Original Research

Cardiopulmonary Responses During Clinical and Laboratory Gait Assessments in People With Chronic Stroke

Jane L. Woodward, Mark Connolly, Patrick W. Hennessy, Carey L. Holleran, Gordhan B. Mahtani, Gabrielle Brazg, Meghan Fahey, Kameswari Maganti, T. George Hornby

J.L. Woodward, PT, DPT, Shirley Ryan AbilityLab, Chicago, Illinois. She is a board-certified neurologic clinical specialist.

M. Connolly, MS, Shirley Ryan AbilityLab.

P.W. Hennessy, PT, DPT, Infiniti Rehab Inc, Portland, Oregon. He is a board-certified neurologic clinical specialist.

C.L. Holleran, PT, DPT, DHS, Division of Physical Therapy, Washington University of St. Louis, St. Louis, Missouri. He is a board-certified neurologic clinical specialist.

G.B. Mahtani, MS, Shirley Ryan AbilityLab.

G. Brazg, PT, DPT, Shirley Ryan AbilityLab. She is a board-certified neurologic clinical specialist.

M. Fahey, DPT, NCS. Shirley Ryan AbilityLab. She is a board-certified neurologic clinical specialist.

K. Maganti, MD, Department of Cardiology, Feinberg School of Medicine, Northwestern University, Chicago, Illinois.

T.G. Hornby, PT, PhD, Department of Physical Medicine and Rehabilitation, Indiana University School of Medicine, Indianapolis, IN 46524 (USA). Address all correspondence to Dr Hornby at: tghornby@iu.edu.

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Background. The 6-Minute Walk Test (6MWT) is a common clinical assessment used to evaluate locomotor function in patients after stroke. Previous work suggests the 6MWT can estimate peak metabolic capacity (VO_2peak) without cardiorespiratory assessments during graded exercise tests (GXTs), which may assist with exercise prescription. However, selected research also indicated increased heart rates (HRs) during 6MWTs beyond levels considered safe without GXTs.

Objective. The goal of this study was to examine cardiorespiratory responses during 6MWTs and GXTs in individuals with chronic stroke and their associations with demographic or clinical characteristics.

Design. The study used a cross-sectional observational design.

Methods. Cardiorespiratory responses were assessed during 6MWTs at self-selected velocity (SSV) and fastest velocity (FV), and during GXTs. Secondary assessments included the lower extremity Fugl-Meyer Assessment, Functional Gait Assessment, gait speeds, and daily stepping activity. Correlation and regression analyses were used to evaluate associations between locomotor performance, cardiorespiratory responses, and clinical and demographic characteristics.

Results. Average HRs during 6MWT-FV were 72% to 76% of the age-predicted maximum (HR_{max}), with 20% of participants exceeding 85% predicted HR_{max}. When normalized to HRs during GXTs, HRs during 6MWT-FV were 86% to 88% of observed HR_{max}. Primary predictors of increased HRs during 6MWTs were resting HR, body mass index, and daily stepping. Distance during 6MWT-FV was a significant predictor of VO_2peak in combination with other variables. Electrocardiographic abnormalities were observed in >80% of participants at rest and 31% demonstrated distinct abnormalities during GXTs, which were not related to 6MWT or GXT performance.

Limitations. In addition to sample size, a primary limitation involved the ability to accurately predict or measure HR_{max} in patients with motor dysfunction after stroke.

Conclusions. Cardiac responses were higher than anticipated during 6MWTs and often exceeded recommended HR thresholds. Clinicians should closely monitor cardiorespiratory responses during 6MWTs.

Associations between cardiovascular and cerebrovascular disease are well documented, with the former present in approximately 75% of patients after stroke, and similar risk factors for both disease processes.[1] Although various cardiovascular abnormalities can precipitate stroke onset and can be detected by electrocardiography (ECG), changes in sympathetic regulation after a stroke can also contribute to early-onset ECG changes.[2] For patients in the chronic stages after stroke (eg, duration of >6 months), physical disability often results in decreased physical activity, which leads to greater deconditioning and can exacerbate cardiovascular and cerebrovascular disease. Previous work suggests many vascular risk factors are not recognized or managed appropriately in patients after stroke,[3,4] and approximately 30% of individuals with chronic stroke demonstrate undiagnosed ECG abnormalities.[5]

The increased risks of cardiovascular compromise in patients after stroke may be of concern with physical exertion that may occur during rehabilitation. Although previous data suggest the cardiac demands of conventional rehabilitation strategies are limited (<55% the age-predicted maximum heart rate [HR_{max}]),[6–8] emerging data suggests that locomotor activities performed at higher cardiovascular intensities (>70% predicted HR_{max}) may substantially augment motor recovery.[9–14] Previous and recent research established the efficacy and safety of high-intensity aerobic training in patients following subacute and chronic stroke, with significant increases in peak metabolic capacity, gait efficiency, or both, as well as walking speed and distance.[11,15–18,20] Greater aerobic capacity has also been linked to reduced risk of cardiovascular or cerebrovascular morbidity or mortality[10] and is recommended for stroke survivors.[10,19] In many aerobic training studies, however, specific enrollment criteria are used and research participants frequently undergo graded exercise tests (GXTs) to assess peak aerobic performance, with concomitant ECG monitoring to ensure safety prior to exercise prescription.[20,21] Performance of GXTs with ECGs is, unfortunately, not standard clinical practice secondary to the cost and availability of equipment and trained personnel.[10]

Recent data suggest that clinical assessments of walking function can estimate peak exercise capacity in patients after stroke without cardiorespiratory assessments.[22,23] In particular, the 6-minute walk test (6MWT) is a standard clinical measure of locomotor function that may reasonably predict peak exercise capacity in patients after stroke, particularly in conjunction with other measures.[24–26] Such findings could augment the ability to safely prescribe aerobic exercise (ie, as a percentage of peak predicted aerobic capacity) in patients after stroke without traditional GXTs. However, recent data suggest the physical exertion during 6MWTs may still be substantial. In patients with chronic stroke with average gait speeds of approximately 0.50 m/s, cardiac exertion during 6MWTs with specific instructions to "walk at your normal comfortable pace" elicited an average of 60% to 65% of age-predicted HR_{max} (100–105 beats/min).[13] Heart rates [HRs] that were higher than anticipated were also reported in a separate group of patients with similar gait impairments with instructions to "walk as far as possible" (mean HR = 112 beats/min).[27] Such HRs are within moderate intensities of aerobic exercise, although selected individuals may approach higher (ie, vigorous) intensities, defined here and previously as 70% to 85% the HR_{max}.[28] In contrast, lower HRs have been reported in other studies during 6MWTs with instructions to walk as far as possible,[23,26] with few individuals exceeding 85% the predicted HR_{max}. Patients in these latter studies were higher functioning, however, with average speeds of approximately 0.80 m/s.[23,26] The combined data suggest cardiorespiratory responses during 6MWTs may vary with both test instructions and the extent of locomotor impairments.

Although the 6MWT may be of clinical value, the potential cardiovascular exertion during testing may pose an increased risk for selected patients after stroke, particularly those with greater impairments in physical and cardiovascular function.[22,23] To date, few studies have investigated the intensities achieved during 6MWTs during different walking conditions across a range of individuals with various gait impairments, and their comparison to responses during maximum walking exercise tests.[23,26] The purpose of this study was to investigate cardiovascular and metabolic responses during 6MWTs and GXTs in individuals with chronic stroke at various levels of gait dysfunction. Using a cross-sectional, observational design, cardiorespiratory data were collected in individuals after stroke during assessments of walking function, including 6MWTs and GXTs. Secondary goals were to evaluate clinical and demographic variables that may predict cardiorespiratory exertion during these assessments. Our primary hypotheses were that individuals with greater gait dysfunction would generate higher HR responses during 6MWT, and 6MWT performance could serve as a surrogate measure of peak metabolic capacity in individuals with chronic stroke.

Methods

Participants

Individuals who were 30 to 85 years old and had a history of chronic (>6 months) hemiparesis following unilateral, non-cerebellar stroke were eligible. Further inclusion criteria consisted of the ability to ambulate without physical assistance for >10 m with assistive devices or braces below the knee (ie, ankle-foot orthosis) as needed but <1.2 m/s at a self-selected speed, the ability to follow 3-step commands, the provision of informed consent, and physician clearance to participate. Participants were excluded if they had significant cardiovascular, metabolic, or respiratory disease that limited exercise participation (eg, previous myocardial infarction or seizure <3 months earlier, previous or current orthopedic injury limiting walking function, uncontrolled congestive heart failure, resting blood pressure of >180/110 mmHg, uncontrolled diabetes, end-stage renal disease, severe infectious or psychiatric disease, or advanced malignancy).

Protocol

All clinical measures were assessed by trained physical therapists in a laboratory setting. Specific measures included walking distance and speeds, and cardiorespiratory data collected during standardized walking tests using portable indirect calorimetry (K4b2; CosMed, Chicago, IL, USA) and a Polar T31 transmitter (Polar, Bethpage, NY, USA) to record HRs. In the event of HR monitor failure, an additional pulse oximeter was worn and HR recorded every minute. Specific metabolic measures include the rate of O_2 consumption (VO_2) and the respiratory exchange ratio (RER), an estimate of metabolic substrate used (ie, ratio of CO_2 expired to O_2 consumed).

For 6MWTs, participants completed 2 separate assessments with instructions to walk at “normal, comfortable speed” (ie, self-selected velocity [SSV]) or to “cover as much ground as possible” (fastest velocity [FV]) around an 80-m walkway. The 6MWT-SSV was used to reduce the potential risk of falls[13,14,29] and to provide a controlled testing condition from 6MWT-FV when greater effort was requested. The order of testing was randomized and a seated rest break of 10 minutes or more was provided between tests to ensure recovery (or until HR reached within 10 beats/min of baseline). Testing was terminated if physical assistance was necessary at any time. Cardiorespiratory responses were averaged over the last 3 minutes of each test.

At least 10 minutes following the final 6MWT, participants completed a graded treadmill test (ie, GXT) with 12-lead ECG and indirect calorimetry. Participants wore a harness without weight-support as a safety catch and used handrails as needed only for balance. Treadmill speed began at 0.1 m/s, with speeds increased every minute by 0.1 m/s until participants experienced significant gait instability that required weight support, the participant requested to stop, or if criterion for terminating exercise testing was reached.[30] Ratings of perceived exertion (RPEs)[31] were collected at each speed and participants were asked if they experienced symptoms of angina or dyspnea throughout testing. Peak treadmill speed was determined as the fastest speed in which a full minute was completed. Metabolic (VO_2 and RER) and HR measures were averaged over the last 30 seconds of each minute of the GXT, and peak values of VO_2 (VO_2peak) and RER were identified. ECG data were recorded for 10 seconds of each minute of the GXT (ie, approximately 30 seconds after each change in treadmill speed).

Additional assessments included the lower-extremity Fugl-Meyer Assessment, Functional Gait Assessment, and walking speeds at SSV and FV (2 trials averaged; Gaitmat [Equitest, Inc, Chalfont, PA, USA]). Daily stepping activity (steps/day) was measured via accelerometers (Modus, Inc, Washington, DC, USA) worn on the paretic ankle for 5 to 14 days after the testing session.

Data Analysis

Cardiorespiratory and HR measures collected during the 6MWT and GXT assessments were reported as absolute values. HRs were also reported as the percent predicted HR_{max}, calculated as [(208 − (0.7 × age)] and reduced by 10 beats/min for individuals prescribed β-blockers.[32] The percent predicted heart rate reserve (HRR) was calculated using the Karvonen formula, age, and resting HR (HR_{rest}), as follows: [($HR - HR_{rest}$)/(predicted $HR_{max} - HR_{rest}$)]. In addition, and consistent with many exercise testing and training studies conducted in patients after stroke,[11,12,16,33] HRs during 6MWTs were also normalized to peak HRs observed during the GXT and quantified as the percent observed HR_{max} and the percent observed HRR**.** Metabolic and HR data were compared to standardized definitions of intensity, with VO_2 evaluated as metabolic equivalents (METs; 1 MET = 3.5 mL of O_2/kg/min). Specific categories of intensity thresholds were defined as follows: low intensity = <3 METs, <55% the HR_{max}, and <40% the HRR; moderate intensity = 3 to 6 METs, 55% to 70% the HR_{max}, and 40% to 60% the HRR; and vigorous to high intensity = >6 METs, >70% the HR_{max}, and >60% the HRR[28]) (however, see other recommendations with various HR thresholds[10,30]).

A cardiologist independently evaluated ECG recordings at rest and during each minute of the GXT, with all resting and exercise-related abnormalities tabulated. In addition, ECG abnormalities were categorized by those considered relative indicators for termination of exercise testing, including presence of conduction deficits (ie, heart block), premature ventricular contractions (PVCs, multi- and unifocal triplets), and ST-segment depression of >2 mm.

Parametric distributions were confirmed using Kolmogorov-Smirnov tests for all data with the exception of duration after stroke, and all data are reported as mean and standard deviation in the text and tables. Participants were classified by their SSV over short distances (<0.4 m/s, 0.4–0.8 m/s, and 0.8–1.2 m/s)[34] to evaluate potential contributions of gait dysfunction to cardiorespiratory responses. Statistical analyses focused on changes in walking and cardiorespiratory responses (gait speed or distance, relative HR responses, VO_2, and RER) during the different walking assessments (6MWT-SSV, 6MWT-FV, and GXT) across participants with various walking abilities (gait speed classifications). Only values for the percent predicted HR_{max} (versus percent HRR or percent observed HRs) were used in statistical analyses to minimize redundancy. Two-way analyses of variance were performed for each dependent variable, with main factors of gait speed classification and locomotor assessments (repeated). Bonferroni corrections were used for multiple comparisons. If significant findings were observed, post hoc Tukey-Kramer assessments were performed to identify specific differences between groups. Comparisons between demographics and clinical presentations (including ECG abnormalities) across participants at different SSV classifications were made using 1-way analyses of variance.

Potential associations between locomotor and cardiorespiratory measures during the 6MWTs with other demographic and clinical characteristics were evaluated using Pearson and Spearman correlations and simple linear regressions. Specific dependent variables of interest included HR responses during both 6MWT at SSV and FV, as well as VO_2peak. Independent variables demonstrating significant correlations were used in stepwise multiple linear regression models to determine the contributions of demographic and clinical characteristics on locomotor and cardiorespiratory performance. Specifically, a potential variable was entered in the regression if it was significantly correlated ($P < .05$) with the primary independent variables of interest. More directly, for HR responses during 6MWT at either SSV or FV, variables were entered into the regression if significantly correlated with either 6MWT variables. For VO_2peak during GXTs, independent variables were entered only if significantly correlated with the primary dependent variable. In addition, the use of β-blockers was also entered as an independent variable, as it directly influences HR responses. Variables contributed significantly to the regression if P was $<.05$ and removed if P was $>.10$. Collinearity was monitored, with variance inflation factors of <3.0 considered to be acceptable.

Conditional logistic regression was subsequently performed to evaluate the contributions of independent predictors to the incidence of percent predicted HR_{max} during 6MWT-SSV or 6MWT-FV achieving >70%, indicating vigorous to higher-intensity thresholds,[28] or >85%, which exceeds American College of Sports Medicine guidelines for cessation of activity without prior GXTs.[30]

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Results
Of the 73 individuals who consented to participate in the study, 11 were unable to obtain medical clearance, 2 walked at SSVs of >1.2 m/s, 1 reported a recent seizure, 1 had a recent knee replacement, 1 was diagnosed with a cerebellar stroke, and 4 had scheduling conflicts. The demographic and clinical characteristics of all 53 participants and of those in each gait speed classification are provided in Table 1.

Electrocardiography was performed at rest and during GXTs for all participants (Tab. 1), although equipment or user error limited storage of ECG data for 5 participants. Of the 48 participants with viable recordings, 85% demonstrated ECG abnormalities at rest and 31% presented with additional abnormalities during exercise; only 8% of participants did not have ECG abnormalities at rest or with exercise. The types and incidence of ECG abnormalities during rest are tabulated in Table 1, with additional delineation of those considered relative indications for exercise testing termination. Specific abnormalities included: first degree atrial ventricular block (27%), left atrial fascicular block (6%), left atrial enlargement (17%), left axis deviation (10%), right bundle branch block (8%), unifocal PVCs (2%; no multifocal or unifocal triplets observed), ST-segment depression of >2 mm (10%), left ventricular hypertrophy (10%), and nonspecific ST-segment repolarization (10%).

During GXTs, there were no significant cardiac events or symptoms that warranted GXT termination, with additional ECG abnormalities during exercise detailed in Table 1. The most frequently observed abnormality was increased presence of unifocal PVCs (observed in 25%), with no evidence of multifocal or triplet PVCs. There was 1 additional incidence of ST-segment depression, but no changes in incidence of conduction deficits, and no participants reported angina or dyspnea. Other events included premature atrial contractions (4%), ventricular couplets (2%), and T-wave inversion (2%). Of the 15 participants who had exercised-induced abnormalities, 11 had additional resting abnormalities; that is, these participants developed further abnormalities with exercise (ie, 1 participant with resting abnormalities experienced ST-segment depression only during exercise). There were no significant correlations with ECG abnormalities at rest or exercise as compared to most demographic or clinical characteristics, with the exception of a low negative association between incidence of resting ECG abnormalities and steps/day ($r = -0.38$; $P = .01$).

Average distance or speeds and cardiorespiratory responses during both 6MWTs and GXTs are presented in Table 2, with selected correlation analyses in Table 3. Differences in average walking distances or speeds were significant across each locomotor assessment and across gait speed classifications ($P < .001$ for both main effects) (Fig. 1A). Average speeds during the 6MWT-SSV were 0.57 m/s (SD = 0.30), which was similar to those at SSV over shorter distances (0.57 [SD = 0.30]), with the linear regression approaching unity ($r = 0.94$; 6MWT-

Table 1.
Demographic and Clinical Characteristics of Participants[a]

Characteristic	All Participants (n = 53)	Participants With Self-Selected Velocities of:		
		<0.4 m/s (n = 18)	0.4–0.8 m/s (n = 20)	>0.8 m/s (n = 15)
Demographics				
Age, y	59 (8.8)	61 (7.4)	58 (8.9)	58 (10)
Sex (no. of men/no. of women)	31/22	9/9	13/7	9/6
Hemiparesis (right/left)[b]	28/25	14/4	10/10	5/10
Duration, mo	64 (86)	46 (41)	55 (3829)	98 (14,731)
BMI, kg/m^2	30 (5.9)	29 (5.8)	29 (5.5)	31 (6.6)
Hypertension (% of participants)	77	72	90	67
CAD (% of participants)	9	11	20	0
CHF (% of participants)	4	0	5	7
Taking β-blockers (% of participants)	47	44	60	33
Impairments and activity				
FM score for lower extremity[c]	21 (18–25)[d]	18	21	24
SSV, m/s	0.57 (0.30)	0.24 (0.10)	0.58 (0.13)	0.86 (0.22)
FV, m/s	0.77 (0.43)	0.31 (0.15)	0.80 (0.22)	1.17 (0.30)
FGA score	14 (5.2)	9.4 (2.4)	15 (4.2)	20 (2.3)
Steps/d	4205 (2731)	2730 (2543)	3570 (1925)	5584 (2702)
Relative incidence of ECG abnormalities (% of participants)				
Resting	41 (85)	14 (88)	16 (89)	11 (79)
ST-segment depression	5 (10)	0 (0)	1 (6)	4 (29)
PVCs	1 (2.1)	1 (6.3)	0 (0)	0 (0)
Conduction block	18 (38)	9 (56)	7 (39)	2 (15)
Exercise induced	15 (31)	3 (19)	9 (50)	3 (21)
ST-segment depression	0 (0)	0 (0)	1 (6)	0 (0)
PVCs	10 (25)	2 (13)	4 (22)	3 (20)
PACs	2 (4)	1 (6)	0 (0)	1 (6)
Ventricular couplet	1 (2)	0 (0)	1 (6)	0 (0)
T-wave inversion	1 (2)	0 (0)	1 (6)	0 (0)
Conduction block	0 (0)	0 (0)	0 (0)	0 (0)

[a]Data are reported as mean (SD) unless otherwise indicated. BMI = body mass index; CAD = coronary artery disease; CHF = congestive heart failure; ECG = electrocardiographic; FGA = Functional Gait Assessment; FM = Fugl-Meyer Assessment; FV = fastest velocity; PACs = premature atrial contractions; PVCs = premature ventricular contractions; SSV = self-selected velocity.
[b]Reported as number of participants with hemiparesis on the left/number of participants with hemiparesis on the right.
[c]Reported as mean unless otherwise indicated.
[d]Reported as mean (range).

SSV = 0.94 × SSV + 0.03). In contrast, speeds during the 6MWT-FV (mean = 0.67 [SD = 0.39]) were slightly slower than those at FV over shorter distances (0.77 [SD = 0.43]; average speed during 6MWT-FV = 0.87 × FV + 0.01), but were strongly correlated (r = 0.95). Both 6MWTs demonstrated moderate to strong correlations with most functional measures, although correlations with demographic variables were not significant with the exception of age and duration after stroke with 6MWT-FV (Tab. 3).

Table 2.
Locomotor and Cardiorespiratory Outcomes During 6-Minute Walk Tests (6MWTs) and Graded Exercise Tests[a]

Measure or Test	All Participants	Participants With Self-Selected Velocities of:		
		<0.4 m/s	0.4–0.8 m/s	0.8–1.2 m/s
Resting HR	77 (14)	78 (13)	78 (13)	73 (15)
6MWT-SSV				
Distance, m	205 (108)[b]	87 (41)[c]	217 (63)[c]	330 (39)[c]
VO_2, mL/kg/min	12 (3.8)[b]	10 (3.0)[c]	13 (2.7)	14 (4.5)
RER, a.u.	0.92 (0.15)	0.92 (0.18)	0.89 (0.13)	0.96 (0.13)
HR, beats/min	111 (22)	111 (25)	111 (21)	111 (20)
% predicted HR_{max}	68 (13)	69 (14)	68 (13)	68 (14)
% predicted HRR	41 (23)	41 (29)	40 (21)	43 (19)
% observed HR_{max}	82 (12)	86 (13)	82 (11)	77 (11)
% observed HRR	60 (25)	64 (32)	60 (22)	54 (19)
6MWT-FV				
Distance, m	243 (140)[b]	93 (43)[c]	262 (92)[c]	396 (61)[c]
VO_2, mL/kg/min	14 (4.9)[b]	11 (3.5)[c]	15 (2.9)	17 (6.7)
RER, a.u.	0.95 (0.17)	0.91 (0.17)	0.96 (0.20)	1.0 (0.13)
HR, beats/min	118 (24)	115 (27)	118 (23)	124 (22)
% predicted HR_{max}	73 (15)	71 (16)	73 (13)	76 (16)
% predicted HRR	50 (27)	45 (32)	49 (21)	58 (28)
% observed HR_{max}	88 (12)	88 (13)	88 (11)	86 (12)
% observed HRR	72 (28)	70 (31)	73 (27)	72 (24)
Graded exercise test				
Speed, m/s	0.97 (0.45)[b]	0.51 (0.25)[c]	1.0 (0.31)[c]	1.4 (0.27)[c]
VO_2, mL/kg/min	17 (7.0)[b]	13 (3.7)[c]	18 (5.2)	21 (9.6)
RER, a.u.	1.1 (0.24)	1.1 (0.21)	1.1 (0.29)	1.2 (0.17)
HR, beats/min	136 (24)	129 (25)	134 (24)	144 (20)
% predicted HR_{max}	84 (14)	81 (15)	85 (13)	88 (13)
% predicted HRR	70 (25)	64 (28)	71 (24)	79 (22)
% observed HR_{max}				
% observed HRR				

[a]Data are reported as mean (SD). Heart rates (HRs) were normalized to the age-predicted maximum HR (HR_{max}) (percent predicted HR_{max} and heart rate reserve [HRR]) and to the highest observed HRs during graded exercise tests (percent observed HR_{max} and HRR). 6MWT-FV = 6-Minute Walking Test at fastest velocity; 6MWT-SSV = 6-Minute Walk Test at self-selected velocity; a.u. = arbitrary units; RER = respiratory exchange ratio.
[b]The *P* value between walking subgroups was <.01.
[c]The *P* value between walking subgroups was <.05.

Cardiorespiratory responses also scaled with greater walking demands but demonstrated smaller differences across gait-speed classifications. Two-way analyses of variance for VO_2, RER, and percent predicted HR_{max} revealed differences across locomotor assessments (6MWT-SSV < 6MWT-FV < GXT). Conversely, there were limited effects of gait speed classifications except for VO_2, with post hoc analyses revealing significantly lower responses only in those within the lower functioning subgroup (0–0.4 m/s) for all testing conditions (SSV shown in Fig. 1B). Average VO_2 during 6MWT-SSVs were 73% to 78% the VO_2peak obtained during GXTs, and 83% to 87% the VO_2peak during 6MWT-FVs. Average METs during the locomotor tests were generally categorized as moderate intensity (ie, 3–6 METs), except those with SSV of <0.4 m/s during 6MWT-SSV categorized as low intensity.

For the percent predicted HR_{max}, the participant population averaged slightly below the vigorous- or high-intensity threshold (ie, <70% the HR_{max}) during

Table 3.
Correlations of Demographics, Clinical Characteristics, and Functional Measures With Cardiorespiratory Measures in 6-Minute Walk Tests (6MWTs) and Graded Exercise Tests (GXTs)[a]

Measure	6MWT-SSV	6MWT-FV	% HR_{max} at SSV	% HR_{max} at FV	VO_2peak in GXT	Speed in GXT
Primary measures						
6MWT-SSV						
6MWT-FV	0.95[b]					
% HR_{max} at SSV	– 0.05	– 0.12				
% HR_{max} at FV	0.10	0.07	0.93[b]			
VO_2peak in GXT	0.41[b]	0.53[b]	– 0.17	– 0.02		
Speed in GXT	0.84[b]	0.88[b]	– 0.22	– 0.05	0.65[b]	
Demographics						
Age	– 0.23	– 0.31[c]	– 0.04	– 0.10	– 0.31[c]	– 0.36[b]
Sex	0.22	0.17	– 0.11	0.03	0.12	0.17
BMI	0.04	0.03	0.25	0.30[c]	– 0.29[c]	– 0.13
Duration	0.21	0.30[c]	– 0.09	– 0.01	0.13	0.25
Hemiparesis	– 0.26	– 0.26	– 0.03	– 0.04	– 0.45[b]	– 0.35[b]
CHF	0.08	0.03	0.14	0.21	0.07	0.08
CAD	– 0.06	– 0.02	0.03	– 0.01	0.17	– 0.02
HTN	– 0.08	– 0.08	– 0.07	0.06	– 0.23	– 0.16
Resting HR	– 0.10	– 0.14	0.50[b]	0.44[b]	– 0.12	– 0.16
Secondary impairments and activity						
FM	0.48[b]	0.51[b]	– 0.14	0.01	0.28[c]	0.55[b]
SSV	0.94[b]	0.92[b]	0.08	0.20	0.42[b]	0.81[b]
FV	0.95[b]	0.95[b]	0.04	0.17	0.48[b]	0.86[b]
FGA	0.85[b]	0.86[b]	– 0.03	0.09	0.44[b]	0.81[b]
Steps/d	0.66[b]	0.64[b]	– 0.33[c]	– 0.23	0.41[b]	0.71[b]

[a] 6MWT-FV = 6-Minute Walking Test at fastest velocity; 6MWT-SSV = 6-Minute Walk Test at self-selected velocity; BMI = body mass index; CAD = coronary artery disease; CHF = congestive heart failure; FGA = Functional Gait Assessment; FM = Fugl-Myer Assessment; HR = heart rate; HR_{max} = maximum HR; HTN = hypertension.
[b] $P < .01$.
[c] $P < .05$.

6MWT-SSV and surpassed this level during the 6MWT-FV and GXT (Tab. 2). Across all groups, 24 participants (45%) presented with HRs of >70% the HR_{max} during the 6MWT-SSV, with 6 individuals (11%) reaching >85% the predicted HR_{max} (Fig. 1C). During the 6MWT-FV, 28 (53%) reached >70% the predicted HR_{max} and 12 (23%) reached >85% the predicted HR_{max}. Calculation of percent predicted HRRs revealed average HRRs within "moderate" intensities (40%–60% the HRR). Normalization of HR responses to peak HRs achieved during the GXT (ie, observed HR_{max}) (Fig. 1D, Tab. 2) indicate average HRs of >80% the observed HR_{max} during both 6MWT-SSV and 6MWT-FV, and >70% the observed HRR, consistent with definitions of vigorous-intensity activities. With this normalization, 46 (87%) and 51 (96%) participants surpassed 70% the observed HR_{max} during the 6MWT- SSV and FV, respectively, whereas 23 participants (43%) and 31 participants (58%) surpassed 85% the observed HR_{max}. In addition, there were 3 individuals who achieved higher HRs during the 6MWT-SSV than during the GXT (all <0.4 m/s), and 8 during 6MWT-FV (3 with SSV <0.4 m/s, 3 between 0.4 and 0.8 m/s, and 2 >0.8 m/s). There were no significant differences between predicted or observed HR_{max} responses in individuals with various degrees of gait impairments.

Evaluation of associations between HR responses and demographic or clinical characteristics revealed specific and consistent findings. For example, there were no associations between 6MWT distances and percent

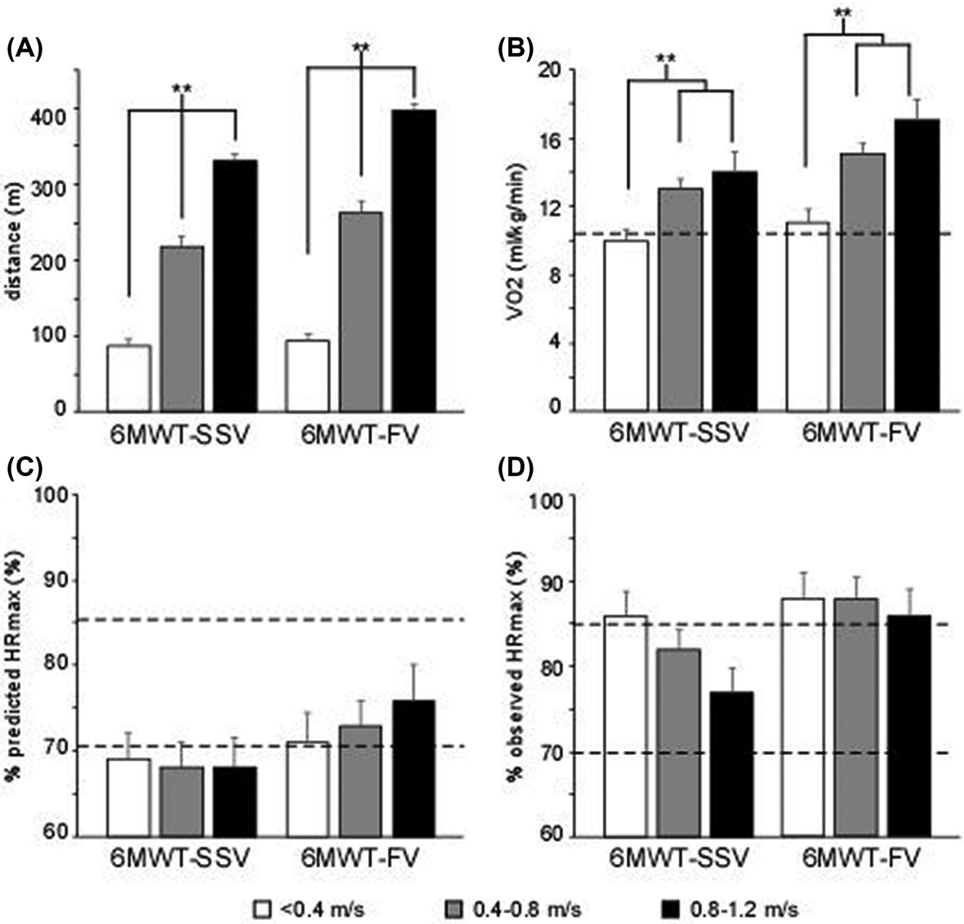

Figure 1.
Differences in walking outcomes (A), VO_2 (B), percent predicted maximum heart rate (HR_{max}) (C), and percent observed HR_{max} (D) during 6-minute walking tests (6MWTs) at self-selected velocities (6MWT-SSV) and fastest velocities (6MWT-FV) across participants with various initial walking impairments (<0.4 m/s, 0.4–0.8 m/s, and 0.8–1.2 m/s). Dotted lines in (B) denote the threshold for low versus moderate intensity using VO_2 or metabolic equivalents (METs) (10.5 mL/kg/min or 3 METs). Dotted lines in (C) and (D) denote thresholds for moderate to vigorous intensity (70% HR_{max}) and vigorous to very high intensity (>85% HR_{max}). Significant differences (∗∗) in distances were observed between walking subgroups during each 6MWT, with lower VO_2 during both 6MWTs in the group with lower functioning (<0.4 m/s).

predicted HR_{max}. Rather, HR responses during either 6MWTs demonstrated low but significant associations with resting HR ($r = 0.44$–0.50), body mass index (BMI) (0.25–0.30), and steps/day (-0.23 to -0.33; $r \geq 0.29$; $P < .05$) (Tab. 3), with specific correlations between selected variables shown in Figure 2. Stepwise, multiple linear regressions incorporating all 3 of the correlated variables and use of β-blockers indicated resting HR, BMI, and steps/day were significant predictors of percent predicted HR_{max} achieved during 6MWT-SSV ($r = 0.70$), although only resting HR and BMI contributed to HR responses during 6MWT-FV ($r = 0.61$; Equation 1 and Equation 2). Conditional logistic regressions were used to estimate variables that contribute to elevated HR responses (>70% or 85% the predicted HR_{max}) during 6MWTs. For 6MWT-SSV, higher resting HRs, faster SSVs, and lower steps/day were significant predictors of reaching >70% the predicted HR_{max}, while higher resting HRs and no use of β-blockers best predicted an incidence of >85% the predicted HR_{max}. For 6MWT-FV, lower steps/day and higher BMI predicted individuals who reached >85% the predicted HR_{max}, with no significant predictors for those who exceeded 70% the predicted HR_{max}. 6MWT-SSV was calculated as follows:

$$\text{percent of predicted } HR_{max} = \left(0.005 \times \text{resting HR}\right) + (0.007 \times \text{BMI}) - \left(1.3\tfrac{\text{steps}}{\text{day}} \times 1000\right) + 0.12. \quad (1)$$

6MWT- FV was calculated as follows:

$$\text{percent of predicted } HR_{max} = \left(0.005 \times \text{resting HR}\right) + (0.009 \times \text{BMI}) + 0.063. \quad (2)$$

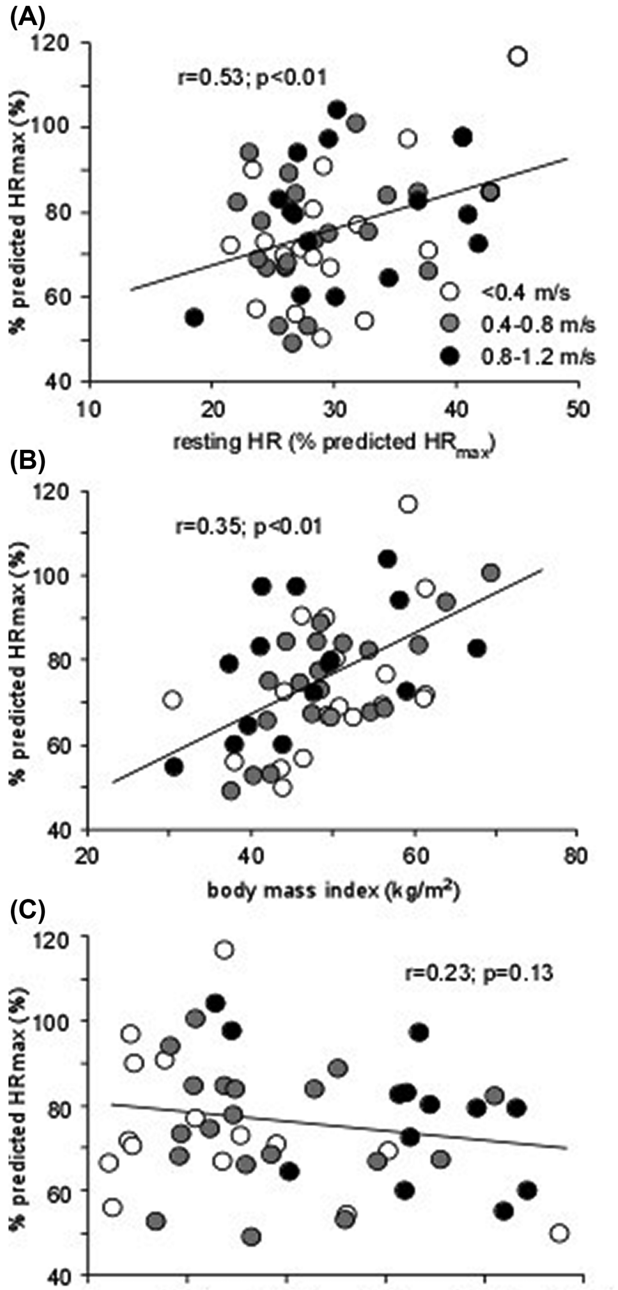

Figure 2.
Correlations between primary associations contributing to increased heart rates (HRs) during the 6-minute walk test at the fastest velocity, including (A) resting HR (percent predicted maximum HR [HR_{max}]), (B) body mass index, and (C) daily stepping activity (steps/day).

For VO_2peak during GXTs, moderate correlations were observed between VO_2peak and peak treadmill speeds ($r = 0.65$), while associations with other demographic characteristics and clinical measures varied. Low to moderate associations were observed between 6MWT distances and VO_2peak, demonstrating the highest correlation with 6MWT-FVs ($r = 0.53$) (Tab. 3). Investigation of these associations (VO_2peak versus 6MWT-SSV or 6MWT-FV distances) within each gait speed classification revealed low correlations ($r = 0.15$–0.30), with the exception of 6MWT-FVs in those with SSVs between 0.80 and 1.2 m/s ($r = 0.62$). Other correlations that were significantly associated with VO_2peak included side of hemiparesis (right), age, and BMI (all $P < .05$) (Tab. 3). Stepwise multiple linear regression used only dependent variables that were correlated to VO_2peak, and indicate 6MWT-FV distance, side of hemiparesis, and BMI were the primary predictors (Equation 3; $r = 0.70$), accounting for 49% of the variance. When replacing 6MWT-FV with 6MWT-SSV, FV over shorter distances, side of hemiparesis, and BMI were significant ($r = 0.63$ or 36% variance), with no contributions of 6MWT-SSV. VO_2peak during GXT was calculated as follows:

$$VO_2\text{peak} = (0.02 \times \text{6MWT-FV}) - (4.45 \times \text{right hemiparesis}) - (0.35 \times \text{BMI}) + 25.5. \quad (3)$$

Discussion

The present study investigated cardiorespiratory responses and locomotor performance during 6MWTs and GXTs in participants with chronic stroke, revealing HRs during 6MWTs that often surpassed thresholds of moderate exercise intensities when normalized to age-predicted HR_{max}. With normalization to the percent observed HR_{max} during GXTs,[11,12,15] average HRs during the 6MWT-FV were within the vigorous or "high" aerobic training ranges. Evaluation of ECG recordings at rest and during exercise indicated a high prevalence of cardiac abnormalities without reported symptoms of angina or dyspnea in the population tested. Nonetheless, the utility of the 6MWT-FV, but not 6MWT-SSV, was confirmed using regression analyses to predict VO_2peak, particularly in combination with other clinical variables.

Elevated HRs during 6MWTs are consistent with previous studies,[26,27] although HRs reported here are slightly higher, including 10 to 12 beats/min (5%–6% the HR_{max}) greater during 6MWT-SSV and 4 to 24 beats/min (2%–11% the HR_{max}) greater during 6MWT-FV.[27] Normalization to the percent observed HR_{max} suggests that aerobic intensities achieved during 6MWT-FVs were within prescribed ranges targeted during specific rehabilitation trials attempting to higher intensities (60%–80% the HRR).[11,12,15] Although the 6MWT may be widely used in clinical assessments of patients with stroke, elevated HRs during testing may be unknown to most clinicians without cardiac monitoring. Of additional potential interest was the finding that average HRs during 6MWTs at either SSV or FV were higher (68%–76% the predicted HR_{max} or 40%–58% the predicted HRR) than those observed during conventional rehabilitation (25%–40% the predicted HRRs).[6–8] The combined findings highlight the potential increased cardiovascular exertion achieved during standardized clinical testing, both beyond traditional physical therapist interventions and often above exercise intensities observed during aerobic training protocols.[11,12,16]

Although HRs increased with increasing tasks demands (eg, GXT > 6MWT-FV > 6MWT-SSV), responses were not accounted for by participants' walking dysfunction, with no differences across gait speed classifications. This latter findings contrast directly with our primary hypothesis. More directly, the data further suggests that the level of gait impairments is not associated with cardiac demands during clinical walking tests. As such, patients with various gait dysfunctions may be equally at risk and therapists should not use potential stroke-related impairments as an indicator of the cardiac demands that may arise with testing. Conversely, consistent predictors of elevated HR responses included higher HR_{rest} and BMI, and lower steps/day. The associations of greater HRs with HR_{rest} and BMI may be expected, although the contributions of steps/day were not necessarily anticipated. Although previous data suggest reduced HR responses following various exercise protocols,[30] the present findings suggest greater daily physical activity without specific exercise prescription may play a similar role in patients after stroke. Nonetheless, increased resting HR and BMI may be variables that can alert clinicians during routine assessments, and steps/day may be collected through indirect estimates of physical activity from commercial accelerometers.[35,36]

Regression analyses suggested that distance during the 6MWT-FV, side of hemiparesis, and BMI were significant predictors of VO_2peak. Other studies have attempted to estimate VO_2 responses after stroke using 6MWT,[22,23,26] although with differing conclusions regarding the predictive values of the 6MWT. In this study, however, the combined variables explained 49% of the variance.[22,23,26] Replacing 6MWT-FV with the 6MWT-SSV revealed that FV at shorter distances, but not 6MWT-SSV, was a significant predictor. The 6MWT-FV test, as typically performed, may be the most accurate assessment to estimate peak aerobic capacity without available equipment or personnel for GXTs.

The high frequency of resting or exercise-related ECG abnormalities observed here, including those considered relative indicators of GXT termination,[30] may be surprising, as only 17% of participants were diagnosed with coronary arterial disease. However, most participants were diagnosed with established cardiac risk factors (eg, hypertension, hyperlipidemia, obesity, diabetes) and demonstrated sedentary behaviors (<5000 steps/day[35]), both of which can precipitate heart disease. The current findings are also consistent with previous research indicating the potential for undiagnosed ECG abnormalities in patients after stroke,[5,37] and concerning given the relatively high cardiac demands observed. Of the specific ECG changes observed, most are associated to the presence of underlying heart disease, including ischemia (ie, conduction blocks, ST-segment depression, PVCs) or various forms of cardiomyopathy (hypertrophy, axis deviation). With the exception of ST-segment depression and selected conduction blocks, most ECG findings are not considered indicators for exercise test cessation, although their presence may still warrant referral to appropriate medical personnel for further evaluation. In the absence of the equipment and personnel required for these recordings, therapists may nonetheless wish to consult with the primary or rehabilitation physician to ensure awareness of the potential cardiac demands that may arise during standard clinical assessments and other interventions.

The combined results highlight the importance of monitoring cardiovascular responses during 6MWTs. Although selected studies have questioned the utility of the 6MWT,[38] the present data confirms the potential value of 6MWT in predictions of peak aerobic capacity (see also Marzolini et al[23]) and has been recently recommended as a standard for neurologic physical therapist practice.[39] Measurement of HRs as well as other signs and symptoms (eg, dyspnea) during clinical assessments can provide clinicians with greater insight into cardiac demands during sustained locomotor activities such as the 6MWT. Importantly, the HRs achieved here, particularly during 6MWT-FV, were above thresholds used in selected clinical trials[40] and greater than HRs achieved during conventional rehabilitation.[6–8] Measurement of HRs during 6MWTs could also allow calculation of changes in cardiovascular demands following various physical therapy strategies (eg, Physiological Cost Index[41]). Finally, continued use of HR monitoring beyond clinical assessments and during treatment sessions will be helpful to ensure the appropriate intensity of clinical rehabilitation, as recommended for patients after stroke.[10,19,42,43]

Limitations of the current study include a relatively small sample size, particularly in each gait speed classification, although the present study incorporated a larger range of gait speeds and more impaired participants as compared to most previous data.[22,23,26,27] A further limitation is the inability to control for medications that alter cardiovascular responses during exercise. Although many agents can alter HR responses, we estimated effects of only those prescribed β-blockers, in which predicted HR_{max} was modestly adjusted (10 beats/min)[32] for 47% of the participants in our study. This calculated decrease of predicted HR_{max} is consistent with data in patients with known coronary artery disease and generally lower aerobic capacity[44] and approximates adjustments used in patients after stroke.[6] However, data from intact individuals indicates HR can decrease as much as 40 to 50 beats/min with β-blockade,[45–47] and our analyses may have overestimated HR_{max}. Related limitations include using predicted HR responses, which can vary substantially for selected individuals, even without medications.[48] Alternatively, observed HR_{max} obtained during GXTs has been used to estimate HR ranges, although these values are much lower than predicted HR_{max}, and likely due, in large part, by the inability of patients after stroke to walk at higher speeds. With the present data normalized to the percent observed HR_{max}, resultant values suggest that >50% of patients exceed recommended exercise thresholds during 6MWTs. The accuracy and consistency of predicted or observed HR_{max} may be difficult to validate in patients after stroke throughout the course of rehabilitation. This remains a limitation for researchers and clinicians, and is an area of further investigation.

Conclusion

The data presented here indicate elevated HR responses during 6MWTs that often exceed recommended thresholds for safe exercise participation without prior cardiovascular screening. Increased HR responses were not related to stroke-related deficits and gait dysfunction, but were related to other variables such as resting HRs, BMI, and daily stepping activity that clinicians may use as "warning signs." Given the potential utility of the 6MWT-FV to predict peak exercise capacity and concomitant increases in HR responses, the use of HR monitoring during clinical assessments appears justified and is recommended to ensure safety during clinical assessments and interventions.

Author Contributions

Concept/idea/research design: J.L. Woodward, P.W. Hennessy, K. Maganti, T.G. Hornby
Writing: J.L. Woodward, P.W. Hennessy, G.B. Mahtani, K. Maganti, T.G. Hornby
Data collection: J.L. Woodward, M. Connolly, P.W. Hennessy, C.L. Holleran, G.B. Mahtani, G. Brazg, M. Fahey, T.G. Hornby
Data analysis: J.L. Woodward, M. Connolly, P.W. Hennessy, G.B. Mahtani, G. Brazg, K. Maganti, T.G. Hornby
Project management: J.L. Woodward, P.W. Hennessy, T.G. Hornby
Fund procurement: T.G. Hornby
Providing participants: J.L. Woodward
Providing facilities/equipment: T.G. Hornby
Providing institutional liaisons: T.G. Hornby
Clerical/secretarial support: J.L. Woodward
Consultation (including review of manuscript before submitting): J.L. Woodward, P.W. Hennessy, C.L. Holleran, G. Brazg, K. Maganti

Ethics Approval

All procedures and analyses were approved by the Northwestern University Institutional Review Board.

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Disclosures

The authors completed the ICJME Form for Disclosure of Potential Conflicts of Interest and reported no conflicts of interest.

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