge and confidence to initiate safe, tailored cardiorespiratory fitness training early after stroke in people with mild-to-moderately severe stroke,<sup>38</sup> as recommended in multiple national guidelines.<sup>1,2,7</sup>

Only one minor adverse event was recorded (exacerbation of a pre-existing knee condition), but this did not limit function or further participation in rehabilitation. There were no cardiovascular adverse events or serious adverse events associated with cardiorespiratory fitness testing. These results are consistent with the previous literature showing the safety of cardiorespiratory fitness testing in chronic stroke<sup>11</sup> and in people with nondisabling or very mild stroke.<sup>14</sup> The feasibility of cardiorespiratory fitness testing remains questionable given that only 66% ( $n = 41$ ) of participants enrolled in this study were able to complete the test in the early subacute phase post-stroke. Of those unable to complete this cardiorespiratory fitness test, 43% ( $n = 9$ ) could not complete the test because they were unable to mount the cycle ergometer due to stroke-related impairments. The majority ( $n = 7$ ) of these participants were assessed as mild-to-moderately severe stroke (NIHSS 5 to 14; Table 3). Stroke-related impairments have been noted previously as a barrier for the completion of cardiorespiratory fitness testing in chronic stroke,<sup>6,39,40</sup> and the results of this current study confirm that this is also true in the early subacute phase. Feasibility of cardiorespiratory fitness testing may be determined by not only the equipment utilized for testing, but also the timing of testing. The feasibility of cardiorespiratory fitness testing is well established in chronic stroke.<sup>9-12</sup> Patients have made greater recovery and stroke impairments may be less likely to impact participation, resulting in a greater number of participants able to complete fitness testing. However, this might miss an opportunity to safely initiate cardiorespiratory fitness training early after stroke, and take advantage of a window of enhanced functional recovery immediately post-stroke.<sup>41</sup>

The protocol used in this study may not be appropriate for all people with stroke across a wide range of stroke-related deficits and comorbid conditions. One third of participants who were unable to complete the fitness test, were not able to commence the protocol (ie, pedal against the indicated starting resistance

[30 watts] or maintain 60 rpm) as a result of stroke-related impairments, indicating the starting resistance or cadence may have been too high. Nearly half ( $n = 17/41$ ) of the participants able to complete the fitness test, ceased testing due to an inability to maintain cadence once resistance was increased at the corresponding heart rate. This may have been particularly evident in participants on beta-blocker therapy ( $n = 4/9$ ) where heart rate response was dampened, resulting in an increase in resistance that may not accurately reflect their aerobic capacity, and thus resulting in an inability to maintain the required cadence.

It is worth noting here that although the submaximal test protocol used was validated in chronic<sup>10</sup> and subacute<sup>42</sup> stroke using a total body recumbent stepper, in this study, for pragmatic reasons, we used a cycle ergometer. These results show that stroke-related impairments can restrict participation in cardiorespiratory fitness testing when using a cycle ergometer. It is possible that more participants might have been able to complete the testing if we had access to a total body recumbent stepper. The total body recumbent stepper may overcome the barrier that stroke-related impairments impose<sup>43</sup>, however the cost of it is likely prohibitive for many hospitals, rehabilitation units, and community-based settings. Similarly, a number of direct measures of cardiorespiratory fitness have been validated in stroke, but the equipment, expertise, and time needed to deliver such tests are unlikely available in most clinical settings.<sup>4,6,10,13</sup> Given the limitations of current testing protocols and procedures, there is a need for an alternative test of high clinical utility for cardiorespiratory fitness in people with stroke. Such a test may increase the uptake of cardiorespiratory fitness testing in clinical practice and subsequently improve clinicians' capacity to deliver safe and individualized doses of cardiorespiratory fitness training.<sup>3,38</sup>

In this study, people with stroke with greater depressive symptoms ( $p = .042$ ) were less likely to complete the fitness test in the early subacute phase post-stroke. In addition, participants who were unable to complete the fitness test in this study population had greater stroke severity, motor impairments, and disability than those who were able to complete the fitness test. Greater disability following stroke is a predictor for post-stroke depression,<sup>20</sup> while post-stroke depression is associated with lower exercise self-efficacy and reduces the likelihood a person may initiate and maintain exercise.<sup>18-20</sup> Greater disability and depressive symptoms in this population may have limited the participant's ability to complete cardiorespiratory fitness testing in the early subacute phase post-stroke. These results highlight the challenges (physical, mental, and emotional) that people with stroke may experience when participating in exercise, and also the need for multidisciplinary interventions that target physical, emotional, and mental well-being in the early subacute



phase post-stroke. This may aid initiation and uptake of cardiorespiratory fitness testing and training, in line with multiple national guidelines.<sup>1,2,7</sup>

Despite previously published literature,<sup>44</sup> similar numbers of female and male participants (male,  $n = 32$ , 51.6%) were recruited to this study (Table 2), although female participants ( $n = 12$ , 57%) were less likely to complete the cardiorespiratory fitness test compared to male participants ( $n = 9$ , 43%). Female participants recorded significantly lower test durations ( $p = .023$ ) and final watts ( $p = .005$ ) compared to male participants. This is consistent with previous literature noting indices of fitness tended to be lower for women compared to men.<sup>16,45</sup> Lower cardiorespiratory fitness indices and endurance in women may also influence further participation in cardiorespiratory fitness interventions and secondary prevention programs.<sup>17</sup> Given that cardiovascular disease is the leading cause of death in women worldwide, there are strong recommendations for the management of cardiovascular disease risk factors such as low cardiorespiratory fitness for women.<sup>46</sup> Despite an abundance of literature noting sex differences in enrollment and participation in rehabilitation programs,<sup>17,47</sup> the specific barriers for participation in fitness testing and training for women is unknown.<sup>17</sup> Understanding these barriers may assist in identifying specific facilitators for improved enrollment and participation in future cardiorespiratory fitness testing and training trials.

## Limitations

Despite utilizing what we considered were broad eligibility criteria to capture a representative cohort of individuals across a wide spectrum of stroke severity and motor impairments, ~70% of participants in this study were classified as mild stroke (NIHSS 0 to 4) and two-thirds were classified as independent (mRS 0 to 2). While the predominantly mild stroke population recruited into this study is representative of people with stroke admitted to the rehabilitation center they were recruited from, it does limit the generalizability of our results to people with greater stroke severity and disability. A large proportion of patients declined to participate in the research due to feeling “overwhelmed” (48%,  $n = 21$ ) with their medical condition, fatigue, and managing multiple rehabilitation appointments daily. This limited recruitment. This brief inpatient rehabilitation window has been established as a challenging and confusing time for people with stroke and can impact recruitment rates.<sup>48</sup> Despite recommendations for the early initiation of cardiorespiratory fitness testing and training,<sup>1,2,7</sup> this early period may not be the optimal time point for at least some people with stroke to begin cardiorespiratory fitness training. Although the results of this study have shown us that individuals with lesser

stroke severity, greater motor function, and mood may be more likely to engage in early cardiorespiratory fitness testing, the optimal time to intervene is likely to vary for each individual.

## CONCLUSION

Cardiorespiratory fitness testing was safe and feasible for more than two-thirds of people with mild and mild-to-moderately severe ischemic stroke and transient ischemic attack in this study population <2 weeks post-stroke. Participants who can complete cardiorespiratory fitness testing in the early subacute phase of stroke recovery can be characterized as having lower stroke severity and disability, greater motor and cognitive function and fewer depressive symptoms.

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## DISCLOSURES

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This is a sub-study of a larger single-center, multi-site, prospective cohort feasibility study (Cardiac Rehabilitation in Stroke Survivors to Improve Survivorship [CRiSSIS]).

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