LONGITUDINAL STUDY OF CHANGES IN EXERCISE CAPACITY AFTER STROKE

by

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DEDICATION

To my loving father, G. S. MacKay,
for teaching me from a young age
the importance of questioning by often replying,
"But, Marilyn, that's just one person's opinion."

To my dear mother, Jean (Ross) MacKay,
for never questioning my ability to fulfill my dreams.

To my terrific husband, Brian MacKay-Lyons,
and our wonderful children, Renée, Alison, and Matthew,
for more than words could ever express.

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ABSTRACT

It has been known for some time that most individuals with stroke have coexisting cardiac disease. What has not been adequately investigated is the cardiovascular response to exercise post-stroke. Knowledge of the responses to exercise after stroke is basic to understanding the physiologic adaptations to activity, prescribing appropriate exercise for rehabilitation, and ensuring a reasoned approach to new therapies.

The primary objective of this thesis was to investigate longitudinally the metabolic and cardiorespiratory responses to exercise over the course of post-stroke recovery. The first challenge was to design a testing protocol that would permit an objective assessment of metabolic response to exercise of individuals early post-stroke. Body weight support (BWS) offsets a percentage of body mass while providing balance support, permitting safe treadmill walking for patients with motor impairments. To validate a testing protocol using the Pneuweight Unweighting System®, 15 healthy adults (55 ± 11 yr) performed 3 graded exercise tests (GXTs): (i) standard treadmill GXT, (ii) treadmill GXT with 15% BWS, (iii) treadmill GXT with 0% BWS. BWS did not affect gas exchange variables although peak tidal volume (Vt) was significantly lower in the 15% BWS test. To validate the protocol for patients early post-stroke, 29 subjects (65 ± 13 yr) performed a symptom-limited treadmill GXT with 15% BWS at 26 ± 9 days post-stroke. No complications were encountered. Peak oxygen consumption ($\dot{V}O_{2peak}$) was 14 ± 5 ml/kg/min (60% of normal values), indicating significantly compromised exercise capacity. This was the first study to document responses to maximal treadmill exercise early post-stroke.

A 2-phase clinical study was conducted to estimate the aerobic component of a stroke rehabilitation program. In Phase 1, heart rate (HR) responses of 20 patients post-stroke (65 ± 13 yr) were monitored at bi-weekly intervals during 189 therapy sessions over the course of rehabilitation. The percentage of total time/therapy session spent in activities that elicited HR responses in the target HR zone was low (5% in physiotherapy, 2% in occupational therapy). Patients were physically inactive for 42% of total time/physiotherapy session and 54% of time/occupational therapy session. No significant changes in HR responses (i.e. resting, mean, peak HR) were found over the 14-week monitoring period. Phase 2 involved 23 of the patients participating in the longitudinal study described below. HR was monitored during physiotherapy sessions at 1, 2, and 3 months post-stroke. The results were comparable to Phase 1: 40% of time/session was spent inactive and HR responses remain stable across sessions. The mean time spent in the target HR zone - determined using $\dot{V}O_2$ data - was 12% of time/session. A significant increase was found in mean energy expenditure (EE) between the 1- and 3-month sessions (1.8 ± 0.4 to 2.6 ± 0.6 kcal/min). The main conclusion was that the stroke program did not provide adequate cardiorespiratory stress to induce a training effect.

The main purpose of the final study was to investigate changes in exercise capacity and EE during level walking over the course of post-stroke recovery. Twenty-five patients (64 ± 14 yr), with first ischemic stroke and mild to moderate disability, performed 15% BWS-facilitated treadmill GXTs at 1, 2, 3, and 6-months post-stroke. Between the 1- and 6-month GXTs, a 17% increase in $\dot{V}O_{2peak}$ (15 ± 5 to 17 ± 7 ml/kg/min) and a 16% decrease in EE while walking at .35 m/sec (3.8 ± 0.3 to 3.2 ± 0.2 kcal/min) were observed. Significant decreases in submaximal $\dot{V}O_2$, HR, rate-pressure product, minute ventilation and Vt also occurred. While improvements in functional measures occurred over the course of recovery, most of the increase in $\dot{V}O_{2peak}$ was realized between the 1- and 2-month GXTs. At 6 months mean $\dot{V}O_{2peak}$ remained low (71% of normative values). These results, together with findings of a low aerobic component to contemporary rehabilitation and the capability of patients early post-stroke to exercise safely to maximal, symptom-limited intensity, support a rationale for incorporating aerobic conditioning into stroke rehabilitation. The results provide baseline data for future research into the effects of an increased aerobic component on cardiorespiratory outcomes and functional recovery.

ABBREVIATIONS

ACSM	American College of Sports Medicine
ADLs	activities of daily living
ADP	adenosine diphosphate
ANOVA	analysis of variance
ATP	adenosine triphosphate
AVO_2 difference	arteriovenous oxygen difference
BI	Barthel Index
BMI	body mass index
BWS	body weight support
C	centigrade
CAD	coronary artery disease
cm	centimeter
CM	Chedoke McMaster
CMDI	Chedoke McMaster Disability Inventory
CO_2	carbon dioxide
COM	center of mass
Cr	creatine
DBP	diastolic blood pressure
DBP_{rest}	resting diastolic blood pressure
ECG	electrocardiographic
EE_{mean}	mean energy expenditure
EE_{walk}	energy expenditure during walking
EMG	electromyographic
GXT	graded exercise test
ΔG	change in free energy
H^+	hydrogen ion
Hg	mercury
hr	hour
HR	heart rate
HR_{max}	maximal heart rate
$HR_{max\text{-}pred}$	predicted maximal heart rate
$HR_{max\text{-}pred/adj}$	predicted maximal heart rate adjusted for β-blocker effect
HR_{mean}	mean heart rate
HR_{peak}	peak heart rate

$HR_{reserve}$	heart rate reserve
HR_{rest}	resting heart rate
HR_{submax}	submaximal heart rate
HR_{target}	target heart rate
ICC	intraclass correlation coefficient
kg	kilogram
l	liter
LACI	lacunar infarct
LE	lower extremity
LOS	length of stay
m	meter
MET	metabolic equivalent
MI	myocardial infarction
min	minute
ml	milliliter
MMSE	Mini Mental Status Examination
n	number
N_2	nitrogen
$NaHCO_3$	sodium bicarbonate
O_2	oxygen
O_2 pulse$_{max}$	maximal oxygen pulse
O_2 pulse$_{peak}$	peak oxygen pulse
OCSP	Oxfordshire Community Stroke Project
PACI	partial anterior circulation infarct
PAQ	Physical Activity Questionnaire
PCr	phosphocreatine
P_i	inorganic phosphate
PO_2	partial pressure of oxygen
POCI	posterior circulation infarct
$\dot{Q}$	cardiac output
$\dot{Q}_{max}$	maximal cardiac output
r	Pearson product-moment correlation coefficient
R	coefficient of reliability
RER	respiratory exchange ratio
RER$_{peak}$	peak respiratory exchange ratio
rPAR-Q	Revised Physical Activity Readiness Questionnaire

RME	rot mean squared
RPE	ratings of perceived exertion
RPP	rate-pressure product
RPP_{max}	maximal rate-pressure product
RPP_{peak}	peak rate-pressure product
RQ	respiratory quotient
R^2	coefficient of determination
RR	respiratory rate
RR_{peak}	peak respiratory rate
RR_{rest}	resting respiratory rate
SBP	systolic blood pressure
SBP_{peak}	peak systolic blood pressure
SBP_{rest}	resting systolic blood pressure
SD	standard deviation
SV	stroke volume
SV_{max}	maximal stroke volume
TACI	total anterior circulation infarct
UE	upper extremity
$\dot{V}CO_2$	carbon dioxide output
$\dot{V}CO_{2\,max}$	maximal carbon dioxide output
$\dot{V}CO_{2peak}$	peak carbon dioxide output
$\dot{V}E$	minute ventilation
$\dot{V}E_{peak}$	peak minute ventilation
$\dot{V}E_{rest}$	resting minute ventilation
$\dot{V}O_2$	oxygen consumption
$\dot{V}O_{2\,max}$	maximal oxygen consumption
$\dot{V}O_{2\,max(pred)}$	predicted maximal oxygen consumption
$\dot{V}O_{2peak}$	peak oxygen consumption
V_t	tidal volume
V_{tpeak}	peak tidal volume
V_{trest}	resting tidal volume
yr	year

ACKNOWLEDGEMENTS

CHAPTER 1: INTRODUCTION

Approximately 50,000 Canadians will have a stroke this year (1). About 95 percent of these individuals will survive the acute phase due to advances in emergency and acute stroke management over the past decade (2), and 60 percent of the survivors will experience persistent neurologic impairments that restrict functional independence long-term (3). Stroke is now the leading cause of disability among adults (4). Moreover, stroke is an age-related phenomenon, in that 75 percent of all strokes occur in people over 65 years of age (5); thus its prevalence is expected to escalate with changing demographics. These trends have tremendous human and economic implications and present major challenges for society.

Traditionally, the extent of recovery post-stroke was viewed as being almost exclusively dependent on the status of the neuromuscular system; consequently, intervention strategies focused on improving the capacity of that system, an approach that has met with limited success in terms of restoring functional independence. Recently, however, growing interest in how multiple systems (neuromuscular, cardiorespiratory, musculoskeletal) interact with each other and with the environment has begun to draw attention away from the neuromuscular system and toward previously unheeded multi-system interactions. Although the neurologic impairments resulting from the stroke itself are major sources of disability, cardiac co-morbidity - present in approximately 75 percent of patients with stroke - may be a significant factor limiting recovery (6). Individuals in the post-recovery phase of stroke identify fatigue as the area of greatest concern and the source of functional limitations (7-9). Further, there is mounting evidence that people with chronic stroke are physically deconditioned (10, 11). Despite the documented involvement of the neuromuscular and cardiovascular systems in this prevalent, debilitating condition, few studies have been conducted on the responses to exercise of individuals post-stroke.

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Knowledge gained from such investigations may lay the foundation for novel therapeutic approaches to improve function and quality of life of survivors of stroke.

In this introductory chapter, an overview of basic principles of exercise metabolism is presented and cardiovascular and respiratory responses to exercise are reviewed. Factors that affect and limit the exercise capacity of healthy individuals and people post-stroke are discussed. In addition, biomechanical and metabolic mechanisms that help to explain variations in the energy expenditure of human locomotion are outlined and related to pathological gait, particularly that of individuals post-stroke. Finally, the overall objective and specific purposes of this thesis are presented.

1.1 Exercise capacity

Exercise capacity can be defined as the body's limit in ability to respond to the physiologic stresses induced by prolonged physical effort. Maximal oxygen consumption ($\dot{V}O_{2max}$), the highest oxygen intake an individual can attain during physical work (12), is generally considered to be the definitive index of exercise capacity (13). Exercise requires increased energy metabolism to fuel the contracting muscle. Thus, exercise capacity is related to the bioenergetic processes occurring in skeletal muscle during dynamic activity.

1.1.1 Energetics of skeletal muscle

At rest skeletal muscle accounts for less than 20 percent of the body's total energy expenditure whereas during exercise most of the increased energy metabolism occurs within the contracting muscle (14). The force-generating interactions of actin and myosin myofilaments require energy supplied by the hydrolysis of terminal phosphate bond(s) of adenosine triphosphate (ATP) by myosin ATPase:

$$ATP \quad \xrightarrow{\text{myosin ATPase}} \quad ADP \; + \; P_i \; + \; \Delta G \qquad [1]$$

where ADP is adenosine diphosphate, P_i is inorganic phosphate and ΔG represents the change in free energy for the reaction under physiologic conditions (15).

Three mechanisms are involved in ATP generation in the muscle - the anaerobic hydrolysis of phosphocreatine (PCr), the aerobic oxidation of substrates, and the breakdown of glycogen or glucose to lactic acid (12). At the initiation of exercise, the high-energy phosphate bonds of pre-existing ATP are split to support the immediate energy requirements of the active muscles. Rephosphorylation of ATP is provided by the rapid hydrolysis of PCr by creatine kinase:

$$\text{PCr} \quad \overset{\text{creatine kinase}}{\longrightarrow} \quad \text{Cr} \; + \; P_i \; + \; \Delta G \qquad\qquad [2]$$

where Cr represents creatine.

While PCr hydrolysis provides immediate energy for ATP regeneration, the major energy source for ATP production during sustained exercise of moderate intensity is oxidative phosphorylation in the mitochondrial electron transport chain (15). Increased intramuscular concentrations of Cr, P_i, and ADP are thought to stimulate oxidative phosphorylation (12). The hydrogen ions (protons) (H^+) and their associated electrons liberated in the catabolic breakdown of substrates (primarily glycogen and free fatty acids) are made available to the cytochrome electron transport chain where the electrons are transferred through a series of oxidation-reduction reactions from sites of high potential energy to those of lower potential energy. The energy released is used to rephosphorylate ATP. Oxygen (O_2) serves as the final acceptor of hydrogen in the electron transport chain, with cytochrome oxidase catalyzing the reaction of O_2 and H^+, yielding water and carbon dioxide (CO_2). The net equation for the aerobic metabolism of glucose is:

$$\text{glucose} + 36\text{ADP} + 36P_i + 36H^+ + 6O_2 \rightarrow 6CO_2 + 36\text{ATP} + 42H_2O \qquad [3]$$
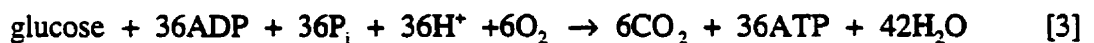
The substrate metabolized affects the amount of O_2 required. Carbohydrates are more efficient than fats in terms of O_2 utilization since they require less O_2 for a given rate of ATP production (15). The respiratory quotient (RQ), the ratio of the CO_2 production by the cells

to the O_2 uptake by the cells, reflects the proportion of carbohydrates and fats being utilized in the metabolic process. At rest, the RQ is about 0.82 that indicates that approximately 60 percent of substrate utilization is derived from fats and the remaining 40 percent from carbohydrates (16). During steady-state exercise the RQ can be estimated from the respiratory exchange ratio (RER), the ratio of CO_2 output by the lungs ($\dot{V}CO_2$) to the O_2 uptake by the lungs ($\dot{V}O_2$). At moderate intensity, steady-state exercise the RER, and hence the RQ, is about 0.95, indicating that carbohydrates comprise about 84% of the substrate used (16). Thus, as the work rate increases, the fuel mixture derives proportionally more from carbohydrate than from lipid stores.

As exercise intensity increases, the amount of O_2 delivered to the electron transport chain becomes insufficient to meet the increased energy requirements. ATP production must be augmented by the anaerobic-glycolytic (Emben-Meyerhof) pathway with obligatory carbohydrate utilization. Glucose or glycogen is converted to pyruvate, which is reduced to lactate, which is the final hydrogen acceptor (17). The net equation for the glycolytic metabolism of glucose is:

$$\text{glucose} + 2P_i + 2ADP \rightarrow 2\text{lactate} + 2ATP \qquad [4]$$

The amount of energy produced by anaerobic means is limited; approximately 19 times more energy is produced by aerobic oxidation.

With the increase in cellular H^+ load with lactate accumulation, there is greater stress on acid-base regulation. The lactate in the blood is buffered by sodium bicarbonate ($NaHCO_3$) and CO_2 is formed:

$$\text{lactate} + NaHCO_3 \rightarrow Na\,\text{lactate} + H_2O + CO_2 \qquad [5]$$
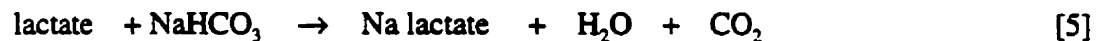
The CO_2 generated in the buffering of lactate is in addition to the ongoing metabolic CO_2 production and, as such, imposes an additional load on the respiratory system. The onset of lactic acidemia, the point at which the rate of lactate production exceeds its rate of removal, is marked by a sudden increase in the rate of $\dot{V}CO_2$ with respect to $\dot{V}O_2$ (15). The exercise intensity at which lactic acidemia occurs is referred to as the lactate threshold

(18). The lactate threshold can be used as an indicator of the energy generation mechanisms involved. Work rates below the threshold are *moderate* - involve little anaerobic metabolism and therefore can be prolonged without the additional stress from metabolic acidemia. Work rates above the threshold are *heavy* - both aerobic and anaerobic mechanisms share in energy generation with the latter providing an increasing proportion of energy as the work rate is increased. *Severe* work rates lead to $\dot{V}O_{2max}$ being attained with its consequent high levels of acidemic stress.

1.1.2 Cardiovascular response to exercise

Exercise requires the interaction of the cardiovascular, respiratory, and neuromuscular systems in order to respond to the energy demands of contracting muscle as well as to the increased concentrations of CO_2 and H^+, the by-products of muscle metabolism. The capacity to respond is reflected by the value of $\dot{V}O_{2max}$. $\dot{V}O_{2max}$ is considered to be the best measure of the functional limits of the O_2 transport system (19). The relationship between cardiovascular function and $\dot{V}O_{2max}$ is described by the Fick equation (19):

$$\dot{V}O_{2max} = \dot{Q}_{max} \quad x \quad max\ AVO_2\ difference \qquad [6]$$

where $\dot{Q}_{max}$ = maximal cardiac output and max AVO_2 difference = maximal systemic arteriovenous oxygen difference. Given that $\dot{Q}_{max}$ equals the product of maximal heart rate (HR_{max}) and maximal stroke volume (SV_{max}), $\dot{V}O_2$ max can be calculated as follows:

$$\dot{V}O_{2max} = HR_{max} \quad x \quad SV_{max} \quad x \quad max\ AVO_2\ difference \qquad [7]$$

Thus, the value of $\dot{V}O_2$ max reflects the integrity of both O_2 transport to the tissues and O_2 utilization by the tissues.

The increase in $\dot{V}O_2$ during exercise is due to the increase in both $\dot{Q}$ and AVO_2 difference. Cardiac output ($\dot{Q}$) at $\dot{V}O_2$ max is increased 3-6 times resting levels, depending on subject's physical condition, with HR increasing 200-300 percent and SV by about 50

percent (19). Over the lower third of the work rate range both HR and SV increase progressively with increasing work rate; thereafter, HR continues to increase while SV remains essentially constant (20, 21). The increase in SV has been attributed to enhanced myocardial contractility with an increase in left ventricular filling pressure and end-diastolic volume (22). In response to the higher myocardial $\dot{V}O_2$ demands, coronary blood flow increases three to five times the resting value (23). Increased venous return, secondary to compression of the veins by contracting muscles and reduced intrathoracic pressure, also contributes to the increased SV (19). At low intensity exercise the increase in HR is mainly the result of a decrease in vagal tone but as the intensity of exercise increases sympathetic stimulation and circulating catecholamines become progressively more important (15). Reduced baroreflex sensitivity as the intensity of exercise progresses limits its role in HR modulation (22).

The increased $\dot{Q}$ is directed predominantly to the regions with heightened metabolic demands - the working muscles. The selective distribution of the increased blood flow is due to both local vasodilation mediated by metabolites, in concert with other factors, acting on the vascular smooth muscle, and vasoconstriction in tissue with low metabolic demand; among the suggested vasodilatory agents are decreased partial pressure of O_2 (PO_2) and elevated levels of H^+, CO_2, potassium, adenosine, and nitric oxide. Previously unused capillaries in the working muscles open which allows for an adequate transit time of red blood cells despite the high flow rates (24). Average blood flow to other vascular beds either remains unchanged (e.g., brain) or decreases (e.g., renal and splanchnic bed) through active vasoconstriction resulting from increased sympathetic discharge (and to some extent by the release of catecholamines from the adrenal medulla). As the intensity of exercise increases, the systolic blood pressure (SBP) increases markedly while the diastolic blood pressure (DBP) either remains unchanged or lowers slightly, resulting in a moderate increase in mean arterial pressure. The reduction in total peripheral resistance resulting

from the vasodilation counteracts the increased driving pressure for flow resulting from the elevated mean arterial blood pressure (12).

During exercise the increase in $\dot{V}O_2$ exceeds the change in $\dot{Q}$; thus the AVO_2 difference must also increase. O_2 extraction from the muscle capillary blood to mitochondria is dependent on an adequate O_2 diffusion gradient (17). During a progressive increase in workload, arterial hemoglobin saturation and arterial O_2 content remain relatively constant at 97 percent and 200 ml/l of blood, respectively, whereas the venous O_2 content decreases substantially due to increased O_2 extraction in the active muscles and the redistribution of blood flow away from the non-exercising muscles and viscera.

1.1.3   Ventilatory response to exercise

As the metabolic rate increases during exercise, the minute ventilation ($\dot{V}E$) increases proportionately to changes in $\dot{V}CO_2$ in order to remove the CO_2 and to regulate pH balance after lactic acidosis develops. The ventilatory response to a given $\dot{V}CO_2$ is greater in older compared to young subjects (25). Below the lactate threshold increases in $\dot{V}E$ are due mainly to increased tidal volume (Vt) while above the threshold the respiratory rate (RR) increases without substantial change in Vt (12). At maximal workloads the O_2 cost of breathing may be as much as 10 percent of the total $\dot{V}O_2$ max, with the accessory inspiratory muscles (e.g., parasternal intercostal muscles, the scalenes) and the expiratory (the abdominals) sharing the mechanical work of breathing with the diaphragm (26). The diaphragm maintains aerobic metabolism even at intense work rates because of its high vascularity and oxidative enzyme activity (27).

In contrast to the predictability of many of the variables associated with the physiological response to exercise in healthy individuals, $\dot{V}E$ requirements for any given level of exercise can vary enormously, depending on the integrated influence of many

variables, e.g., ventilation/perfusion mismatch, partial pressure of alveolar CO_2, $\dot{V}CO_2$ and $\dot{V}O_2$ (17).

At the initiation of exercise dilatation of the pulmonary vascular bed results in perfusion of unperfused and underperfused areas of the lungs and reduced pulmonary vascular resistance; hence pulmonary blood flow is increased without a significant increase in pulmonary artery pressure (27).

1.2 Measurement of exercise capacity

$\dot{V}O_2$ max is a stable and highly reproducible characteristic of an individual when measured under standardized conditions that assure i) adequate duration and work intensity by at least 50 percent of total muscle mass; ii) independence from motivation or skill of the subject; and iii) standardized environmental conditions (19). Under these conditions, $\dot{V}O_2$ max tests have a high coefficient of reliability (R = 0.95), with repeated measurements varying only 2-4 percent (28). Thus, measurement of $\dot{V}O_2$ max is recognized as the most quantitative and reproducible method of assessing maximal aerobic capacity (29). The optimal duration of a graded exercise test (GXT) is 8-17 minutes (30). Underestimations of $\dot{V}O_2$ max may result from work rate increments that are either too large or too small. Excessive increments may limit the ability to respond to rapid rates of change in metabolic demands whereas prolonged tests may induce boredom, lack of motivation, excessive hyperthermia, subject discomfort, ventilatory fatigue, or altered substrate utilization (30).

The exercise modality can affect the $\dot{V}O_2$ max value attained. Recruitment of at least 50 percent of total muscle mass is much more likely to be met while walking than while cycling, particularly in a deconditioned population. About 85-90 percent of the $\dot{V}O_2$ max

achieved with treadmill testing can be attained with bike ergometry and only 70 percent can be achieved with either arm or supine ergometry (19).

The principal criterion to indicate maximal effort during $\dot{V}O_{2\,max}$ testing is attainment of a plateau in $\dot{V}O_2$ beyond which there is less than 150 ml/min increase despite increases in workload (28). Since a true measure of $\dot{V}O_{2\,max}$ is precluded when this criterion is not achieved a more accurate term for the value obtained without a plateau is peak $\dot{V}O_2$ ($\dot{V}O_{2\,peak}$). Plateauing of $\dot{V}O_2$ is frequently not observed in deconditioned or elderly individuals (31) or in patients with heart disease.

Because of the linear relationship between $\dot{V}O_2$ and HR, $\dot{V}O_{2\,max}$ can be estimated from HR measurements taken during submaximal exercise. However, while $\dot{V}O_{2\,max}$ is relatively unaffected by many stresses (e.g., dehydration, changes in body temperature, acute starvation), HR is markedly affected, thus limiting the accuracy of the estimation (19).

1.3   Factors affecting exercise capacity

The three main factors that contribute to differences in exercise capacity among healthy individuals are, in order of ascending importance, sex, age, and level of habitual physical activity.

1.3.1   Gender

Absolute and relative $\dot{V}O_{2\,max}$ are lower in women than in men of similar age, weight, and level of physical fitness (32). The $\dot{V}O_{2\,max}$ of women has been reported to be 77 percent of that of men, after adjusting for body weight and activity level (33). However, despite the reduced O_2-carrying capacity in women due to lower hemoglobin concentration,

this gender difference is removed when the $\dot{V}O_2$ max per kg of fat-free mass is calculated (34, 35). Thus, the gender difference is largely a result of the greater percentage of body fat in women.

1.3.2 Age

Physical limitations associated with aging, resulting not only from intrinsic age-associated structural and functional changes but also from inactivity, loss of coordination and flexibility, and co-morbidities (e.g., arthritis, cardiovascular disease), restrict the capacity to engage in physical work. Consequently, there is a steady, age-related decline in $\dot{V}O_2$ max, averaging about one percent per year (0.4-0.5 ml/kg/min/y) between 25 and 75 years (34, 36, 37). The rate of decline in exercise capacity is not related to sex but is significantly affected by the increasingly sedentary lifestyles and greater percentages of adipose tissue associated with aging, factors which confound identification of unique age-dependent changes (37). A large portion of the decline in $\dot{V}O_2$ max appears to be due to reduced O_2-transporting capacity, secondary to decreased HRmax. Structural changes in cardiac tissue include a decrease in the capillary-fibre ratio within the myocardium and an increase in the ratio of collagen to muscle resulting in myocardial stiffness. Decreased myocardial contractility, secondary to reduced ventricular compliance and depressed β-adrenergic responsiveness, is reflected in reduced ejection fraction, a hallmark of cardiovascular aging (38).

Whether there are declines with age in SV and AVO_2 difference remains controversial (39). Ogawa et al. (35) reported that 50 percent of the decline in $\dot{V}O_2$ max could be explained by smaller SV, with the remainder due to lower HRmax and reduced AVO_2 difference. Diminished oxidative capacity of the working muscles has been attributed to alterations in mitochondrial structure and distribution, changes in the microcirculation of skeletal muscle, and sarcopenia (loss of skeletal muscle mass) secondary to reductions in

number and size of fibers, particularly type II fibers (12, 37). Capillary density, capillary-to-muscle fiber ratio, and muscle enzyme activity are not affected by aging; thus, the oxidative capacity of the remaining muscle fibers is maintained in the elderly (40).

Age-related changes in ventilatory function, including decreased compliance of the lungs secondary to reduced elastic recoil of the lung and calcification and stiffening of the cartilagenous articulations of the ribs, limit the increase in $\dot{V}E$ during exercise (40). In addition, reduced diffusion capacity across the alveolar-capillary membrane result in a decrease in arterial O_2 tension of 2.1 - 4.1 mm Hg per decade (40).

1.3.3   Level of habitual physical activity

The extremes in activity level - from bedrest to endurance training - have been investigated in terms of effect on $\dot{V}O_2$ max.

1.3.3.i   Physical inactivity

The cardiovascular alterations that occur with physical inactivity in some ways parallel the changes that occur with aging, including reduced $\dot{V}O_2$ max and $\dot{Q}$max. Deconditioning explains a significant proportion of the age-related decline in $\dot{V}O_2$ max. In fact, if physical activity and body composition remain constant over time, the expected rate of decline in aerobic power is reduced by about 50 percent (to approximately 0.25 ml/kg/min/y) (37).

A mean decrease in $\dot{V}O_2$ max of 15 percent has been reported in healthy, middle-aged men after 10 days of bedrest with post-recumbent orthostatic stress being the principal factor limiting exercise tolerance (41). Decreases in $\dot{V}O_2$ max, as high as 28 percent, demonstrated in young, healthy subjects after three weeks of recumbency were attributed almost exclusively to decreases in SV, secondary to impaired myocardial function and increased venous pooling (42). However, inactivity also leads to significant peripheral

changes with decreases in oxidative enzyme concentrations, mitochondria, and capillary density resulting in a greater propensity to fatigue (15).

1.3.3.ii Training-induced adaptations to maximal exercise

Adaptations to the chronic physiologic stresses imposed by endurance training are evident during both maximal and submaximal exercise. Training programs that involve dynamic exercise of adequate intensity, duration, and frequency provoke both central and peripheral adaptations in proportion to the degree of stress imposed on the heart and on the working skeletal muscles, respectively (26). To induce central adaptations, training must incorporate use of large muscle mass activities in order to attain high levels of $\dot{V}O_2$ and $\dot{Q}$. In contrast, to induce local adaptations the training regime may involve small or large muscle mass. However, attainment of an exercise capacity that exceeds the pretraining maximal cardiovascular capacity will occur only with involvement of large muscle mass. While central adaptations can be demonstrated during exercise with trained or nontrained muscles, local adaptations are evident only during exercise performed using trained muscle groups, the latter reflecting specificity of training (26).

The principal indicator of a training effect during maximal exercise is attainment of a higher $\dot{V}O_{2\,max}$ than was achieved in the pre-trained state. No differences have been found in relative increases in $\dot{V}O_{2\,max}$ for men and women when they are trained under same intensity, frequency and duration (43). Further, the greatest increments in relative $\dot{V}O_{2\,max}$ with training at any age or either sex occur with the lowest initial values of $\dot{V}O_{2\,max}$ although absolute $\dot{V}O_{2\,max}$ increments decline with advancing age (44). Thus, individuals with similar relative exercise capacity demonstrate comparable exercise trainability, regardless of age or sex (45).

Increased $\dot{V}O_{2\,max}$, and hence, exercise capacity, following training in middle-aged and older adults is largely due to improved $\dot{Q}_{max}$ (20). It has been well established that

HR_{max} is unchanged or slightly reduced following training (26); thus the improved $\dot{Q}_{max}$ is associated with greater SV_{max}. Increased SV_{max} results in augmented maximal flow capacity, reflecting the combined effects of peripheral and central adaptations. The principal peripheral adaptation contributing to improved SV_{max} is reduced peripheral vascular resistance to blood flow in trained muscles. With training there is a decrease in vasoconstriction in the non-working muscles, possibly the result of reduced activation of the sympathetic vasoconstrictor nerves; thus, a training-induced increase in $\dot{Q}_{max}$ can occur without a concomitant increase in mean arterial pressure (26). Improved venous return may also contribute to increased $\dot{Q}_{max}$. The O_2 pulse, the quotient of $\dot{V}O_2$ and HR, at maximal exercise increases with aerobic conditioning. Training does not, however, affect the blood hemoglobin content (46) nor does it have a substantial effect on coronary blood flow or flow through the other vascular beds.

The main central adaptation contributing to improved SV_{max} appears to be improved myocardial performance secondary to enhanced intrinsic myocardial contractility (26). Endurance training, if prolonged and intense, can also result in signs of volume overload - an increased left ventricular end-diastolic volume and mass (26). The effects of training on myocardial perfusion and ejection fraction remain unclear (47). According to Stratton et al. (38) the mechanism underlying training-induced augmentation of SV is age-dependent - due primarily to increased ventricular ejection fraction in young subjects and to increased end-diastolic volume in older subjects.

In young subjects as much as 50 percent of the augmentation in $\dot{V}O_{2\ max}$ may be due to increases in the AVO_2 difference in the exercising muscle tissue (42, 48). The improved AVO_2 difference has been attributed to improvements in several components of the oxidative energy transfer process, particularly in type 1 fibers, allowing the trained muscle to function at a lower PO_2. Increases are observed in the size and number of mitochondria, myoglobin levels, Krebs' cycle enzymes (e.g., succinate dehydrogenase), and respiratory

chain enzymes (e.g., cytochrome oxidase) (15, 19). Increased capillary density facilitates exchange of gases, substrates, and metabolites as blood flows through the capillary (24). The adaptations resulting from these training effects, including increased O_2 extraction, greater capability for aerobic energy production, and decreased lactate production in the conditioned muscles, contribute to enhanced aerobic capacity for physical work and delayed onset of fatigue (49).

Endurance training also protects against the decline in age-related ventilatory function with significant increases in maximal $\dot{V}E$ and the percentage of maximal voluntary ventilation used at maximal exercise (50, 51). However, training appears to have relatively little direct effect on the lung parenchyma, airways, and capillary-to-fiber ratio in the diaphragm (27). Dempsey and Fregosi (27) postulated that the intermittent increases in metabolic rates typical of most training regimes do not provide a sufficient stimulus for chronic pulmonary adaptation.

1.3.3.iii Training-induced adaptations to submaximal exercise

After endurance training, several variables associated with the physiological responses to exercise exhibit smaller deviations from resting conditions at a given submaximal workload. The reduction in submaximal HR induced by training is confined, in part, to exercise with trained muscles (44). The mechanisms underlying this bradycardic response are not completely known. It is not fully explained by increased vagal activity, reduced sympathetic-adrenergic drive, or a training-induced reduction in resting HR (HRrest) (52). Another adaptation to exercise training that may contribute to reduced submaximal HR is the increase in total blood volume, resulting from expanded plasma volume (53). Although arterial blood pressure at a similar relative work rate is often unchanged with training, the rate-pressure product (RPP) at any given submaximal work load is lower (35). Since RPP has been shown to be highly correlated with myocardial $\dot{V}O_2$, it serves as a useful indicator of cardiac efficiency (54).

With the decrease in submaximal HR and the concomitant increase in SV, $\dot{Q}$ at a given submaximal workload is unchanged in healthy subjects compared to pretraining values (20). At a given workload, an increase in submaximal A$\dot{V}O_2$ difference in trained muscle appears to be counterbalanced by reduced blood flow to the working muscle due to a decreased vasodilatory effect as well as a less pronounced decrease in blood flow to the non-exercising muscles resulting from depressed sympathetic reflex activity (26). The net result is that $\dot{V}O_2$ at a given submaximal workload is either unchanged (20) or somewhat reduced (55) in response to training.

The extent of decrease in HR$_{rest}$ depends on the intensity of the training sessions and may result from a reduction in the intrinsic cardiac rate or from a change in the balance between sympathetic and parasympathetic activity in the heart toward greater dominance of the parasympathetic component (26). A recent study concluded that the small magnitude of training-induced change in HR$_{rest}$ is of minimal physiological significance (53).

Other indices of endurance training adaptations to submaximal exercise include an increase the percentage of $\dot{V}O_{2\,max}$ at which the SV plateaus. The demand for increased anaerobic metabolism as exercise intensity increases is delayed secondary to the improved capacity for aerobic exercise; thus the lactate threshold is elevated and the $\dot{V}E$ at a given submaximal workload is reduced (52). Ratings of perceived exertion (RPE) for a particular workload are generally reduced.

1.4 Factors limiting exercise capacity in healthy individuals

The factors limiting the capacity of healthy individuals to respond to physical work have not been identified conclusively. It is generally agreed that the respiratory system does not impose limitations on $\dot{V}O_{2\,max}$ (12, 19). Most evidence suggests that the diaphragm does not become fatigued during maximal work rates (27). Similarly, the

metabolic capacity of the muscles has not been implicated as a principal limiting factor (49). Involvement of only 50 percent of total muscle mass is required to attain $\dot{V}O_{2\,max}$ whereas if the metabolic capacity of the muscle were limiting $\dot{V}O_{2\,max}$, adding additional muscles would raise the maximal $\dot{V}O_2$ level (19). Furthermore, training studies, such as the investigation by Gollnick et al. (56), have demonstrated a greater increase in the aerobic potential of trained muscle than in $\dot{V}O_{2\,max}$ values, a finding that speaks against the oxidative capacity of muscle being the major limiting factor. These observations point to the cardiovascular system imposing an upper limit on $\dot{V}O_{2\,max}$. Since low maximal AVO_2 difference rarely is a major limiting factor, the main cardiovascular limitation to exercise in healthy individuals appears to be $\dot{Q}_{max}$.

1.5 Exercise capacity following stroke

There is a paucity of documentation of exercise capacity post-stroke, particularly in the early phases of recovery. The unique constellation of neuromuscular impairments resulting from cerebrovascular accidents argues against using normative data from healthy populations to predict the exercise capacity of individuals with stroke. The prevalence of cardiac disease in the stroke population reinforces the imprudence of estimating exercise capacity of patients with multi-system involvement using information based on studies of individuals without disability or with other disabilities. A major obstacle to investigation of patients post-stroke has been the lack of testing protocols that can accommodate the often pervasive neuromuscular impairments, and that are safe and well tolerated. The studies that have documented cardiovascular responses to maximal exercise will be discussed below.

Four studies measured $\dot{V}O_{2\,peak}$ post-stroke, and despite differences in selection criteria and testing protocol, the results are remarkably similar. All four studies involved samples of patients with chronic stroke whose mean age ranged from 52 to 58 years and they used

bicycle ergometry as the mode of $\dot{V}O_{2peak}$-testing. The earliest investigation reported a mean $\dot{V}O_{2peak}$ of 13.4 ml/kg/min among seven female, one to three years post-stroke (57). A decade later, Bachynski-Cole and colleagues (58) documented a mean $\dot{V}O_{2peak}$ of 16.1 ml/kg/min in eight males who were, on average, 3.8 months post-stroke. In a training study of patients with chronic stroke, the mean baseline $\dot{V}O_{2peak}$ of the 19 experimental subjects (8 males and 11 females) was 16.7 ml/kg/min and that of the 23 control subjects with stroke (15 males and 8 females) was 15.1 ml/kg/min (59). In the most recent study a mean $\dot{V}O_{2peak}$ of 17.7 ml/kg/min was documented in a group of 30 men with a mean post-stroke interval of 10 months (60). After adjusting for the gender-related reduction in $\dot{V}O_{2peak}$ values of the female subjects in the above studies, the $\dot{V}O_{2peak}$ values reported are remarkably similar.

The 87 subjects in the above-mentioned studies were in the post-recovery phase since most functional recovery occurs within the first three months post-stroke (61). Whether improvements in exercise capacity occur during the recovery phase has not been investigated. It is apparent, however, that after the period of maximal recovery and participation in stroke rehabilitation, significant functional aerobic impairment persists with exercise capacities between 50 and 70 percent of the values expected for healthy individuals of similar age, sex, and habitual activity status. $\dot{V}O_{2max}$ of less than 84 percent of normative values is interpreted as being pathologic (12). An exercise capacity of 15 ml/kg/min is considered the minimum level required to meet the physiological demands needed for independent living (62). Further, exercise capacity has been used as predictor of mortality among patients with coronary artery disease (CAD) - those with $\dot{V}O_{2max}$ levels of less than six metabolic equivalents (METs) or 21 ml/kg/min designated as a high mortality group and those with a capacity exceeding 10 METs or 35 ml/kg/min designated as an excellent survival group (29). However, the usefulness of this predictive capacity of $\dot{V}O_{2max}$ is limited in patients post-stroke since not all patients have CAD, and threshold

MET levels would need to be adjusted for the older age and reduced activity level of the stroke population.

1.5.1 Neuromuscular impairments

The most common manifestations of neuromuscular impairment post-stroke are muscle weakness, postural instability, incoordination, abnormal muscle tone, and loss of range of motion (63). The extent of impairment depends on the location and size of the cerebrovascular lesion. Hemiparesis reduces the pool of motor units available for recruitment during physical work, thereby limiting exercise capacity. McComas and associates (64) estimated that only half of the normal number of motor units were functioning between the second and sixth month post-stroke. Dietz and colleagues (65) postulated that this reduction in motor unit activation may be due to degeneration of the corticospinal tract with subsequent transynaptic changes in the motoneurons. Denervation potentials (e.g., fibrillation and positive sharp waves) have been noted in electromyographic (EMG) studies of hemiparetic muscles (66) and significant morphological changes at the neuromuscular junctions in hemiparetic muscle have been reported (67). Degeneration of alpha motoneuron should result in muscle atrophy. However, evidence of atrophy of muscle in the hemiparetic extremities has been an inconsistent finding, possibility due to differences in subject selection in terms of chronicity of lesions, severity of motor impairment, and level of physical activity. While neither Landin et al. (68) nor Jacobsson (69) found atrophy in their subjects with mild to moderate hemiplegia, other investigators have demonstrated selective atrophy of type II fibers in patients with upper motor neuron lesions (65, 70, 71). Chokroverty and Medina (72) suggested that signs of denervation, rather than being a direct consequence of stroke, may be secondary to prolonged pressure being exerted on peripheral nerves during periods of prolonged immobilization.

Alterations in muscle metabolism and fiber type recruitment pattern during dynamic exercise have been documented in patients with hemiparesis. Landin et al. (68) found evidence of reduced blood flow, increased lactate production and diminished oxidative capacity in the paretic leg muscles of eight male patients with chronic hemiplegia. Significant decreases in blood flow, $\dot{V}O_2$, glucose uptake, and workload of the paretic leg relative to the non-paretic leg were observed during two-leg exercise on a cycle ergometer. When comparing one-legged exercise involving either the hemiparetic or contralateral extremity, $\dot{V}O_2$, and glucose uptake by the working leg were similar bilaterally but lactate release was significantly greater and blood flow, muscle glycogen concentration, and ATP concentration were substantially lower in the paretic leg. The authors hypothesized that the reduced oxidative capacity of paretic muscles may be attributed to an increased number and activation of the glycolytic type II muscle fibers as well as to alterations in the structure of mitochondria. Findings from an earlier study by the same investigators of reduced activity of succinate dehydrogenase in both the paretic and nonparetic leg muscles of patients with hemiplegia were interpreted as evidence that physical inactivity secondary to the neurologic disease may contribute as much to the low oxidative potential as the disease process itself (73). Jacobsson and colleagues (69) observed a greater proportion of type II fibers (both subtypes A and B) in the tibialis anterior of 10 patients with hemiplegia in comparison to healthy control groups. In addition, Young and Mayer (74) documented, in their subjects with long-term hemiplegia, a unique fiber type characterized by slow twitch contraction times and increased fatigability.

1.5.2   Cardiovascular co-morbidity

As many as 75 percent of people with cerebral infarction also have cardiac disease (6) and, in some cases, cardiovascular disease appears to be the major limiting factor restricting a successful rehabilitation outcome (75). Moreover, long-term stroke survivors are at greater risk of dying from cardiac disease than from any other cause, including a

second stroke (75). The prevalence of CAD among patients post-stroke is in the range of 60 to 70 percent (76-78). Roth (6) reported that 46 percent of patients admitted for stroke rehabilitation had evidence of CAD by history of myocardial infarction (MI), angina, or coronary bypass surgery, in contrast to the value of 28 percent found by Harvey et al. (79). The disparity in these figures may be explained by the observation that cardiac dysfunction is often undiagnosed in patients with known cerebrovascular disease (76, 80, 81). In a study involving 200 patients with transient ischemic attacks, stroke, or carotid bruit but without clinical evidence of CAD, only 14 percent of the patients had normal coronary arteries while 40 percent had advanced or severe CAD (with stenosis of more than 70 percent of the lumen diameter of one or more coronary arteries) and the remaining 46 percent had mild to moderate CAD (with less than 70 percent stenosis) (81).

A high incidence of CAD post-stroke should not be unexpected since stroke and CAD share similar predisposing factors (e.g., age, hypertension, diabetes mellitus, cigarette smoking, sedentary lifestyle, and hyperlipidemia) and pathogenic mechanisms (e.g. atherosclerosis) (6). Atherosclerosis is a generalized process and postmortem studies have indicated a close association between the number and degree of stenosing lesions in the coronary and carotid arteries (82, 83). Hachinski and Norris (84) differentiated the cardiac co-morbidities associated with stroke using three categories: (i) *causal*, with emboli that originate from left atrial thrombi, heart valves, or the ventricular wall causing a cerebrovascular accident; (ii) *consequential*, with the overactivity of the sympathetic nervous system accompanying stroke resulting in myocardial injury or dysrhythmias; and (iii) *coincidental*, with hypertension and ischemic heart disease leading to both CAD and stroke. The last category accounts for the majority of cardiovascular co-morbidity post-stroke with hypertension found in the majority, and ischemic heart disease found in two-thirds of patients with stroke (76, 77, 81). Cardioembolic phenomena cause 15 to 20 percent of all strokes (84-86). Current understanding of the mechanisms underlying the neurohumoral and electrophysiologic consequences of stroke on the heart is incomplete. It

appears that cardiac events such as cardiac arrhythmias, arterial hypertension, and sudden cardiac death that have been attributed to underlying central nervous system dysfunction result primarily from changes in sympathetic nervous system activity (87).

The exercise capacity of individuals with CAD is typically 60 to 70 percent of that of healthy, sedentary people, depending on the severity of CAD (14). The reduction in $\dot{V}O_2$ max is due primarily to diminished $\dot{Q}$max rather than a change in AVO_2 difference (46). In some patients with CAD the main limiting factor appears to be decreased left ventricular contractility secondary to residual ischemia, resulting in a progressive decrease in ejection fraction and SV with exercise. In other individuals with CAD $\dot{Q}$max may be limited more by reductions in HRmax as a consequence of adverse symptoms (e.g., angina) or chronotropic incompetence, the inability of the heart to increase its rate in proportion to the metabolic demands of exercise (22). The mechanisms underlying chronotropic incompetence remain unclear but impairments associated with this dysfunction include myocardial ischemia, sinus node disease, autonomic dysfunction, and left ventricular dysfunction (39). A range of prevalence figures have been reported for chronotrophic incompetence among patients with CAD, from 14 percent (88) to 29 percent (89).

Only one study investigated the effect of cardiac involvement on responses to submaximal exercise post-stroke (78). The patients with stroke (n=50) demonstrated greater increases in arterial blood lactate levels and lactate-pyruvate ratio than did the healthy control subjects but the subgroup of 37 patients with stroke and heart disease showed significantly greater deviations from the normative data. These observations were interpreted to indicate increased anaerobic metabolism during exercise in patients post-stroke with cardiac co-morbidity.

1.5.3   Respiratory dysfunction

Respiratory function following hemispheric stroke is usually affected to only a modest extent, notwithstanding the relatively high occurrence of respiratory complications (e.g.,

pulmonary embolism, aspiration pneumonia) (90). Respiratory dysfunction may be a direct result of the stroke (e.g., muscle weakness, impaired breathing mechanics) or may be secondary to cardiovascular dysfunction or lifestyle factors (e.g., physical inactivity, high incidence of smoking (79)).

Both reduced and paradoxical chest wall movement as well as impaired diaphragmatic excursion contralateral to the stroke have been described (90, 91). Decreased EMG activity of both the diaphragm and intercostal muscles on the paretic side has been documented in patients early post-stroke (92). Recently, Similowski et al. (93) found, using cortical magnetic stimulation, that there is no bilateral motor representation of each hemidiaphragm. In a study of the respiratory status of 19 patients with chronic stroke, Haas et al. (3) found that the mean $\dot{V}E$ while walking on level ground at 25 cm/sec was almost twice that of the control values and the average arterial O_2 tension was 74 mm Hg, the latter being suggestive of mild hypoxemia. The profound fatigability experienced by these patients was attributed, in part, to respiratory insufficiency as indicated by decreased lung volumes, impaired mechanical performance of the thorax, low pulmonary diffusing capacity, and ventilation-perfusion mismatching (3). Hypoxemia and abnormal mechanics of ventilation were also documented in a study of 12 patients, aged 38 to 75, with acute cerebral infarction (94). Annoni and colleagues (95) suggested that the poor respiratory tolerance to effort observed post-stroke may be secondary to restricted thoracic excursion resulting from weakness, hypotonicity, and incoordination of the trunk musculature. This suggestion is supported by an earlier finding, based on a sample of 54 hemiplegic subjects, that the extent of expiratory dysfunction post-stroke is related to the degree of motor impairment, particularly hemi-abdominal muscle weakness (96). Delayed loss of inspiratory capacity after stroke appears to be due to the gradual development of rib cage contracture (96).

1.5.4   Longitudinal changes in physical status

Few longitudinal investigations of changes in physical status have been conducted of patients with stroke. This is surprising given the tremendous potential of this neurologic population to serve as a model for studying not only changes in single systems (neuromuscular, cardiorespiratory, musculoskeletal) during physiologic and functional recovery but also the effect of multi-system interaction on recovery. The neuromuscular system has received the most attention in the literature, with greater emphasis on evolution of impairments and abilities than on underlying physiologic mechanisms. In fact, functional recovery post-stroke is often attributed solely to improved neurologic status with little consideration of the role that the cardiorespiratory and musculoskeletal systems may have in limiting or enhancing recovery. Systematic documentation of changes in the cardiorespiratory function, including changes in response to exercise, is lacking in the literature. Thus, our current knowledge of the post-stroke adaptability of the cardiorespiratory system is largely limited to findings from training studies of patients with chronic stroke.

1.5.4.i   Recovery of motor control and functional mobility

The relative contributions of intrinsic neuroplasticity, resolution of acute pathophysiologic change, and behavioral compensation to functional recovery post-stroke are unknown (97). It is becoming clear, however, that recovery of patients post-stroke cannot be explained solely on the basis of improved neuromuscular function. Roth and colleagues (98) determined that only 2-36 percent of the variance in disability following stroke is explained by neurologic impairment.

The changes in motor function post-stroke have been well documented, and a predictable, stepwise recovery pattern has been identified (99). The majority of patients show considerable recovery within the first few months but the exact time course and

extent of recovery are less certain. Duncan and colleagues (100) emphasized the distinction between recovery of impairment-level attributes (e.g., motor control, muscle strength, muscle tone, range of motion) and disability-level attributes (e.g., bed mobility, transfers, gait, self-care). For their cohort of 95 patients, the most rapid improvement in motor impairment of the upper and lower extremities occurred in the first 30 days. Consistent with that observation was the finding of a plateau in upper extremity function by three weeks post-stroke in 80 percent of 421 patients (101). Newman (102) reported that 80 percent of motor recovery occurred in the first six week post-stroke. In a study of 113 patients with stroke, the magnitudes of change in motor control of the upper and lower extremities in the 16 week interval between onset of stroke and discharge from rehabilitation were 25 and 33 percent, respectively (103).

Impairment variables alone have been found to be insufficient prognostic indicators of recovery (103). Attention must also be paid to functional abilities which tend to improve over a longer time span than do impairment-level attributes. Mayo et al. (104) noted continuing progress toward independent function (e.g., sitting, walking, stair climbing) at four to six months post-stroke in a group of 93 patients. Studying 976 patients with stroke, Wade and Langton Hewer (105) found that the incidence of total dependence in activities of daily living decreased from 58 percent at one week post-stroke to nine percent at six months post-stroke. In the largest published study of recovery from stroke a plateau in functional recovery was observed within a post-stroke interval of 12.5 weeks in 95 percent of 1,197 patients (106). This finding concurs with the often-quoted conclusion by Skilbeck et al. (61) that "the majority of recovery occurs within three months. Although improvement is seen thereafter, it does not reach statistical significance." Independence in walking, the principal goal of most stroke survivors (107), is achieved by 60-70 percent during that interval (108-110). The extent of recovery is dependent on the status during the early post-stroke period. Shiavi et al. (111) compared the gait patterns of 12 patients at one month and one year post-stroke and documented improved speed and symmetry on post-

testing. Those patients who initially walked at very slow speed (less than .28 m/sec) retained abnormal EMG patterns bilaterally at one year post-stroke.

1.5.4.ii Changes in cardiovascular status

As already mentioned, change in cardiovascular function during the period of recovery post-stroke has not been investigated and thus its contribution to functional recovery is unknown. Nevertheless, Gresham et al. (112) proposed that "much of the disability of stroke victims appears to be due to coexisting cardiovascular disease." There are indications, mainly from the results of training studies, that improvements in cardiovascular adaptation to physical work are possible, at least in the post-recovery, chronic stages of stroke. In the first training study, 12 weeks of aerobic conditioning by seven patients with long-term stroke resulted in a 20 percent reduction in mean submaximal HR at a fixed work rate on a bicycle ergometer (113). Macko and associates (114) demonstrated that the training effects of a 6-month treadmill conditioning program involving eight males with chronic stroke were progressive, with a mean decrease in submaximal HR of nine percent at three months of training and a further mean reduction of six percent in the remaining three months. The single patient with stroke who participated in a 10-week training study by Wolman and Cornall (115) demonstrated no change in submaximal HR at a fixed load.

Four studies involved longitudinal measurements of $\dot{V}O_{2peak}$ in patients with chronic stroke. Potempa et al. (59) documented a mean increase of 13 percent in $\dot{V}O_{2peak}$ in 19 patients who participated in a 10-week program of aerobic conditioning using cycle ergometry. Interestingly, the magnitude of change in $\dot{V}O_{2peak}$ is comparable to the 12.8 percent mean gain realized by 23 males with CAD following a 12-week walk-jog program (116) and the 15 percent mean improvement recorded in a group of 20 patients with chronic atrial fibrillation after participation in a walking program (117). Two other intervention studies investigated changes in $\dot{V}O_{2peak}$ in patients with disabilities, some of

whom were post-stroke (118, 119). Separate data for the subgroup with stroke were not provided in either study, thus limiting comparability. Santiago et al. (118) reported that after 12 weeks of physical conditioning involving five patients with stroke, the overall mean change in $\dot{V}O_{2peak}$ was 27.3 percent as measured using a combined arm-leg ergometer. In contrast, the mean $\dot{V}O_{2peak}$ measured with arm ergometry in 16 patients with CAD and co-existing long-term stroke or amputation did not change from a baseline value of 12 ± 3 ml/kg/min following six months of a home-based conditioning program (119). A recent study by Fujitani and colleagues (60) reported a mean improvement in $\dot{V}O_{2peak}$ of 19 percent in 30 ambulatory males after a post-rehabilitation period of 9.4 months that involved 'no special supervised training'.

Discrepancies in the effects of training post-stroke on cardiovascular parameters in the aforementioned studies could be due to many factors, including differences in subjects, mode and intensity of training, compliance with exercise regime, and GXT testing mode. Most of the studies provided evidence of improved cardiovascular fitness post-stroke. Whether improvement results from central or peripheral adaptations to exercise or both remains unknown. It is likely that the mechanisms underlying the improvement are similar to those involved in training-induced adaptations of patients with CAD because of the high incidence of CAD among patients with stroke as well as comparable improvements following training among patients with stroke and with CAD but without stroke. Fergueson et al. (120) demonstrated significant increases in exercise capacity in 26 patients with CAD and exertional angina pectoris after six months of physical training. Although there was evidence of skeletal muscle adaptations (e.g., increased succinate dehydrogenase activity and muscle hypertrophy), central adaptations (e.g., reduced myocardial $\dot{V}O_2$ requirements, increased maximal coronary blood flow) were more highly correlated with both increased exercise capacity and reduced submaximal HR responses. Training-induced cardiovascular adaptations to exercise have also been documented after MI. A mean

increase of 66 percent in peak treadmill workload and a significant reduction in submaximal HR were demonstrated in 28 men who participated in eight weeks of physical training initiated 3-11 weeks post MI (121). However, in the same study, a mean improvement of 34 percent was found in 30 men allocated to the no training condition, suggesting the possibility of 'spontaneous improvement' in cardiovascular function following MI. Similarly, Savin et al. (122) documented a 23 percent increase in mean $\dot{V}O_{2\,max}$ over an eight week period in patients with MI who underwent no formal exercise training. In a subsequent study involving patients early after MI, Sheldahl et al. (123) reported that 21 of 62 patients (34 percent) attained higher HR_{peak} values with out-of-hospital activities, such as self-care and walking, than with the predischarge GXT. That the aerobic requirements of many daily activities may exceed the threshold intensity for cardiorespiratory conditioning in debilitated patients may provide an explanation for the phenomenon of 'spontaneous' improvement. In the previously mentioned study by Fujitani and colleagues, (60) significant improvements were noted in $\dot{V}O_{2peak}$ in community-dwelling patients post-stroke who were not participating in supervised exercise. Bjuro and colleagues (57) showed that while patients in the chronic post-stroke period performed household tasks such as vacuuming and bed making, their $\dot{V}O_2$ levels during these activities were 75-88 percent of $\dot{V}O_{2peak}$, almost twice that of the healthy control subjects. However, the $\dot{V}O_2$ during domestic tasks was measured using a Douglas bag carried in a harness on the back of the subject, which could have affected the validity of the measurements for both control and experimental subjects.

In summary, the neuromuscular, cardiovascular, and to a lesser extent, respiratory impairments, of patients with stroke appear to contribute to the low exercise capacity characteristic of this patient population. The low aerobic capacity is likely related to abnormalities in both central and peripheral mechanisms involved in O_2 transport and utilization, either as direct or secondary consequences of stroke. The evolution of exercise

capacity over the course of post-stroke recovery has not been investigated but findings from training studies suggest that enhanced adaptations to exercise are possible in patients in the chronic post-stroke period. There is also indirect evidence of partial 'spontaneous recovery' of exercise capacity post-stroke (60) . Training studies have also demonstrated reductions in the energy cost of walking post-stroke - the topic of the next section.

1.6 Energy expenditure during locomotion

Walking is the principal form of human physical activity, and for many people is the only departure from a sedentary life (124). Human locomotion is a complex phenomenon requiring the interaction of the neuromuscular and musculoskeletal systems to coordinate joint motion and muscular activity in the lower extremities, the pelvic, and the trunk in order to advance the body through space (125). Although there is a variety of possible strategies to produce locomotion, the dominant influences that shape gait kinetics and kinematics appear to be the minimization of metabolic energy costs and the reduction of musculoskeletal stresses. In this section, biomechanical and metabolic factors will be discussed in relation to the energy expenditure of normal gait and that of individuals post-stroke.

1.6.1 Biomechanical factors

The total muscular work of walking equals the sum of the external work (i.e., the work to accelerate and lift the center of mass (COM) at each step) and internal work (i.e., the work of accelerating and decelerating the limbs relative to the trunk) (126). Often the mechanical power associated with locomotion is assessed by calculating only the external work, resulting in an underestimation of the total energy requirements since significant energy expenditure may be needed in changing the limb position with little effect on the whole-body COM position (127). For an accurate interpretation of the metabolic energy

costs of walking, the biomechanical factors affecting both external and internal work need to be considered.

1.6.1.i External work

The energy level of a body is the sum of its potential and kinetic energies. When the energy level is not constant, as is the case with locomotion, work must be done to produce the change in energy level. Energy changes involving leg segments account for about 80 percent of the total energy costs of walking, with the remaining 20 percent due to energy changes in the arms, trunk and head (128). The work done by the muscles across the joints results in the forward translation of the body from one point to another. Assessing the external work of walking involves studying the behavior of the body's COM over the gait cycle. During walking the body vaults over a relatively stiff stance limb and the COM reaches its peak at mid-stance and lowest level at double support. In normal gait the movement of the COM in the plane of progression follows a smooth undulating or sinusoidal path with a total vertical excursion of 4.6 cm in the healthy adult male, the "locomotory dead space" (129). The gravitational potential energy of the COM is maximized at mid-stance and the kinetic energy of the COM is at its minimum value since the negative horizontal ground reaction force tends to decelerate the body during the first half of stance (130). During the second half of stance, the gravitational potential energy is minimized and the kinetic energy increases due to the accelerating effect of the positive horizontal ground reaction force. In other words, the fluctuations in the gravitational potential energy versus the kinetic energy of the COM are approximately 180 degrees out-of-phase with each other (131). In an idealized 'inverted pendulum' model of locomotion (with rigid struts representing the legs and a point mass representing body mass) no work would be done since all the kinetic energy would be converted into potential energy during the first half of stance and stored until needed again as kinetic energy during the second half of stance. In human gait, however, the lower extremities do not behave exactly as rigid

struts and complete recovery of mechanical energy is not achieved. Knee flexion occurs during stance to reduce the ground reaction force and the vertical movements of the COM (132). Therefore, despite the fact that 60-70 percent of the mechanical energy required to lift and accelerate the COM is conserved by this pendulum-like energy transfer mechanism, (133) the net result is a continual expenditure of energy (130).

Saunders (130) related the 'arc of translation' of the COM to the energy expenditure of walking and identified 'determinants' of normal gait that maximize energy transfer and minimize metabolic costs. Pelvic rotation about the vertical axis, lateral pelvic tilt, and 15 degrees of knee flexion in early stance all reduce the vertical displacement of the COM. Knee and ankle interactions during stance smooth out the arc of translation, preventing abrupt changes in the direction of motion that require a high energy expenditure. Lastly, horizontal shift of the pelvis displaces the COM laterally over the stance limb, with the shift minimized by the tibiofemoral angle. This lateral displacement of the COM also describes a smooth sinusoidal curve with the total excursion of about 4.4 cm (130).

1.6.1.ii Internal work

When the force generated by muscle results in either a concentric or eccentric contraction, movement of the joint results and *work*, the product of force by distance, is said to have been performed by the muscular activity. The work done during locomotion results not only in the forward translation of the body (external work) but also in the dissipation of significant amounts of energy in the rotations of the lower extremity segments while accelerating and decelerating the limbs relative to the trunk (internal work). The two components of walking that account for most of the energy expended are the internal work of moving the legs and the external work involved in the forward progression of the body and vertical oscillations of the COM (127). The total change in energy during level walking reflects equal amounts of positive and negative internal work, both of which require metabolic energy (127, 128). According to Williams et al. (134), positive work

results in increased segmental energy derived from concentric muscle contractions, transfer of energy between limb segments, and elastic storage. Negative work results in decreased segmental energy from eccentric muscle contractions and non-muscular sources such as joint range-of-motion limitations and internal musculoskeletal resistance (134). Muscular activity generates the most mechanical work whereas the contributions from elastic storage and from limitations in joint range are minimal in walking (as opposed to running) (126).

A useful measure of the effect of muscle contraction in the production of segmental rotations during gait is the *moment of force* which the muscle can exert. The moment of force is defined as the product of the tension in the muscle and the lever arm of the muscle, the perpendicular distance between the insertion of the muscle and the axis of rotation (135). During locomotion the muscles operate by exerting moments about joints, resulting in relatively small angular displacements. The net muscle moment about a joint reflects the net moment produced by all of the muscles at the joint. During the swing phase the limb swings forward passively after the muscles initiate motion, and at certain walking speeds, there is almost no lower extremity muscle activity in the swing limb (136). In contrast, significant net muscle moments occur during the stance phase, with the largest at the ankle (mainly a plantarflexion moment). In fact, the single most important muscle group for power generation during the normal gait cycle is the ankle plantarflexors during push-off (137). Olney et al. (138) calculated that the plantarflexors accomplish about the same amount of positive work as the hip flexors and extensors together. Substantially lower net moments occur at the hip and knee; however, there is more coactivation of antagonistic muscles at the hip and knee and higher agonist forces are required to exert a given net muscle moment. The pattern of net muscle moment at hip and knee varies dramatically among individuals but the limb kinematics are remarkably similar, supporting the hypothesis that different motor strategies may be used to produce kinematically normal gait provided that the overall objective of minimizing the total muscular effort is attained (139). This concept underscores the flexibility of human gait whereby changes in muscle

activation and net muscle moment at one joint are offset by changes at another joint. In spite of this flexibility, one of the dominant features of human locomotion is the stereotypical nature of gait which has been attributed to the automaticity bestowed by preprogrammed central locomotor commands (140).

The net *power* output at a joint, the rate of doing internal work, can be calculated from the product of the net muscle moment and the joint angular velocity (131). When the net muscle moment and the angular velocity are both in the same direction, there is net power production at the joint, whereas, when they are in opposite directions, there is net power absorption at the joint (131). However, determination of net power is problematic because the power generation at a joint is not necessarily limited to muscles that cross that particular joint because biarticular muscles can contribute to within-segment and between-segment energy transfers that are difficult to quantify. Also, the energy costs of co-contraction of antagonistic muscles and of isometric contractions to support the body against gravity do not appear as mechanical energy costs (141).

1.6.2   Metabolic factors

The primary determinants of the $\dot{V}O_2$ during dynamic exercise are the amount of work done and the efficiency of the muscles (17). Muscular efficiency is defined as the ratio of the work accomplished to the energy expended during steady-state work (142). While the term muscular efficiency is accepted as a global measure of the relationship between mechanical power (work rate) and physiological energy expenditure (submaximal $\dot{V}O_2$) (143), inconsistent calculations and interpretations of the term have led to confusion. First, the adjective "muscular" is somewhat misleading since most, but not all, of the energy consumed during locomotion can be attributed to energy consumption by muscles performing mechanical work. The assumption underlying the use of submaximal $\dot{V}O_2$ values in the denominator of the muscular efficiency calculation is that all ATP is supplied

by oxidative respiration; however, submaximal $\dot{V}O_2$ reflects the metabolic energy costs only as long as the workload remains aerobic (134). Further, submaximal $\dot{V}O_2$ is typically measured under steady-state conditions but the time to achieve steady-state is dependent on various factors that can be difficult to assess (e.g., time to steady-state is directly related to the work intensity (144) and inversely related to the level of cardiovascular fitness (17)). Donovan and Brooks (145) contend that the term "steady-state" is conceptually flawed because the homeostatic conditions reflected in the term are not met; rather, many variables including $\dot{V}O_2$, HR, SV, $\dot{V}E$, tissue temperature, and substrate utilization remain in a dynamic flux during exercise. As stated by Whipp and Wasserman (146) "the living organism is never in true equilibrium with its environment." Donovan and Brooks (145) prefer the term "steady-rate" $\dot{V}O_2$ to refer to the $\dot{V}O_2$ measured at a constant work rate.

A significant source of ambiguity with the term "muscular efficiency" lies in the use of different measures for the numerator. The measure of mechanical work selected can have a marked effect on the value of muscular efficiency obtained. Inherent in all measures of mechanical power is a substantial amount of uncertainty due to difficulties in ascertaining the amount of actual work performed (134). Considerable amounts of the total work done may be omitted in the calculations. Often, only the external work performed is calculated, thereby excluding the internal work involved in moving the limbs and breathing, resulting in underestimations of the true efficiency (146). Furthermore, some of the metabolic energy requirements are not reflected in the measurement of mechanical work (e.g., isometric contraction). As well, the inability to accurately account for energy savings from transfers between kinetic and potential energy may yield misleading information. As a consequence of these factors, widely divergent values for efficiency of walking appear in the literature. To complicate matters further, different terms have evolved without agreement on their definitions (e.g., "overall efficiency", "gross efficiency", "net efficiency", "delta efficiency", "work efficiency", "motor efficiency", "mechanical

efficiency", "physiological efficiency") (146, 147). Less contentious is the term "economy of movement" which appears to be universally accepted as the steady-state aerobic demand (submaximal $\dot{V}O_2$) required to perform a given task (148). Cavanagh and Kram (147) advocate the use of the term "economy" because it is both conceptually clear and practical for evaluating the efficiency of performing endurance activities. The O_2 cost of level walking can be expressed as $\dot{V}O_2$ per kilogram of body weight per unit distance traveled (ml/kg.m) (149). Alternatively, energy expenditure of level walking at steady state O_2 kinetics may be expressed in units of kcal/min using the caloric equivalent for a liter of O_2 at a measured RER, assuming nonprotein substrate utilization (16, 150).

Muscular efficiency is dependent on the efficiency of both phosphorylative-coupling and contraction-coupling processes (146). Whipp and Wassermann (146) calculated the efficiency of muscular work as the product of phosphorylative-coupling efficiency (60 percent) and contraction-coupling efficiency (49 percent) to derive an overall muscular efficiency of 29 percent. The mean muscular efficiency of walking calculated using estimations of the external work performed has been reported to be 31.3 percent (range 25.2-48.7 percent) (145). Using a more complicated biomechanical approach to determine the internal and external work performed, efficiency ratios for walking of 43-67 percent have been calculated (151). However, these mean values for efficiency of walking are somewhat meaningless since the actual efficiency is dependent upon the speed of walking, as discussed below.

1.6.3   Factors affecting energy expenditure during walking

Several variables have been investigated in relation to their effects on energy expenditure during gait. Despite identification of many influential factors, the interaction of these factors does not fully explain intersubject differences in economy of movement (148).

1.6.3.i   Speed of walking

Research has clearly and consistently found that speed of walking has a significant effect on energy expenditure. A U-shaped speed-economy relationship is apparent for normal gait, with the minimum aerobic demand occurring at 1.2-1.4 m/sec (126, 152-154) and very gradual decreases in efficiency over the range of 0.5 to 2 m/sec (127). Interestingly, the preferred speed of walking approximates the most economical speed, reflecting the tendency of biological systems to self-optimize. At the speed where the aerobic demand is the lowest, the magnitudes of the fluctuations in kinetic and gravitational potential energy are similar; thus energy exchange is maximized and the muscular work minimized (126, 155). Duff-Raffaele and associates (156) presented evidence in support of the hypothesis that the higher energy costs at slow speeds may be due to the internal work of moving the legs relative to the trunk accounting for a greater proportion of total energy consumption than at the most economical speed. In addition to decreased biomechanical energy transfer at velocities exceeding the optimal speed, changes in the recruitment profile of muscle fiber types contribute to the reduction in efficiency. At low speeds, the Type I slow-twitch fibers tend to be selectively recruited, whereas the energetically inefficient Type II fast-twitch fibers are recruited at higher speeds, especially at speeds corresponding to work rates of 70-80 percent of $\dot{V}O_2$ max (143). As the walking speed increases, a speed is eventually reached where running requires less metabolic energy than walking.

Since there is a direct relationship between stride length and walking speed, the effect of stride length on the energy cost of walking has been a topic of study. At a fixed walking speed, the aerobic demand increases curvilinearly as stride length is either shortened or lengthened from the preferred length (157). Minetti et al. (129) demonstrated that the external work rate was more accurate than either internal or total work rate in predicting the preferred stride frequency, and hence stride length, at any given speed of walking. Hreljac and Martin (158) hypothesized that the $\dot{V}O_2$- stride length relationship may be due to

minimizing jerk and maximizing smoothness of movement while walking with the preferred stride length. However, they found that only 6-8 percent of the variation in $\dot{V}O_2$ could be explained by variations in jerk-cost, suggesting that optimizing smoothness of movement and minimizing energy costs are not complementary performance criteria during walking. In contrast, Morio et al. (159) found that walking speed accounts for almost 60 percent of the variation in $\dot{V}O_2$.

1.6.3.ii Age

Waters et al. (160) demonstrated that the $\dot{V}O_2$ of walking at preferred speed did not significantly differ between adults (20-59 years) and senior subjects (60-80 years), averaging 12.1 ml/kg/min and 12.0 ml/kg/min, respectively. However, significant differences were seen in both the preferred speed of walking (80m/min and 74 m/min, respectively) and the O_2 demand expressed as a percentage of $\dot{V}O_2$ max (32 and 48 percent, respectively). Thus, older individuals not only have reduced muscular efficiency and higher relative energy costs of walking but also smaller aerobic reserves, and consequently, decreased ability to accommodate any additional physiologic penalties such as a gait disorder.

The reasons for the higher relative energy costs of walking in older individuals have been investigated to a limited extent. The more sedentary lifestyles associated with aging may be a factor since about five percent of the variation in energy expenditure is negatively related to usual physical activity level (159). To avoid confounding age-related differences in the energy expenditure of walking with those caused by morbidity and physical inactivity, Larish et al. (161) compared healthy, physical active seniors with a mean age of 70.5 years to young adults with a mean age of 25.6 years and found that an age-related difference in the economy of gait persisted with significantly higher energy costs for the older group at each of the common walking speeds. The investigators suggested that the reduced stride length of the older subjects, possibly secondary to an age-related decline in

joint flexibility, may account, in part, for the decreased efficiency of gait. Bassey and colleagues (162) found that the leg muscle power of older, frail women was highly correlated with walking speed (r = .93), accounted for up to 86 percent of the variance in walking speed. This finding of reduced power may help to explain the documented reduction in both vertical and horizontal ground reaction forces at fixed walking speeds of older adults in comparison to young subjects (161). Alternatively, the reduced ground reaction forces may reflect a strategy to minimize the musculoskeletal stresses associated with walking.

1.6.3.iii Gender

No gender-related differences were found in the energy expenditure of treadmill walking after adjustment for differences in resting metabolic rate, percent body fat, usual physical activity level, and velocity of walking in 26 healthy subjects with a mean age of 66.4 years (159). This finding is consistent with that of Davies and Dalsky (163) who reported a lack of gender-specific decrement in economy of walking at 60 percent of $\dot{V}O_2$ max in 98 healthy subjects with a mean age of 70 years.

1.6.3.iv Body mass and body mass distribution

The energy cost of walking is not affected by body mass (148) nor by stature (164) when expressed as net cost per kilogram of fat free mass. The significance of the distribution of mass is less clear; some evidence suggests that individuals with less mass concentrated in the limbs and more mass concentrated closer to the body's main axes of rotation require less muscular effort to accelerate the limbs (148).

1.6.3.v Joint range of motion

The independent effect of joint range of motion on the economy of movement has not been well studied. It has been postulated that decreased flexibility, a characteristic associated with aging, may result in altered gait pattern that is less economical because of

increased resistance to motion near the extremes of the available range (148). However, Gleim et al. (165) found that in 100 healthy individuals with a mean age of 33 years nonpathologic decreases in musculoskeletal flexibility of trunk and lower limb segments were associated with decreased steady-state $\dot{V}O_2$ for treadmill walking and jogging.

1.6.3.vi Walking surface and grade

Walking on a soft surface results in energy-consuming deformation of the surface and therefore the energy expenditure is greater than walking on a hard surface at the same velocity (127). Comparisons of energy costs of treadmill and over-ground walking have yielded conflicting results. Pearce and colleagues (153) found that the energy cost of treadmill walking was about four percent less than floor walking at fixed, self-selected walking speeds of 1-2 m/sec. The investigators hypothesized that the treadmill motor contributed to the mechanical work in lifting the COM. In contrast, Ralston (166) found that the energy contribution by the treadmill for walking speeds of 0.8 m/sec and 1.6 m/sec was insignificant.

Muscular efficiencies for uphill walking have been reported from 25-36 percent, (145, 151) but such values are somewhat meaningless since efficiency is dependent on walking speed and grade. Internal work is thought to have little influence on the economy of grade walking since the stride frequency, and hence the internal work, remain relatively constant at each speed regardless of the gradient (167). The efficiencies of both negative and positive external work at a given gradient decrease with increasing speed (167). When the grade is manipulated, the main energy expenditure above 15 percent grade is due to the vertical lift of the body because the vertical oscillations of the COM disappear (127); thus almost all the external work is positive (167). Since the energy cost of positive work are dramatically higher than that of negative work, the efficiency of uphill walking decreases as grade increases. In fact, the most economical condition is walking downhill on a 10 percent gradient (167). The external work rate for walking at grades of 15 percent can be

estimated with reasonable accuracy as the product of the body weight, walking speed, and percent gradient (145). However, Dean (127) cautioned that since grade walking is more complex than level walking, total energy expenditure is difficult to calculated accurately.

1.6.3.vii Psychogenic factors

The findings of the limited number of studies that have attempted to manipulate energy metabolism using hypnosis or meditation suggest that factors of a psychogenic nature can influence resting as well as exercise metabolism (168). Morgan (168) cited various studies that demonstrated significant decreases in energy costs in terms of $\dot{V}O_2$ at fixed exercise intensities after meditation or hypnosis. One explanation advanced for the reductions in $\dot{V}O_2$ is that certain psychological procedures might reduce an exercise-induced "emergency reaction" and its associated sympathetic activity which require O_2 in excess of that required by the actual workload (168).

1.6.4 Energy expenditure during walking post-stroke

In some forms of pathological gait, the final pathway of the COM is essentially the same as that of healthy individuals in that it is the most economical to maintain. Overt pathological disturbances can have surprisingly little influence on the fundamental pattern when loss of one function is compensated for by exaggeration of other unaffected segments (139). However, if compensation is ineffective, as is often the case with walking post-stroke, several determinants of normal gait may be lost, with consequent high energy costs of locomotion, an inevitable cardiovascular burden, and limitations in the type and duration of daily activities (130).

Some of the strategies used by individuals post-stroke to reduce the absolute energy expenditure of walking are not dissimilar to those used by healthy older people. Hash et al. (169) found that the mean $\dot{V}O_2$ at preferred walking speed of 19 subjects who were, on average, 54 years old and six weeks post-stroke, was actually lower than that of the control

subjects but that the energy cost at a fixed velocity (0.35 m/sec) was about three times higher than control values. In an earlier study involving 10 patients early post-stroke with a mean age of 62 years, the mean energy cost of walking at a speed of 0.45 m/sec was about twice the normative average value (170). In comparison, Corcoran et al. (171) documented in 15 patients in the chronic post-stroke period and with a mean age of 45 years energy expenditures that were 51-67 percent higher than control subjects walking at the same slow speed. These investigators noted that use of ankle-foot orthoses reduced energy costs between 10-13 percent. Discrepancies in the magnitude of increases in energy expenditure post-stroke in comparison to normative data may be explained by differences in subjects' age, severity of stroke, post-stroke time interval, use of orthoses, and walking speed.

The optimal walking speed in terms of energy expenditure for patients post-stroke has been reported to be 1.25 m/sec which is in the range of that of healthy individuals (172). However, many patients post-stroke are unable to walk at this speed, for reasons that include decreased power, instability, fear of falling, and avoidance of musculoskeletal stress. Furthermore, the slope of the energy-speed curve for patients with stroke is greater than that of control subjects; thus patients post-stroke pay a higher price in $\dot{V}O_2$ for a given increment in speed (171).

1.6.4.i Mechanisms underlying increased energy expenditure

The mechanisms underlying the elevated cost of hemiparetic gait have not been fully investigated. Reductions in the oxidative capacity of paretic musculature could explain part of the muscular inefficiency. However, Francescato and associates (173) reported that while the energy costs of walking were higher in 20 patients post-stroke than in healthy subjects matched for age, weight, and walking speed, RER values were the same for both groups and were unaffected by speed of walking. The interpretation of these findings was that mechanical impairments are more likely than metabolic impairments to contribute to the

higher energy costs of hemiparetic gait. The limitations of this study in terms of sample size and methodology do not provide a good basis for general conclusions regarding the relative contributions of metabolic and mechanical mechanisms in inflating energy costs of walking post-stroke.

The prominent role that spasticity was thought to play in elevating the energy costs of hemiparetic gait has been downplayed over the past few decades. In 1963, Bard (174) reported that metabolic cost of walking in 15 patients post-stroke was significantly related to the degree of clinical spasticity, the measurement of which was limited to a qualitative classification (i.e., mild, moderate, severe). Knutsson and Richards (175) recorded premature plantarflexor EMG activity in the stance phase of gait in nine of 26 of their subjects with stroke and attributed this abnormal activity to excessive stretch activation of the plantarflexors. However, Ada et al. (176) presented evidence suggesting that plantarflexor muscle spasticity does not contribute to gait dysfunction post-stroke. In their study, nine of 14 ambulatory subjects in the chronic post-stroke period exhibited resting tonic stretch plantarflexion reflexes but reflex activity during active contraction was not different from that of control subjects. This is in agreement with the findings in other studies of low plantarflexor activity on the paretic side during the stance phase of gait (177, 178). Berger et al. (178) concluded that reflex activity contributes minimally to the production of plantarflexor muscle tension during hemiparetic gait. Biomechanical analyses of the gait of 18 patients with a mean post-stroke interval of two months demonstrated that the pattern of motion of the paretic lower extremity was more strongly correlated with muscle weakness than with degree of spasticity or balance control (179). In addition, other studies have found a lack of correlation between knee extensor muscle spasticity and walking speed (180, 181). Berger et al. (178) postulated that hypertonia demonstrated in hemiparetic muscles after stroke may be due to alterations in mechanical muscle fiber properties resulting from impaired supraspinal input as opposed to enhanced motoneuron activity associated with spasticity.

Olney and associates (141) conducted a comprehensive biomechanical analysis of gait energetics post-stroke in order to identify the source of inefficiencies in the gait cycle. In their sample of 10 ambulatory patients (mean age of 59 yr; mean post-stroke interval of 3.7 yr), the mean energy conservation across the gait cycle was estimated to be 48 percent. The investigators postulated that the speed of walking (mean velocity of 0.42 m/sec) was too slow to generate the kinetic energies required for normal levels of energy transfer, thus reducing the efficiency of pendular mechanism. The instantaneous energy curves of the leg segments, although low in magnitude, followed a normal gait pattern while the abnormal curves of the combined head, arms and trunk segment contributed significantly to low energy-conserving exchanges. Later, the same group of investigators repeated biomechanical analyses of gait post-stroke to determine the effect of walking speed on gait energetics (138). Using 30 patients subdivided into three groups according to preferred speed of walking, they demonstrated that the reduced amplitude of the instantaneous energy curves of lower limb segments were particularly evident at slow walking speeds. Similarly, Francescato et al. (173) noted a greater disparity in the energy costs of normal and hemiparetic gait at slow speeds.

The findings of low kinetic energy production in the studies by Olney et al. (138, 141) are consistent with the results of EMG investigations of locomotion post-stroke. Peat and colleagues (177) documented in 20 subjects post-stroke loss of the normal phasic pattern of muscle activity during gait with significant reduction in activity of all of the major muscle groups of the paretic lower extremity. These investigators also noted significant asymmetry in the stance time expressed as a percentage of the total cycle with a mean stance time of 67 percent on the more affected side and 80 percent on the less affected side. However, walking speed of the subjects was not reported; both the extent of joint power and the degree of temporal symmetry in weight-bearing are directly related to walking velocity post-stroke (138). Shiavi et al. (111) also noted compensatory changes in the EMG pattern of leg musculature contralateral to the hemiparetic lower extremity, including

prolonged muscle activation and increased coactivation. While Knutsson and Richards (175) found that depressed EMG activity in the hemiparetic leg musculature was relatively common, they cautioned against generalization because of marked variation in EMG patterns among patients. They identified three broad classes of abnormal patterns of muscle activation in the gaits of 22 patients post-stroke - underactivation, premature activation of the calf muscles in stance, and coactivation of several or all muscles during part of gait cycle. Other investigators have reported significantly different inter-subject EMG patterns and highly reproducible intra-subject patterns (177, 182, 183).

Morita et al. (184) found that in 58 patients in the chronic post-stroke period the stage of motor recovery of the paretic lower extremity was highly correlated with the degree of both vertical and anterior-posterior ground reaction forces, the velocity of walking, and stride length and was inversely related to the lateral component of the ground reaction force. The latter result corroborates an earlier finding of excessive lateral displacement of the COM in hemiparetic gait (182).

In addition to reduced power generation of the paretic extremity musculature, decreased excursion of lower extremity joints may contribute to higher energy costs of walking post-stroke. Joint-angle disturbances on affected side include reduced knee flexion in stance, reduction of knee flexion range in swing, and occasional loss of dorsiflexion during the swing phase and at initial contact (140). Plantarflexion shortening may obstruct the energy transfer from potential to kinetic energy during the second half of stance (141) and stride length may be compromised by the inability to simultaneously extend the knee and flex the hip in terminal swing (125). Also, lack of reciprocal arm swing may in turn restrict the pelvic motion required for optimal energy exchange. However, differences in energy expenditure between walking with natural arm swing and with no arm swing are insignificant in healthy individuals (127).

1.6.4.ii Longitudinal changes in energy expenditure

Few investigators have documented changes in the energy cost of walking over the course of post-stroke recovery. In a group of 10 patients with stroke a mean reduction of 30 percent in the energy expenditure of walking at a speed of 0.45 m/sec was documented after participation in physical rehabilitation (170), which is consistent with the 23 percent improvement reported by Hash (169). In the previously described training study by Potempa and colleagues (59), the investigators postulated that because the magnitude of training-mediated improvements in peak workload (43 percent) and exercise time (40 percent) were greater than that of $\dot{V}O_2$ max (13 percent), muscular efficiency probably improved to a greater extent than aerobic capacity. In the only investigation specifically designed to study the effects of training on the energy costs of walking post-stroke, Macko and associates (114) presented preliminary evidence of training-induced reductions in energy expenditure of hemiplegic gait.

1.7 Use of body weight support to facilitate walking post-stroke

Body weight support (BWS) systems have been developed recently to mechanically offset a percentage of body mass while providing external balance support, thereby permitting treadmill walking of patients in the early stages of neurologic recovery (185, 186). The typical system consists of a vest similar to parachute harness which is attached to an overhead support. Unweighting of a prescribed amount of body mass is achieved by vertical displacement through the supporting frame using a weight and pulley or a pneumatic system. Visintin and Barbeau (187) reported attainment of a more normal gait pattern using treadmill walking with 40 percent BWS in seven individuals with spastic paresis. Recently, Hesse et al. (188) compared treadmill walking with 0, 15, and 30 percent BWS to floor walking in 18 patients with chronic hemiparesis and found that the preferred speed of treadmill walking was less than that of overground walking due to

reduced cadence on the treadmill. In addition, greater symmetry of weight-bearing was recorded during treadmill walking irrespective of the extent of BWS, and both premature plantarflexor activity and antigravity muscle activity decreased with increasing BWS. Researchers from the same laboratory (189) demonstrated that treadmill training with BWS was more effective than conventional physiotherapeutic techniques in improving the walking velocity and gait ability of seven nonambulatory hemiparetic patients. Visintin et al. (190) corroborated these findings in a recent randomized study of 100 individuals averaging 73 days post-stroke, half of whom received six weeks of BWS-treadmill training while the other half had six weeks of gait training bearing full body weight.

1.8   Purpose of the thesis

The extensive neuromuscular and cardiorespiratory impairments associated with stroke are likely to adversely affect both exercise capacity and muscular efficiency, with consequent effects on functional mobility and resistance to fatigue. However, little knowledge exists regarding the response of patients post-stroke to exercise, particularly during the early post-stroke recovery period. The overall objective of this thesis was to investigate longitudinally the metabolic and cardiorespiratory responses to exercise over the course of post-stroke recovery. The next four chapters summarize studies conducted to address this objective. These chapters were written as independent papers; thus some redundancy in content was unavoidable.

The first challenge was the design of an exercise testing protocol that would permit assessment of exercise capacity of patients post-stroke in the functional upright position. To date the use of the preferred testing mode - the treadmill - has been limited because of the motor and postural impairments of people with stroke. However, given the success of facilitating paretic gait with BWS, it seemed conceivable that this strategy could be useful in permitting safe and efficacious testing early after stroke. Thus, one purpose of this thesis

was to validate the use of a BWS-facilitated treadmill exercise protocol, first with healthy individuals (Chapter 2), and then with people less than one month post-stroke (Chapter 3).

Despite the fact that stroke constitutes the single most common diagnostic category of patients undergoing physical rehabilitation, details regarding the mode, intensity, and duration of rehabilitative activities are lacking in the literature. The extent of physical activity, in terms of the intensity and duration of metabolic stress, can affect the extent of adaptation to exercise. Therefore, in order to carry out a comprehensive investigation of the responses to exercise, the level of physical activity of the subjects should be documented. Consequently, a clinical study was conducted, the main purpose being to estimate the aerobic component of stroke rehabilitation sessions through continuous HR monitoring (Chapter 4). Secondary purposes were to (i) determine the daily and total duration of stroke rehabilitation sessions over the course of recovery; (ii) estimate the aerobic component of occupational therapy and physiotherapy sessions; (iii) estimate the mean energy expenditure of physiotherapy sessions; (iv) determine the extent to which the sessions provided metabolic stress sufficient to induce a training effect; (v) identify the particular therapeutic interventions that elicited adequate and excessive cardiovascular stress.

The principal purpose of the final study was to investigate changes in exercise capacity and the energy expenditure in level walking over the course of post-stroke recovery (Chapter 5). Secondary purposes were to (i) document changes in functional status, exercise capacity, and energy cost of level treadmill walking over the same time period; (ii) determine the relationships among changes in exercise capacity, energy cost of walking, and functional status.

1.9   References

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CHAPTER 2: EFFECT OF BODY WEIGHT SUPPORT ON EXERCISE CAPACITY OF HEALTHY INDIVIDUALS

2.1 Introduction

Over the past two decades the conceptual framework guiding neurologic rehabilitation has undergone changes that have had significant clinical implications. With the emergence of the systems model of motor control, the historical focus on the neuromuscular system has been replaced with an emphasis on how multiple systems (neuromuscular, musculoskeletal, cardiorespiratory) interact with each other and with the environment to affect functional outcomes (1). This broader perspective has led to the need for multidimensional databases, prompting adaptation of evaluative techniques traditionally not considered to be in the domain of neurologic physical therapy. One such technique is the testing of exercise capacity.

It is becoming clear that recovery of patients with neurologic involvement cannot be attributed solely on the basis of improved neuromuscular function. Roth and colleagues (2) determined that only 2-36 percent of the variance in disability following stroke is explained by neurologic impairment. Indeed, Gresham et al (3) proposed that "much of the disability of stroke victims appears to be due to coexisting cardiovascular disease." Approximately 75 percent of people with stroke also have cardiac disease (4) and chronic stroke survivors often have abnormally low exercise capacity (5-7). There is some evidence of compromised cardiorespiratory fitness in patients with other neurologic diagnoses including post-polio syndrome (8), Parkinson's disease (9), Guillain-Barre Syndrome (10), traumatic brain injury (11, 12), cerebral palsy (13), multiple sclerosis (14), and spinal cord injuries (15, 16).

The limited investigation of exercise testing of neurologic populations conducted to date has been restricted to those individuals with chronic neuromotor deficits. There is a need to develop procedures that will permit assessment of patients with recently acquired

disability since it is typically this group who are actively engaged in rehabilitation. Given the high probability of significant motor and postural impairments in the acute and subacute stages, the challenge is to design safe and efficacious methods of testing. Maximal oxygen consumption ($\dot{V}O_2$max) is generally accepted as the definitive index of exercise capacity (17), as well as the best measure of the functional limit of the cardiovascular system (18). While most investigators studying oxygen consumption ($\dot{V}O_2$) of neurologic patients have relied on cycle and wheelchair ergometers, treadmill walking is the testing modality of choice for several reasons. To facilitate measurement of true $\dot{V}O_2$max approximately 50 percent of the total muscle mass must be recruited; this condition is much more likely to be met while walking than while cycling, particularly in a deconditioned population (18). Also, the upright posture is used for the majority of mobility tasks. Both measured $\dot{V}O_2$max values and aerobic training are task-specific, that is, specific to the exercise modality employed (19) or the task being trained (18, 20). Thus, to ensure clinically relevant interpretation of patient's status, this task specificity should be reflected in the testing protocol.

Body weight support (BWS) systems have been developed recently to mechanically offset a percentage of body mass while providing external balance support, thereby permitting treadmill walking of patients in the early stages of neurologic recovery (21, 22). The typical system consists of a vest similar to parachute harness which is attached to an overhead support. Unweighting of a prescribed amount of body mass is achieved by vertical displacement through the supporting frame using a weight and pulley or a pneumatic system. Visintin and Barbeau (23) reported attainment of a more normal gait pattern using treadmill walking with 40 percent BWS in seven individuals with spastic paresis. Recently, Hesse et al. (24) compared treadmill walking with 0, 15, and 30 percent BWS to floor walking in 18 patients with chronic hemiparesis and found greater symmetry of weight-bearing during treadmill walking irrespective of the extent of BWS, and

reduction in both premature plantarflexor activity and antigravity muscle activity with increasing BWS. Researchers from the same laboratory recommended in an earlier study that an upper limit of 30 percent of BWS should be used to facilitate treadmill walking in order to avoid significant reductions in muscle activation (25). The EMG amplitude of the lower extremity muscles elicited during BWS-facilitated locomotion has been shown to be closely associated with peak limb load (26). Harkema et al. (26) suggested that optimal limb loading provides the appropriate level of sensory input required for lumbosacral spinal cord modulation of efferent output to facilitate the generation of stepping. Studies of treadmill stepping in cats following thoracic spinal transection have also demonstrated the importance of proprioceptive inputs in modulating the motor pools for locomotion (27). In a pilot study comparing the effects of 15, 30, and 50 percent BWS on the biomechanics of hemiparetic gait, Hassid and colleagues (28) found that 15 percent BWS optimized the symmetry of loading during the stance phase. This finding intimates that unweighting of 15 percent of body mass was most effective in providing step-related sensory feedback to the locomotor networks of the brainstem and spinal cord.

To date, there have been no reports of the application of BWS to facilitate treadmill testing of neurologic patients. Mangione et al. (29) applied an unweighting technique to reduce the ground reaction forces and associated stress during submaximal treadmill testing of 27 patients with osteoarthritis of the knee. An inverse relationship was found between the degree of unweighting (0, 20, and 40 percent) and $\dot{V}O_2$ at a given submaximal workload. This result is consistent with previous evidence indicating that recruitment of muscle mass at submaximal workloads is less with BWS than with full weight bearing (30) and that submaximal $\dot{V}O_2$ levels are proportional to the muscle mass used in performing the task under investigation (31).

For meaningful interpretation of the measurements of exercise capacity in patients with pathology, comparison to normative reference values is desirable. Thus, $\dot{V}O_{2\,max}$

values obtained using BWS-facilitated treadmill testing must be shown to be comparable to those obtained under standard testing conditions. The purpose of this preliminary study was to investigate the feasibility of using a BWS-facilitated maximal treadmill exercise testing protocol with healthy adults by determining if the results obtained under the condition of 15 percent BWS are comparable to those obtained when testing under the standard, full weight-bearing condition. In addition, we wanted to determine if the presence of the harness support alone, without BWS, would affect test results. If deemed to be a valid testing modality, BWS-facilitated treadmill testing would then be used in a study to measure exercise capacity of neurologic patients. A level of 15 percent BWS was chosen since the research findings discussed above suggest that low percentages of unweighting enhance the gait pattern of individuals with neurologic involvement without significantly altering the peak muscle mass recruited, and thus the peak $\dot{V}O_2$ levels attainable. Therefore, we anticipated that the $\dot{V}O_2$ max values attained using 15 percent BWS would be similar to those measured in the standard test and in the test using the harness support without BWS.

2.2 Methods

2.2.1 Subjects

Volunteers over 40 years of age were recruited from the community by word of mouth. None of the subjects had a history of cardiovascular disease, musculoskeletal abnormalities or pulmonary disease that would preclude maximal exercise. The subjects demonstrated various levels of physical fitness but none had participated in specific physical training during the preceding six months. Potential subjects were asked to complete the Revised Physical Activity Readiness Questionnaire (rPAR-Q) which has been demonstrated to be a reliable screening tool for exercise testing (32) (Appendix 1). High

concurrent validity of the rPAR-Q has been demonstrated in its use with adults 60-69 years of age (33). A total of 17 subjects with no positive responses to the rPAR-Q questions were given a detailed explanation of the study and were asked to sign the informed consent form which was approved by the university's research ethics committee (Appendix 2).

Two of the subjects, a 60 year old male and a 61 year old female, were withdrawn from the study and referred to a cardiologist because of abnormal electrocardiographic (ECG) responses during their first exercise test. Of the remaining 15 subjects, 10 had never smoked and five were former smokers (mean of 7.0 pack-years, where pack-year is number of packs/yr x years of smoking; years since quitting 31 ± 16 yr]. Other background characteristics are summarized in Table 1. The Physical Activity Questionnaire (PAQ) was used as a general measure of the physical activity level of each subject (34) (Appendix 3). This questionnaire involves asking the subject to indicate the frequency and duration of their participation over the past year in 11 forms of physical activity. A score for each activity is derived from the product of the length of time of participation per session (in hr), the number of sessions per week and the number of seasons of participation per year. A total activity score is the sum of the individual scores and can be categorized as: score > 18, *very active*; 1-18, *active*; and 0, *inactive*.

Table 1. Subject characteristics

Subjects	n	Age *yr*	Height *cm*	Mass *kg*	BMI	PAQ
females	8	55.1 ± 13.6	166.0 ± 6.8	70.5 ± 11.2	25.6 ± 4.5	29.4 ± 17.4
males	7	56.4 ± 9.4	177.2 ± 6.8	74.9 ± 11.3	24.0 ± 3.1	25.6 ± 10.5
Total	15	55.2 ± 11.3	171.4 ± 8.6	72.6 ± 11.1	24.8 ± 3.9	27.6 ± 14.2

Data are means $\pm$ SD. BMI: body mass index (mass/height^2); PAQ: Physical Activity Questionnaire.

2.2.2 Study protocol

All testing took place in the exercise testing laboratory. Each subject participated in a familiarization session and performed three maximal treadmill GXTs, with an interval of 48 hours between tests. The sequence of the following experimental conditions was randomized for each subject: (i) *no BWS* - standard GXT; (ii) *0% BWS* - GXT with harness support and no unweighting; (iii) *15% BWS* - GXT with harness support and 15 percent of body mass displaced.

2.2.2.i   Familiarization Session

One week prior to the initial exercise test, each subject visited the laboratory to become familiar with the testing equipment, the exercise protocol, and the unweighting procedure, and to practice breathing with the respiratory mouthpiece, headgear and noseclip in place. Each subject was fitted with a harness of the appropriate size. The subjects became comfortable with treadmill walking with and without BWS in less than five minutes, consistent with a previous report that only 1-2 minutes are required for most healthy individuals to habituate to treadmill walking (35).

2.2.2.ii   GXT protocol

The three GXTs performed by each subject were conducted at the same time of the day in a temperature-controlled laboratory with temperature maintained at 22 ± 2 °C and relative humidity of 45-60 percent. Subjects were requested to avoid food and smoking for at least two hours, refrain from drinking caffeinated beverages for at least six hours and avoid heavy exertion or exercise for 12 hours. A progressive exercise test was performed using a calibrated motorized treadmill* in accordance with standard American College of Sports Medicine (ACSM) criteria (36). The Naughton-Balke protocol (2.5% grade increment/2 min at a constant velocity of 1.3 m/sec) was the test protocol used for all tests.

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*Model 18-60, Quinton, 3303 Monte Villa Parkway, Bothel, WA 98021-8906

Testing was preceded by a 3-minute warm-up at level grade using a velocity of 0.9 m/sec and was followed by a 2-minute cool-down at level grade and a velocity of 1.0 m/sec. Subjects were requested to avoid using the handrails of the treadmill for support because such support can increase the total treadmill time and reduce submaximal values of $\dot{V}O_2$ (37). Termination of testing followed ACSM guidelines (36). Subjects were instructed to use the 'thumbs down' signal to indicate their desire to terminate the test. Criteria for a maximal effort included attaining at least two of the following: i) increase in $\dot{V}O_2$ of less than 100 ml in the final minute of exercise ($\dot{V}O_2$ plateau), ii) maximal heart rate (HRmax) within 10 b/min of age-predicted HRmax (220 - age), iii) peak respiratory exchange ratio (RERpeak) of greater than 1.10 (38).

Expired gas was analyzed using open-circuit spirometry using a SensorMedics 2900 Metabolic Measurement Cart[†] to determine $\dot{V}O_2$, $\dot{V}CO_2$, minute ventilation ($\dot{V}E$), RER, and tidal volume (Vt). Expired volumes were passed through a 3-1 mixing chamber where the percentages of O_2 and CO_2 were analyzed by a mass spectrometer (accuracy $\pm$ 0.02 percent). Calibration of gases was done using standard gases (26% O_2/74% N_2 and 16% O_2/4% CO_2/80% N_2) and verified before each test. Volume calibration using a 3-liter syringe was also verified prior to each test. Subjects wore a nose clip and breathed room air through a one-way directional valve system attached to a mouthpiece. Maximal values for exercise parameters were averaged over the last 30 seconds.

Electrical activity of the heart was continuously monitored using a 10-lead electrocardiogram. Skin sites were abraded with fine sandpaper and alcohol to remove surface epidermis and oil in order to minimize impedance. To ensure good contact, each electrode was tapped vigorously after placement while monitoring the corresponding lead on the oscilloscope. In addition, each lead was slackened prior to application of the BWS

[†] Sensormedics, 22705 Savi Ranch Parkway, Yorba Linda, CA 92687

harness to avoid undue tension on the leads during the exercise tests. HR was obtained from the RR interval on the ECG recording. HR_{rest} was determined after the subject had rested for 10 minutes while seated in a chair placed on the treadmill belt. This measurement was taken just prior to the exercise test with the respiratory mouthpiece, headgear and noseclip in place. HR_{max} was the average HR during the last 30 seconds of exercise. Maximal O_2 pulse (O_2 pulse$_{max}$) was calculated using the formulae O_2 pulse$_{max}$ = $\dot{V}O_2$ max/HR_{max}. Right brachial artery SBP and DBP were measured using a calibrated mercury sphygmomanometer. Resting SBP (SBP_{rest}) and resting DBP (DBP_{rest}) were measured subsequent to determining HR_{rest}. During exercise testing blood pressure was measured every 2 minutes and every minute during recovery until returning to baseline. Maximal rate-pressure product (RPP_{max}), an index of myocardial oxygen consumption (39), was calculated as the product of HR_{max} and peak SBP (SBP_{peak}) divided by 100.

In the *15% BWS* and *0% BWS* GXTs the Pneuweight Unweighting System[‡] was used (Figure 1). This system provides vertical displacement of a prescribed amount of weight using pneumatic pressure. This particular unweighting device accommodates the 5 cm vertical displacement of the center of gravity that occurs in the normal gait cycle, thus permitting a normal gait pattern. The harness, weighing approximately 0.7 kg, was applied to the subject's chest and leg straps attached to the harness were placed around each upper thigh for additional support. The harness was then attached to the overhead supporting frame by two clips. In the *15% BWS* GXT, the unweighting dial was set to allow displacement of 15 percent of body mass.

Exercise time, the time from the initiation to termination of the exercise protocol excluding the warm-up and cool-down, was recorded. Predicted $\dot{V}O_2$ max ($\dot{V}O_2$ max(pred)) was calculated in ml/kg/min using the ACSM formula for treadmill walking: $\dot{V}O_2$ max(pred) = [(3.5 ml/kg/min) + (speed (m/min) x 0.1) + (grade (fraction) x speed (m/min) x 1.8)] (36).

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‡ Quinton, 3303 Monte Villa Parkway, Bothel, WA 98021-8906

Measured $\dot{V}O_2$ max was expressed as a percentage of $\dot{V}O_2$ max(pred). Subjective exertion on the treadmill was recorded at the end of each stage of exercise and at peak exercise using the modified RPE on a scale of 0 (*nothing at all*) to 10 (*very, very strong*) (40). Subjects were asked to point with the index finger to the number indicative of their RPE. In addition, at the conclusion of each testing session, each subject was asked to identify the reason for termination of the test and to respond to the open-ended question *"How did you feel during and after the exercise test?"* At the end of the final session the subjects were also asked *"Please comment on the harness support system. Did you prefer to do the exercise test with or without the support?"* The responses were documented verbatim.

Figure 1. Experimental set-up. Anterior view of body weight support system with harness, overhead suspension and treadmill. The electrocardiograph is to the left and the metabolic measurement cart is to the right of the treadmill.

2.2.2.iii   Data analysis

One-way analysis of variance (ANOVA) for repeated measures using the within-subject factor of experimental condition and Bonferroni *post hoc* testing were applied to detect statistically significant differences in the dependent variables across the three experimental conditions. To ascertain the potentially confounding effect of order of the experimental conditions, the ANOVAs of all dependent variables were repeated using testing order as a between-subject factor. All statistical tests were performed with an alpha level set at 0.05.

2.3 Results

The order of testing conditions did not affect the results of the exercise tests. The requirements for the designation of a 'maximal effort' were met with all tests, and in 27 of the 45 tests, all three criteria were achieved. The HRmax criterion was achieved by all subjects while three subjects (two 61-yr-old males, one 71-yr-old male) were unable to attain a RERpeak greater than 1.10 and three other subjects (one 43-yr-old female, one 46-yr-old male, one 56-yr-old male) did not attain a $\dot{V}O_2$ plateau during the last minute of exercise. In all tests the subjects voluntarily requested termination of the tests. For the *no BWS and 0% BWS* GXTs, the reason for termination was consistent within individual subjects, six offering dyspnea as the main reason and the remaining nine claiming general fatigue. However, in the *15% BWS* GXT, four of the latter group stopped due to dyspnea, yielding a total of 10 in this experimental condition whose reason for termination was respiratory difficulty.

Maximal values of relative $\dot{V}O_2$, exercise time, and HRmax achieved by each of the 15 subjects for each testing condition are illustrated in Figure 2. Neither $\dot{V}O_{2\,max}$ nor

HRmax were affected by the testing condition but exercise time was significantly longer in the *15% BWS* GXT.
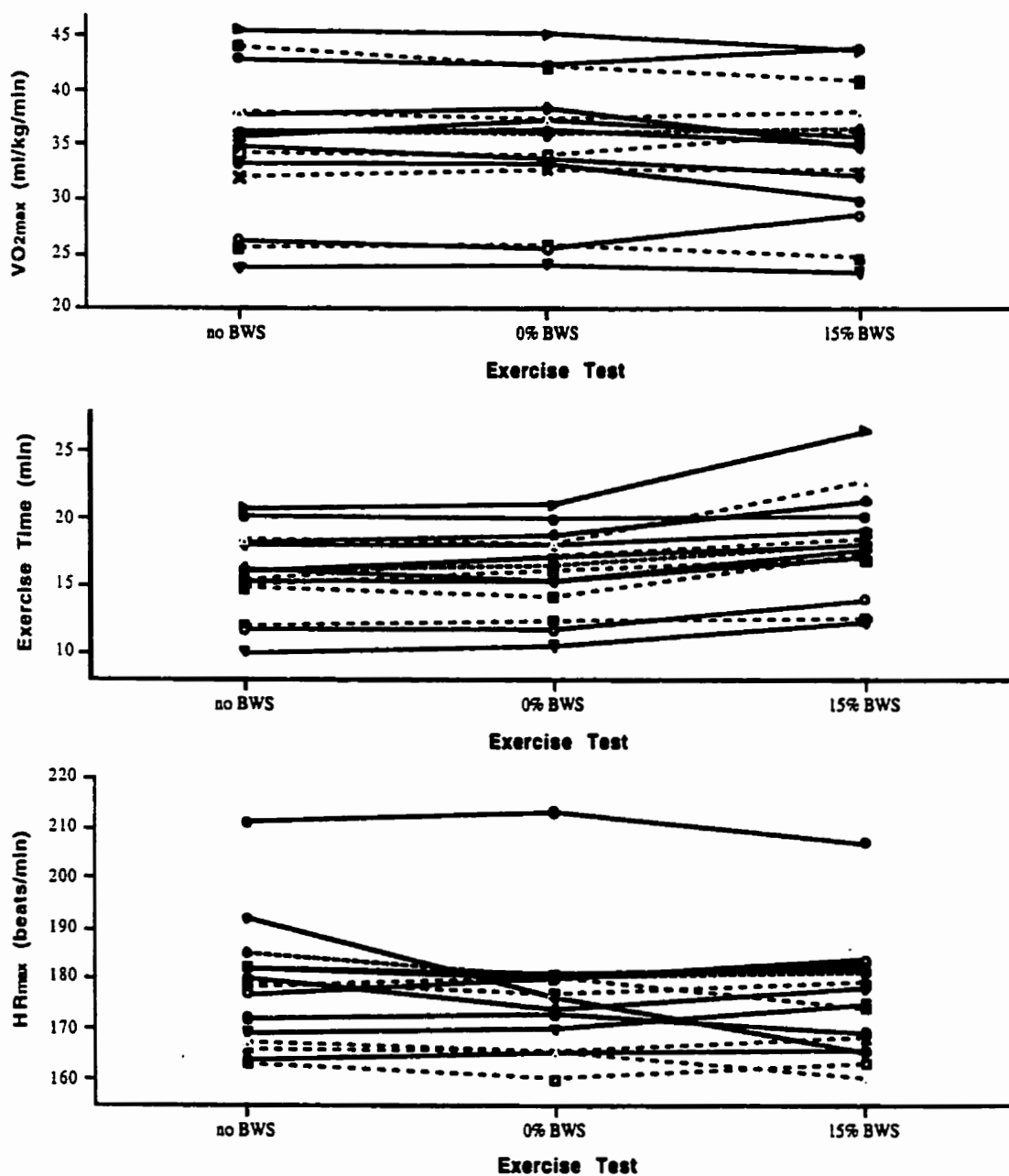
Figure 2. V̇O₂ max, exercise time and HRmax for each of the 15 subjects across the three testing conditions.

Relative and absolute $\dot{V}O_2$ max, $\dot{V}CO_2$ max, HRmax, O_2 pulsemax, RPPmax, $\dot{V}E$peak,

RRpeak, and RPEpeak were not influenced by the testing condition (Table 2). However,

Vtpeak was significantly lower in the *15% BWS* condition than in the *no BWS* condition.

Exercise time was significantly longer in the *15% BWS* condition than in the either the *no*

BWS or the *0% BWS* conditions by averages of 12.4 and 13.8 percent, respectively. The

mean percentage of predicted $\dot{V}O_2$max was significantly lower in the *15% BWS* condition

than in the other two conditions. In the standard *no BWS* GXT the mean ($\pm$ SD) $\dot{V}O_2$max

was 32.9 ± 7.2 ml/kg/min for female subjects and 37.6 ± 5.0 ml/kg/min for male subjects.

Table 2. Physiologic Variables at Peak Exercise Intensity across GXTs

Variable	GXT		
	No BWS	0% BWS	15% BWS
$\dot{V}O_2$max *ml/kg/min*	35.1 ± 1.7	34.9 ± 1.6	34.4 ± 1.6
% $\dot{V}O_2$max (pred)	83.8 ± 1.3	83.4 ± 1.2	74.4 ± 2.4*§
$\dot{V}O_2$max *l/min*	2.53 ± 0.14	2.52 ± 0.14	2.49 ± 0.14
$\dot{V}CO_2$ max *ml/kg/min*	40.1 ± 1.9	39.9 ± 1.8	39.1 ± 2.0
RERpeak	1.15 ± 0.07	1.15 ± 0.08	1.14 ± 0.06
HRmax *beats/min*	177.8 ± 12.5	175.9 ± 12.3	175.6 ± 11.7
O_2 pulsemax *ml/beat*	14.3 ± 0.80	14.2 ± 0.80	14.2 ± 0.78
RPPmax	338.5 ± 13.8	334.0 ± 9.9	339.7 ± 12.5
$\dot{V}E$ peak *l/min*	88.4 ± 5.0	89.8 ± 5.3	85.8 ± 5.4
Vtpeak *l*	2.57 ± 0.14	2.51 ± 0.13	2.36 ± 0.12†
RRpeak *breaths/min*	35.0 ± 1.7	36.4 ± 2.2	36.9 ± 2.5
Exercise time *min*	15.9 ± 0.78	16.1 ± 0.78	18.1 ± 0.96‡ll
RPEpeak *0-10*	7.9 ± 0.31	7.5 ± 0.39	7.3 ± 0.57

Data are means±standard errors for all 15 subjects. $\dot{V}O_2$ max: maximal O_2 uptake; % $\dot{V}O_2$max (pred): measured $\dot{V}O_2$ max expressed as a percentage of predicted $\dot{V}O_2$ max; $\dot{V}CO_2$max: maximal CO_2 production; RERpeak: peak respiratory exchange ratio; HRmax: maximal heart rate; O_2 pulsemax: maximal O_2 pulse; RPPmax: maximal rate-pressure product; $\dot{V}E$peak: peak minute ventilation; Vtpeak: peak tidal volume; RRpeak: peak respiratory rate; RPEpeak: peak ratings of perceived exertion. * $p<0.01$, † $p<0.001$, and ‡ $p<0.0001$ denote significant differences from no BWS test; § $p<0.01$ and l $p<0.0001$ denote significant differences between 0% BWS test and 15% BWS tests.

For comparative purposes $\dot{V}O_2$ values during treadmill testing across the testing conditions were normalized by expressing $\dot{V}O_2$ values as percentages of the highest value of $\dot{V}O_{2\,max}$ obtained during the standard *no BWS* test. Similarly, exercise time was normalized by expressing it as a percentage of the exercise time recorded during the *no BWS* test (Figure 3).
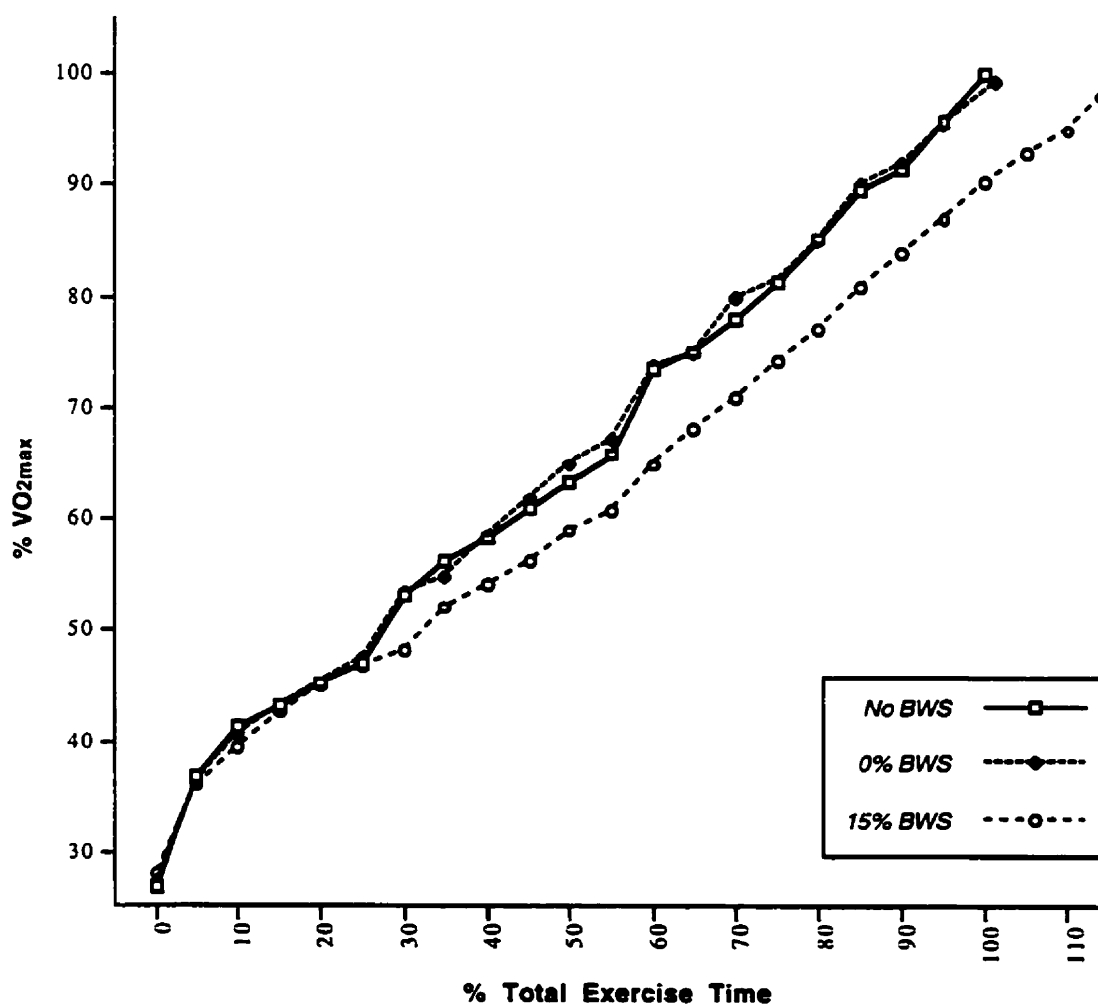
Figure 3. Mean $\dot{V}O_2$ for all subjects over exercise time across the three testing conditions. Values are normalized for comparative purposes by expressing $\dot{V}O_2$ as a percentage of the $\dot{V}O_{2\,max}$ recorded in the standard *no BWS* test and expressing exercise time as a percentage of the total exercise time of the *no BWS* test.

All subjects reported that the harness was comfortable to wear. However, nine subjects preferred testing without BWS because the harness was perceived to have had a mild restrictive effect on respiration toward the end of the test. This group included the four subjects whose reason for terminating the exercise test changed from fatigue in the *no BWS* and *0% BWS* conditions to dyspnea in the *15% BWS* condition. In addition, the V_{tpeak} values for each of these four subjects were lowest in the *15% BWS* condition, and in two female subjects (48.7 and 60.5 yr), $\dot{V}_{Epeak}$ and $\dot{V}_{O_2 max}$ values were also lowest in that condition. The remaining six subjects preferred using the harness because of the security it provided during testing, two of whom stated that the harness also provided back support which they felt enhanced their performance. However, their test results did not reflect this observation.

2.4   Additional experiments

Four preliminary investigations were also conducted to explore aspects of the unweighting mechanism. Future experimentation would be necessary before conclusions could be drawn regarding these points of inquiry.

2.4.1   Calibration of unweighting system

The first of these brief experiments investigated the precision of the unweighting mechanism of the Pneuweight® BWS System. A dead weight of 5 kg placed on the treadmill was attached to the overhead support and the unweighting dial was gradually turned. At precisely 5 kilograms on the dial the weight lifted off the treadmill. A similar result was found when the experiment was repeated using a 10 kilogram weight, providing preliminary evidence that the calibration of the unweighting mechanism appeared to be precise under these somewhat crude testing conditions.

2.4.2   Effect of treadmill grade on extent of unweighting

The purpose of the next experiment was to determine if the grade of the treadmill affected the precision of the unweighting mechanism. Each of two healthy subjects, wearing a BWS harness, stood on a digital strain gauge scale placed on the treadmill. With the treadmill at 0 percent grade, 15 percent of the subject's body mass was unweighted and the reading on the scale was recorded. The percentage of body mass that was unweighted was determined using the formula: % BWS = [(total body weight - reading on scale)/total body weight] x 100. This procedure was repeated for treadmill grades of 5%, 10%, and 15%. The results summarized in Table 3 suggest that increases in treadmill elevations from 0% to 15% do not systematically affect the precision of unweighting of 15% of body mass. The error in precision of providing 15% BWS using the Pneuweight® BWS System appears to be in the order of ± 0.9%. Thus the potential error in calibration exceeded that found in the preceding study where dead weights of much smaller mass were used and the actual point at which unweighting occurred was limited to visual observation.

Table 3. Percentage of BWS while unweighting 15% of body mass using the Pneuweight® BWS System and altering treadmill grade from 0% to 15%

Treadmill grade (%)	Subject 1	Subject 2
0	14.8	14.4
5	15.4	14.7
10	14.7	14.2
15	16.1	15.6
% BWS*	15.25±0.64%	14.72±0.62%

*Values are mean ± SD.

2.4.3   Effect of handrail support on extent of unweighting

The next series of experiments investigated the effects of handrail support on the precision of unweighting by the Pneuweight® BWS System. Handrail support has been shown to influence the results of treadmill exercise testing by reducing the aerobic demands

of walking (41). Although the subjects in the present study did not use handrail support, we anticipated that future application of the same exercise test method for patients post-stroke with significant balance problems might necessitate the use of such support. Thus, we were interested in investigating whether the unweighting mechanism used in the Pneuweight® BWS System adjusts for the additional unweighting resulting from use of handrail support. Each of two healthy subjects (weighing 62.7 and 62.4 kg) stood on a digital strain gauge scale placed on the treadmill. In the first condition the subject was fully weight bearing and in the second condition 15% BWS was applied. The effect of fingertip support (light contact of the fingertips of the second to fifth digits of the left hand with the left handrail of the treadmill) on body weight recorded on the scale was measured using treadmill elevations of 0%, 5%, 10%, and 15%. The experiments were repeated using 'moderate' support, instructing the subjects to "Use your left hand on the left handrail to provide moderate support."

Percentages of BWS in the various conditions were determined by the formula used in the preceding set of experiments. The results are summarized in Table 4. The effect of fingertip support on the percentage of BWS in the full weight bearing condition varied greatly across the treadmill grades and between the two subjects, despite their similar body mass. Fingertip support in this condition had minimal effect on the extent of unweighting of Subject 1 until 15 percent of treadmill elevation whereas a substantial effect was observed at all grades in the case of Subject 2. With 15 percent of body mass unweighted by the Pneuweight® System, the effect of fingertip support on the extent of unweighting was minimal. In the full weight bearing condition, moderate handrail support resulted in unweighting of about 15 percent in subject 1 and 11 percent in subject 2 whereas with 15 percent of unweighting by the Pneuweight® System, moderate handrail support contributed an additional 5% BWS in subject 1 and 10 percent in subject 2. Subject I reported difficulty attaining and maintaining 'moderate' support through the left hand while being unweighted 15 percent of body mass.

Although such variable results derived from only 2 subjects precludes a conclusive interpretation, it would appear that Pneuweight® BWS System does not adjust for additional unweighting through handrail support and that both fingertip and moderate support can contribute substantially, and to highly variable extents, to the total percentage of BWS. This preliminary observation suggests that whenever feasible, either fingertip or moderate handrail support should be discouraged during BWS-facilitated exercise testing. More investigation is warranted of the influence of handrail support on the actual versus desired extent of unweighting.

Table 4. Percentage of BWS with fingertip versus moderate handrail support while unweighting 0% and 15% of body mass and altering treadmill grade from 0% to 15%

	Fingertip handrail support				Moderate handrail support			
	0% unweighted		15% unweighted		0% unweighted		15% unweighted	
Treadmill Grade	Subj. 1	Subj. 2	Subj. 1	Subj. 2	Subj. 1	Subj. 2	Subj. 1	Subj. 2
0	0.6	1.6	16.7	15.0	17.4	10.8	17.6	26.3
5	0.3	4.7	17.0	15.0	13.6	9.2	17.5	25.0
10	0.6	4.7	15.9	14.7	16.7	12.0	24.0	22.8
15	3.0	7.3	15.2	15.2	14.2	12.0	20.2	25.6
% BWS*	1.1	4.6	16.2	15.0	15.5	11.0	20.1	25.0
	±1.3	±2.3	±0.8	± 0.2	±1.9	±1.3	±3.2	±1.5

*Values are mean±SD.

2.4.4   Effect of additional weight on $\dot{V}O_2$ max

In the final pilot experiment the $\dot{V}O_2$ max and total exercise time attained with overweighting of 15% of body mass were compared to those recorded in the other three test conditions (no BWS, 0% BWS, and 15% BWS). We expected that exercise time would be reduced but $\dot{V}O_2$ max would not differ from that attained in the other GXTs. The rationale was that while the submaximal workload would be increased by the additional weight, thereby increasing the $\dot{V}O_2$ values at any given submaximal work rate and

shortening the total exercise time, the muscle mass recruited at maximal effort would be similar to that in the other conditions, hence the $\dot{V}O_2$ max level attained would not be altered. Indeed, it has been demonstrated that activation of muscles in excess of that required to elicit $\dot{V}O_2$ max (about 50 percent of total muscle mass) has no effect on the peak $\dot{V}O_2$ level attainable (18).

In this simple experiment one subject, a 42-year-old female, repeated the exercise protocol of the principal study but with a dead weight equaling 15 percent of her body mass attached to the waist. The results were as anticipated - total exercise time was decreased to 83.3 percent of the *no BWS* test (from 14.4 min to 12 min) while the $\dot{V}O_2$ max value of 42.2 ml/kg/min attained with an additional 15 percent of body weight was consistent with the value of 43.1 ml/kg/min attained in the *no BWS* test (Fig. 4).
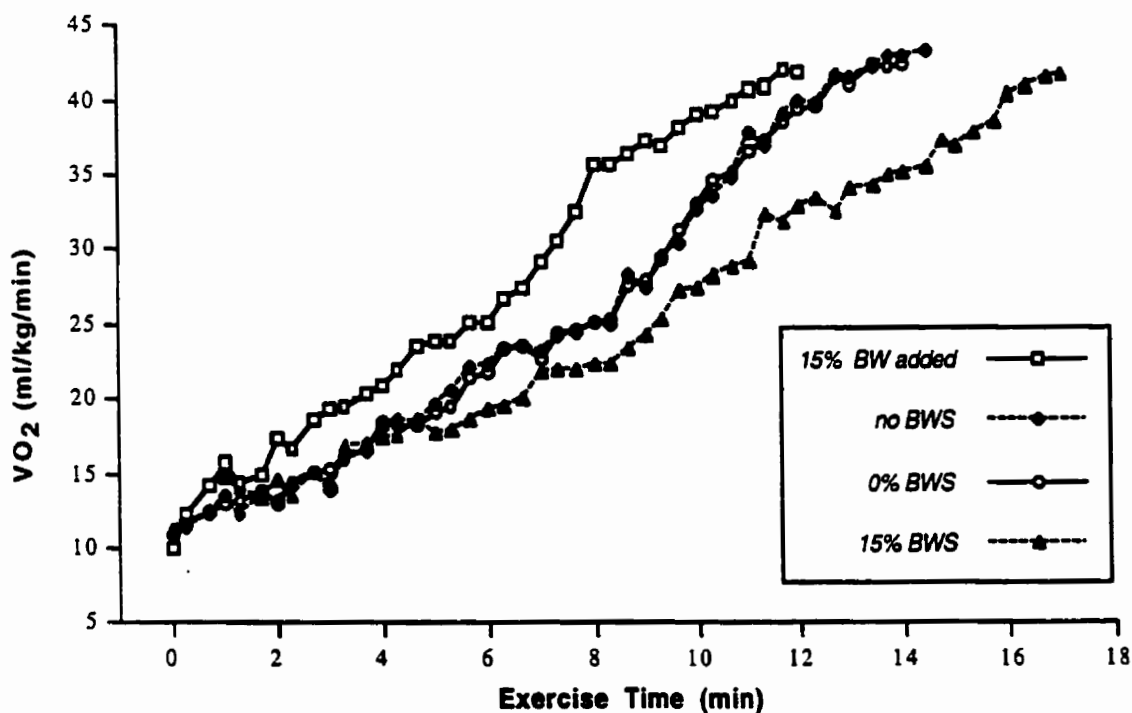
Figure 4. Changes in $\dot{V}O_2$ of one subject (42 yr-old female) during 4 maximal treadmill exercise tests: *15% BW added* - with no harness but 15 percent of body mass added; *no BWS* - with no harness and no body weight support (BWS); *0% BWS* - with harness but no unweighting; *15% BWS* - with harness and unweighting of 15 percent of body mass.

2.1 Discussion

To accurately interpret data obtained from maximal exercise tests, it is important to ensure that the subjects have demonstrated maximal effort. While every subject in the present study met the required two of three criteria for designation of $\dot{V}O_2$ max in all tests, only nine (60 percent) achieved all three criteria. Despite the fact that use of HRmax as an absolute criterion has been discouraged due to high inter-subject variability of HRmax (standard deviation of ± 11 beats/min) (42), all subjects met this criterion. Also, although it is not uncommon for subjects to fail to demonstrate a plateau in $\dot{V}O_2$ (38), 12 (80 percent) of the subjects met this criterion. That three subjects over 60 years of age did not achieve a RERpeak greater than 1.10 is consistent with previously reported reductions in RERpeak values at maximal effort in individuals over 60 years (43). As further assurance that the tests represented maximal effort, the $\dot{V}O_2$ max values documented in this study are comparable to the findings of previous studies. Recently, Jackson and colleagues (44) conducted maximal exercise treadmill tests with 160 healthy males over the age of 55 years (mean age 58.0 ± 3.0 yr) and reported a mean $\dot{V}O_2$ max of 33.2 ± 6.0 ml/kg/min. In addition, the extent of variability in the $\dot{V}O_2$ max measurements can be compared using the coefficient of variation, a dimensionless number expressing the standard deviation as a proportion of the mean (45). The coefficients of variation for $\dot{V}O_2$ max were 18.5 percent and 18.1 percent, respectively, in this study and in the study by Jackson et al. (44).

As anticipated, neither the presence of the harness support in the *0% BWS* condition nor the harness plus unweighting in the *15% BWS* condition affected the end-point values of the main respiratory gas exchange variables measured during exercise testing. At any given submaximal stage of exercise, the energy expenditure and cardiorespiratory responses were less in the unweighted condition, in keeping with the aforementioned fact that $\dot{V}O_2$ is proportional to the muscle mass recruited; hence the greater exercise duration to

elicit a maximal response. However, since the $\dot{V}O_2$ max level attained was not significantly different than that of the standard test, the assumption is that the application of 15 percent of BWS does not reduce the total muscle mass activated at peak effort below the threshold required to attain a true $\dot{V}O_2$ max. This assumption is consistent with previous investigations that concluded that low percentages of unweighting do not significantly alter the peak muscle mass recruited (25, 26).

The effects of 15% BWS observed in this study are analogous to the influence of handrail support on treadmill GXT results. Measured $\dot{V}O_2$ max is not different with or without handrail support but submaximal $\dot{V}O_2$ levels are significantly reduced and total exercise time is significantly increased when handrail support is permitted (41, (46). The reduction in aerobic demands of walking with handrail support results in a shift of the exercise time/$\dot{V}O_2$ curve to the right (41), similar to the right shift observed in the present study in the *15% BWS* test, as shown in Figure 2. Thus, there appears to be a common trend in the effects of 15% unweighting of body mass and the use of handrail support on the response to treadmill exercise testing. Indeed, the use of moderate handrail support used by the two subjects in the brief pilot experiment described in section 2.4.3 resulted in reductions in weight bearing of 15.5 and 11 percent, respectively.

Application of the ACSM formula to estimate $\dot{V}O_2$ max during treadmill walking resulted in overestimates of the actual $\dot{V}O_2$ max achieved, consistent with previous observations that the estimated steady-state requirements of the last treadmill stage attained often overestimate the achieved $\dot{V}O_2$ max (17). The substantial overestimation in the *15% BWS* test (134 percent) was anticipated since peak treadmill speed and elevation - parameters used in the formula - were greatest in the unweighted condition. Clearly, the ACSM formula is inappropriate for the test conditions in this study. A revision to the ACSM formula has recently been suggested for exercise protocols with relatively small

workload increments between stages, such as the Naughton-Balke used in the present study (17). Application of this revised formula in the standard *no BWS* test reduced the overestimation of $\dot{V}O_{2max}$ from 119 to 103 percent. Interestingly, application of another formula by the same authors (17), adapted for use when handrail support is permitted during testing, decreased the overestimate of $\dot{V}O_{2\,max}$ for the *15% BWS* test from 134 to 103 percent. This finding corroborates the above-stated suggestion that the testing conditions imposed by *15% BWS* test appear to be similar to those encountered with a standard maximal treadmill test allowing handrail support.

The differences in $\dot{V}O_{2\,max}$ values on repeated testing under the three testing conditions varied, on average, by 2 percent, which is within the reported 2-4 percent of variability for repeated measurements of $\dot{V}O_{2\,max}$ among healthy individuals (31). However, although differences in $\dot{V}O_{2\,max}$ across the three testing conditions were neither statistically or clinically significant, there was a trend toward lower $\dot{V}O_{2\,max}$ values in the tests using *15% BWS*, with 12 subjects (80 percent) demonstrating their lowest $\dot{V}O_{2\,max}$ values in the unweighted condition. This observation may be explained by the protracted exercise time in the *15% BWS* condition, with nine subjects (60 percent) exceeding the upper limit of the "optimum duration of 8-17 minutes" for maximal treadmill tests (47). Buchfuhrer et al. (47) reported a decrease, albeit not statistically significant, in $\dot{V}O_{2\,max}$ when tests lasted more than 17 min. The investigators suggested that the reduction in $\dot{V}O_{2\,max}$ during prolonged tests may be due to elevated body temperature, increased dehydration, altered substrate utilization, subject discomfort or ventilatory fatigue. Whereas Buchfuhrer et al. (47) noted an increase in the incidence of low back pain during prolonged exercise testing, no subject in the present study complained of back pain and two subjects claimed that the harness provided back support. While reduction in $\dot{V}O_{2\,max}$ values with unweighting does not appear to be substantial, avoidance of very small

workload increments between stages (i.e. < 0.5 METs) of a testing protocol using BWS may help to offset the potential for exercise time to exceed 17 minutes.

The ventilatory parameters, $\dot{V}E_{peak}$, Vt_{peak}, and RR_{peak} attained in the standard *no BWS* test are consistent with previous reports (48). The finding of significantly lower Vt_{peak} values in the *15% BWS* condition than in the *no BWS* and *0% BWS* conditions suggests that restriction in chest wall excursion is due to combination of the circumferential pressure exerted on the thorax by the harness vest and the upward force imposed by the vertical displacement of body mass. This reduction in Vt_{peak} without concomitant changes in the $\dot{V}E_{peak}$ implies a compensatory increase in respiration rate. Two of the subjects who preferred the *no BWS* condition recorded their lowest values for $\dot{V}O_2 max$, Vt_{peak} and $\dot{V}E_{peak}$ in the *15% BWS* condition and terminated that testing session because of dyspnea. While definitive conclusions cannot be drawn from data on two subjects, this clustering of findings suggests that caution may need to be exercised in the use of BWS for individuals with compromised respiratory function. Further investigation of the effect of unweighting on respiratory function is warranted.

The exercise testing protocol and application of the BWS harness were well-tolerated by the subjects, and unweighting did not affect the end-point values of the principal respiratory gas exchange variables. These findings support further study of the application of this testing method for those individuals in neurologic rehabilitation whose neuromuscular limitations preclude standard exercise testing. However, we anticipate that the Naughton-Balke protocol would be too demanding for this population. A more appropriate protocol might be an individualized, low-velocity method such as that used by Macko and colleagues (5) for testing patients with chronic stroke.

2.5.1 Study limitations

The conclusions reached in this study may have limited application because of the small sample size. Also, the subjects were relatively inexperienced with treadmill walking, thus the results may have been affected by learning or habituation. However, this possibility is unlikely since the order of testing did not affect the results. Based on the findings of one of the preliminary experiments, calibration of the degree of unweighting in the Pneuweight® BWS System may be somewhat inaccurate. If this is the case, the results obtained in the 15% BWS condition could be somewhat spurious.

2.6 Conclusions

Unweighting of 15 percent of body mass had no effect on the end-point values of the principal respiratory gas exchange variables measured during $\dot{V}O_{2\,max}$ treadmill testing of 15 healthy adults over the age of 40 years. Thus, study of its application in treadmill exercise testing of individuals with neurologic dysfunction is warranted. The findings in the present study of comparable respiratory end-points attained with or without use of 15% BWS are important to ensure validity of future comparisons of test results of neurologically-compromised subjects. Reduction in V_{tpeak} values with unweighting suggests that caution should be exercised when using unweighting with individuals who manifest compromised respiratory function. Further study of the effects of varying percentages of unweighting on respiratory gas exchange variables of individuals with and without pathology would extend the clinical usefulness of this technique.

2.7 References

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Revised Physical Activity Readiness Questionnaire (rPAR-Q)*

Please read the following questions carefully and answer each one honestly. Check ( ) YES or NO.

YES	No	
☐	☐	1. Has your doctor ever said that you have a heart condition <u>and</u> that you should only do physical activity recommended by a doctor?
☐	☐	2. Do you feel pain in your chest when you do physical activity?
☐	☐	3. In the past month, have you had chest pain when you were not doing physical activity?
☐	☐	4. Do you lose your balance because of dizziness or do you ever lose consciousness?
☐	☐	5. Do you have a bone or joint problem that could be made worse by a change in your physical activity?
☐	☐	6. Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or a heart condition?
☐	☐	7. Do you know of <u>any other reason</u> why you should not do physical activity?

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Subject   Date

*Reference: Cardinal BJ, Esters L, Cardinal MK. Evaluation of the Revised Physical Activity Readiness Questionnaire in older adults. Med. Sci. Sports Exer. 1996;28:468-472.

2.9 Appendix 2

**Queen Elizabeth II
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<u>Informed Consent</u>

Title of Study: *Effect of body weight support on exercise capacity of healthy individuals*

Principal Investigator:	• Marilyn MacKay-Lyons, M.Sc. (PT), Doctoral Student, Department of Physiology & Biophysics, Dalhousie University; Tel: 902-494-2632 or 902-473-8622
Associate Investigators:	• Lydia Makrides, Ph.D., Professor and Director, School of Physiotherapy, Dalhousie University • Stephen Phillips, M.D., Neurologist and Director, Acute Stroke Service, Queen Elizabeth Health Sciences Centre • Stephanie Speth, MSc., Certified Exercise Specialist, Cardiac Prevention and Rehabilitation Research Centre • Michael Allen, M.D., Staff Physician, Cardiac Prevention and Rehabilitation Research Centre

Introduction

We invite you to take part in a research study at the QEII Health Sciences Centre. This study has been approved by Dalhousie University and QEII Research Ethics Committees. Taking part in this study is voluntary. The quality of your health care will not be affected by whether you participate or not. Participating in this study might not benefit you, but we might learn things that will benefit others. You may withdraw from the study at any time without affecting your care. The study is described below. The description tells you about the risks, inconvenience, or discomfort which you might experience. You should make sure that any questions you have about the study are answered to your satisfaction.

What is the purpose of this study?

Treadmill exercise tests are used to find out how well the heart, lungs and leg muscles function while exercising. For a person who has had a stroke it is difficult to do a treadmill exercise test without support. The new Pneuweight System can provide this support. The person wears a safety vest, similar to a life jacket, around the chest which is attached to an overhead bar. This support system can also be used to remove some of the body weight to make walking on the treadmill easier for a person who has had a stroke. However, at present we do not know how this support system affects the results of the standard exercise test. The purpose of this study is to find out what the effect of this support system is on exercise tests done by healthy people. This information will be used to help us understand how the harness affects the exercise tests done by people with stroke who are unable to do the test without support.   **Please turn to page 2**

Effect of body weight support on exercise capacity of healthy individuals.

Who can take part in the study?
The 15 healthy adults in this study:
• will live in the community within commuting distance of the QEII;
• will have completed the Physical Activities Readiness Questionnaire (Par-Q) and answered 'no' to all questions;
• will be able to provide informed consent.

How are participants selected?
Healthy adults will be recruited from the community by word of mouth and asked to complete the revised PAR-Q. Those people with no positive answers on the PAR-Q questions will be given a detailed explanation of the study by the principal investigator and asked to sign this consent form.

What does the study involve?
All testing will be done at the Cardiac Prevention and Rehabilitation Research Centre (CPRRC) located on the 9th floor of the Abbie Lane Building. You will make four visits to CPRRC and each visit will take 45- 60 minutes.

Your first visit to CPRRC will be a practice session and you will not do an exercise test. Your body weight and height will be measured. You will then be shown the room where the treadmill exercise testing will be done. You will see the treadmill and the safety vest attached to an overhead support that may be worn during the exercise test to prevent falling. We will fit you with the right vest and give you a chance to practice walking on the treadmill while wearing the vest. You will be shown the equipment used during the exercise test to measure the oxygen and carbon dioxide in the air that you breath out (e.g. mouthpiece, noseclip, headgear, and metabolic cart). You will be given a chance to practice breathing with the mouthpiece and noseclip in place. While wearing the mouthpiece you will be unable to speak so you will be instructed to use the following hand signals: 'thumbs up' means everything is fine, 'thumbs down' means you want to stop and have the mouthpiece removed.

You will do three exercise tests, with at least 48 hours between each test. Each test will be done at the same time of the day (that is, if the first test is done in the morning, the other two tests should also be done in the morning). Before coming for each test:
• avoid a heavy meal on the day of the test;
• avoid eating for about one hour before the test (but drink fluids as needed to satisfy thirst);
• avoid smoking for at least 2 hours;
• avoid drinking caffeinated beverage for at least six hours;
• avoid heavy exertion or exercise for 12 hours
• wear lose, comfortable clothes and footwear appropriate for walking.

Effect of body weight support on exercise capacity of healthy individuals.

For one of the three exercise tests, the safety vest will be worn and 15% of your body weight will be taken up by the overhead support (Test W). For another test, the safety vest will be worn but no body weight will be removed (Test V). The other test will follow the routine method and a vest will not be worn and no body weight will be removed (Test R). The order of testing will be decided randomly, by having you draw one of three papers which has one of the test names (Test B, V or R) written on it. This will be the first test. The next paper that you draw will be the second and the remaining one will be the third test.

To record your heart rate and the electrical activity of your heart, an electrocardiogram (ECG) will be done during each exercise test. The ECG electrodes will be attached to your chest. To make sure there is a good connection between the skin and the electrodes, your skin will be rubbed with alcohol and fine sandpaper before the electrodes are attached. Hair on the skin may need to be shaved. A cuff will be placed around your right arm to measure your blood pressure. If the test is Test V or Test W, the safety vest will be put on. After the mouthpiece and noseclip have been put in place, you will rest for 15 minutes, seated in a cushioned chair. Resting heart rate and blood pressure will be measured at the end of this rest.

You will then step onto the treadmill and, if the safety vest is worn, it will be attached to the overhead support. For the next three minutes you will walk on the treadmill at a low speed to complete your warm-up. The exercise test will begin at a very easy level and will gradually become more difficult. You will be asked to keep walking until you are limited by severe fatigue or discomfort. When you signal to stop, the treadmill will be slowed down and turned off. You will be closely monitored during the test by an exercise specialist who will take your blood pressure, follow your ECG tracing and measure the air that you will be breathing through the mouthpiece. The noseclip makes sure that all the air you breathe out is measured. A physician will also be present for the first test. If we see any reason to stop the test, you will be asked to stop at once and the treadmill will be turned off. After the testing is over you will remain seated until rested.

Are there any risks or discomforts?
Exercise testing is a routine procedure done at CPRRC. However, it is possible that certain unfavorable changes may occur during or after the test. Should any of these happen to you, you may stop the exercise test. These may include abnormal blood pressure, dizziness, fainting, disorders of the heart beat, leg cramps and very rarely, heart attack. However, in our exercise facilities, with the presence of well-trained staff, the likelihood of such risks is small. Emergency equipment and experienced staff are available to deal promptly with any unusual situations.

What are the possible benefits?
By agreeing to participate in this study, you will be contributing valuable information. This information will be used to help answer important questions about the effects of the support system on the standard exercise test. Then, when we use this support for when testing people with stroke, we will have a better idea of how the support is affecting the results of the tests. In addition, you will be given the results of your own tests, which will give you an idea of your level of fitness. We can provide advice to you about safe levels of physical activity, based on your test results. Also, we will let your doctor know if the tests show any unusual findings.

Effect of body weight support on exercise capacity of healthy individuals.

Other important information

1. **Confidentiality:** All information gathered during the study will be kept confidential. The information collected from this study will be published, as well as presented at scientific conferences but your name will not be used in any reports or publications. Your records will be kept in a locked file cabinet. Only the staff involved in the research study will see them.

2. **Costs:** There will be no costs to you for being in this study. You will not be charged for any of the costs of the exercise tests. If you become injured while participating in this study, medical treatment will be available to you. None of your legal rights will be waived. The investigators still have their legal and professional responsibilities.

3. **Questions or Problems:** If you have any questions about this study, please contact Marilyn MacKay-Lyons at the CPRRC (902-473-8622) or at Dalhousie University (902-494-2632). There is also voice mail at these numbers.

I have read the description of the study. I have been given the opportunity to discuss the study. My questions have been answered to my satisfaction. I understand that I will be given a copy of this consent form for my own records. I hereby consent to take part in this study.

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Signature of Subject   Date

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Signature of Study Investigator   Date

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Signature of Witness   Date

2.10 Appendix 3

PHYSICAL ACTIVITY QUESTIONNAIRE (PAQ)

Instructions to subjects:
"We need to get an idea of your level of physical activity. Think back over the last year. Together we will fill in the chart below for each activity you did in the last year."

ACTIVITY	SEASONS YOU DID ACTIVITY?	# OF TIMES/WK	HOW LONG EACH TIME?	SCORE
Walking for Exercise	spring summer fall winter	1 2 3+	__hr__min	☐
Running or Jogging	spring summer fall winter	1 2 3+	__hr__min	☐
Gardening/ Yard Work	spring summer fall winter	1 2 3+	__hr__min	☐
Home exercise	spring summer fall winter	1 2 3+	__hr__min	☐
Golf	spring summer fall winter	1 2 3+	__hr__min	☐
Tennis	spring summer fall winter	1 2 3+	__hr__min	☐
Bowling/ curling	spring summer fall winter	1 2 3+	__hr__min	☐
Swimming	spring summer fall winter	1 2 3+	__hr__min	☐
Bicycling	spring summer fall winter	1 2 3+	__hr__min	☐
Social dancing	spring summer fall winter	1 2 3+	__hr__min	☐
Heavy Housework	spring summer fall winter	1 2 3+	__hr__min	☐

TOTAL SCORE: ☐

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Subject   Date

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* Reference: Jaglal SB, Krieger N, Darlington G. Past and recent physical activity and risk of hip fracture. Am J Epidemiol 1993;138:107-118.

CHAPTER 3: EXERCISE CAPACITY EARLY AFTER STROKE

3.1 Introduction

While neurologic recovery post-stroke has been extensively studied, surprisingly little knowledge exists regarding exercise capacity in the early post-stroke period. As a consequence, functional recovery post-stroke is usually attributed solely to improved neurological status; thus intervention strategies are focused on improving the neuromuscular system. In 1968 Iseri and colleagues (1) stressed that "prospective studies taking into consideration all the factors which might influence rehabilitation including an objective assessment of metabolic response to exercise are needed to determine the specific role played by abnormalities of the cardiovascular system."

An accurate indication of the functional limit of the cardiovascular system would be of particular benefit in the early stages of recovery post-stroke when there is a well-recognized 'window of opportunity' to optimize functional recovery. Indeed, Newman (2) reported that 80 percent of neurologic recovery and gains in functional ability occur within the first six weeks post-stroke. Measurement of $\dot{V}O_{2\,max}$ is the definitive index of functional exercise capacity (3). Using the treadmill as the $\dot{V}O_{2\,max}$ test modality is preferable to other methods such as cycle and wheelchair ergometers for the following reasons. To facilitate measurement of true $\dot{V}O_{2\,max}$ approximately 50 percent of the total muscle mass must be recruited; this condition is much more likely to be met while walking than while cycling, particularly in a deconditioned population (4). Also, since measured $\dot{V}O_{2\,max}$ is specific to the exercise modality employed (5), testing should be performed in the most functional position. In the case of patients recovering from stroke the upright posture is used for the majority of mobility tasks. Thus, to ensure clinically relevant interpretation of results, this task specificity should be reflected in the protocol.

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A major methodological impediment to investigating exercise responses in the upright position has been lack of a test protocol that can accommodate the motor and postural impairments and that is well tolerated by patients with stroke. Corcoran and Brengelmann (6) stated that while the treadmill is the tool of choice for studying the energy cost of ambulation post-stroke, feelings of anxiety and insecurity elicited during treadmill walking preclude the use of this testing mode for patients with stroke. Most investigators have relied on the use of other modalities, mainly cycle ergometers, and have restricted testing to the chronic stroke population (7-15). A recent study introduced a bridging activity as a mode for submaximal stress-testing of patients post-stroke (16). However, the authors found that this test did not differentiate between the patients post-stroke and the healthy control subjects in terms of HR_{peak} and $\dot{V}O_{2peak}$. We found only one study that used a treadmill protocol. Macko and his colleagues (17) reported successful use of a low-velocity treadmill protocol to test HR_{peak} of 30 patients who were, on average, two years post-stroke. ($\dot{V}O_{2peak}$ was not measured.) The authors concluded that although there is a need for testing in the early post-stroke period, use of their protocol may not be feasible due to physical limitations in the subacute phase.

Body weight support (BWS) systems have recently been developed to mechanically offset a portion of body weight, thereby permitting treadmill ambulation of patients in the early stage of neurologic recovery. Such support could potentially overcome the restrictions on exercise testing imposed by poor motor control and balance reactions allowing tests to be conducted with greater safety and at a much earlier time in the post-stroke recovery phase than would otherwise be feasible. Recently, we validated the use of 15 percent BWS-facilitated testing with 15 healthy individuals (Chapter 2). The use of BWS did not affect the end-points of the principal respiratory gas exchange variables and thus did not confound interpretation of the results of $\dot{V}O_2$ max testing.

The main purpose of this study was to determine if a treadmill exercise protocol using 15 percent BWS would be a safe and efficacious method of documenting exercise

capacity early post-stroke. By safe is meant that the testing procedure should not place the patient at a greater risk of complications than that of routine exercise tests. Retrospective data from some 2,000 facilities regarding 500,000 clinical exercise tests that involved patients with and without known cardiovascular impairment reported a rate of MI of 3.6 per 10,000 and a death rate of 0.5 per 10,000 (18). For the testing procedure to be considered efficacious, the design of the protocol should be appropriate for the subjects under study, permitting maximal volitional effort, resulting in symptom-limited termination of testing, and yielding valid and reliable data.

To be truly efficacious, the end-point $\dot{V}O_2$ values should be 'maximal'. According to Rowell (4), $\dot{V}O_{2\,max}$ is a unique, stable, and highly reproducible value of $\dot{V}O_2$ of a given individual that can be obtained under a variety of conditions whereas $\dot{V}O_{2peak}$ represents the highest value of $\dot{V}O_2$ reached under a specific set of circumstances. In the case of deconditioned or elderly individuals, which would include most patients with stroke, the rigorous criteria for $\dot{V}O_{2\,max}$ are usually not met (19) and attainment of $\dot{V}O_{2peak}$ is an acceptable standard of testing efficacy. If the test protocol used in this study were to be found to be safe and efficacious, then the data collected would represent the first documentation of exercise capacity early post-stroke. The same protocol would be used in a subsequent study to document changes in exercise capacity during recovery from stroke.

3.2 Methods

3.2.1 Pilot study

In order to select criteria for participation in this study and to develop an appropriate exercise protocol we conducted a pilot study involving six patients who were characteristic of the type of subjects we anticipated studying in the principal investigation. All were within two months post-stroke and ambulated more than 15 meters with single or quad

canes and with minimal or standby assistance of one physiotherapist. Two subjects wore molded ankle-foot orthoses. We used the Chedoke McMaster (CM) Stages of Recovery to screen potential subjects according to level of motor impairment of the involved lower extremity (20) (Appendix 1). The CM Assessment, which involves having the patient perform increasingly complex motor tasks of the arm, hand, leg and foot (20), has been extensively investigated in terms of reliability and validity (21). Stage 1 is assigned when flaccid paralysis is present and Stage 7 when movement is 'normal'. Stage 3 is described as that stage of neurological recovery where "active voluntary movement occurs without facilitation, but only in the stereotyped synergistic patterns" and Stage 4 as the stage in which "synergy patterns and simple movements out of synergy are possible" (20). Two patients were at Stage 3 of CM Stage of Recovery of the Leg (CM-Leg) two at Stage 4, and two at Stage 5.

The subjects were brought to the exercise testing laboratory where they performed treadmill walking with 15 percent BWS (see Chapter 2). The effects of treadmill speed and grade on the quality of the gait pattern were observed in order to determine the ability of the patients to manage this mode of exercise as well as to develop an appropriate exercise protocol. The speed was slowly increased in increments of 0.04 m/sec from an initial speed of 0.27 m/sec to ascertain a suitable range of velocities for the exercise protocol. Four of six of the subjects walked at self-selected speeds of 0.35-0.4 m/sec and were unable to walk speeds greater than 0.5 m/sec due to difficulty advancing the affected leg during the swing phase. In addition, the patients with CM-Leg of Stage 3 required constant physical assistance to support and advance the affected leg. Thus, we ascertained that the minimal degree of motor control required to independently advance the affected leg on the treadmill with use of 15 percent BWS was equivalent to greater than Stage 3.

The patients were able to tolerate gradual increments in treadmill grade from 0 percent to 10-15 percent, at which point they complained of substantial discomfort in the calf muscles, which caused them to terminate the walking trial. This discomfort was

presumably due to stretching of the posterior tibial muscles during the stance phase at the higher treadmill elevations.

Prior to the pilot test we assumed that use of the handrails while treadmill walking with 15 percent BWS would be unnecessary due to the support provided by the unweighting system. However, three subjects were unwilling to walk without the additional support. It became clear that handrail support would be required by some patients in the principal study.

From this pilot work, we concluded that a standard exercise protocol would be too challenging for patients early post-stroke and elected to use an individualized protocol. It was also apparent that the subjects could tolerate greater increments in grade than in speed. Thus we selected a progressive, patient-specific, protocol for the principal investigation that involved manipulating the grade in the early stages and the speed in the later stages. During the initial 2 minutes each subject would walk at a self-selected speed and 0 percent treadmill grade, after which there would be a 2.5 percent increase in grade every two minutes until an incline of 10 percent was reached, and, thereafter, a 0.05 m/sec increase in speed every two minutes. Due to the observed rapid onset of fatigue in some patients, the warm-up phase would be to limited to one minute.

3.2.2 Subjects

Consecutive patients admitted to the Acute Stroke Service of the Queen Elizabeth II Health Sciences Centre in Halifax were screened for eligibility. Inclusion criteria required diagnosis of a first ischemic stroke; post-stroke interval of less than 1 month; CM-Leg greater than Stage 3; age greater than 17 years; score in excess of 23 on the Mini Mental Status Examination (MMSE) (22); and ability and willingness to provide informed consent. Exclusion criteria were the absolute and relative contraindications for exercise testing outlined by the American College of Sports Medicine (ACSM) (23) (Appendix 2). Prospective subjects who met the criteria were given a detailed explanation of the study and

were asked to sign the informed consent form which was approved by the Research Ethics Committees of both the university and health care facility (Appendix 3).

The minimum criterion of CM-Leg greater than Stage 3 was established after the pilot study. The 18 year minimum age was used to restrict the sample to adults with stroke; patients less than 18 years are classified as pediatric patients and are managed at the children's hospital. An upper limit on age was not imposed since there are no contraindications regarding age in maximal exercise testing. Patients in their seventh, eighth and ninth decades of life who met the ACSM-stipulated exclusion criteria have been tested without incident (24). The criterion of a MMSE of greater than 23 was selected since lesser scores are interpreted as evidence of the presence of dementia (25).

The Oxfordshire Community Stroke Project (OCSP) classification was used to classify cerebral infarction into four subtypes: total anterior circulation infarct (TACI), partial anterior circulation infarct (PACI), posterior circulation infarct (POCI), and lacunar infarct (LACI) (26). The Barthel Index (BI) was used to classify the subjects by level of functional dependence (27) (Appendix 4). The BI, reported to be more robust than the other scales of activities of daily living (28), assesses 10 activities of self-care and mobility, yielding two subscores and one combined score, ranging from 0 to 100. The scores reflect the amount of assistance required, and hence, the extent of functional involvement.

The Physical Activity Questionnaire (PAQ), recently developed by Jaglal et al. (29) to determine pre-morbid physical activity level, was completed by asking subjects to indicate the frequency and duration of participation in 11 activities during the year preceding their stroke (see Chapter 2). A score for each activity is derived based on the product of the length of time of participation per session, the number of sessions per week and the number of seasons (i.e. spring, summer, fall, winter) of participation. A total activity score is derived from the sum of the individual activity scores and can be categorized as: very active, greater than 18; active, 1-18; and inactive, 0.

The clinical history of each subject was recorded, noting smoking habits and co-morbidities such as hypertension, diabetes mellitus, and CAD. Clinically significant CAD was based on the presence of at least one of the following: MI by history or ECG, angina pectoris, or coronary artery bypass graft surgery (30).

3.2.3 Study protocol

All testing took place in the exercise testing laboratory. One week prior to the exercise test, each subject visited the laboratory for a familiarization session similar to that described in Chapter 2. In addition to being made familiar with the testing equipment and procedures, each patient was fitted with a BWS harness and walked on the treadmill with 15 percent BWS at a self-selected, comfortable speed, in part to become familiar with weight-supported treadmill walking but also to identify the initial treadmill speed for the actual exercise test.

In preparation for the exercise test, subjects were requested to maintain their regular medication schedule, to avoid food and smoking for at least two hours, refrain from drinking caffeinated beverages for at least six hours and avoid heavy exertion or exercise for 12 hours. The methods for data collection are described in detail in Chapter 2. In brief, the symptom-limited exercise test was performed using a calibrated motorized treadmill. Handrail support was permitted as needed but subjects were encouraged to minimize the pressure applied to the rail. Subjects were instructed to use maximal effort and to display the 'thumb down' signal when they wished to terminate the test. Termination of testing followed ACSM guidelines (23). For those subjects who were smokers at the time of their stroke, a Nellcor NPB-40 pulse oximeter with a finger probe was used to monitor arterial oxygen saturation during exercise testing. The probe was placed on the distal phalanx of the left third digit. Oxygen saturation less than 85 percent was used as the criterion to terminate the exercise test (31).

Expired gas was analyzed using open-circuit spirometry to determine $\dot{V}O_2$, $\dot{V}CO_2$, $\dot{V}E$, RER, and V_t. Peak values for exercise parameters were the averages of values recorded during the last 30 seconds of the test. The term 'peak' was deemed more appropriate than the term 'maximal' to describe the highest values recorded since we anticipated that many subjects would not attain a true $\dot{V}O_2$ max (4).

A 10-lead electrocardiogram provided continuous monitoring of HR and cardiac electrical activity and the Pneuweight® Unweighting System unweighted 15 percent of body mass. HR_{rest} was determined after the subject had rested for 5 minutes sitting in a chair placed on the treadmill belt. This measurement was taken just prior to the exercise test with the respiratory mouthpiece, headgear and noseclip in place. HR_{peak} was the average HR during the last 30 seconds of exercise and was expressed as a percentage of maximal age-predicted HR_{max} [$HR_{max-pred}$ = (220 - age)]. O_2 pulse$_{peak}$ in ml O_2/beat was calculated using the formula O_2 pulse$_{peak}$ = (1000 x $\dot{V}O_{2peak}$)/HR_{peak}. Right brachial artery SBP and DBP were measured using a calibrated mercury sphygmomanometer. Resting SBP and DBP were measured subsequent to determining HR_{rest}. During exercise testing blood pressure was measured every 2 minutes and every minute during recovery until returning to baseline. Peak rate-pressure product (RPP_{peak}), an index of myocardial oxygen consumption (32), was calculated as the product of HR_{peak} and peak SBP divided by 100.

Exercise time, the time from the initiation to termination of the exercise protocol excluding the warm-up and cool-down, was recorded. Subjective exertion on the treadmill was recorded at the end of each stage of exercise and at peak exercise using the modified RPE on a scale of 0 (*nothing at all*) to 10 (*very, very hard*) (33). Subjects were asked to point to the number indicative of their RPE. In addition, at the conclusion of each testing session, each subject was asked to identify the reason for termination of the test.

As a check on the reliability of the testing protocol, we conducted a test-retest study by having a subsample of subjects perform two GXTs within 3-4 days at two months post-stroke. Being mindful of the substantial physical involvement and tremendous emotional stress confronting many of the subjects in the early post-stroke period, we decided to delay reliability testing until two months after stroke. Nevertheless, most subjects remained reluctant to perform two tests in such a short time interval. Six subjects (three from the dependent group and three from the independent group) consented to participate in the reliability substudy.

3.2.4 Data analysis

Descriptive statistics (mean, standard deviation, range, frequency) were used to characterize the subjects and the variables of the exercise tests. Independent t-tests for unequal sizes were used for between-group comparisons of normally distributed continuous variables and the Mann-Whitney U-test for ordinal variables. Chi-square analysis was used to determine the relationship between nominal variables and the Fisher's exact test was applied to 2x2 contingency tables. Pearson product-moment correlation coefficients were computed to assess relationships between continuous variables. Alpha level was set at 0.05.

Multiple linear regression was used to examine the effects of various independent variables on the dependent variable $\dot{V}O_{2peak}$ (34). Because of the documented correlation of age with $\dot{V}O_{2peak}$, age was treated as a forced variable. Least-square regression lines were calculated for $\dot{V}O_2$ and HR against exercise time for each of the six subjects who participated in the reliability tests. The slopes and intercepts were compared using the intraclass correlation coefficient ($ICC_{(3,1)}$) (35). $ICC_{(3,1)}$s were also calculated for $\dot{V}O_{2peak}$ and HR_{peak} values measured in the reliability tests.

3.3 Results

3.3.1 Subjects

Although 44 patients who met the screening criteria were initially recruited for participation in this study, only 29 (66 percent) performed the GXT, including 20 white males, 2 black males and 7 white females. Older females were particularly reluctant to participate. Of the 15 subjects who did not participate, 10 (67 percent) withdrew after the familiarization session due to test anxiety, two had a progression of their neurologic status prior to the time of testing, and the remaining three did not offer a reason for their withdrawal from the study. Characteristics of the participants and non-participants are compared in Table 5. Statistically significant differences were seen in age and sex, with the participant group being younger and consisting of more males than females (76 percent male) while the non-participant group included more females than males (33 percent male).

Table 5. Comparison of characteristics of non-participants and participants

Characteristics	Non-participants (n=15)	Participants (n=29)
Age yr	71.3±11.4 (41-88)	64.9±13.5* (29-83)
Sex	5M:10F	22M:7F*
Side of stroke	7R:8L	18R:11L
Barthel Index	74.0±11.2 (56-98)	76.7±12.6 (59-98)
History of CAD	10/15 (67%)	17/29 (59%)
β-blocker medication	8/15 (53%)	15/29 (52%)

Data are means ± SD or counts (percentages). *p<0.01

The participants were divided into two disability categories according to their BI. Ten subjects were classed as 'Independent' (BI > 90) and the remaining 19 were classified as 'Dependent'. It should be noted that the patients in the Independent group exhibited mild disability; Skilbeck et al (36) emphasized that a BI of 100 does not necessarily imply normality, but only that the patient can manage without attendant care. Background

characteristics of the participants are compared according to group in Table 6. Statistical analysis revealed a significantly longer interval between the stroke and exercise test for the Dependent group.

Table 6. Characteristics of participants grouped according to level of disability

Characteristic	Dependent (n=19)	Independent (n=10)	Total (n=29)
Age *yr*	66.6±14.0	61.7±13.0	64.9±13.7 (29-83)
Sex	13M:5F	8M:2F	22M:7F
Weight *kg*	78.4±16.7	87.1±10.8	81.4±15.3 (50-115)
BMI *kg/m²*	26.9±4.0	28.0±3.0	27.3.0±3.6 (20-35)
Time post-stroke *days*	28.4±7.9	21.5±9.1*	26.0±8.8 (20-35)
Side of stroke	12R:7L	6R:4L	18R:11L
OCSP classification			
TACI	4 (21%)	0	4 (14%)
PACI	6 (32%)	1 (10%)	7 (24%)
POCI	4 (21%)	0	4 (14%)
LACI	5 (26%)	9 (90%)	14 (48%)
CM Stage of leg *1-7*	5.2±0.7	5.5±0.7	5.3±0.7 (4-6)
CM Stage of foot *1-7*	4.3±1.2	4.5±1.7	4.3±1.4 (1-7)
Barthel Index *0-100*	72.2±9.1	93.8±3.2	79.8±12.6 (59-98)
Ambulatory aid			
no aid	0	8 (80%)	8 (28%)
single cane	10 (53%)	2 (20%)	12 (41%)
quad cane	6 (31%)	0	6 (21%)
walker	3 (16%)	0	3 (10%)
History of CAD	11/19 (58%)	4/10 (40%)	15/29 (52%)
β-blocker medication	10/19 (53%)	5/10 (50%)	15/29 (52%)
Diabetes mellitus	5/19 (26%)	2/10 (20%)	7/29 (24%)
PAQ	7.4±10.4	3.7±5.4	5.6±8.9 (0-36)
History of smoking	12/19 (63%)	6/11 (55%)	18/29 (62%)
Amount smoked *pk-*	41.0±24.2	35.2±15.5	39.1±21.4 (5-74)

Data are means ± SD or counts (percentages). BMI: body mass index (mass/height²); OCSP classification: see text for details; CM: Chedoke McMaster; CAD: coronary artery disease; PAQ: Physical Activity Questionnaire; amount smoked: by those with history of smoking expressed as pack-years (pk-yr) [# yr of smoking x average # of packages of cigarettes/day]; *p<0.05.

That 52 percent of the participants had a history of CAD is consistent with previous incidence reports of 58 percent (37), 60 percent (38), and 70 percent (1). Roth (39)

reported that 46 percent of patients admitted for comprehensive rehabilitation had evidence of CAD. Fifteen subjects were on β-blocker medications, 13 of which were β_1-selective blockers (metoprolol, atenolol) and the remaining two being non-selective (propranolol, labetalol). No subject took digitalis or other mediations known to affect response to exercise. The incidence of diabetes among the participants (24 percent) is in keeping with a report that 280 out of 945 (30 percent) of patients admitted for comprehensive rehabilitation had preexisting diabetes (40) but is lower than the 40 percent prevalence documented in the Copenhagen Stroke Study (41). While a total of 18 participants (62 percent) had a history of smoking, 13 had quit prior to the time of their stroke. This prevalence exceeds a previously reported prevalence of 47 percent for patients in stroke rehabilitation (40).

3.3.2 General response to exercise testing

All but one subject were highly motivated, the majority claiming that their performance during testing enhanced their outlook on recovery from the stroke. No complications were encountered during or following the tests. The harness support was described as being comfortable and reducing anxiety related to fear of falling. Despite the presence of BWS and instructions that discouraged the use of handrail support, 18 (62 percent) of the subjects used the handrail during testing. The mean walking speed at initiation of testing was 0.39 ± 0.12 m/sec (median, 0.35 m/sec) and at the last completed stage was 0.54 ± 0.30 m/sec (median, 0.44 m/sec).

The majority of subjects (83 percent) terminated the exercise test of their own volition while, in the five remaining cases, testing was terminated by the investigators due to excessive increases in blood pressure. In one patient, a 64-year-old male, blood pressure rose unexpectedly to 268/130 mm Hg during the fourth stage of exercise. Testing was terminated immediately and the patient was referred to a cardiologist. No ECG abnormalities were detected and at no time during or after the test did the patient experience angina or signs of poor perfusion (e.g., lightheadedness, cynanosis, confusion, pallor,

nausea). One subject had to stop due to previously undiagnosed leg claudication. Table 7 compares the reasons for GXT termination in this study to those of a previous study involving 30 subjects who were of similar age (mean, 65 years) but with a longer post-stroke interval (mean of 26 months), and faster walking speed (mean, 0.71 m/sec) than the subjects in the present investigation (17). Arterial oxygen saturation was monitored during testing for five subjects and readings did not fall below 85 percent at any point during the GXTs.

Table 7. Reasons for GXT termination in the present study of patients early post-stroke compared with a previous study of patients in the later post-stroke period (17)

Reason for Test Termination	Present Study (n=29)	Macko Study (n=30)
Volitional fatigue	8 (28%)	23 (77%)
Hemiparetic leg fatigue	3 (11%)	1 (3%)
Nonhemiparetic leg fatigue	5 (17%)	1 (3%)
Leg claudication	1 (3%)	1 (3%)
Cardiopulmonary signs/symptoms	12 (41%)	4 (13%)
dyspnea	7 (24%)	1 (3%)
ST-segment depression	0	3* (10%)
SBP > 260 or DBP > 115 mm Hg	5 (17%)	0

Data are counts (percentages). *One subject had ST-segment depression accompanied by dyspnea.

3.3.3 Reliability of responses to GXTs

The $ICC_{(3,1)}$ for the $\dot{V}O_{2peak}$, HR_{peak}, slopes of $\dot{V}O_2$ and HR data, and intercepts of $\dot{V}O_2$ and HR data of the six subjects involved in the test-retest reliability study were 0.94, 0.93, 0.96, 0.88, 0.94 and 0.92, respectively. These values are consistent with those reported by Potempa and colleagues (14) in a reliability study involving 25 subjects in the chronic post-stroke period. Figure 5 shows the regression lines for $\dot{V}O_2$ and HR against exercise time.
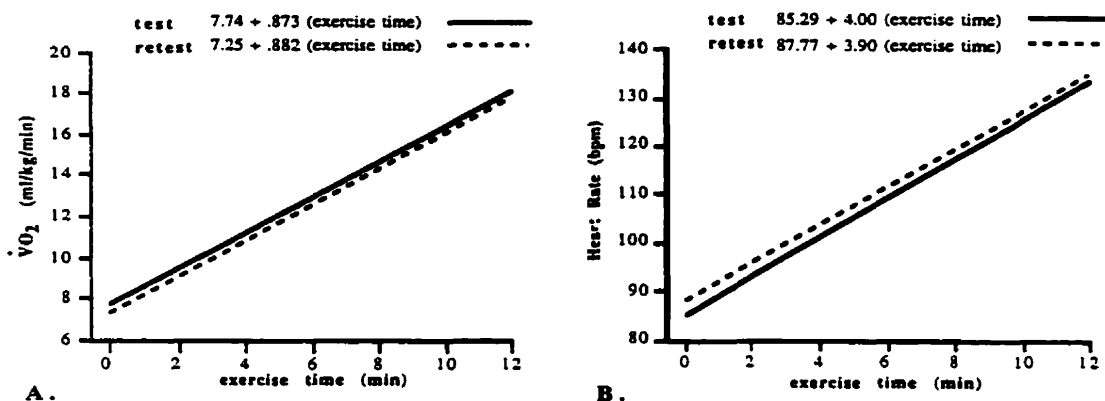
Figure 5. Average least square regression lines for the test-retest reliability study; (A.) $\dot{V}O_2$ against exercise time. (B.) HR against exercise time.

3.3.4 Attainment of $\dot{V}O_2$ max

Eighteen (62 percent) of the subjects achieved one or more of the minimum criteria commonly used to identify achievement of $\dot{V}O_2$ max (19, 24). Table 8 shows the percentages of subjects who attained the various criteria. Fifteen subjects (52 percent) were on β-blocker medication at the time of testing. Adjusting for the HR-lowering effect of this type of medication by using the formula [HRmax-pred/adj = 85% (220-age)] (42, 43) resulted in a 2.5-fold increase in the numbers of subjects who met the HRmax criteria.

Table 8. Percentages of subjects achieving criteria for attainment of $\dot{V}O_2$max

Subjects	SBPpeak >200 mm HG	RERpeak > 1.00	RERpeak >1.10	HRpeak <15 b/min	HRpeak <10 b/min	HRpeak adjusted for β-blocker* <15 b/min	HRpeak adjusted for β-blocker* <10 b/min
Dependent	4 (21%)	10 (53%)	0	3 (16%)	1 (5%)	10 (53%)	3 (16%)
Independent	4 (40%)	7 (70%)	0	2 (20%)	1 (10%)	3 (30%)	2 (20%)
Total	8 (28%)	17 (59%)	0	5 (17%)	2 (7%)	13 (45%)	5 (17%)

Data are counts (percentages). RERpeak: respiratory exchange ratio at peak exercise intensity; HRpeak: heart rate at peak exercise intensity, expressed as <15 or <10 beats/min of predicted HRmax[220-age]; SBPpeak: systolic blood pressure at peak exercise intensity. * adjustment in predicted HRmax [85% (220-age)] for HR-lowering effect of β-blocker medication.

3.3.5 Physiologic variables at peak exercise intensity

Physiologic measurements at peak exercise intensity are summarized in Table 9. Relative and absolute $\dot{V}O_2$peak values were significantly higher for the independent group compared to the dependent group but when expressed as a percentage of the normative value this group difference was not evident. Peak HR attained was similar for the groups and represented 80 ± 10 percent of predicted HRmax. The subgroup of 14 subjects not on β-blocker medication achieved 86 ± 8 percent of predicted HRmax while the group on β-blockers attained 74 ± 7 percent of predicted HRmax, the difference being statistically significant (p=.0003). The difference in mean O_2 pulsepeak of the group of subjects taking β-blockers compared with the non-β-blocker group was not statistically significant (10.1 ± 3.5 versus 9.1 ± 3.2 ml/beat). For the overall group mean RPP values increased from 109.3 ± 17.3 at rest to 224.0 ± 65.6 at peak exercise, with an overall mean increase in RPP during exercise of 112.0 ± 68.3.

Table 9. Physiologic variables at peak exercise intensity of subjects grouped according to level of disability

Variable	Dependent (n=19)	Independent (n=10)	Total (n=29)
$\dot{V}O_2$peak $mL/kg/min$	13.0±3.1	17.1±7.0*	14.4±5.1 (9-32)
$\dot{V}O_2$peak % normative	58.0±15.3	63.6±17.3	60.0±16.0 (37-89)
$\dot{V}O_2$peak L/min	1.02±0.32	1.51±0.64¥	1.2±0.50 (.5-2.7)
$\dot{V}CO_2$peak $mL/kg/min$	12.7±3.3	17.2±7.9*	14.5±5.7 (8-35)
RERpeak	0.99±0.06	1.00±0.08	1.00±0.06 (.88-1.09)
HRpeak beats/min	123.1±20.1	123.1.4±17.6	123.1±18.9 (93-144)
% of HRmax-pred	80.1±9.5	78.7±10.3	79.6±9.6 (60-93)
O_2 pulsepeak $mL/beat$	8.3±2.1	12.1±4.0¥	9.6±3.3 (4.4-20.3)
RPPpeak	220.7±65.1	237.0±69.2	224.0±65.6 (113-395)
SBPpeak $mm Hg$	177.2±32.8	190.2±32.5	181.7±32.7 (154-268)
DBPpeak $mm Hg$	93.8±14.5	105.6±12.7	98.2±14.8 (80-130)
$\dot{V}E$peak L/min	39.2±12.3	47.8±21.8	42.1±16.4 (22-68)
Vtpeak l	1.3±0.3	1.7±0.7*	1.4±0.53 (0.7-2.6)
RRpeak breaths/min	31.0±7.2	27.6±4.2	29.8±6.4 (20-51)
Exercise time min	8.5±4.1	9.2±5.7	8.7±4.6 (2-16)
RPEpeak 0-10	5.3±1.7	6.7±0.7*	5.9±1.5 (5-9)

Data are means ± SD. $\dot{V}O_2$peak: peak O_2 consumption; $\dot{V}O_2$peak % normative: % of sex and age-adjusted normative values; $\dot{V}CO_2$peak: peak CO_2 output; HRpeak: peak heart rate; % HRmax (predicted): % of (220-age); SBPpeak: peak systolic blood pressure; DBPpeak: peak diastolic blood pressure; RPPpeak: peak rate-pressure product; $\dot{V}E$peak: peak minute ventilation; Vtpeak: peak tidal volume; RPEpeak: peak ratings of perceived exertion. * p<0.05; ¥ p<0.01.

Mean Vtpeak values were higher for the independent group than the dependent group, averaging 68 percent and 57 percent, respectively, of the age and sex-adjusted normative values (44). Mean $\dot{V}E$peak values did not differ significantly between groups and were about 56% of the normative values (44). The average exercise time (8.7 min) was within the optimal range of 8-17 minutes for $\dot{V}O_2$ max testing (45). However, in a previous study we found that the GXT duration was artificially prolonged by about 14 percent when 15 percent BWS was used (see Chapter 2). Therefore, after adjusting for the

effects of unweighting using a factor of 14 percent, the optimal lower limit increases to about nine minutes, a target which 13 (45 percent) subjects, nine in the dependent group and five in the independent group, failed to achieve.

3.3.6 Prediction of $\dot{V}O_{2peak}$

In the multiple linear regression analysis the variables age and BI were significant in predicting relative and absolute values of $\dot{V}O_{2peak}$ (Table 10). The additional independent variables BMI, PAQ, and pack-year history of smoking were not significant factors in explaining the $\dot{V}O_{2peak}$ values. Similarly, the use versus non-use of handrails did not significantly affect the peak measurements.

Table 10. Multivariate prediction of relative and absolute $\dot{V}O_{2peak}$

	variables	Coefficient	SE	t	p	R^2	Adjusted R^2	Multivariate p
Relative $\dot{V}O_{2peak}$	age	-.200	.053	-3.76	.001	.475	.435	0.0002
	BI	.150	.056	2.67	.0129			
Absolute $\dot{V}O_{2peak}$	age	-.022	.004	-4.49	.0001	.563	.530	<0.0001
	BI	.016	.005	3.18	.0038			

R^2; coefficient of determination

3.4 Discussion

The primary purpose of this study was to determine whether a BWS-facilitated treadmill GXT protocol is a safe and efficacious method of measuring exercise capacity with patients early post-stroke. The trial involved testing 29 subjects with mean age of 65 years, mild to moderate disability, and an average post-stroke interval of 26 days. The fact that 34 percent of the subjects who had been recruited ultimately did not participate underlines the previously reported difficulty in conducting studies of patients early post-stroke (46). The subjects who withdrew differed from the participants in age and sex

distribution; thus the results of this study cannot be interpreted as being truly representative of those patients with stroke who meet the screening criteria.

3.4.1 Safety of GXT protocol

When considering the safety of exercise testing post-stroke, Macko and colleagues (17) speculated that in the early post-stroke period adverse cardiorespiratory responses such as hypotension and cardiac dysrhythmia may occur during testing. Continuous ECG monitoring and frequent blood pressure monitoring in our protocol reduced the possibility of these unwanted events. One patient had an excessive hypertensive response during testing but showed no signs of poor perfusion. The possibility of falling during treadmill testing due to unresolved problems with postural control and gait has also been raised (47). The use of the BWS system mitigated against this mishap. Since adverse events did not occur during or following the testing procedure, we can conclude that the protocol is safe, at least for the specific set of conditions under which this study was conducted.

3.4.2 Efficacy of GXT protocol

The issue of efficacy is more complex. The physical limitations of the subjects in this study precluded the application of a standardized protocol. Rather, a patient-specific protocol was used with less than one MET increments in each 2-minute stage. The use of individualized protocols that depart from standard methods have been previously validated for testing functional exercise capacity of untrained, sedentary individuals (3, 48). Although 18 subjects used handrail support, the regression analysis revealed that the use of support did not have a significant effect of peak measurements. This finding concurs with previous reports (48, 49).

The reliability study conducted in conjunction with the present investigation, albeit involving only six subjects, provides evidence that the data generated using the BWS-facilitated protocol are highly reproducible. This result is consistent with findings of high

reliability for exercise testing of healthy subjects (50) and subjects in the chronic post-stroke period (14).

A truly efficacious test of exercise capacity would be one in which *bona fide* $\dot{V}O_2$ max values were attained. However, based on previous investigations involving deconditioned and elderly subjects (19), we anticipated that attainment of such a goal would not be realistic for the subjects under study. Indeed, only 55 percent of the subjects exercised for a duration generally considered sufficient to generate a true $\dot{V}O_2$ max despite their willingness to exert maximal effort. Moreover, when the test results were subjected to the more rigorous criteria for $\dot{V}O_2$ max - a $\dot{V}O_2$ plateau, RER greater than 1.15, HR_{peak} within 10 beats/min of $HR_{max-pred}$) (19) - only two subjects could be interpreted as having achieved that end-point.

When considering the efficacy of our protocol relative to other designs, it is instructive to compare our findings with other studies. However, since this is the first study to report on the exercise capacity of individuals in the early post-stroke period, the comparison is restricted to studies involving patients at later stages of recovery (Table 11). The results, in terms of mean values of $\dot{V}O_{2peak}$ and HR_{peak} as well as the extent of variability in these values, are surprisingly similar given the substantial differences in testing methods and chronicity of the subjects as well as the potential for enormous heterogeneity in demographic and physical characteristics of patients post-stroke. In the three studies that involved testing of exercise capacity later in post-stroke recovery (8, 14, 51), the mean relative $\dot{V}O_{2peak}$ values were higher than in the present study. The cycle ergometer was used in all three studies; and $\dot{V}O_2$ max values of healthy individuals have been reported to be approximately 6-11 percent less when measured using cycle ergometry than when using a treadmill (4, 45). The confounding effect of exercise mode may be offset by the fact that the subjects in the present study were, on average, about a decade older than those in the other studies. Suomimen and colleagues (52) demonstrated that

$\dot{V}O_{2peak}$ decreases at a rate of at least 0.25 ml/kg/min each year of life for nondisabled males, and a similar trend has been shown for females (53). However, these trends may not apply to individuals post-stroke; hence, a longitudinal study of changes in exercise capacity over the course of recovery following stroke is warranted.

Table 11. Reported cardiovascular responses to maximal exercise testing of individuals post-stroke*

Mode of testing	Subjects	Age	Time post-stroke	$\dot{V}O_2$peak ml/kg/min	$\dot{V}O_2$peak l/min	HRpeak	% HRmax	End-points	Study
treadmill	n=29 22M:7F	65±14	26±9 days	14.4±5.1	1.2±0.5	123±19	80±10	volitional fatigue	present study
treadmill	n=30 27M:3F	65±8	2±2 yr	NT	NT	129±14	84±10	volitional fatigue	(17)
cycle ergometer	n=30 30 M	54	10 mo	17.7±4.2	1.1±0.3	125±21	75†	fatigue	(51)
cycle ergometer	n=2 2M	42, 49	11/35 wk	NT	NT	124/124	70/73	exhaustion	(54)
cycle ergometer	n=42 8M:11F(E) 15M:8F(C)	56±12	long-term	16.7±4.3(E) 15.1±4.8(C)	NR	142±23 128±26	87† 78†	exhaustion R>1.15	(14)
wheelchair ergometer	n=70 33M:37F	63±13	NR	NT	NT	121±24	77±14	exhaustion	(13)
cycle ergometer	n=19 10M:9F	66±12	8 wk-15 yr	NT	NT	104±22	NR	volitional fatigue	(10)
cycle ergometer	n=8 8M	52±10	4±3 mo	16.1±4.2	1.3±0.3	126±15	76±12	exhaustion	(8)
supine ergometer	n=10 6M:4F	72	9.5 wk	NT	NT	102±18	67±11	exhaustion	(12)
cycle ergometer	n=8 8 F	58±7	1-3 yr	13.4±3.8†	0.8±0.2	123±24	76†	NR	(15)

*Format of table is revised from Potempa (14) pg. 340. E: experimental; C: control; †calculated using mean values provided. NR: not reported; NT: not tested.

In all of the studies examining the cardiovascular responses to exercise post-stroke HRpeak was measured (see Table 11). In the only other study using the treadmill as the mode of exercise, and with a sample of similar size and age but a longer post-stroke interval and fewer subjects on β-blockers, the mean HRpeak was about 5 percent higher than in the present study (17). Also, a mean increase of 133 percent in RPP was attributed

to exercise as compared to 112 percent in the present study, suggestive of higher peak myocardial oxygen demand in the sample of patients in the chronic post-stroke period. The lowest HR_{peak} (102 ± 18 beats/min) was reported in a study using a supine ergometer (12). This finding is consistent with reports of lower hemodynamic measurements during exercise in supine than upright due to a fall in arterial driving pressure for blood through exercising muscle in the LE (55). Potempa et al. (14) reported the highest HR_{peak} (142 ± 23 beats/min, equivalent to 87 percent of age-related HR_{max}) using the cycle ergometer. HR_{max} values are approximately 1-2 percent lower using a cycle ergometer than those obtained using a treadmill (56). Thus, the HR_{peak} values recorded in that study, together with attainment of mean RER values of 1.22 ± 0.03 for the same group of subjects, suggest that these subjects used greater effort during testing, and hence probably achieved a closer approximation of $\dot{V}O_{2\ max}$ than did subjects in the other studies. However, the subjects in the Potempa study (56) were almost a decade younger and were in the post-recovery phase of stroke, two factors that could positively influence the testing conditions. Longitudinal investigations of exercise capacity after stroke have not been conducted.

The observation that β-blocking agents, mainly of the β_1-selective class, did not significantly alter peak exercise capacity ($\dot{V}O_{2peak}$, exercise duration) is in accordance with other studies of untrained sedentary individuals (42) (43). However, in contrast to the findings by Cohen-Solal and others (42) of increased O_2 pulse$_{peak}$ to compensate for the decrease in HR during exercise, O_2 pulse$_{peak}$ was not statistically different in the present study.

3.4.3 Possible mechanisms underlying low $\dot{V}O_{2peak}$

The data provided evidence of an abnormally low exercise capacity (mean of 14.4 ml/kg/min; about 60 percent of normative values) for patients in the early stages of recovery post-stroke. Values for $\dot{V}O_{2\ max}$ of less than 84 percent of normative values are interpreted

as being pathologic (57). An exercise capacity of 15 ml/kg/min is considered the minimum level required to meet the physiological demands needed for independent living (58). Further, exercise capacity has been used as predictor of mortality among patients with CAD - those with $\dot{V}O_2$ max levels of less than 21 ml/kg/min designated as a high mortality group and those with a capacity exceeding 35 ml/kg/min designated as an excellent survival group (59). However, the usefulness of this predictive capacity of $\dot{V}O_2$ max is limited in patients post-stroke since threshold $\dot{V}O_2$ max levels would need to be adjusted for the older age and reduced activity level of the stroke population.

The mechanisms underlying the observed reduction in exercise capacity cannot be ascertained from methods used in this study. Neuromuscular, cardiovascular, and respiratory limitations could contribute to poor adaptive responses to physical activity. What follows are brief overviews of each of these potential contributing factors.

3.4.3.i   Neuromuscular impairments

Hemiparesis reduces the pool of motor units available for recruitment during physical work, thereby limiting exercise capacity. The extent of the effect depends on the location and severity of the cerebrovascular lesion. In the present study, regression analysis demonstrated a significant correlation between $\dot{V}O_2$peak and BI, the latter reflecting the extent of neuromuscular involvement. McComas and associates (60) estimated that only half of the normal number of motor units were functioning between the second and sixth month post-stroke. Dietz and colleagues (61) postulated that this reduction in motor unit activation may be due to degeneration of the corticospinal tract with subsequent transynaptic changes in the motoneurons. Denervation potentials (e.g., fibrillation and positive sharp waves) have been noted in electromyographic (EMG) studies of hemiparetic muscles (62) and significant morphological changes at the neuromuscular junctions in hemiparetic muscle have been reported (63). Degeneration of alpha motoneuron should result in muscle atrophy but evidence of atrophy in hemiparetic muscles has been an

inconsistent finding. While neither Landin et al. (64) nor Jacobsson (65) found atrophy in their subjects with mild to moderate hemiplegia, other investigators have demonstrated selective atrophy of type II fibers in patients with upper motor neuron lesions (61, 66, 67). Chokroverty and Medina (68) suggested that signs of denervation, rather than being a direct consequence of stroke, may be secondary to prolonged pressure being exerted on peripheral nerves.

Alterations in muscle metabolism and fiber type recruitment pattern during dynamic exercise have been documented in patients with hemiparesis. Landin et al. (64) found evidence of reduced blood flow, increased lactate production and diminished oxidative capacity in the paretic leg muscles of eight male patients with chronic hemiplegia. The authors hypothesized that the reduced oxidative capacity of paretic muscles may be attributed to an increased number and activation of the glycolytic type II muscle fibers as well as to alterations in the structure of mitochondria. Findings from an earlier study by the same investigators of reduced activity of succinate dehydrogenase in both the paretic and nonparetic leg muscles of patients with hemiplegia was interpreted as evidence that physical inactivity secondary to the neurologic disease may contribute as much to the low oxidative potential as the disease process itself (69). Jacobsson and colleagues (65) observed a greater proportion of type II fibers (both subtypes A and B) in the tibialis anterior of 10 patients with hemiplegia in comparison to healthy control groups. In addition, Young and Mayer (70) documented, in their subjects with long-term hemiplegia, a unique fiber type characterized by slow twitch contraction times and increased fatigability.

3.4.3.ii   Cardiovascular co-morbidity

The prevalence of CAD among patients post-stroke is in the range of 60 to 70 percent (1, 37, 38) and, in some cases, cardiovascular disease appears to be the major limiting factor restricting a successful rehabilitation outcome (71). In the present study, 59 percent of the participants had documented CAD. Moreover, numerous reports have

shown that long-term stroke survivors are at greater risk of dying from cardiac disease than from any other cause, including a second stroke (3-5). The exercise capacity of individuals with CAD is typically 60 to 70 percent of that of healthy, sedentary people (72) and the reduction appears to be due primarily to diminished $\dot{Q}_{max}$ rather than a change in AVO_2 difference (73).

Only one study has investigated the effect of cardiac involvement on responses to submaximal exercise post-stroke (1). The 50 patients with stroke demonstrated greater mean increases in arterial blood lactate levels and lactate-pyruvate ratio than did the healthy control subjects but the subgroup of 37 patients with stroke and heart disease showed significantly greater deviations from the normative data. These observations were interpreted to indicate increased anaerobic metabolism during exercise in patients post-stroke with cardiac co-morbidity.

3.4.3.iii   Respiratory dysfunction

Respiratory function following hemispheric stroke is usually affected to only a modest extent, notwithstanding the relatively high occurrence of respiratory complications (e.g., pulmonary embolism, aspiration pneumonia) (74). Thus, although the $\dot{V}E_{peak}$ and Vt_{peak} were only 56 percent and 62 percent, respectively, of normative values in the present study, it is unlikely that respiratory function was the principal factor limiting exercise capacity. Respiratory dysfunction may be a direct result of the stroke (e.g., muscle weakness, impaired breathing mechanics) or may be secondary to cardiovascular dysfunction or lifestyle factors (e.g., physical inactivity, high incidence of smoking (40)).

Hypoxemia and abnormal mechanics of ventilation (75) as well as decreased EMG activity of both the diaphragm and intercostal muscles on the paretic side (76) have been documented in patients with acute cerebral infarction. Reduced and paradoxical chest wall movement as well as impaired diaphragmatic excursion contralateral to the stroke have been described (74, 77). Haas et al. (78) found that the mean $\dot{V}E$ of 19 patients with chronic

hemiplegia while walking at a controlled speed on level ground was almost twice that of the control values and the average arterial O_2 tension was 74 mm Hg, the latter being suggestive of mild hypoxemia. The profound fatigability experienced by these patients was attributed, in part, to respiratory insufficiency as indicated by decreased lung volumes, impaired mechanical performance of the thorax, low pulmonary diffusing capacity, and ventilation-perfusion mismatching (78).

Annoni and colleagues (79) suggested that the poor respiratory tolerance to effort observed post-stroke may be secondary to restricted thoracic excursion resulting from weakness, hypotonicity, and incoordination of the trunk musculature. This suggestion is supported by an earlier finding, based on a sample of 54 hemiplegic subjects, that the extent of expiratory dysfunction post-stroke is related to the degree of motor impairment, particularly hemi-abdominal muscle weakness (80). Delayed loss of inspiratory capacity after stroke appears to be due to the gradual development of rib cage contracture (80).

3.4.4 Study Limitations

As in the previous clinical studies of physiologic responses to exercise post-stroke, the study population was small and represented a sample of convenience. Moreover, there were significant differences in the characteristics of those who participated and those who did not, with the latter group being older and consisting of more females than males. Thus, the findings of this study cannot be generalized to the general population of individuals post-stroke and more investigation is necessary to specifically define the population who can safely undergo testing using the protocol under study. Individualized exercise protocols were used that were nonstandardized and patient-specific, with a shortened warm-up period of one minute to offset the rapid onset of fatigue. The use of handrail support and 15 percent BWS may have confounded the findings in ways that we have not yet identified. In addition, the fact that many subjects did not achieve the criteria commonly used to identify attainment of $\dot{V}O_2$ max limits the interpretation of the results.

3.5   Conclusion

A safe and efficacious method of assessing exercise capacity in the early post-stroke period is important to inform the need for, and design of, cardiovascular training regimes for individuals involved in stroke rehabilitation. This study is the first, to our knowledge, to report the response of patients early post-stroke to symptom-limited treadmill exercise. The test procedure achieved the objective of documenting exercise capacity early in the recovery phase in a functionally relevant posture, an objective that has yet to be achieved using any other protocol. Twenty-nine subjects with a mean age of 65 years and with mild to moderate disability safely performed a 15% BWS-facilitated, incremental, patient-specific exercise test at a mean post-stroke time interval of 26 days. Peak oxygen consumption was, on average, about 60 percent of norm-referenced values, indicating compromised exercise capacity in the early post-stroke recovery phase. Further research is required to elucidate the physiologic bases for this low capacity. The relative contributions of neuromuscular, cardiovascular and respiratory impairments remain to be clarified. Also, there is a clinical need to document the pattern of change in physiologic responses to exercise over the course of recovery (i) to determine if there is a need to introduce aerobic conditioning to an already personnel and time-intensive program of rehabilitation, and if so, (ii) to identify factors (e.g., timing, intensity, and rate of progression) that would inform the design of a safe and effective training protocol. These objectives are addressed in Chapter 4 and 5.

3.6 References

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3.7 Appendix 1

Chedoke-McMaster Stages of Recovery: Leg (CM-Leg)

Instructions: Start at Stage 4. Starting position is indicated. Check ( ) each box as appropriate and stage the patient at the highest stage in which the patient achieves at least 2 ticks (3 checks at Stage 3).

Stage 1:

□ • Not yet at Stage 2

Stage 2: <u>Crook lying</u>:

□ • Resistance to passive hip or knee flexion

□ • Facilitated hip flexion

□ • Facilitated hip extension

Stage 3: <u>Crook lying</u>:

□ • Full hip extension

□ • <u>Abduction</u>: Adduction to neutral

□ • Hip flexion to 90°

Stage 4:

□ • Hip flexion to 90°, then extension synergy

□ • Bridging hips with equal weight-bearing

□ • <u>Sit</u>: Knee flexion beyond 100°

Stage 5:

□ • <u>Crook lying</u>: Extension synergy, then flexion synergy

□ • <u>Sit</u>: Raise thigh off supporting surface

□ • <u>Stand on strong leg with support</u>: Hip extension and knee flexion

Stage 6:

□ • <u>Sit</u>: Lift foot off floor 5 times in 5 seconds

□ • <u>Stand on strong leg with support</u>: Trace pattern forward, side, back, return

□ • <u>Stand on strong leg with support</u>: Full range internal rotation

Stage 7:

□ • <u>Stand unsupported</u>: Rapid high stepping 10 times in 5 seconds

□ • <u>Stand unsupported</u>: Trace a pattern quickly: forward, side, back, reverse

□ • <u>Stand on involved leg with support</u>: Hop

Stage of leg □

Reference: Gowland C, VanHullenaar S, Torresin W, Moreland J, Vanspall B, Barrecca S, Ward M, Huijbregts M, Stratford P, Barclay-Goddard R. Chedoke-McMaster Stroke Assessment: Development, Validation, and Administration Manual, Chedoke-McMaster Hospitals and McMaster University, 1995.

3.8   Appendix 2

ACSM Contraindications for Exercise Testing

Absolute Contraindications

- recent acute or complicated myocardial infarction (MI);
- unstable angina,
- uncontrolled ventricular dysrhythmia;
- uncontrolled atrial dysrhythmia that compromises cardiac function;
- third-degree A-V block;
- acute congestive heart failure;
- severe aortic stenosis;
- dissecting aneurysm;
- myocarditis/pericarditis;
- thrombophlebitis or intracardiac thrombi;
- recent systemic or pulmonary embolus;
- acute infection;
- significant emotional distress (psychosis).

Relative Contraindications

- uncontrolled hypertension (resting diastolic blood pressure (DBP) exceeding 115 mm Hg and/or resting SBP exceeding 200 mg Hg;
- moderate valvular disease;
- electrolyte abnormalities (e.g. hypokalemia, hypomagesaemia);
- fixed rate pacemaker;
- frequent or complex ventricular ectopy;
- ventricular aneurysm;
- chronic infectious disease (e.g. mononucleosis, hepatitis, AIDS);
- uncontrolled metabolic diseases (e.g. insulin dependent diabetes mellitus, thyrotoxicosis, myxoedema);

Reference: American College of Sports Medicine - Guidelines for exercise testing and prescription, 5th edition, 1995.

3.9 Appendix 3

Q≡

Queen Elizabeth II
Health Sciences Centre
Cardiac Prevention and Rehabilitation Research Centre
Abbie J. Lane, 9th Floor
Halifax, B3H 3G2

<u>Informed Consent</u>

Title of Study: *Exercise capacity early after stroke.*

Principal Investigator:	• Marilyn MacKay-Lyons, M.Sc. (PT), Doctoral Student, Department of Physiology and Biophysics, Dalhousie University; tel: 494-2632 or 473-8622
Associate Investigators:	• Lydia Makrides, Ph.D., Professor and Director, School of Physiotherapy, Dalhousie University
	• Stephen Phillips, M.D., Neurologist and Director, Acute Stroke Service, Queen Elizabeth Health Sciences Centre
	• Stephanie Speth, MSc., Certified Exercise Specialist, Cardiac Prevention and Rehabilitation Research Centre
	• Tom Currie, M.D., Emergency Room Physician, QEII

Introduction
We invite you to take part in a research study at the QEII Health Sciences Centre. Taking part in this study is voluntary. The quality of your health care will not be affected by whether you participate or not. Participating in this study might not benefit you, but we might learn things that will benefit others. You may withdraw from the study at any time without affecting your care. The study is described below. The description tells you about the risks, inconvenience, or discomfort which you might experience. You should make sure that any questions you have about the study are answered to your satisfaction.

What is the purpose of this study?
Treadmill exercise tests are used to find out how well the heart, lungs and leg muscles function while exercising. At present there is little information about the function of people with stroke during such tests. The purpose of this project to study how people with stroke respond to treadmill exercise testing and to see if the responses change over the course of stroke rehabilitation. Also, we want to see if improvements in physical function (such as turning in bed, standing from sitting, walking) following a stroke are related to changes in response to treadmill exercise testing.

Who can take part in the study?
The patients in this study will:
• have been admitted to the Queen Elizabeth II Health Sciences Centre (QEII);
• have had an ischemic stroke within the past month;
• have some control of movement of the affected leg;
• be able to understand simple commands;
• be free of any indication that they should not have a treadmill exercise test as shown by the results of the medical history, electrocardiogram, blood tests, and chest x-ray taken during their present hospital admission. **Please turn to page 2.**

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How are participants selected?

Patients admitted to the QEII who meet the conditions described above will be told about the study by Dr. S. Phillips, neurologist and Director of the Acute Stroke Service. The names of people who agree to participate will be given to Marilyn MacKay-Lyons, a physiotherapist and the principal investigator of the study. She will visit each person to review details of the study, answer questions, and obtain a signed copy of this form.

What does the study involve?

All testing will be done at the Cardiac Prevention and Rehabilitation Research Centre (CPRRC) located on the 9th floor of the Abbie Lane Building of the QEII. While you are a patient of the QEII Infirmary, you will be brought to the CPRRC by wheelchair. After discharge from the Infirmary, transportation to CPRRC will be arranged for you.

Before the first visit to the CPRRC, one of the researchers will visit you in your hospital room for about 30 minutes to explain the study. Your medical records will also be reviewed at this time and throughout your rehabilitation to record information about your physical function that has been reported by your physiotherapist at the QEII.

You will visit the CPRRC five times. Each visit will take about one hour.
Visit #1: practice session to see the lab and try out the treadmill
Visit #2: exercise test about one month after your stroke
Visit #3: exercise test about two months after your stroke
Visit #4: exercise test about three months after your stroke
Visit #5: exercise test about six months after your stroke

Practice Session: Your first visit to CPRRC will be a practice session and you will not do an exercise test. Your body weight and height will be measured. Also, the strength of your grip will be measured by having you grip a hand-held gripping device three times with either hand.

You will then be shown the room where the treadmill exercise testing will be done. You will see the treadmill and a safety vest that is attached to an overhead support. This vest, similar to a life jacket, will be worn during each exercise test to prevent falling. This support can also take up some of your body weight to make it easier to walk on the treadmill. We will fit you with the right vest and give you a chance to practice walking on the treadmill while wearing the safety vest. You can hold the handrails lightly for support. A arm sling can be worn if support for your weak arm is required. Also, you will be shown the equipment used during the exercise test to analyze the air that you breath out (e.g. mouthpiece, noseclip, headgear, and metabolic cart). You will be given a chance to practice breathing with the mouthpiece and noseclip in place. While wearing the mouthpiece you will be unable to speak so you will be instructed to use the following hand signals: 'thumbs up' means everything is fine, 'thumbs down' means you want to stop and have the mouthpiece removed.

Exercise Tests: Within one week you will return to the testing room to do a treadmill exercise test. Before coming for the test you will be asked to:
• have a light meal;
• avoid smoking for at least 2 hours;
• avoid drinking caffeinated beverage for at least 6 hours;
• avoid heavy exertion or exercise for 12 hours;
• wear lose, comfortable clothes and footwear appropriate for walking;
• bring your walking aid and arm support sling, if you use these aids.

To record your heart rate and the electrical activity of your heart, an electrocardiogram (ECG) will be done during each exercise test. The ECG electrodes will be attached to your chest. To make sure there is a good connection between the skin and the electrodes, your skin will be rubbed with alcohol and fine sandpaper before the electrodes are attached. Hair on the skin may need to be shaved. A cuff will be placed around your right arm to measure your blood pressure. The safety vest will be put on. After the mouthpiece and noseclip have been put in place, you will rest for 15 minutes, seated in a cushioned chair. Resting heart rate and blood pressure will be measured at the end of this rest.

You will then step onto the treadmill and the safety vest will be attached to the overhead support. During each test 15% of your body weight will be removed to make walking easier.

For the next minute you will walk on the treadmill at the low speed to complete your warm-up. The exercise test will begin at a very easy level and will gradually become more difficult. You will be asked to keep walking until you are limited by severe fatigue or discomfort. When you signal to stop, the treadmill will be slowed down and then turned off. You will be closely monitored during the test by a physician and an exercise specialist who will take your blood pressure, follow your ECG tracing and measure the air that you will be breathing through the mouthpiece. The noseclip makes sure that all the air you breathe out is measured. If we see any reason to stop the test, you will be asked to stop at once and the treadmill will be turned off. After the testing is over you will remain seated until rested.

The same method will be used for each exercise test.

Are there any risks or discomforts?
Exercise testing is a routine procedure done at CPRRC. However, it is possible that certain unfavorable changes may occur during or after the test. Should any of these happen to you, you may stop the exercise test. These may include abnormal blood pressure, dizziness, fainting, disorders of the heart beat, leg cramps and very rarely, heart attack. However, in our exercise facilities, with the presence of well-trained staff, the likelihood of such risks is small. The safety harness provides added safety by preventing falls. Emergency equipment and experienced staff are available to deal promptly with any unusual situations.

What are the possible benefits?
By participating in this study, you will be contributing valuable information. This information will be used to help answer important questions about the functioning of the heart, lungs and leg muscles after a stroke. By finding out more about the cardiovascular function, we can then come up with better ways of improving this function during rehabilitation. You will be made aware of your own results of each exercise test and the overall results of the study after the study has been completed. Also, we will let your doctor know if the tests show any unusual findings. **Please turn to page 4.**

Other important information

1. **Confidentiality**: All information gathered during the study will be kept confidential. The information collected from this study will be published and presented at scientific conferences but your name will not be used. Your records will be kept in a locked file cabinet. Only the staff involved in the research study will see them.

2. **Costs**: There will be no costs to you for being in this study. You will not be charged for any of the costs of the exercise tests. If you become injured while participating in this study, medical treatment will be available to you. None of your legal rights will be waived. The investigators still have their legal and professional responsibilities. Funds will be made available for transportation to the exercise testing lab.

3. **Questions or Problems**: If you have any questions about this study, please contact Marilyn MacKay-Lyons at the CPRRC (902-473-8622) or at Dalhousie University (902-494-2632). There is voice mail at these numbers.

I have read the description of the study. I have been given the opportunity to discuss the study. My questions have been answered to my satisfaction. I understand that I will be given a copy of this consent form for my own records. I hereby consent to take part in this study.

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Signature of Subject   Date

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Signature of Study Investigator   Date

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Signature of Witness   Date

3.10 Appendix 4

Barthel Index

Guidelines:
- Index should be used as record of what a patient does, not what he is capable of doing.
- Main aim is to establish degree of independence from any help (physical or verbal).
- The need for supervision means that the patient is not independent.
- Patient's performance should be established using best evidence (e.g. asking patiient, family, nurses). However, direct testing is not required.
- Usually performance over the preceding 24-48 hr is important, but longer periods may be relevant.

Self-Care Index	"Can do by Myself"	"Can do with Help"	"Cannot do at all"
1. Drinking from a cup	4	0	0
2. Eating	6*	0**	0
*Eats normal uncut-up food, cooked & served by others. ** food cut up but feeds self			
3. Dressing upper body	5*	3**	0
*Selects & puts on all clothes (may be adapted) ** needs help with buttons, zippers etc.			
4. Dressing lower body	7	4	0
5. Putting on a brace or artificial limb	0	2	0 (N/A)
6. Grooming*	5	0	0
*doing teeth/hair, fitting false teeth, shaving, washing face			
7. Washing or bathing	6	0	0
8. Controlling urination	10*	5	0
*includes independent with catheter		(accident)	(incontinent)
9. Controlling bowels	10	5	0
		(accident)	(incontinent)
Mobility Index			
10. Getting in & out of chair*	15	7	0
*from bed to chair & back			
11. Getting on & off toilet*	6	3**	0
*includes undressing, cleaning, dressing; ** can wipe self and do some of above			
12. Getting in & out of tub or shower	1*	0	0
* gets in & out unsupervised & washes self			
13. Walking 50 yards on the level	15	10	0
14. Walking up/down1 flight of stairs	10*	5	0
* must carry walking aid			
15. If not walking: propelling or pushing w/c	5	0	0 (N/A)

Reference: Mahoney FI, Barthel DW. Functional evaluation: The Barthel Index. Maryland State Medical Journal 1965;14:61-65.

CHAPTER 4: ESTIMATION OF THE AEROBIC COMPONENT OF CONTEMPORARY STROKE REHABILITATION

4.1 Introduction

This year the direct and indirect costs associated with stroke care in Canada will be in the order of $2.7 billion (1). The majority of patients with disability post-stroke undergo comprehensive physical rehabilitation which, being both time and personnel intensive, contributes significantly to the overall economic and human burden. Despite the indisputable impact on society, surprisingly little specific information exists regarding the nature of stroke rehabilitation services. As stated by Gladman and colleagues (2), "we do not know what it is in the 'black box' of a stroke unit that is effective because the trials [of stroke rehabilitation] did not systematically measure the interventions." This lack of documentation has allowed new therapeutic strategies to be introduced without clear delineation of their indications, contra-indications, and effectiveness - a situation that may well be contributing to an unjustifiable escalation in services and costs. One intervention that is beginning to be incorporated into stroke rehabilitation programs is aerobic fitness training (3).

It has been known for some time that most individuals with stroke have coexisting cardiac disease (4-8), a finding which is not unexpected since stroke and CAD share similar pathogenic mechanisms (9). However, what has not been adequately investigated - either under controlled laboratory conditions or during physical rehabilitation sessions - is the cardiovascular response to exercise post-stroke. Knowledge of the responses to exercise after stroke is basic to understanding the physiologic adaptation to activity, to prescribing appropriate exercise for rehabilitation, and to ensuring a reasoned approach to implementing new therapies.

Substantial evidence suggests that functional outcome post-stroke is adversely affected by coexisting cardiac disease (10-13). Gresham et al. (13) proposed that "much of the

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disability of stroke victims appears to be due to coexisting cardiovascular disease." Furthermore, most patients with stroke have abnormally low exercise capacity (14-16). With the widespread acceptance of the effectiveness of cardiac rehabilitation in improving the cardiorespiratory fitness of people with cardiac disease (17, 18), attention to the role of aerobic conditioning post-stroke is warranted. Rehabilitation specialists must be aware of the demands that various interventions place on the cardiovascular system in order to induce adequate metabolic stress to enhance exercise capacity. Hjeltes (19) speculated that the low physical endurance of patients in the chronic post-stroke period is a consequence of the relatively static nature of the typical stroke rehabilitation program.

Knowledge of the intensity of rehabilitation sessions is also needed to minimize cardiac complications. Therapists often prescribe exercises for patients post-stroke without full knowledge of their patients' cardiac status and without monitoring HR and blood pressure (3, 16). In a study of 106 patients post-stroke, Roth and colleagues (20) noted that over 50 percent of the subjects demonstrated abnormalities of HR, blood pressure, and ECG pattern during physical therapy sessions. Iellamo et al. (21) investigated the HR and BP responses to exercises employed in physical therapy and found that "even submaximal endurance-type exercise yields an elevated functional stress on the cardiovascular system which could precipitate hazardous events in subjects with unrecognized cardiac diseases."

The overall aim of current stroke rehabilitation techniques is to recover neuromuscular function (22). Although conventional clinical protocols do not specifically address cardiorespiratory function, the possibility exists that an aerobic training effect may occur insidiously over the course of rehabilitation. Patients with low basal levels of exercise capacity, a category that applies to most patients in stroke rehabilitation, experience the most benefit in terms of cardiovascular conditioning, even at relatively modest levels of physical exercise (23). However, the information necessary to ascertain the aerobic component of post-stroke therapeutic sessions (e.g., mode, intensity, frequency, and duration) has not been documented. What has been published in the stroke rehabilitation

literature provides little insight regarding the intensity of therapy. Behavioral mapping techniques have been used to sample the activity of patients at specific intervals over the course of the day (24-28). The most striking finding of these studies is how little therapy the patients received. Lincoln and colleagues (25) concluded that "the proportion of time in therapeutic activity was low in all locations, with patients spending many hours sitting and doing nothing." In the studies cited above, however, 'intensity' of therapy was equated erroneously with time rather than with the metabolic stress induced by therapeutic interventions.

Wade et al. (28) recommended that attention be redirected from the *amount* to the *content* of therapy. Monitoring of individual patients participating in therapy provides more accurate information on activity patterns than does reviewing health records or conducting interviews (29). While $\dot{V}O_2$ cannot be measured directly without interfering with therapy, target HR (HR_{target}) has been used extensively to monitor exercise intensity (30). The use of HR_{target} is based on the essentially linear relationship between HR and $\dot{V}O_2$ (31, 32). The ACSM guidelines recommend that achieving an aerobic training effect requires exercise of large muscle groups at a frequency of 3-5 times a week, for a duration of 20-60 minutes and at an intensity of 60-90 percent of HR_{max} (33).

In the only published study of cardiovascular monitoring of patients post-stroke participating in physical therapy, the authors concluded that the activities performed during physical therapy were of appropriate intensities for this population and that the patients "may" have derived a cardiovascular training effect from their exercise program (20). However, the post-stroke time interval of the subjects, the duration of elevations in HR, and the criteria for determining a training intensity were not reported. Furthermore, the conclusions were based on a single observational session per subject which was not scheduled at a standardized post-stroke interval.

There are compelling reasons for investigating the intensity of occupational therapy sessions for patients post-stroke. First, the role of the occupational therapist is to promote

recovery through purposeful activity (34) and patients post-stroke often have significant disability in activities of daily living, such as household tasks and leisure pursuits (35). Secondly, cardiorespiratory limitations contribute to this disability. Bjuro et al. (36) found that $\dot{V}O_2$ requirements of performing household tasks (e.g., bed making, vacuuming, cleaning bathroom) were considerably higher among women with chronic hemiplegia compared with healthy women (75-88 percent versus 42-45 percent of $\dot{V}O_2$ max, respectively). Finally, training is task-specific, that is, the benefits are specific to the task being learned (37, 38). Therefore to enhance task performance of patients post-stroke, these skills must be trained.

Further study is necessary before determining whether specific cardiac rehabilitation strategies would be redundant or beneficial additions to contemporary stroke rehabilitation. The overall purpose of this two-phase study was to estimate the aerobic component of an existing stroke rehabilitation program by documenting the HR responses of individuals post-stroke during standard physical and occupational therapy sessions over the course of the rehabilitation.

4.2 Study design

This descriptive, longitudinal study was conducted in two phases, the details of which are described in separate sections below. In summary, Phase 1 involved monitoring the HR and activities of patients with stroke during physiotherapy and occupational therapy sessions at bi-weekly intervals over the course of rehabilitation. Phase 2 involved monitoring the HR of patients during physiotherapy sessions at 1,2,3, and 6 months post-stroke and estimating the mean energy expenditure (EEmean) during these sessions by relating the HR responses to each individual subject's HR-$\dot{V}O_2$ curve established in the laboratory.

4.3   Phase 1 Methods

4.3.1   Purpose

The purposes of Phase 1 were three-fold:

i) To estimate the extent to which patients were within their HR_{target} zone during physiotherapy and occupational therapy sessions.

ii) To determine if the extent of exceeding the HR_{target} zone changed over the course of stroke rehabilitation.

iii) To identify those activities in which the patient participated during physiotherapy and occupational therapy that resulted in HR responses within and above the HR_{target} zone .

4.3.2   Subjects

Subjects included patients with the diagnosis of a first ischemic stroke who were designated by the acute stroke team as having 'rehabilitation potential' using the criteria of (i) mild to moderate deficits, (ii) motivated to participate in rehabilitation, (iii) ability to learn and participate in the rehabilitation program; (iv) good psychosocial support (39). Patients with pacemakers were excluded and those patients who ultimately failed to complete at least 14 weeks of rehabilitation were withdrawn from the study. Informed consent, approved by the Queen Elizabeth II Health Sciences Center Research Review Board, was obtained from all patients prior to their inclusion in the study (Appendix 1). Recruitment was consecutive until 20 patients who met all of the criteria had been enrolled.

4.3.3   Monitoring protocol

Heart rate was recorded continuously during regular physical and occupational therapy sessions on a consistent day at bi-weekly intervals from initiation of physiotherapy and occupational therapy in the acute setting to discharge from out-patient rehabilitation. The BI was calculated at the time of the first monitoring session to reflect the level of functional

dependence (40). The Polar Vantage XL Heart Rate Monitor* was used to record and store the HR data which were downloaded for further analysis using the Polar Computer Interface. The monitoring device consisted of a sensor/transmitter placed securely around the chest and a receiver/monitor worn around the wrist. In cases of inadequate contact between the chest wall and the sensor, conductive gel was applied. Just prior to the therapy session, baseline HR_{rest} was obtained after a 5-minute period of quiet sitting, whenever feasible. Periodically throughout the recording session the position of the sensor/transmitter was checked to ensure proper functioning. Recording near strong electromagnetic sources, such as electrotherapy equipment, was avoided since interference from such sources can yield inaccurate HR data.

Coincidental with HR monitoring, a trained observer, either a physiotherapist or a student of physiotherapy, recorded the activities in which the patient engaged in terms of duration, patient position, extremity involvement, equipment used, and overt signs and symptoms of exertion. A list of 48 possible activities was field tested with five different patients. The revised list included 60 activities categorized according to position of the patient (i.e., lying, sitting, standing) (Appendix 2). During the therapy sessions the observer used a hand-held stop watch synchronized with the HR monitor to record the duration and HR response of each activity. In cases where the patient and therapist were engaged in a discussion or conversation, the nature of the exchange was noted. Similarly, the observer recorded signs of possible physical exertion (e.g., sweating, pallor, dyspnea, dizziness, chest pain) and of overt emotional behavior (e.g., crying, laughing, shouting). While the observer tried to remain as unobtrusive as possible throughout the session, both the patient and therapist were aware of the observer's presence, and the intent of the research was disclosed.

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*Polar USA, Inc., 470 West Avenue, Stamford, CT 06902

4.3.4   Data analysis

Although data were collected over the complete course of rehabilitation for each patient, statistical analysis was limited to the data related to the first 14 weeks post-stroke; subsequent to that period the data were unbalanced due to varying times of discharge from rehabilitation. Descriptive statistics including means, standard deviations, and ranges were calculated for all dependent variables. Variables included total duration of each session, amount in time per session spent actively participating in therapeutic interventions in lying, sitting, and standing, and amount of time spent 'inactive' from a cardiorespiratory perspective. The latter category included resting, listening, or talking in a static position, and receiving passive therapeutic treatments such as manual stretches and passive ranging. Recorded HR was averaged over 15 seconds intervals for purposes of data reduction. Variables associated with HR monitoring included HR_{rest}, HR_{mean}, HR_{peak}, and percentage of age-predicted maximal HR ($HR_{max-pred}$) attained using the formula $HR_{max-pred} = 220$-age (33). For those patients taking beta-blocking medication, the formula was adjusted [$HR_{max-pred/adj} = 85\%$ (220-age)] to accommodate the HR-lowering effect of this type of medication (41, 42). The HR_{target} zone was determined using the most common clinical method - the Karvonen formula - adapted for the very unfit: HR_{target} zone = [40 - 85% ($HR_{max-pred/adj}$ - HR_{rest})] + HR_{rest} (33). Time per session and percentage of total time/session in which HR was within the HR_{target} zone for intervals of at least 30 consecutive seconds were calculated and activities that elicited a HR response within zone were identified. In addition, the percent increase from HR_{rest} over the course of each session was calculated using the formula [100 x (HR_{peak}-HR_{rest}/HR_{rest}] (20).

Inferential statistics were applied to analyze the activity distribution in occupational therapy and physiotherapy and to determine the extent to which the HR_{target} was attained during physiotherapy and occupational therapy sessions over the course of rehabilitation. One-way repeated measures ANOVAs were used with one within-subject factor (time post-stroke). Bonferroni *post hoc* testing was applied to detect statistically significant

differences in the dependent variables across the four tests. The software program, BMDP-5V - Unbalanced Repeated Measures Models with Structured Covariance Matrices was selected for the ANOVAs since this program was designed specifically for small data sets with limited missing data (43) . Independent t-tests for unequal sizes and Chi-square analysis were used for comparing demographic and clinical characteristics of subjects with and without CAD. Paired t-tests were applied to compare the duration of physiotherapy and occupational therapy sessions and Pearson product-moment correlation coefficients (r) were computed to assess relationships between HR and activity data. All statistical tests were performed with an alpha level set at 0.05.

4.4 Phase 1 results

4.4.1 Subjects

Over the course of the study five participants were withdrawn from the study due to discharge from rehabilitation at less than 14 weeks post-stroke. Characteristics of the final 20 subjects are summarized in Table 12. The finding that 30 percent of the subjects had preexisting diabetes is in agreement with the incidence of 30 percent reported in a study of 945 patients involved in comprehensive rehabilitation (44). The incidence of CAD, based on the presence of at least one of the following: MI by history or ECG, angina pectoris, or coronary artery bypass graft surgery (10), is consistent with previously reported figures of 60 percent (6) and 70 percent (4). Subjects with CAD were significantly older than those without CAD (70.4 ± 7.9 years versus 53.3 ± 13.8 years, respectively; p=0.004). Also, acute length of stay (LOS) was significantly longer for those patients with CAD compared to those without CAD (25.3 ± 11.6 days versus 17.6 ± 9.3 days; p= 0.03). One participant, a 73-year-old male without prior history of CAD, died of a myocardial infarct just prior to discharge from outpatient therapy at 17 weeks post-stroke.

Table 12. Demographic and clinical characteristics of subjects (n=20)

age *years*	65.0±13.1 (40-84)
sex	11M:9F (55% M)
side of stroke	13R:7L (65% R)
Initial Barthel Index *0-100*	36.6±16.9 (7-64)
hypertension	14/20 (70%)
CAD	13/20 (65%)
β-blocking medication	12/20 (60%)
diabetes	6/20 (30%)
history of smoking	10/20 (50%)
acute LOS *days*	28.0±10.3 (12-46)
inpatient and outpatient rehabilitation *weeks*	10.9±1.7 (7.8-14.6)
duration of physiotherapy *minutes/day*	54.8±7.2 (39-70)
duration of occupational therapy *minutes/day*	40.8±7.0* (30-49)

Data are means ± SD (ranges) or counts (percentages). CAD: coronary artery disease; β-blocker: beta blocking; LOS: length of stay. *Comparison of duration of occupational therapy and physiotherapy (P<0.01).

4.4.2 Activity analysis

A total of 189 sessions (109 physiotherapy and 80 occupational therapy sessions) were monitored. Some sessions could not be monitored due to cancellations, holidays, and scheduling conflicts between the observers and therapists. The therapists in the stroke program included 10 physiotherapists with 13.4±5.7 years of clinical experience (10.0±4.9 years of neurophysiotherapy practice) and six occupational therapists with 8.3±3.8 years of practice (6.7±2.7 years in neurotherapeutics). The general approach to stroke rehabilitation involved a combination of contemporary task-oriented therapeutic strategies and traditional neuromuscular facilitative techniques (22).

Physiotherapy sessions were significantly longer than occupational therapy sessions (p<0.01). The ANOVA results indicated that neither the duration of physiotherapy nor occupational therapy sessions changed significantly over the course of study. The percentages of total therapy time spent inactive, and active in lying, sitting, and standing positions are illustrated in Figure 6. Significantly more time was spent in lying (p=0.0002)

and standing (p<0.0001) during physiotherapy than during occupational therapy, and more time was spent inactive (p=0.0003) and sitting (p=0.006) during occupational therapy than during physiotherapy. In physiotherapy, the majority of the 'inactive' period was spent in sitting or standing and involved therapists instructing the patient on new motor skills, resting between activities, waiting for the physiotherapist, or for equipment to become available, and performing passive interventions, particularly passive ranging and joint mobilization. In occupational therapy considerable 'inactive' time was spent in sitting while waiting for the occupational therapist and while discussing issues with the occupational therapist related to discharge planning, equipment needs, and home management. Although the ANOVA results indicated significant differences over time in the percentage of time spent active in standing during physiotherapy (p=0.005) and in the percentage of time spent active in sitting during occupational therapy (p=0.004), *post hoc* testing using the Bonferroni correction for multiple comparisons did not reveal significant differences. These findings suggest that the study lacked adequate power to identify the source of the differences in the ANOVA findings.
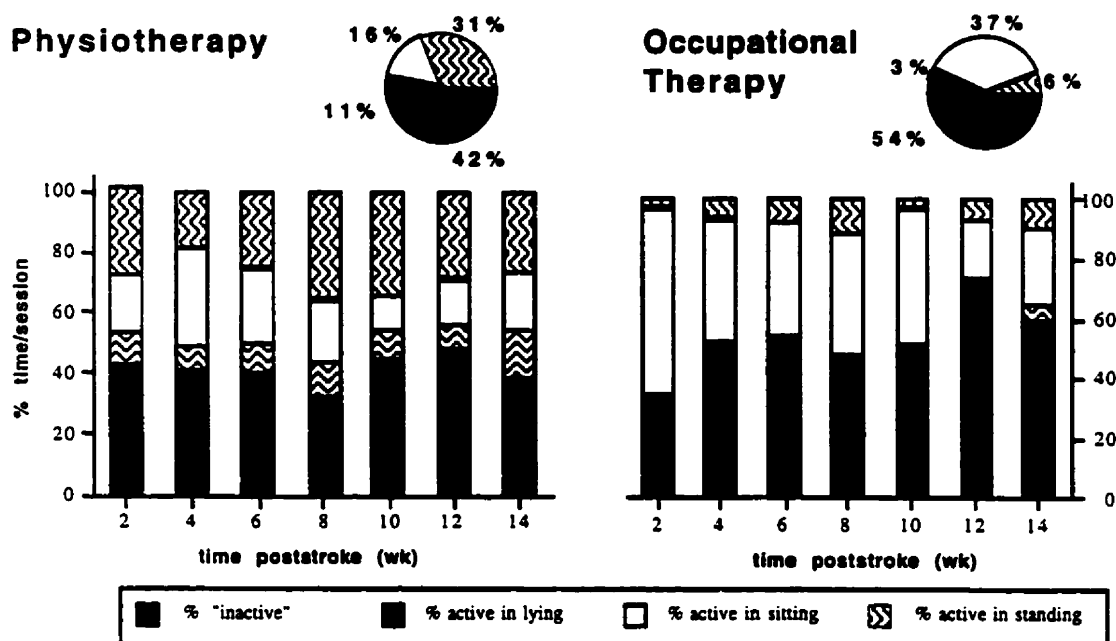
Figure 6. The pie charts illustrate the overall mean percentages of time per session spent inactive and active in lying, sitting and standing positions across the course of rehabilitation and the column graphs illustrate the mean percentages at biweekly intervals.

4.4.3 Heart rate responses

Overall mean values of HRmean, HRpeak, and time within the HRtarget zone were found to be significantly higher during physiotherapy compared with occupational therapy sessions, indicating that the intensity of physiotherapy was greater than that of occupational therapy (Table 13). No significant differences were found in any of these variables between patients with and without CAD. On average, HR responses were below the HRtarget zone for approximately 95 percent of the total time spent in physiotherapy sessions and 98 percent in occupational therapy sessions. However, there was substantial variability in the data, with the medium percentages being higher (99 percent and 100 percent, respectively). Further, the mean period over which HR responses within the HRtarget zone was sustained without interruption was only 0.84 ± 0.23 minutes. All but two

patients (a 72-year-old female and a 78 year-old female) exceeded the lower limit of the HR$_{target}$ zone at some point during physiotherapy while five failed to reach their HR$_{target}$ zone during any of their occupational therapy sessions.

Table 13. Heart rate responses during physiotherapy and occupational therapy

	Physiotherapy			Occupational Therapy		
	mean±SD	median	range	mean±SD	median	range
HR$_{rest}$ *beats/min*	72.2±11.1	68.8	52-106	70.2±11.3	68.3	54-94
HR$_{mean}$ *beats/min*	82.1±17.4	78.4	56-125	71.9±12.1*	70.2	59-108
HR$_{mean}$ *%HRmax-pred*	59.0±9.8	58.2	40-85	55.0±10.8†	52.3	42-80
HR$_{peak}$ *beats/min*	104.0±24.3	95.0	74-159	90.5±23.6*	83.0	66-157
HR$_{peak}$ *%HRmax-pred*	74.6±11.7	71.2	45-119	68.7±18.9*	65.7	44-116
change in HR/session %	42±31	38	10-56	29±24*	18	5-42
time in HR$_{target}$ zone *min*	2.83±1.01	0.4	0-19	0.71±0.34†	0	0-9
time in HR$_{target}$ zone *% of session*	4.8±2.1	0.7	0-29	1.8±0.8†	0	0-21

HR$_{rest}$: resting heart rate; HR$_{mean}$: mean heart rate; HR$_{peak}$: peak heart rate; HR$_{target}$: target heart rate; change in HR/session: [(HR$_{peak}$-HR$_{rest}$)/HR$_{rest}$ x 100]. $^*p<0.05$; $^\dagger p<0.01$.

To compare HR responses among the subjects over the course of rehabilitation, HR values were normalized by expressing them as percentages of the HR$_{max-pred}$. The ANOVA results did not reveal any significant differences over the course of physiotherapy or occupational therapy in normalized mean values of HR$_{peak}$, HR$_{mean}$, HR$_{rest}$, and HR while inactive and during activities in standing, sitting, and lying. These findings were in contrast to our expectations of a progressive increase in the intensity of the sessions over the course of rehabilitation. Figure 7 displays the HR curves for these variables. The relatively stable values for mean HR$_{rest}$ over the course of rehabilitation alleviated our concerns regarding accuracy of these measurements obtained in the often noisy physiotherapy and occupational therapy departments. As well, these values were comparable to the mean HR$_{rest}$ of 19 patients post-stroke, with an average age of 66 years, measured after 15 minutes of recumbency in a quiet room (45). As anticipated, HR responses were highest during activities in standing and lowest during activities in lying

and while inactive. The overall HR$_{mean}$ and HR$_{peak}$ responses were consistently higher during physiotherapy sessions but there were no statistically significant trends of increasing HR responses over the course of rehabilitation.
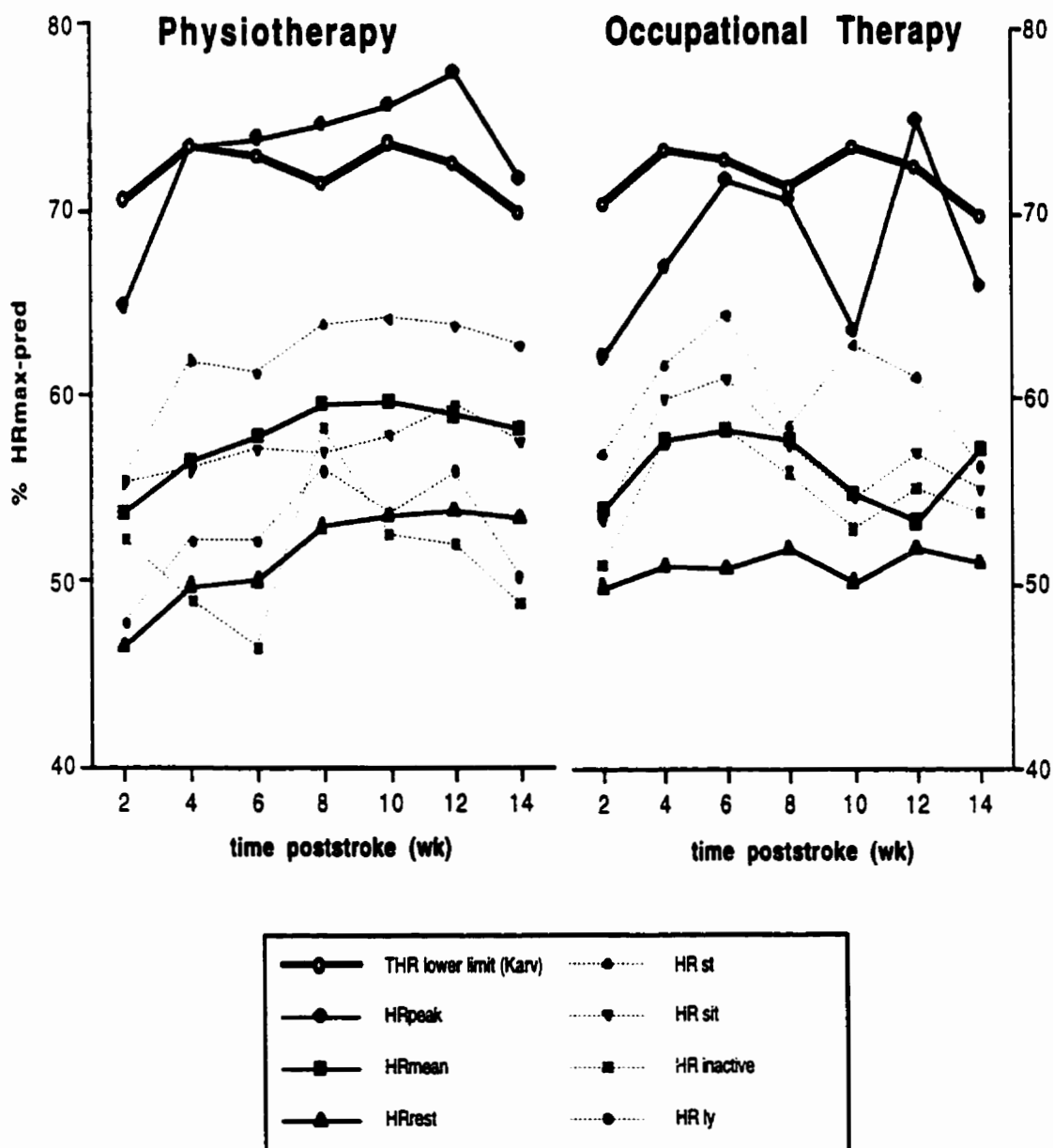
Figure 7. Average resting HR (HR$_{rest}$), mean HR (HR$_{mean}$), and peak HR (HR$_{peak}$) expressed as a percentage of maximal HR (HR$_{max-pred}$ = age - HR$_{rest}$) during the biweekly physiotherapy and occupational therapy sessions. The lower limit of the target heart rate zone (THR$_{lower limit}$) was calculated using the Karvonen formula. See text for details.

4.4.4   Activities achieving HR$_{target}$

Percentage of time within HR$_{target}$ zone was positively correlated with time spent in standing activities (r=.704; p= 0.0001) and negatively correlated with time spent in sitting (r=-0.504; p=0.01). Activities that induced HR responses within the HR$_{target}$ zone are listed in Table 14. At no time did the HR response of any patient surpass the upper limit of the HR$_{target}$ zone. Overt signs of physical exertion were not observed during any of the occupational therapy sessions and only infrequently during physiotherapy sessions. Only two patients in physiotherapy and none in occupational therapy had their blood pressure monitored during the therapy sessions.

Table 14. Activities in physiotherapy and occupational therapy that elicited HR responses within the HR$_{target}$ zone

Physiotherapy	Occupational Therapy
treadmill walking	walking with cane
walking unaided	stepping
walking with walker/wheeled walker	resting in sitting after walking
walking with cane	ADLs in standing - making a bed
stair climbing/stepping	sit-to-stand transfers
resting in standing after walking	wheelchair-to-chair transfers
resting in sitting after walking	wheelchair-to-bath transfers
Kinetron exercises	propelling wheelchair
balancing exercises in standing	ADLs in sitting - dressing
upper extremity exercises in standing	balancing exercises in sitting
resisted lower extremity exercises in standing	
wheelchair -to-chair/bed transfer	
sit-to-stand transfers	
stand-to-floor transfers	
resisted upper extremity exercises in sitting	
arm ergometry in sitting	
balancing exercises in sitting	

4.5   Phase 2 Methods

4.5.1   Purpose

The purposes of Phase 2 included:

i) To determine if the trends in HR responses and activity analyses during physiotherapy observed in Phase 2 are consistent with those seen in Phase 1.

ii) To compare estimates of the aerobic component of physiotherapy sessions derived using data from the GXTs to estimates calculated using age-related normative data.

iii) To estimate the EEmean of patients post-stroke while participating in physiotherapy sessions.

4.5.2   Subjects

The cohort of subjects who participated in the longitudinal study of exercise capacity after stroke (see Chapter 3) were recruited for participation in this study; hence the inclusion and exclusion criteria were the same as those outlined in Chapter 3. Ultimately, 27 of the 29 subjects consented to involvement in this study.

4.5.3   Monitoring protocol

Since there was little evidence in Phase 1 of an aerobic component to the occupational therapy sessions, HR monitoring in Phase 2 was limited to physiotherapy sessions. The monitoring protocol was the same as that used in Phase 1 but monitoring was limited to once at one, two, three and six-months post-stroke to coincide with the scheduling of serial GXTs. Monitoring was done within two days prior to or after the GXT. In addition to the data collected in Phase 1, observers noted if the patients were being treated specifically for shoulder pain since this complication has been shown to be related to the amount of therapy provided (46). Only those subjects who continued to participate in physiotherapy were monitored; thus the number being monitored decreased over time as patients were discharged.

4.5.4 Data Analysis

In addition to the analyses used in Phase 1, independent t-tests for unequal sizes were applied to compare continuous variables characterizing the Phase 1 and 2 samples and the Mann-Whitney U-test was used for ordinal variables. Chi-square analysis was used to determine the relationship between nominal variables and the Fisher's exact test was applied to 2x2 contingency tables. Alpha level was set at 0.05.

Four formulae were used to calculate the lower and upper limits of the HR_{target} zone, two of which are applied frequently in cardiac rehabilitation programs ($HR_{target(Karv)}$, $HR_{target-pred}$) while the other two require data obtained from GXTs (Table 15). We chose to use very conservative formulae to calculate the lower limit of HR_{target} since it is well established that relatively modest levels of physical exercise can induce a training effect of people with low basal levels of exercise capacity (47, 48). The percentage of $HR_{reserve}$ used was 40 percent in the $HR_{target(Karv)}$ formula and 50 percent in the $HR_{target(Karv/GXT)}$ formula to offset the difference between $HR_{max-pred}$ and $HR_{peak(GXT)}$ (see Chapter 3). Designating the $HR_{target(GXT)}$ as the criterion measure, the lower limit of $HR_{target(GXT)}$ calculated using each of the other three formulae was compared to that derived using $HR_{target(GXT)}$ by ANOVA with *post hoc*, two-tailed t-test comparisons with Bonferroni correction. We also compared the HR_{target} values obtained using the $HR_{target(GXT)}$ formula to the values obtained using the other three formulae by calculating the $ICC_{(3,1)}$s and by deriving the root mean squared (RMS) error of the HR_{target} using the formula [RMS error = square root of the sum of squared differences between the two HR_{target} values divided by the number in the sample] (49).

Table 15. Formulae for calculating lower and upper limits of target heart rate zone

Formula	Equation	Reference
$HR_{target(GXT)}$	HR at 40-85% $\dot{V}O_2peak(GXT)$	(33)
$HR_{target(Karv/GXT)}$	[50-85% ($HR_{peak\ (GXT)}$ - HR_{rest})] + HR_{rest}	(33)
$HR_{target(Karv)}$	[40-85% ($HR_{max-pred/adj}$ - HR_{rest})] + HR_{rest}	(33)
$HR_{target-pred}$	60-85% $HR_{max-pred/adj}$	(16)

A gross estimate of EE$_{mean}$ during physiotherapy was calculated using the method of McArdle et al. (50). The HR responses of an individual subject obtained during each physiotherapy session were applied to that subject's HR-$\dot{V}O_2$ curve established from the corresponding GXT data. The caloric equivalents were determined from the $\dot{V}O_2$ and the RER corresponding to the HR responses (51, 52). Since basal EE of females is lower than males (53), group mean values were calculated separately for male and female subjects. Further, since only five females participated in the study, their data were not subjected to statistical analysis.

4.6   Phase 2 results

4.6.1   Subjects

Of the 27 subjects who agreed to participate, four were discharged from rehabilitation prior to their 1-month GXT, leaving the final sample size of 23. Characteristics of the subjects are summarized in Table 16. The statistically significant difference found in sex distribution between Phase I and Phase 2 subject populations is readily explained by differences in ease of subject recruitment for the two studies. Female candidates were willing to have their HR monitored during therapy but were reluctant to perform GXTs, the latter being a necessary criterion for participation in the Phase 2 study. Five patients (21 percent) in Phase 2 experienced shoulder pain during the monitoring period, an incidence similar to that of 23 in 98 patients (25 percent) reported by Wade et al (28). Subjects with CAD were significantly older (69.4±13.2 yr versus 60.1±9.4 yr; p<0.05) than subjects without CAD but were comparable in terms of severity of stroke. Acute LOS was significantly shorter for Phase 2 subjects, possibly because of a trend of less severe strokes among Phase 2 subjects as well as the introduction of a hospital administration mandate to reduce LOS. Consistent with Phase 1 results, acute LOS of subjects with CAD was significantly longer than for those without CAD (21.5±11.5 days versus 15.2±7.8 days;

p= 0.05). The mean duration of physiotherapy sessions in Phase 2 was comparable to that of Phase 1. However, in the subgroup of patients experiencing shoulder pain, the mean treatment time was higher (65.0 ± 8.3 min/day). Since only five patients were participating in physiotherapy sessions at six months post-stroke, the data collected during these sessions were not included in the statistical analyses. Three of these five patients were among the subgroup who had shoulder pain, corroborating previous reports of a positive correlation of the presence of shoulder pain and extent of physiotherapy post-stroke (46).

Table 16. Demographic and clinical characteristics of subjects (n=23)

age *years*	65.8 ± 13.5 (29-83)
sex	18M:5F* (78% M)
side of stroke	15R:8L (65% R)
initial Barthel Index *0-100*	44.9 ± 18.8 (0-73)
hypertension	13/23 (57%)
CAD	12/23 (52%)
β-blocking medication	11/23 (48%)
diabetes	6/23 (26%)
history of smoking	15/23 (65%)
acute LOS *days*	17.9 ± 10.2† (3-46)
inpatient rehabilitation LOS *days*	19.0 ± 15.3 (0-58)
outpatient rehabilitation *weeks*	8.9 ± 3.7 (2.3-24.2)
duration of physiotherapy *min/day*	53.8 ± 7.2 (20-72)

Data are means $\pm$ SD (ranges) or counts (percentages). CAD: coronary artery disease; β-blocker: beta blocking; LOS: length of stay. Comparison of Phase 1 and Phase 2 subjects: *p<0.05; †p<0.01.

4.6.2 Activity analysis

Sixty-five sessions were monitored. The mean percentages of time spent 'inactive' and active in lying, sitting and standing are shown in Figure 8. The ANOVA analysis revealed a statistically significant reduction in the proportion of time spent active in sitting between one and three months post-stroke (p=0.01). In comparing those subjects with CAD to those without CAD, the former spent longer in lying (7.3 ± 4.2 min versus 3.6 ± 2.1

min; p=0.04) and a shorter period in standing (14.8±5.0 min versus 19.1±5.5 min; p=0.03). As well, for the subgroup with shoulder pain the mean percentage of time spent inactive increased to 64 percent and the time spent active in standing decreased to 14 percent for those sessions during which the pain was treated. The reduction in activity of this subgroup contributed to the higher mean proportion of time spent inactive during the 3 and 6-month sessions.
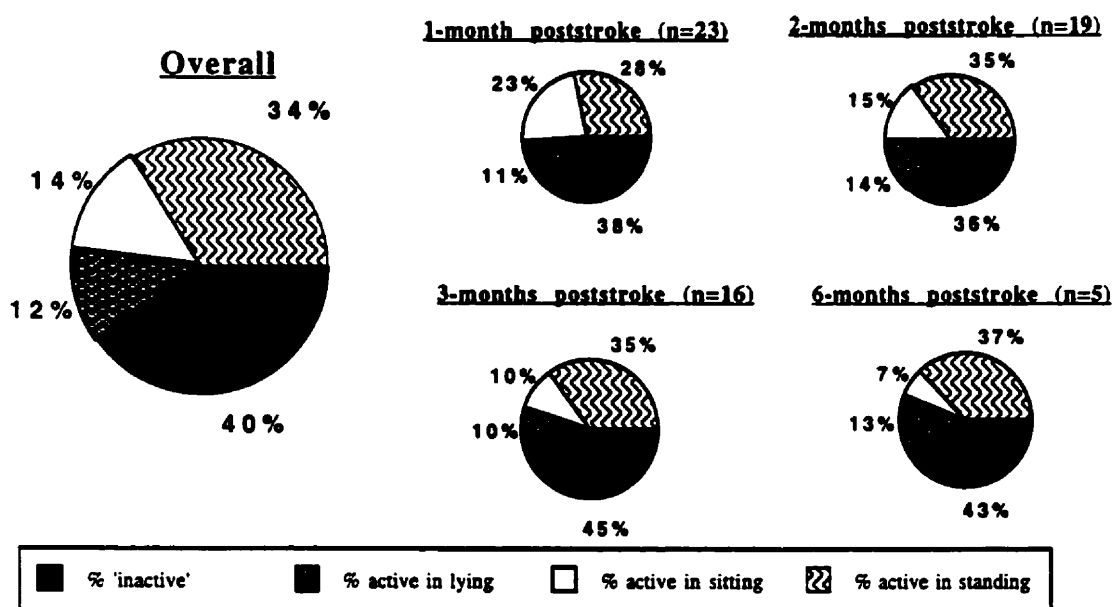
Figure 8. The mean overall percentage of time per physiotherapy session spent inactive, and active in lying, sitting and standing positions as well as the percentages for the different monitoring periods.

4.6.3   Heart rate responses

Heart rate recordings of two of the 65 sessions monitored were discarded from analysis because of inaccurate data, possibly due to interference from electromagnetic sources or from inadequate contact between the chest wall and the sensor of the HR monitoring device. The HR responses recorded during physiotherapy sessions at 1,2, and 3 months post-stroke (Table 17) were similar to those of Phase 1 (see Table 13). The

ANOVAs comparing HR parameters at 1,2, and 3 months post-stroke did not reveal statistically significant differences.

In comparing HR responses of those with and without CAD, the only statistically significant difference was in mean HRmean across the monitored sessions (76.0±11.3 beats/min and 86.8±15.2 beats/min, respectively; p=0.03). However, this finding may be attributed to the age difference between these groups since HRmean values were comparable when expressed as a percentage of HRmax-pred.

Table 17. Heart rate responses during physiotherapy sessions at 1,2, and 3-months post-stroke

Measurement	1-month (n=23)	2-months (n=19)	3-months (n=16)	Overall
Length of session *min*	49.3±10.6	52.0±12.0	54.2±7.8	53.8±7.6
HRrest *beats/min*	72.0±12.5	74.4±14.2	72.0±15.6	73.2±14.5
HRmean *beats/min*	80.6±14.8	81.0±13.8	79.7±17.0	80.1±15.2
HRmean *% HRmax-pred*	56.3±8.5	56.8±9.3	55.3±9.2	56.2±8.6
HRpeak *beats/min*	102.9±20.9	105.7±24.2	98.9±20.3	102.2±21.7
HRpeak *% HRmax-pred*	71.9±13.0	73.8±15.3	69.8±11.5	71.8±13.2
change in HR/session *%*	43.2±19.4	37.2±20.1	38.6±20.4	39.8±20.9

Data are means ± SD. HRrest: resting heart rate; HRmean: mean heart rate; HRpeak: peak heart rate; HRtarget: target heart rate; change in HR/session: [(HRpeak-HRrest)/HRrest x 100]. *P<0.05; †P<0.01.

Since significant differences were not seen in HR responses during sessions monitored at 1,2, and 3-months post-stroke, the HR data were pooled to compare the four formulae used to calculate the lower limit of the HRtarget. The ICC(1,3)s of the relationships between the criterion measure - HRtarget(GXT) - and HRtarget(Karv/GXT), HRtarget(Karv), and HRtarget-pred were .826, .917, and .891, respectively. The HRtarget values calculated using the criterion measure, HRtarget(GXT), were significantly different from the values calculated using the other three formulae (Figure 9). The RMS error of the HRtarget calculated using HRtarget(Karv/GXT), HRtarget(Karv) and HRtarget-pred relative to HRtarget(GXT) were 18.8, 20.0 and 15.3, respectively. Relative to the criterion measure, the HRtarget(Karv/GXT) and the

HRtarget(Karv) formulae overestimated the HRtarget by an average of 10 and 12 beats/min, respectively, and the HRtarget-pred formula underestimated the HRtarget by 3.4 beats/min, on average.
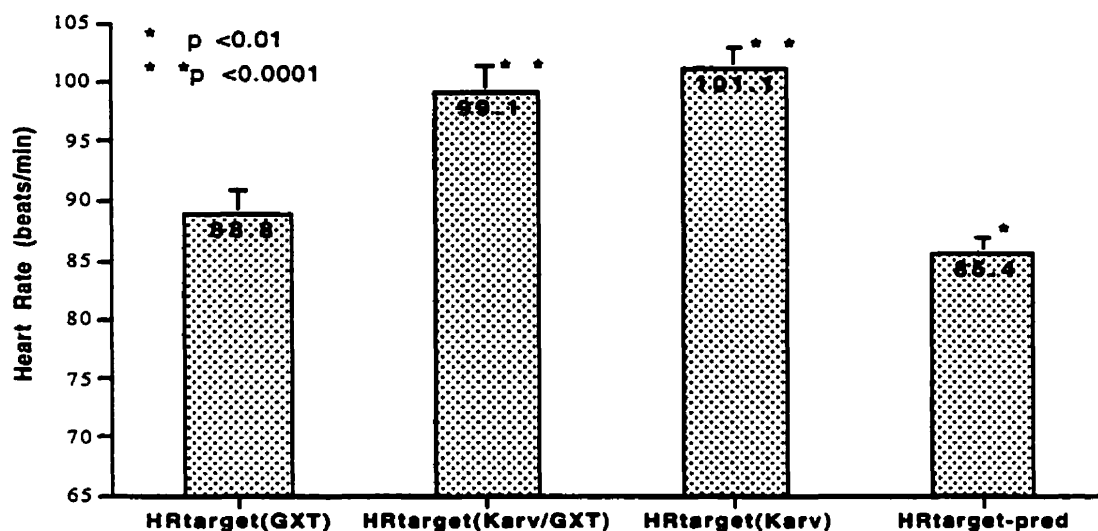
Figure 9. Lower limit of HRtarget estimated using the HRtarget(Karv/GXT), HRtarget(Karv), and HRtarget-pred formulae compared with that derived using the criterion measure of HRtarget(GXT). Error bars are positive values of standard error.

Table 18 shows the mean estimated time and relative time (expressed as a percentage of the total session) spent within the HRtarget zone across sessions, calculated using the four HRtarget formulae. Because of the extent of inter-subject variability, both means and medians are presented. The ANOVA results revealed a significant increase in the time spent within the HRtarget(GXT) zone (p=0.017) with *post hoc* testing indicating that the difference was between the 1-month and 3-month sessions (4.57±3.27 minutes versus 8.84±6.19 minutes, p=0.013). No statistically significant differences were found in the amount of time spent within the HRtarget zone between subjects with and without CAD. The activities that induced a HR response within the HRtarget zone, regardless of which formula was applied, were similar to those reported in Phase 1 (see Table 14).

Table 18. Overall mean time spent in the HR$_{target}$ zone per session estimated using four HR$_{target}$ formulae

formula	Time in HR$_{target}$ zone per session *min*			% of session in HR$_{target}$ zone		
	mean±SD	median	range	mean±SD	median	range
HR$_{target(GXT)}$	7.3±5.8	2.3	0-18	13.5±12.6	2.4	0-26
HR$_{target(Karv/GXT)}$	3.7±2.6	0.7	0-14	7.5±6.3	1.4	0-18
HR$_{target(Karv)}$	2.2±1.7	0.0	0-11	5.4±4.4	0.0	0-15
HR$_{target-pred}$	11.6±10.6	6.3	0-22	24.1±19.3	13.1	0-32

To underline the variability of intensity of physiotherapy sessions and the corresponding HR responses, the HR recordings of two patients are illustrated in Figure 10. The HR responses of a 67 year-old male at three months post-stroke (Figure 10A) were among the highest of all subjects despite the fact that the patient was inactive for 56 percent of the session. He exceeded the lower limit of his HR$_{target(GXT)}$, HR$_{target(Karv/GXT)}$, HR$_{target(Karv)}$, and HR$_{target-pred}$ zones for 10 minutes (22 percent), four minutes (nine percent), 2.5 minutes (six percent), and 14.5 minutes (31 percent of total session), respectively. At no time were symptoms of exertion observed during activities that elicited HR responses within the HR$_{target}$ zone (e.g., weight-resisted leg exercises in lying, walking, and stair climbing). In contrast, a 76-year-old female at three months post-stroke was inactive for 32 percent of her physiotherapy session and exceeded the lower limit of her HR$_{target(GXT)}$, HR$_{target(Karv/GXT)}$, HR$_{target(Karv)}$ and HR$_{target-pred}$ zones for one minute (two percent), 0 minutes, 0 minutes, and 3.5 minutes (seven percent), respectively (Figure 10B). Her HR responses were sustained continuously within the HR$_{target-pred}$ zone for 0.75 minutes while walking with a single cane and for 2.5 minutes while performing reciprocal leg movements on the Kinetron®.
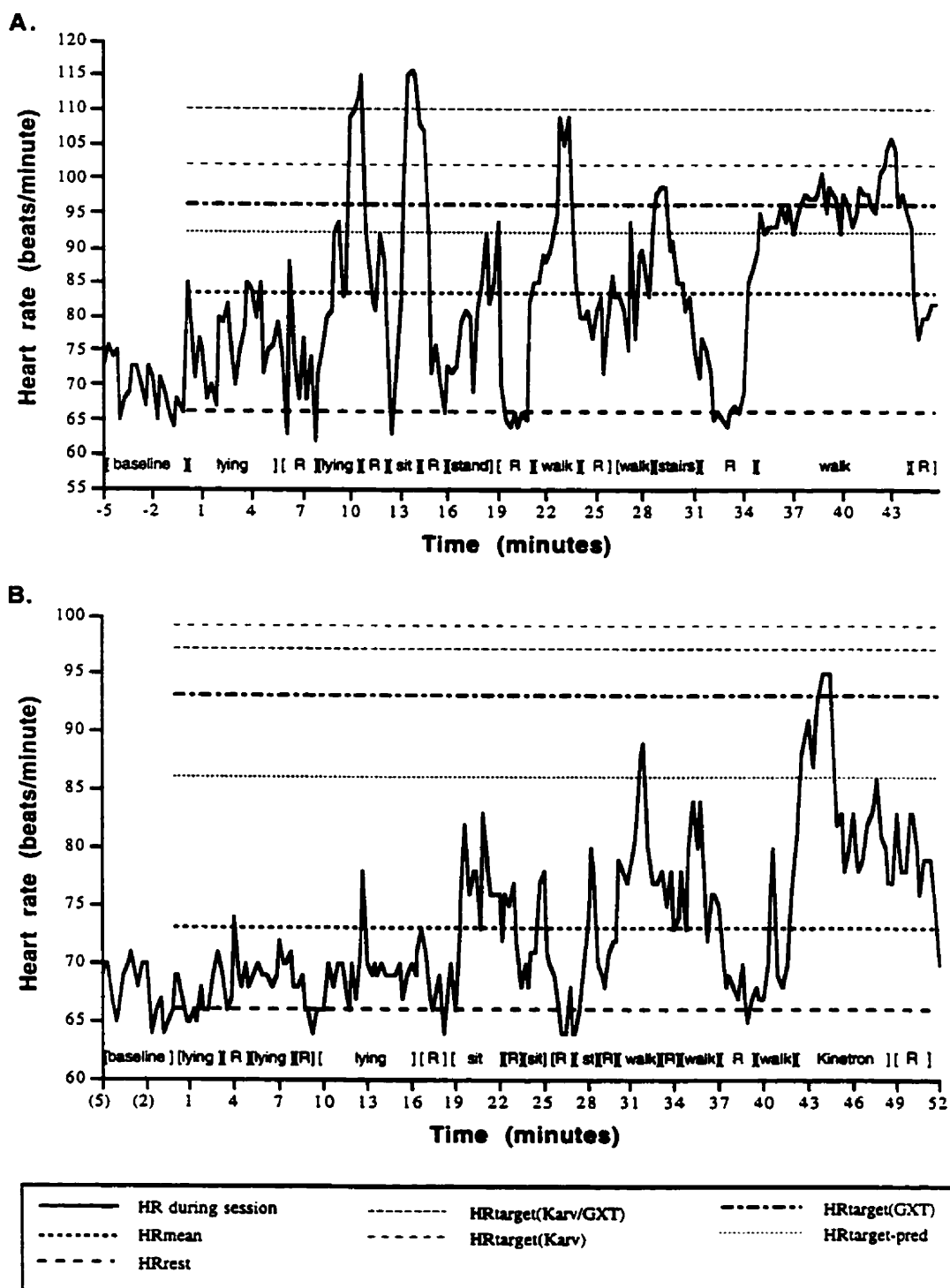
Figure 10. Heart rate responses during physiotherapy of a 65-year-old male (A.) and a 76-year-old female (B.) at 3 months post-stroke. In each graph the lower limits of the four HRtarget zones are indicated and the activities in which the patient was engaged are noted above the x-axes. R refers to resting or inactive and st means activities in standing.

4.6.4 Mean energy expenditure

Estimated EEmean of male and female patients for physiotherapy sessions at 1,2, and 3-month post-stroke are presented in Table 19. The EEmean values during the 1,2, and 3-month sessions were 18 percent, 27 percent, and 32 percent, respectively, lower in the female subgroup. Statistically significant increases were found for the subgroup of males in mean $\dot{V}O_2$ and EEmean between the 1-month and 3-month post-stroke sessions. Nevertheless, using the Five-level Classification of Physical Activity Based on Exercise Intensity (54), the mean level of activity for both male and female subjects would be classified as *light* over the course of rehabilitation. In the 1-month post-stroke GXT, the lower limit of the HRtarget(GXT) was achieved by the majority of patients by the end of the warm-up, which involved level walking at the individual's preferred walking speed. During the GXTs at two and three months post-stroke this target was reached by the second stage, which involved walking at an incline of 2.5 percent at the individual's preferred walking speed. For the majority of subjects their RPE on the Borg scale1-10 corresponding to their lower limit of HRtarget(GXT) was 3 ('moderate').

Table 19. Heart rate and estimated energy expenditure for male and female patients during physiotherapy sessions

	Male subjects			Female Subjects		
	1-month (n=18)	2-months (n=16)	3-months (n=14)	1-month (n=5)	2-months (n=3)	3-months (n=2)
HRmean *beats/min*	82.9±14.9	82.4±14.0	81.9±17.3	74.2±12.1	74.8±13.7	73.8±16.8
$\dot{V}O_2$ at HRmean *l/min*	0.36±0.06	0.46±0.12	0.54±0.13ʳ	0.32±0.10	0.34±0.11	0.37±0.17
RER at HRmean	0.85±.0.04	0.84±0.06	0.81±0.04	0.89±.0.04	0.90±0.06	0.88±0.04
EEmean *kcal/min*	1.80±0.36	2.25±0.61	2.58±0.56*	1.48±0.42	1.65±0.59	1.75±0.73

Data are means ± SD. HRmean: mean heart rate; $\dot{V}O_2$: oxygen consumption; RER: respiratory exchange ratio; EEmean; mean energy expenditure. Significant difference between 1-month and 3-month values: *p<0.01; ʳp<0.001.

4.7   Discussion

4.7.1   Methodological issues

The main challenge in measuring the aerobic component of a stroke rehabilitation program is to determine the relative metabolic demand without interfering with the activities being performed. Intensity and duration are the most important parameters for determining the extent of metabolic stress (47). Often HR data is relied upon as the principal indicator of exercise intensity (as in Phases 1 and 2 of the present study) and energy expenditure (as in Phase 2) because of the approximately linear relationships among HR, exercise intensity, and $\dot{V}O_2$ (31, 32). Before discussing the findings of the present study, the benefits and shortcomings of this applied methodology must be considered.

4.7.1.i   Determining exercise intensity

It is clear from the literature that estimation of exercise intensity is dependent on the formula used to determine the HR_{target} zone. The Karvonen formula, the most widely applied clinical method of HR_{target} determination, uses HR_{rest} and age-related $HR_{max-pred}$ as reference points to calculate an individual's $HR_{reserve}$. Davis and Convertino (55) found that large differences in HR_{rest} values did not significantly affect the value of the HR_{target} generated with the Karvonen formula. However, Londeree et al. (56) reported that only 73 percent of the variability in $HR_{max-pred}$ was accounted for by age and that the 95 percent confidence interval of individual $HR_{max-pred}$ is 45 beats/min. Various physiologic and pathologic factors influence HR_{max} (57), thereby affecting the accuracy of HR_{target} determination. Although we adjusted for the use of β-blocking agents in calculating $HR_{max-pred}$, the adjustment does not reflect the inter-subject and dose-related variability in responses to these agents (41, 42). Further, chronotrophic incompetence, the inability of the heart to increase its rate in proportion to the metabolic demands of exercise (58), is relatively common in individuals with CAD, with prevalence figures ranging from 14

percent (59) to 29 percent (60). Over 50 percent of the subjects in our study had documented CAD.

In addition to reliance on HR$_{max-pred}$, another limitation with the Karvonen formula is the underlying assumption that work intensity among individuals is similar if the relative percentage of HR$_{reserve}$ is the same. HR$_{target}$ determination based solely on HR data fails to account for the considerable inter-subject variability in HR response to exercise; hence a given HR$_{target}$ may reflect a range of metabolic intensities (49, 61-63). Goldberg et al. (63) found overestimation of HR$_{target}$ using 77 percent of HR$_{reserve}$ in the Karvonen formula among people of low fitness and concluded that this formula may be excessive for unfit individuals. To offset this concern we used a very conservative percentage of HR$_{reserve}$ (40 percent) but found the formula HR$_{target(Karv)}$ not only overestimated HR$_{target}$ but also deviated most from the criterion measure, HR$_{target(GXT)}$. The latter finding is in keeping with a previous study comparing HR$_{target}$ formulae (49).

In our study 'artifact' was introduced when using the HR$_{target-pred}$ formula for subjects with abnormally high HR$_{rest}$. In such cases we occasionally found that the lower limit of HR$_{target}$ was exceeded during periods of inactivity (e.g., with the subject calmly sitting in a wheelchair awaiting the physiotherapist). These observations corroborate previous reports of significant overestimates of exercise intensity (and underestimates of HR$_{target}$) when the HR$_{target(pred)}$ formula is applied (55, 64).

The above-mentioned considerations raise doubts regarding the validity of estimating the aerobic component of a program using HR data, particularly in a population with a wide age range and with a high incidence of cardiac disease. The application of GXT data in Phase 2 helped to alleviate this concern. Calculating HR$_{target}$ by using the HR recorded at a specified percentage of the $\dot{V}O_2$peak (40 percent in the percent study) is a more definitive, individualized approach. Despite the accepted notion that 40 percent of $\dot{V}O_2$ max corresponds to approximately 50 percent of HR$_{max}$ (33), the mean lower limits of HR$_{target(GXT)}$ and HR$_{target-pred}$ were similar (63 percent, 60 percent of HR$_{max/adj}$,

respectively). This finding is in agreement with the observations by Swain et al (65) that

40 percent of $\dot{V}O_2$ max corresponded to 63 percent of HR$_{max}$. The ICC between HR$_{target}$

values calculated using the HR$_{target(GXT)}$ and HR$_{target-pred}$ formulae was high and the RMS

was the lowest of all comparisons. Thus, for at least those subjects in the population under

study without abnormally high HR$_{rest}$, the HR$_{target-pred}$ formula used in this study may serve

as a more reasonable, albeit more conservative, proxy for HR$_{target}$ determination than the

commonly used HR$_{target(Karv)}$ formula.

RPE has been shown to reflect exercise intensity (66) and is highly correlated with

several physiologic measures including HR, $\dot{V}O_2$, RR, and lactate levels (67). The fact

that most subjects in Phase 2 reported a rating of 3 at the point of attaining the lower limit

of their HR$_{target(GXT)}$ lends support to the use of RPE for determination of an appropriate

training intensity since 3 (or 'moderate') is considered to be the threshold for a

cardiorespiratory training in unfit individuals (68, 69).

4.7.1.ii Determining duration of aerobic component

Duration of the aerobic component is determined by simply measuring the time in

which HR is within the HR$_{target}$ zone. However, what remains unclear is the minimum

time interval over which HR must be sustained within the zone to impose a metabolic stress

on the cardiovascular system. In the present study we selected a minimum interval of 30

seconds. Using electrically-stimulated dog gracilis muscle as a model, Connett et al. (70)

demonstrated an exponential rise in $\dot{V}O_2$ during the rest-work transition, with a half-time

of about 15 seconds. They also reported that prior to achieving a steady-state $\dot{V}O_2$ plateau

at about 60 seconds, the energy needed for tension development was provided by a burst

of glycolysis during the first 5 seconds of work followed by continuous PCr hydrolysis.

Thus, all three mechanisms of ATP generation are stimulated almost immediately when

muscle contraction begins, with the contribution of oxidative phosphorylation to the energy

balance increasing and that of PCr hydrolysis declining as a steady-state condition is

approached. Medbø and Tabata (71) stated that "anaerobic processes may not provide ATP much faster than aerobic processes even during short bursts of exercise like 30 seconds of bicycling." Walloe and Wesche (72) demonstrated a substantial increase in the velocity of blood flow in human quadriceps muscle after the first 2-second contraction of that muscle during rhythmic exercise sustained for 1-6 minutes. The time to reach steady-state is usually between 1-3 minutes and is inversely related to the exercise intensity (73) and directly related to the fitness of the individual (74).

4.7.1.iii Estimating mean energy expenditure

Energy expenditure during physical activity is obviously dependent on the intensity and duration of the activity, factors which have been discussed above. In situations where direct measurement of $\dot{V}O_2$ is impractical, energy expenditure can be estimated by relating telemetered HR during the activity to the subject's HR-$\dot{V}O_2$ curve established during a GXT (50) - the methodology used in Phase 2. A major concern regarding this technique is that the conditions in which the field and laboratory data are collected are not analogous; in the laboratory extraneous factors are controlled and the activity is usually of a continuous, incremental, dynamic nature (e.g., treadmill walking) involving large muscle groups whereas in the field the activity is often an intermittent, static/dynamic (or isometric/isotonic) nature involving a mixture of small and large muscle groups, and factors that affect the dependent variables are not well controlled. Maas and colleagues (75) studied the accuracy of using the HR-$\dot{V}O_2$ relation established in treadmill running to predict energy expenditure involved in static weight-holding and static/dynamic weight-carrying while treadmill running in eight healthy young adults. The researchers found that $\dot{V}O_2$ predictions from measured HR were relatively accurate for the static/dynamic task but were generally overestimated for the static task.

In addition to the nature of the task (static versus dynamic) and the time course (transient versus steady-state), the type of exercise (arm versus leg), body position during

exercise (supine, sitting) and level of training (untrained versus trained) can affect the $\dot{V}O_2$- HR relation. Bernard et al. (76) found that the slope of the $\dot{V}O_2$-HR curve was higher in the first minute of low-intensity dynamic exercise than during steady-state exercise; thus, a measured HR in the rest-work transition yielded an inflated $\dot{V}O_2$ estimate. The underlying physiologic mechanism was not investigated but a sudden sympathetic resetting of the arterial baroreflex at the onset of exercise was hypothesized. Also, Vokac et al. (77) noted that during the rest-work transition, the HR response during arm exercise was less than that during leg exercise of comparable intensity, and that HR during arm work was no different in sitting than in standing. In contrast, Stenberg and colleagues (78) observed greater HR responses at a given $\dot{V}O_2$ during steady-state arm exercise compared to leg exercise, as well as during arm or leg exercise in sitting compared to supine. These researchers also noted that the effect of HR differences between steady-state arm and leg exercises on the $\dot{V}O_2$-HR relationship was somewhat offset by higher $\dot{V}O_2$ during arm exercise at any given submaximal workload. Lastly, the same HR during submaximal exercise after training represents a higher relative exercise intensity and energy expenditure (74). Despite these limitations in predicting $\dot{V}O_2$ from HR data, Åstrand and Rodalh (79) argued against the need for simulating the actual activity in determining the HR-$\dot{V}O_2$ relation for predictive purposes, stating that "the use of the recorded HR as a basis for the estimation of workload may be acceptable even in many work situations involving arm work or the use of small muscle groups."

4.7.2   Exercise intensity and energy expenditure in therapy sessions

Although the HR responses (HR$_{rest}$, HR$_{mean}$, HR$_{peak}$, % HR$_{max-pred}$) during therapy sessions in Phase 1 and 2 were unchanged over the course of rehabilitation, the mean time spent within the HR$_{target}$ zone in physiotherapy (as calculated for Phase 2 data using the criterion measure - the HR$_{target(GXT)}$ formula) and the corresponding mean EE$_{mean}$ increased

significantly between the first and third month post-stroke. These seemingly inconsistent results underline the limitations of using HR data alone to determine exercise intensity and support the rationale for using formal GXTs to establish appropriate HR_{target} levels for stroke rehabilitation. Nevertheless, our main conclusion from the Phase 1 and 2 results was that the exercise intensity was inadequate from the perspective of cardiorespiratory training. We used the most conservative threshold levels for aerobic conditioning and observed little evidence of physical exertion when these levels were exceeded. The Phase 2 subjects demonstrated during the GXTs that they could safely exercise at higher intensities than they did during therapy sessions and threshold HR_{target} values were reached very early in testing. Furthermore, a disproportionate amount of time was spent being 'inactive' in terms of cardiorespiratory stress. The mean time spent within the HR_{target} zone during therapy sessions, irrespective of the HR_{target} formulae used, was well below the minimum duration of 20 minutes recommended to improve exercise capacity (18, 33). High energy cost components were too intermittent to have significant effects on cardiovascular function; thus the EE_{mean} relative to the total session time was low.

Our results did not support the concern raised by Bachynski-Cole and Cumming (16) that occupational therapy sessions for patients post-stroke may involve periods of intense, isometric work that induce undue cardiac stress. The findings also contradict those of the only published investigation on the intensity of physiotherapy for patients post-stroke (20). Roth and colleagues (20) interpreted a mean change in HR of 36 percent during physiotherapy as sufficient to derive a training effect yet the authors failed to determine a HR_{target} zone and to measure the duration over which the HR was elevated. In the present study, the overall ranges of HR responses during both physiotherapy and occupational therapy sessions were of a magnitude equal to or greater than that reported by Roth et al. (20) but HR values within or approaching the HR_{target} zone were transient and did not reflect metabolic stresses sufficient to enhance cardiorespiratory fitness. The activities that elicited the greatest HR responses were consistent with those identified in the Roth study

(20), and included mainly standing activities and transitional movements (e.g. sitting to standing, standing to sitting on the floor).

Roth and colleagues (20) hypothesized that participation in exercise programs may be limited for patients post-stroke with CAD because of their compromised coronary circulation and decreased cardiac reserves. Moldover (80) expressed concern that the exercise intensity of rehabilitation activities for patients post-stroke with CAD may be unnecessarily limited by excessive cardiac precautions. In our study, no differences were identified in HR responses or intensity of therapy sessions between subjects with and without CAD. There was some indication, based on the limited population of females in Phase 2, that the intensity of physiotherapy may have been lower for the female patients. The mean EE$_{mean}$ during physiotherapy was 18 percent lower for the small subgroup of female patients than for the male subgroup, about 11 percent of which could be attributed to gender-related differences in basal EE (53). In addition, those patients experiencing shoulder pain spent 50 percent less time in standing activities per physiotherapy session and 150 percent more time inactive than did the subjects without that complication.

The reasons for not systematically addressing cardiorespiratory status in stroke rehabilitation are no doubt multifaceted. Since lack of motor and postural control is often the most obvious limiting factor in terms of functional recovery, a preoccupation with improving neuromuscular function is understandable. The observation that experienced therapists in this study and in previous studies (3, 16) did not monitor HR and BP of patients post-stroke, even in patients with well-documented cardiac disease, suggests a disregard for cardiorespiratory functioning. Lamb and Frost (81) assert that "exercise physiology and prescription seem poorly understood [by physiotherapists] and they are undervalued as clinical skills", a sentiment shared by Paley (82). The risk of falls, aggravation of spasticity, and detrimental cardiac responses to the dynamic activities and overload necessary to achieve a training effect may have been deterrents to higher exercise intensities. Lack of time for conditioning may also have been an issue, although the

average time spent in physiotherapy and occupational therapy per day in the present study was over twice the values reported in a meta-analysis by Kwakkel et al. (83).

4.7.3 Study limitations

The most important limitation of this study, that of using HR to estimate exercise intensity, has been discussed at length in Section 4.7.1. The sample of subjects studied, while manifesting characteristics typical of patients participating in stroke rehabilitation, was small and female patients were under-represented in Phase 2. Also, data collection was restricted to physiotherapy and occupational therapy sessions since numerous behavioral mapping studies have indicated that the activity level of patients post-stroke while not engaged in therapy is inordinately low (24-28). Finally, although the stroke rehabilitation program under study appeared to be representative of the contemporary programs, there may have been nuances unbeknownst to us and specific to this program that affected the results.

4.8   Conclusions

Despite the fact that stroke and CAD share common risk factors and pathophysiologic processes, the approach to physical rehabilitation of these conditions is dramatically different.   Key components of cardiac rehabilitation are retraining the cardiorespiratory system through aerobic exercise - the intensity of which is prescribed using a HR_{target} zone - and ongoing monitoring of HR, blood pressure, and perceived exertion.   The main finding of this longitudinal, two-phase study is that stroke rehabilitation, as currently delivered, does not provide significant cardiorespiratory stress. We determined that the estimated aerobic component of physiotherapy over the course of rehabilitation was low, and that of occupational therapy was negligible, for patients post-stroke with and without CAD.   As well, cardiorespiratory responses were not monitored by the therapists supervising the therapy sessions.   The need for and benefit of aerobic

conditioning appear to be largely overlooked, and as a consequence, potentially modifiable cardiovascular limitations are not addressed using the current therapeutic strategies. Since it is becoming increasingly apparent that the majority of patients post-stroke have limited exercise capacity, these observations have significant implications in terms of clinical practice. Our findings support a rationale for incorporating the goals and principles of cardiac rehabilitation into stroke rehabilitation programs. Further research on the efficacy of increasing the aerobic component of these programs in enhancing functional outcomes is warranted.

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4.10 Appendix 1

**Queen Elizabeth II
Health Sciences Centre**
Cardiac Prevention and Rehabilitation Research Centre
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Informed Consent

Title of Study: *Estimation of the aerobic component of contemporary stroke rehabilitation.*

Principal Investigator:	• Marilyn MacKay-Lyons, M.Sc. (PT), Doctoral Student, Department of Physiology and Biophysics, Dalhousie University; tel: 494-2632 or 473-8622
Associate Investigators:	• Lydia Makrides, Ph.D., Professor and Director, School of Physiotherapy, Dalhousie University

Introduction
We invite you to take part in a research study at the QEII Health Sciences Centre. Taking part in this study is voluntary. The quality of your health care will not be affected by whether you participate or not. Participating in this study might not benefit you, but we might learn things that will benefit others. You may withdraw from the study at any time without affecting your care. The study is described below. The description tells you about the risks, inconvenience, or discomfort which you might experience. You should make sure that any questions you have about the study are answered to your satisfaction.

What is the purpose of this study?
The purpose of this study is to determine how activities performed during physical and occupational therapy sessions over the course of the stroke rehabilitation affect the heart rate. We want to find out if these sessions are too challenging, challenging enough, or not challenging enough on the heart to provide an exercise training effect.

Who can take part in the study?
The 20 patients with stroke participating in this study will:
• have been admitted to the Queen Elizabeth II Health Sciences Centre (QEII);
• have had an ischemic stroke within the past month;
• be involved in physical and occupational therapy;
• not have a pacemaker;
• provide informed consent.

How are participants selected?
Patients admitted to the QEII who meet the conditions described above will be told about the study by Dr. S. Phillips, neurologist and Director of the Acute Stroke Service. The names of people who agree to participate will be given to Marilyn MacKay-Lyons, a physiotherapist and the principal investigator of the study. She or one of her physiotherapy students will visit each person to review details of the study, answer questions, and obtain a signed copy of this form.

What does the study involve?

If you choose to participate in this study, your physical and occupational therapy sessions will not be changed in any way. Every two weeks a physiotherapist or physiotherapy student involved in the study will monitor your heart rate during your usual physiotherapy and occupational therapy sessions at the Halifax Infirmary or the Nova Scotia Rehabilitation Centre. In order to monitor your heart rate you will be required to wear a heart rate monitor that is fastened securely around your chest and a heart rate recorder (similar to a watch) that is worn on your wrist. These devices will keep a record of your heart rate during the therapy sessions. The person monitoring the session will also record on paper the types of activities in which you participate during therapy.

Are there any risks or discomforts?

The heart rate monitor around your chest should be 'snug' but should not cause any irritation. If the monitor feels uncomfortable, the person monitoring the session will adjust the length.

What are the possible benefits?

By participating in this study, you will be contributing valuable information. By studying what happens to heart rate during stroke rehabilitation, we hope to assist therapists in designing safe and effective exercises and activities for patients with stroke.

Other important information

1. **Confidentiality**: All information gathered during the study will be kept confidential. The information collected from this study will be published and presented at scientific conferences but your name will not be used. Your records will be kept in a locked file cabinet. Only the staff involved in the research study will see them.

2. **Costs**: There will be no costs to you for being in this study.

3. **Questions or Problems**: If you have any questions about this study, please contact Marilyn MacKay-Lyons (0-902-473-8622) or at Dalhousie University (0-902-494-2632). There is voice mail at these numbers.

I have read the description of the study. I have been given the opportunity to discuss the study. My questions have been answered to my satisfaction. I understand that I will be given a copy of this consent form for my own records. I hereby consent to take part in this study.

---   ----------------------------
Signature of Subject   Date

---   ----------------------------
Signature of Study Investigator   Date

---   ----------------------------
Signature of Witness   Date

4.11   Appendix 2

HEART RATE MONITORING STUDY
DATA SUMMARY FORM

SESSION DATA

Subject's name:_____ Code #:_____

Date of session:_____Time of session:_____

Session #:_____Weeks since stroke:___

Session (and #): PT ___OT____ Name of therapist: _____

Therapy location: NHI__NSRC__Room__Gym___Other__Specify___

Frequency: daily___other__Specify_____home ex program: no/yes

Description ( ):In-pt ___Out-pt___Assessment___Treatment___Both:____

Known Cardiac Disease: no____yes___   Berg Score:_____/56

Timed Up & Go: amb aid_____I^{st} sec_____ 2^{nd}_____sec Mean_____sec

Additional Comments re Mobility/Progress: _____

_____

_____

_____

HEART RATE DATA

Age:_____Est HRmax (= 220 - age):_____HR reserve (= HR_{max} - HR_{rest}):_____

Target HR Zone (= [40-85% HR reserve] + HR_{rest})_____to_____

HR-altering medication:no____yes___Type:_____Dose:____

Effect on HR:_____Altered Target HR Zone:_____

Length of Session:_____min   Mean HR for session: _____bpm

Resting HR:_____bpm Max HR achieved:____bpm %Est HRmax achieved:_____%

Under HR zone:_____min_____%

Within HR zone:_____min_____%

Over HR zone:_____min_____%

Additional Comments/Observations: _____

_____

_____

_____

_____

_____

_____

_____

ACTIVITY LOG

Activity	#	Duration (min)	% total	Mean HR	HR Range	Below (min)	Target %	Within (min)	Target %	Above (min)	Target %
pre-session HR baseline	0										
supine: resting**	1										
supine: LE ex -no wt	2										
supine: LE ex - wt	3										
supine Trunk ex	4										
supine: UE ex -no wt	5										
supine: UE ex - wt	6										
prone: resting**	7										
prone: LE ex -no wt	8										
prone: LE ex - wt	9										
prone Trunk ex	10										
prone: UE ex -no wt	11										
prone: UE ex - wt	12										
R sd ly: resting**	13										
R sd ly: LE ex -no wt	14										
R sd ly: LE ex - wt	15										
R sd ly Trunk ex	16										
R sd ly: UE ex -no wt	17										
R sd ly: UE ex - wt	18										
L sd ly: resting**	19										
L sd ly: LE ex -no wt	20										
L sd ly: LE ex - wt	21										
L sd ly Trunk ex	22										
L sd ly: UE ex -no wt	23										
L sd ly: UE ex - wt	24										
Ly: passive ranging	25										
Ly: stretching	26										
Total for Ly no rest											
Sitt: resting**	27										
Sitt: LE ex -no wt	28										
Sitt: LE ex - wt	29										
Sitt Trunk ex/balance	30										
Sitt: UE ex -no	31										
Sitt: UE ex - wt	32										
Sitt: arm ergometer	33										
Sitt: muscle stimulation	34										
Sitt: manual dexterity	36										
Sitt: cogn/perception	36										
Sitt: ADL- dressing	37										
Sitt: ADL- washing	38										
Sitt: ADL - kitchen	39										
Sitt: transfers to sitt	40										
Sitt: transfers to st	41										
Sitt: transfers to bath	42										
Sitt: transfers to ly	43										
Sitt: Other-	44										
Total Sitt no rest data											
St: resting**	45										
St: LE ex -no wt	46										
St: LE ex - wt	47										
St Trunk ex/balance	48										
St: UE ex -no wt/reach	49										
St: UE ex - wt	50										
St: ADL's	51										
St: stretching	52										
Walking unaided	53										
Walking with walker	54										
Walking with cane	55										
Stairs	56										
Stepping	57										
Treadmill	58										
Kinetron	59										
Running	60										
Total for St no rest											
Total for Resting**											
TOTAL SESSION											

CHAPTER 5: CHANGES IN EXERCISE CAPACITY DURING RECOVERY FROM STROKE

5.1 Introduction

There is evidence in the literature of abnormally low exercise capacity in patients in the chronic post-stroke period (1, 2). We recently corroborated this finding in a group of 29 patients early post-stroke (see Chapter 3). What has not been reported, however, is the extent of change in aerobic capacity over the course of recovery post-stroke. As a result, the contribution of changes in the cardiorespiratory system to overall functional recovery is unknown. The notion of cardiovascular adaptations to exercise as important determinants of stroke outcomes has not be adequately addressed. Gresham et al. (3) suggested, without supporting evidence, that "much of the disability of stroke victims appears to be due to coexisting cardiovascular disease."

Documenting longitudinal changes in exercise capacity and corresponding changes in functional status would be of value in exploring the interaction between the cardiorespiratory and neuromuscular systems in the recovery process. Also, baseline data on the effects of contemporary stroke rehabilitation on cardiorespiratory fitness would be useful in determining the need for aerobic conditioning in the early stages post-stroke, the period during which physical rehabilitation takes place and potential for functional recovery is maximized.

There are indications, mainly from the results of training studies, that improvements in cardiovascular adaptation are possible, at least in the post-recovery stages of stroke (1, 4-7). In two studies that measured $\dot{V}O_{2peak}$ before and after a training period involving patients with chronic hemiplegia, mean improvements in $\dot{V}O_{2peak}$ of 19 percent (8) and 13 percent (1) were reported. Other training studies have relied on submaximal parameters as indices of a training effect. In 1979 Brinkman et al. (4) documented an average reduction of 20 percent in submaximal HR at a fixed work rate after 12 weeks of

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aerobic conditioning by patients with long-term stroke. More recently, Macko and associates (5) demonstrated a mean decrease in submaximal HR of 15 percent with a 6-month treadmill conditioning program for patients in the chronic post-stroke period. The single patient with stroke who participated in a 10-week training study by Wolman and Cornall (6) demonstrated no change in submaximal HR at a fixed load.

In a clinical investigation related to the present study, we concluded that the aerobic component of an existing stroke rehabilitation program was inadequate to elicit significant improvements in cardiorespiratory status (see Chapter 4). Based on this finding, it is unlikely that clinically significant improvements in cardiovascular adaptation occur with current therapeutic interventions. However, the possibility exists that we overestimated the exercise intensity needed to improve exercise capacity during the post-stroke recovery period. Alternatively, a 'spontaneous' increase in exercise capacity may occur after stroke, such as that reported in deconditioned patients soon after MI (9). Thus, longitudinal measurements of exercise capacity are required to ascertain the extent of change in exercise capacity.

In addition to exercise capacity, another potentially modifiable factor that can adversely affect stroke outcome is the energy expenditure of physical activity. The energy expended in walking post-stroke has been a topic of excessive study (5, 10-15), in part because improved walking ability is the principal goal of most stroke survivors (16) and also because, for many individuals, walking represents the only departure from a sedentary life (17). After stroke, several determinants of normal gait may be adversely affected, with consequent high energy costs of locomotion, an inevitable cardiovascular burden, and limitations in the type and duration of daily activities (18). The extent of change in energy expenditure during walking over the course of recovery post-stroke has not been adequately addressed. However, it is reasonable to assume, given the substantial and progressive neuromuscular recovery observed in this period, that muscular efficiency, and hence the energy cost of walking, would likewise improve.

In the present study we investigated changes in exercise capacity and related variables of individuals at 1-, 2-, 3-, and 6-months post-stroke and the relationship of these changes to improvements in functional status. In addition, we also studied longitudinal changes in the energy expenditure during level walking at a fixed speed across GXTs. The principal research hypotheses were that (i) changes in exercise capacity over the 6-month post-stroke period would not be significant, (ii) changes in motor recovery and functional status would be significant and correlate poorly with change in exercise capacity, and (iii) changes in energy expenditure during walking would be significant.

5.2 Methods

5.2.1 Subjects

Data for this study were collected as an extension of an observational cohort study originally designed to investigate the exercise capacity of patients early post-stroke (see Chapter 3). The subjects who had undergone exercise testing at one month post-stroke were asked to return for retesting at two, three, and six months post-stroke. Testing at set post-stroke intervals rather than at specific events such as admission and discharge is in keeping with the recommendations of Jongbloed (19). A six-month period was chosen because most recovery post-stroke has occurred by this time (20). The subjects participated in the usual course of rehabilitation, as prescribed by stroke team members not affiliated with the study. No attempt was made to influence the extent or content of stroke rehabilitation or to restrict or alter the daily activities of the subjects. The subjects were grouped as Dependent or Independent according to their Barthel Index at the one-month GXT (see Chapter 3).

5.2.2 Testing protocol

The testing protocol used in the initial tests was repeated in the subsequent tests with the same initial speed, progression of speed and grade, and use of 15% body weight support (see Chapters 2 and 3 for details). Also, the tests were physician-monitored and conducted at consistent times of the day. Those subjects who used handrail support during the 1-month GXT were instructed to use the same support for the remaining three tests, and at no time was the gait pattern manually facilitated by the investigators. At the time of each GXT, the subjects were asked to report changes in their daily activities since their previous test. Within two days of each GXT, the impairment and disability status was evaluated using the following outcome measures:

• Chedoke McMaster Stages of Recovery of the Leg (CM-Leg) and Foot (CM-Foot) (21): as described in Chapter 3.

• grip strength (grip): A Jamar hand dynamometer was used to measure grip strength of the less affected and more affected hand with the subject seated and the shoulder in neutral position, elbow flexed to 90°, wrist extended to 30°, and in 15° of ulnar deviation. Each subject was instructed to hold the dynamometer and to follow the instructions: "squeeze harder, harder, and relax" (22). The mean of two consecutive measurements was used in data analysis.

• Berg Balance Test (Berg) (23): Each subject performed 14 balance tasks, graded on a 5-point criterion-referenced scale. This test has been shown to have high inter- and intra-rater reliability and validity (24).

• walking speed (speed): Each subject walked 10 meters independently at self-selected speed over level ground supported by any ambulatory aids and orthotic devices used in everyday ambulation. Gait speed over 10 meters has been found to be valid and reliable measure to use with patients early post-stroke (25).

• Timed Up and Go Test (TUG) (26): Each subject stood up independently from an armchair, walked 3 meters, turned, returned to the chair and sat down. This test of

mobility and postural adjustments has been found to have high test-retest reliability, with an interclass correlation coefficient (ICC) of 0.99, and high inter-tester reliability (ICC = 0.99) (27).

• Chedoke-McMaster Disability Inventory (CMDI) (28): The subject performed 14 mobility and locomotion tasks, each scored on a 7-point criterion-referenced scale.

5.2.3 Data Analysis

Descriptive statistics including means, standard deviations and ranges were calculated for all dependent variables measured during the GXTs (i.e., resting, submaximal, and peak values for relative and absolute $\dot{V}o_2$, HR, SBP, DBP, RPP, O_2 pulse, $\dot{V}E$, Vt, RR, as well as peak workload and exercise time) and the functional measures (i.e., CM-leg, CM-foot, grip, Berg, speed, TUG, and CMDI).

To estimate the energy expenditure during level walking on the treadmill (EEwalk) $\dot{V}o_2$ and RER were averaged over the last 30 seconds of the first stage of each GXT. EEwalk was then determined using the caloric equivalent for a liter of O_2 at the measured RER (29, 30). To permit comparisons with normative data the $\dot{V}o_2$ values were adjusted to compensate for the use of 15% BWS. By the end of the first stage, the subjects had been walking on the level at a constant speed for three minutes (i.e., 1-minute warm-up and 2-minute); thus steady-state respiration could be reasonably assured (31) (32). However, the energy costs involved in subsequent 2-minute stages of the GXTs could not be determined with confidence since steady-state conditions were not met.

Inferential statistics were applied to determine the extent of change across testing intervals in the functional variables and in the GXT variables measured at peak exercise intensity as well as submaximal values averaged over the last 30 seconds of each of the first six stages of the GXT. One-way repeated measures analyses of covariance (ANCOVAs) were used with one within-subject factor (GXT) and one non-time-varying

covariate (age). Bonferroni *post hoc* testing was applied to detect statistically significant differences in the dependent variables across the four tests.

The analyses were repeated using two-way ANCOVAs with one within-subject factor (test), one non-time varying covariate (age) and one of two grouping factors (Dependent or Independent group or presence or absence of CAD). The software program, BMDP-5V - Unbalanced Repeated Measures Models with Structured Covariance Matrices (33) was selected for the ANCOVAs since this program was designed specifically for small data sets with limited missing data. The program offers a choice of models for the covariance structure - (i) compound symmetry, with two covariance parameters and where the responses have a common variance and covariance; (ii) first-order autoregressive, with two covariance parameters and where the covariance matrix is banded such that adjacent responses are more closely related than distant responses; and (iii) unstructured, where the covariance matrix is fully parameterized with unique variances and covariances in the matrix. For the majority of the ANCOVAs in the present study, compound symmetry was the model of choice since it was associated with the largest Akaike's Information Criterion.

For those variables in which statistically significant differences between tests were identified by the ANCOVAs, percentage change (% Δ) scores were calculated [% Δ score = (Variable$_{test\ B}$ -Variable$_{testA}$/Variable$_{testA}$) * 100] in order to adjust for the effect of the initial value on the extent of change. To examine the relationship between changes in $\dot{V}O_{2peak}$ and functional measures, multiple linear regression was applied with % Δ $\dot{V}O_{2peak}$ as the dependent variable and % Δ scores in functional measures, age, BMI, and responses to the Physical Activity Questionnaire (PAQ) as independent variables. Least squares regression lines were calculated for $\dot{V}O_{2}$ and HR against exercise time for each of the four GXTs. Pearson product-moment correlation coefficients were computed to assess

relationships between continuous variables. All statistical tests, except the Bonferroni *post hoc* testing, were performed with an alpha level set at 0.05.

5.3 Results

5.3.1. Subjects

Twenty-seven (93 percent) of the 29 subjects who had performed the initial exercise test at about 1-month post-stroke participated in this longitudinal study. The two subjects who did not participate had moderate disability - a 64-year-old male who had an excessive hypertensive response during the initial test and an 83 year-old-female who declined because of the anxiety she experienced during the first test. Data of two subjects were eliminated from the analysis - one 49-year-old male with mild disability who relocated 10 weeks post-stroke and a 72-year-old female with moderate disability who quit after the second test. Background characteristics of the 25 participants grouped according to level of disability at the time of the first exercise test are summarized in Table 20. There were no statistically significant differences between this subsample and the larger sample of 29 subjects who had performed the initial exercise test (see Table 6, Chapter 3). Statistically significant differences were found between the Dependent and Independent groups in the BI on admission to the acute stroke unit and on length of stay (LOS) at both the acute stroke unit and rehabilitation centre. The discharge destination from in-patient rehabilitation of all subjects was home with spouse or other relatives. Of the seven subjects who had been employed at the time of their stroke, five had returned to work by the 6-month GXT.

Table 20. Characteristics of participants grouped according to level of disability at 1-month post-stroke

Characteristic	Dependent (n=16)	Independent (n=9)	Total (n=25)
age *yr*	64.9±14.4	62.7±12.7	64.1±13.6 (29-82)
sex	13M:3F	7M:2F	20M:5F
weight *kg*	79.9±12.8	87.7±11.2	82.7±12.6 (64-115)
BMI *kg/m²*	26.8±3.5	28.4±2.9	27.4±3.3 (20-35)
side of stroke	11R:5L	6R:3L	17R:8L
OCSP classification			
TACI	4 (25%)	0	4 (16%)
PACI	5 (31%)	0	5 (20%)
POCI	3 (19%)	0	3 (12%)
LACI	4 (25%)	9 (100%)	13 (52%)
admission BI *0-100*	37.8±18.1	57.6±13.8*	45.2±19.0 (0-73)
acute LOS *days*	20.0±8.7	10.9±3.1*	16.7±8.4 (3-38)
IP rehab LOS *days*	25.8±15.7	9.1±9.3*	19.8±15.8 (0-58)
OP rehab *weeks*	12.5±10.0	8.6±12.1	10.8±10.9 (0-35)
ambulatory aid			
no aid	0	6 (67%)	6 (24%)
single cane	8 (50%)	3 (33%)	11 (44%)
quad cane	6 (38%)	0	6 (24%)
walker	2 (13%)	0	2 (8%)
history of CAD	10/16 (63%)	3/9 (33%)	13/25 (52%)
β-blocker medication	9/16 (56%)	4/9 (44%)	13/25 (52%)
diabetes mellitus	6/16 (38%)	2/9 (22%)	8/25 (32%)
PAQ	7.6±10.7	3.7±5.8	6.2±9.2 (0-36)
history of smoking	10/16 (63%)	6/9 (67%)	16/25 (64%)
amount smoked *pk-yr*	38.4±25.7	38.5±13.6	38.4±21.5 (5-74)

Data are means ± SD (ranges) or counts (percentages). BMI: body mass index (mass/height²); OCSP classification: see Chapter 3 for details; admission BI: Barthel Index on admission to acute hospital; LOS: length of stay; IP rehab: in-patient rehabilitation; OP rehab: out-patient rehabilitation; CAD: coronary artery disease; PAQ: Physical Activity Questionnaire; amount smoked: by those with history of smoking expressed as pack-years (pk-y) [# y of smoking x average # of packages of cigarettes/day]. *Between-group difference, P<0.01.

5.3.2 General response to exercise testing

The testing procedure was tolerated well by all subjects and there were no complications during or following the GXTs. Several subjects stated that they looked forward to the GXTs because they felt empowered by their performance. Based on visual inspection and feedback from subjects, the gait pattern of most patients appeared to

improve in terms of symmetry and coordination when treadmill walking as opposed to overground walking, particularly with slight treadmill elevations (usually between 2.5-7.5 percent). The testing schedule was adhered to in that the 1-month GXT took place 26±6 days post-stroke, the 2-month GXT at 58±6 days post-stroke, the 3-month GXT at 90±8 days post-stroke, and the 6-month GXT at 184±18 days post-stroke. A total of five GXTs were missed, four due to inclement weather and sickness and the fifth because the subject (a 72-tear-old male) had a second stroke at 5 months after his initial insult.

In 89 of the 95 (94 percent) GXTs performed the subjects terminated testing of their own volition whereas, in five of the six remaining GXTs, testing was terminated by the investigators due to excessive increases in blood pressure (Table 21). On one occasion testing was stopped due to painless S-T segment depression, which would be categorized as a nonischemic response by DeBusk et al. (9). Only five subjects had a consistent reason for termination across all tests; this subgroup included one male with previously undiagnosed intermittent claudication, one male - a long-term smoker - with dyspnea, two males with volitional fatigue, and one female with fatigue localized to the hemiparetic leg. The number of subjects who stopped exercise due to cardiopulmonary signs and symptoms decreased and the number who stopped due to volitional fatigue increased across tests.

Table 21. Reasons for termination of exercise tests at 1,2,3, and 6-months post-stroke

Reason for Test Termination	1-month (n=25)	2-month (n=24)	3-month (n=24)	6-month (n=22)
Volitional fatigue	5 (20%)	7 (29%)	9 (38%)	11 (50%)
Hemiparetic leg fatigue	4 (16%)	4 (17%)	3 (13%)	1 (4.5%)
Non-hemiparetic leg fatigue	5 (20%)	6 (25%)	7 (29%)	6 (27%)
Back pain	0	1 (4%)	0	1 (4.5%)
Leg claudication	1 (4%)	1 (4%)	1 (4%)	1 (4.5%)
Cardiorespiratory signs/symptoms	10 (40%)	5 (21%)	4 (17%)	2 (9%)
dyspnea	7 (70%)	5 (100%)	2 (50%)	1 (50%)
ST-segment depression	0	0	1 (25%)	0
SBP > 260 or DBP > 115 mm Hg	3 (30%)	0	1 (25%)	1 (50%)

Data are counts (percentages).

5.3.3 Comparability of GXTs

The effort exerted by the subjects during each of the four GXTs was compared by examining several variables at peak exercise intensity. The data presented in Table 22 show that the percentage of subjects attaining $\dot{V}O_2$ max criteria was relatively consistent over the four GXTs. In addition, there were no statistically significant differences in mean values of HRpeak, percentage of HRmax-pred, RERpeak, and RPEpeak across the GXTs (Table 23).

Table 22. Attainment of $\dot{V}O_2$ max during exercise tests at 1,2,3, and 6-months post-stroke using commonly employed criteria

GXT	met ≥ 1 criteria	SBPpeak >200 Torr	RERpeak >1.00	>1.10	HRpeak <15 b/min	<10 b/min	HRpeak adiusted for ß-blocker <15 b/min	<10 b/min
1-month (n=25)	16 (64%)	8 (32%)	14 (56%)	0	5 (20%)	2 (8%)	12 (48%)	5 (20%)
2-month (n=24)	15 (63%)	7 (29%)	14 (61%)	3 (13%)	8 (33%)	8 (33%)	12 (50%)	9 (38%)
3-month (n=24)	17 (71%)	6 (25%)	14 (58%)	2 (8%)	6 (25%)	6 (25%)	10 (42%)	9 (38%)
6-month (n=22)	14 (64%)	4 (18%)	12 (55%)	4 (18%)	8 (36%)	7 (32%)	9 (41%)	10 (45%)

Data are counts (percentages). SBPpeak: systolic blood pressure at peak exercise intensity; RERpeak: respiratory exchange ratio at peak exercise intensity; HRpeak: heart rate at peak exercise intensity, expressed as <15 or <10 beats/min of predicted HRmax[220-age]; adjusted for ß-blocker: adjustment in predicted HRmax [85% (220-age)] due to HR-lowering effect of ß-blocker medication.

Table 23. GXT variables at peak exercise intensity at 1,2,3, and 6-months post-stroke

Variable	1-month	2-month	3-month	6-month
HRpeak beats/min	122.8±19.4 (93-176)	126.6±29.3 (83-187)	123.3±26.7 (82-174)	126.1±25.2 (92-187)
% HRmax-pred	79.1±9.5 (60-99)	81.1±15.6 (53-113)	80.0±13.9 (51-114)	82.4±13.1 (63-103)
% HRmax-pred/adj	85.4±8.7 (67-100)	89.8±13.7 (62-113)	86.7±12.7 (58-114)	88.2±11.7 (70-111)
RERpeak	1.00±0.07 (0.82-1.08)	1.00±0.09 (0.84-1.20)	1.00±0.07 (0.84-1.12)	1.00±0.08 (0.90-1.18)
RPEpeak 0-10	6.1±1.2 (5-9)	6.2±1.3 (5-9)	6.0±1.4 (4-9)	6.4±1.2 (5-9)

Data are means ± SD (range). HRmax: peak heart rate; % HRmax-pred: % of [220-age]; % HRmax-pred/adj: adjusted for ß-blocker; RERpeak: peak respiratory exchange ratio; RPEpeak: peak rating of perceived exertion.

5.3.4 Peak oxygen consumption and related variables across GXTs

Peak values of relative $\dot{V}O_2$ attained by each subject in the Dependent and Independent groups are illustrated in Figure 11. The difference in $\dot{V}O_2$peak between groups in the 1-month GXT was statistically significant (13.4 ± 3.2 ml/kg/min versus 17.3 ml/kg/min, respectively, $p<0.05$). Two line graphs in the Dependent group are highlighted. The thick solid line (━━━) represents the data of a 66-year-old male who, after discharge from rehabilitation at 17 weeks post-stroke, joined a fitness club and participated in treadmill walking 4 times per week. The thick broken line (■ ■ ■) represents the data of a 76-year-old male who experienced depression after discharge from rehabilitation at 10 weeks. Soon after his 3-month GXT his wife bought him a treadmill which he used daily. Both subjects were continuing to treadmill walk at the time of the 6-month GXT.
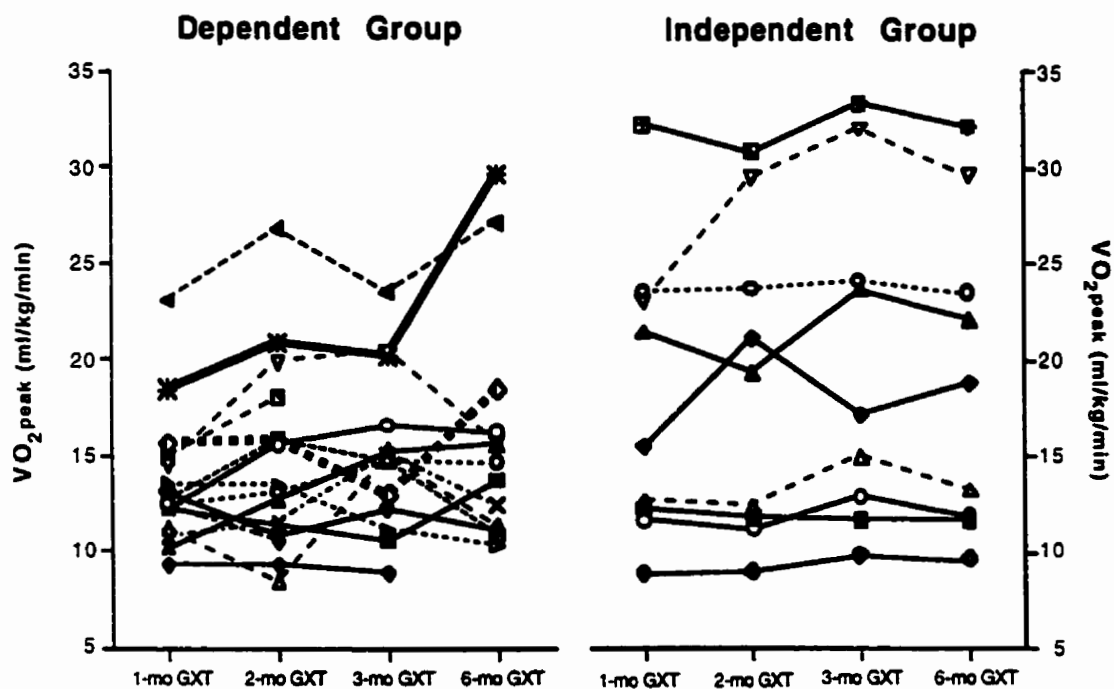

Figure 11. Peak oxygen consumption ($\dot{V}O_2$peak) across the GXTs for each subject in the dependent and independent group. See text for details regarding the highlighted solid and broken lines that represent data of subjects in the Dependent Group.

As shown in Table 24, the increases in relative and absolute $\dot{V}O_{2peak}$ between the 1-month and the 6-month GXTs (16.9 and 18 percent, respectively) were found to be statistically significant on *post hoc* testing. A mean gain of 10.8 percent in relative $\dot{V}O_{2peak}$ was observed between the 1- and 2-month (representing 65 percent of the total change in $\dot{V}O_{2peak}$ over the course of the study) but this gain did not reach statistical significance. Age was a significant covariate. One grouping factor, presence or absence of CAD, was not statistically significant, the other grouping factor, Dependent versus Independent group, was significant (mean difference in $\dot{V}O_{2peak}$ was 2.28 ml/kg/min for the Dependent group and 1.91 ml/kg/min for the Independent group, p=0.04). Statistically significant differences were also found in exercise time and workload$_{peak}$ between the 1-month GXT and each of the other GXTs. In addition, significant differences were found in exercise time and workload$_{peak}$ between the 2-month and 3-month GXTs and between the 2-month and 6-month GXTs. Mean differences in O_2 pulse$_{peak}$, SBP$_{peak}$, DBP$_{peak}$, and RPP$_{peak}$ across GXTs were not statistically significant. A statistically significant increase in mean body weight was observed between the 2-month and 6-month GXTs. Seventeen of the 22 (77 percent) tested at six months post-stroke gained weight since the first GXT with an average gain of 2.2 kg. The source of the gain (i.e., fat, muscle, water) could not be determined from the data. However, at the 6-month testing session the majority of subjects claimed to be inactive and confessed to excessive eating to curb boredom; thus the increased weight may have been in the form of fat.

Table 24. Variables measured at rest and at peak GXT intensity at 1,2,3, and 6-months post-stroke

Variable	1-month	2-month	3-month	6-month	Overall p
weight *kg*	83.1±13.2 (64-119)	82.4±12.7 (64-115)	83.3±13.2 (64-113)	85.4±13.5* (64-116)	.01
BMI *kg/m²*	27.5±3.5 (20-37)	27.2±3.2 (20-35)	27.5±3.6 (20-35)	28.1±4.2* (20-38)	.01
HR$_{rest}$ *beats/min*	72.6±11.6 (60-105)	71.3±11.2 (56-96)	71.2±11.8 (53-96)	70.1±9.1 (57-90)	NS
$\dot{V}O_2$peak *ml/kg/min*	14.8±5.3 (9-32)	16.4±6.5 (9-31)	16.7±6.4 (9-33)	17.3±7.0† (10-32)	.003
$\dot{V}O_2$peak *% normative*	61.7±16.0 (37-90)	65.7±18.9 (36-100)	66.3±19.6 (36-107)	71.3±23.1† (32-124)	.008
$\dot{V}O_2$peak *l/min*	1.25±0.50 (0.6-2.7)	1.37±0.63 (0.6-2.8)	1.44±0.69 (0.6-2.9)	1.48±0.64† (0.7-2.7)	.006
$\dot{V}CO_2$peak *ml/kg/min*	14.5±6.0 (7-35)	16.6±7.3‡ (7-33)	16.7±7.6 (8-36)	17.4±8.2 (9-34)	.003
O_2 pulse$_{peak}$ *ml/beat*	10.1±3.3 (6-20)	10.7±4.0 (6-21)	11.5±4.5 (6-24)	11.5±3.8 (7-20)	NS
SBP$_{rest}$ *mm Hg*	144.2±18.1 (95-180)	149.6±14.9 (130-190)	147.7±14.3 (124-180)	145.7±16.1 (120-180)	NS
DBP$_{rest}$ *mm Hg*	83.7±10.6 (60-108)	85.7±8.3 (68-100)	86.7±8.6 (70-100)	86.6±8.5 (68-100)	NS
SBP$_{peak}$ *mm Hg*	182.7±33.0 (120-268)	184.0±23.3 (135-246)	182.8±19.6 (140-220)	183.5±21.3 (140-250)	NS
DBP$_{peak}$ *mm Hg*	96.7±14.4 (74-120)	97.2±12.0 (70-122)	98.0±12.2 (70-120)	97.5±10.9 (75-120)	NS
RPP$_{peak}$	227.4±67.6 (113-395)	236.3±73.4 (129-391)	228.1±65.3 (115-354)	233.4±61.5 (143-365)	NS
Exercise time *min*	9.3±4.6 (2-16)	12.1±5.5§ (2-23)	13.5±5.4 ‖¶ (4-24)	15.0±5.2 #* (6-26)	<.0001
Workload$_{peak}$ *kg-m/min*	360±394 (183;25-1550)	494±436‡ (342;44-1411)	553±491 ‖¶ (467;30-1610)	615±501 #* (424;98-1815)	<.0001

Data are means ± SD (range) or (median; range). NS: non-significant; $\dot{V}O_2$peak: peak O_2 consumption; $\dot{V}O_2$peak *% normative:* % of sex, age, height and weight-related normative values; $\dot{V}CO2$peak: peak CO_2 production; SBPpeak: peak systolic blood pressure; DBPpeak: peak diastolic blood pressure; RPPpeak: peak rate-pressure product. * 2- vs 6-mo GXTs, p<.0.01; † 1- vs 6-mo GXTs, p<0.01; ‡ 1- vs 2-mo GXTs, <0.01; § 1- vs 2-mo GXTs, p<0.001; ‖ 1- vs 3-mo GXTs, p<0.001; ¶ 2- vs 3-mo GXTs, p<0.01; # 1- vs 6-mo GXTs, p<.0.001.

5.3.5 Submaximal oxygen consumption and related variables across GXTs

Submaximal values of GXT variables were averaged over the last 30 seconds of each stage of the GXTs to identify significant differences in the values across tests and to determine at what stages these differences occurred. No significant differences in submaximal values for O_{2pulse}, SPB, and DBP were found at any stage. Statistically significant differences were noted in submaximal $\dot{V}O_2$, HR and RPP, the overall trend being a gradual reduction in submaximal values at each stage across tests (Figure 12). Submaximal $\dot{V}O_2$ values at stages two and three differed between the 1- and 6-month tests. Submaximal HR values were significantly lower at several stages between the 1-and 3-month GXTs as well as between the 1- and 6-month GXTs. These differences could not be attributed to changes in medication since such changes were minimal. Differences in submaximal RPP were significant at stages 3-5 between the 1- and 6 months tests and between the 1- and 3-month tests as well as at stages 4 and 5 between the 2- and 6-month tests.
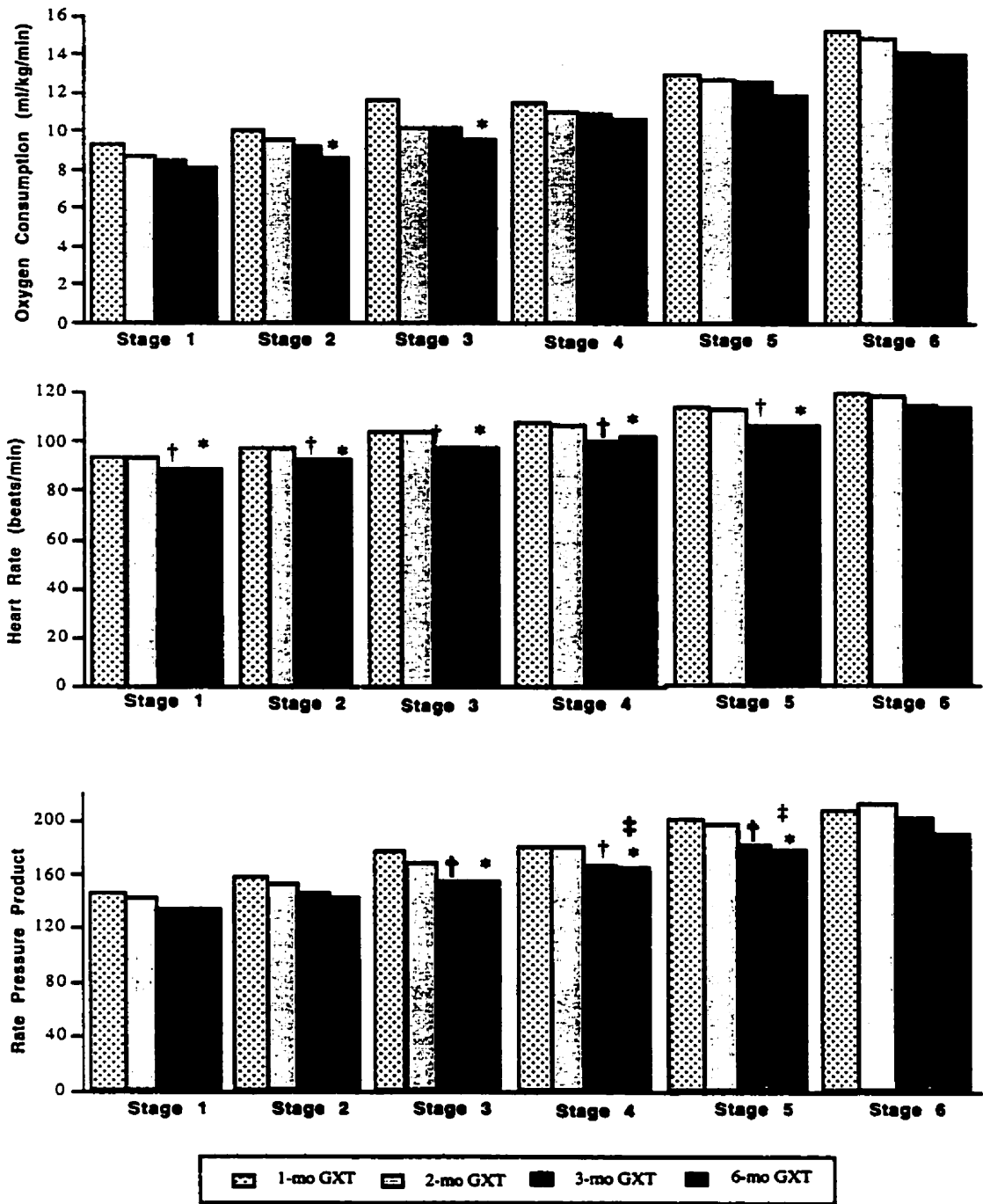
Figure 12. Comparison of physiologic variables at the end of the first 6 stages of the four GXTs * 1 vs 6-mo GXTs, p<0.01; † 1 vs 3-mo GXTs, <0.01; ‡ 2 vs 6-mo GXTs, p<0.001.

The regression lines for $\dot{V}O_2$ and HR against exercise time for each of the four GXTs illustrated in Figures 13 and 14 show the shift to the right with each subsequent GXT, with the exception of HR at the 6-month test.
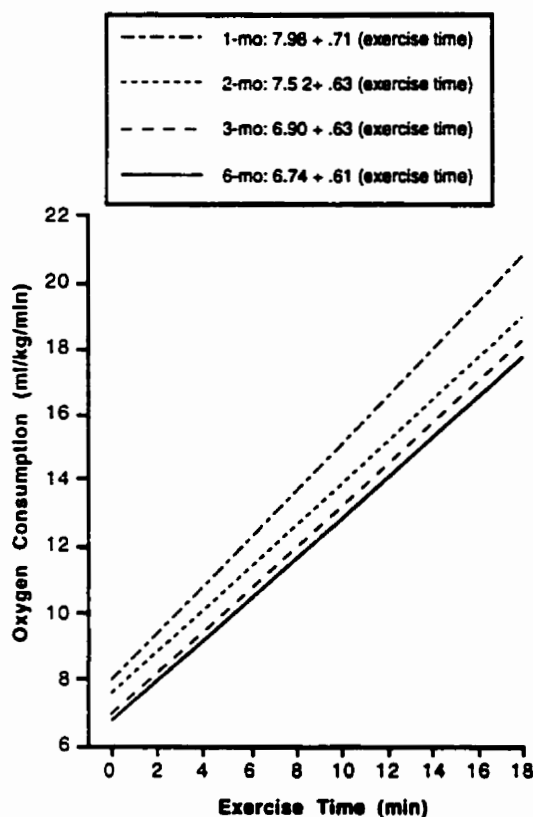
Figure 13. Least squares regression lines and equations for $\dot{V}O_2$ against exercise time for the four GXTs.
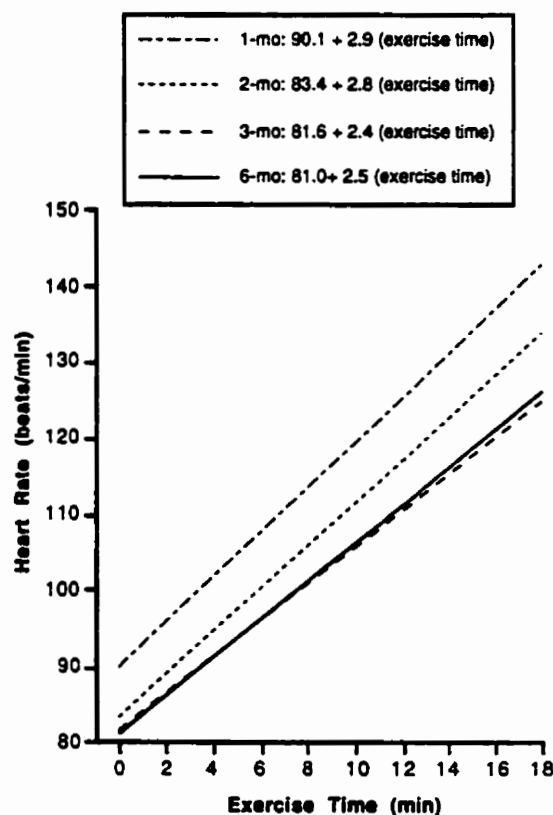
Figure 14. Least squares regression lines and equations for HR against exercise time for the four GXTs.

5.3.6 Peak respiratory variables across GXTs

No statistically significant differences were found in resting and peak values of the respiratory variables $\dot{V}E$, V_t, and RR across the GXTs (Table 26). The values for $\dot{V}E_{rest}$ and V_{trest} were somewhat higher, and RR_{rest} slightly lower, than those reported in a study of 19 patients with chronic hemiplegia (34) (10.1 l/min, 0.55 l, and 18.5 breaths/min

versus 8.2 l/min, 0.44 l, and 18.9 breaths/min, respectively). Overall mean $\dot{V}$Epeak and

Vtpeak values across tests were approximately 61 percent and 67 percent of the age and sex-adjusted normative values (35).

Table 25. Respiratory variables at rest and peak exercise intensity at the 1,2,3, and 6-month GXTs

Variable	1-month	2-month	3-month	6-month
$\dot{V}$E rest l/min	9.8±2.5 (4-15)	10.0±2.3 (6-15)	10.3±3.1 (6-18)	10.2±2.6 (5-16)
$\dot{V}$E peak l/min	44.1±16.7 (22-87)	48.3±21.6 (21-96)	46.4±21.3 (24-96)	48.9±23.6 (22-96)
Vtrest l	0.56±0.2 (0.3-1.6)	0.53±0.08 (0.4-0.8)	0.54±0.13 (0.3-0.8)	0.55±0.14 (0.3-0.8)
Vtpeak l	1.52±0.51 (0.7-3.0)	1.54±0.55 (0.7-3.1)	1.59±0.63 (0.6-3.0)	1.64±0.53 (0.9-2.8)
RRrest breaths/min	18.2±4.4 (10-28)	19.3±4.5 (12-29)	19.3±3.5 (13-25)	18.9±3.8 (12-25)
RRpeak breaths/min	28.4±5.1 (20-39)	30.9±6.3 (21-46)	29.4±6.6 (17-42)	29.1±7.2 (19-47)

Data are means ± SD (range). $\dot{V}$Erest: resting minute ventilation; $\dot{V}$Epeak: peak minute ventilation; Vtrest: resting tidal volume; Vtpeak: peak tidal volume; RRrest: resting respiration rate; RRpeak: peak respiration rate.

5.3.7 Submaximal respiratory variables across GXTs

The submaximal values for respiratory variables were averaged over the last 30 seconds of each stage of the GXTs in order to identify significant differences in the values across tests and to determine at what stages these differences occurred. Statistically significant differences were found in $\dot{V}$E values at most stages between the 1- and 3-month GXTs and between the 1- and 6-month GXTs (Fig. 15). Differences in Vt values were significant at the sixth stage of exercise between the 1-month and all subsequent GXTs, as well as at the second stage between the 1- and 3-month GXT. The only statistically significant difference in RR was found in the 1-month versus 3-month value at the fifth stage.
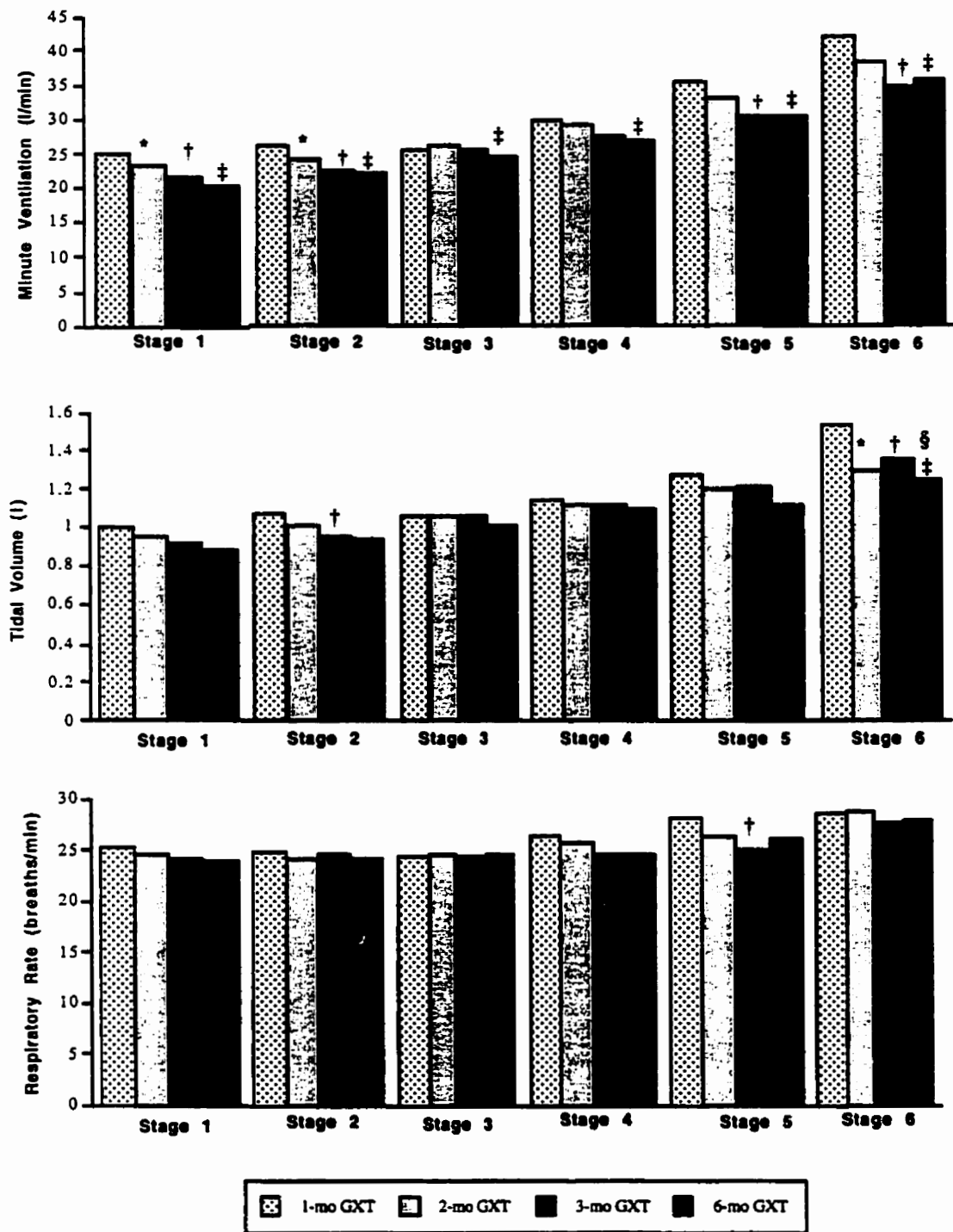
Figure 15. Respiratory variables at the end of the stages 1-6 of the four GXTs; * 1- vs 2-month GXTs, $p<0.01$; † 1- vs 3-month GXTs, $p<0.01$; ‡ 1- vs 6-month GXTs, $p<0.001$; § 3- vs 6-month GXTs, $p<0.001$.

5.3.8 Estimated energy expenditure during level walking across GXTs

Since speed of walking has a significant effect on energy expenditure (14, 36-38), the subjects were grouped according to the walking speed during GXT stage 1; six males were in the Faster Speed group (walking speed of .65 m/sec), the remaining 14 males and the five females in the Slower Speed group (walking speed of .35 m/sec) (Table 26). Although basal energy expenditure of females is lower than males (39), we found no statistically significant differences in EEwalk between males and females, consistent with a previous study (40). ANOVA results using pooled data for the male and female subjects in the Slower Speed group revealed significant decreases in mean $\dot{V}O_2$ and mean EEwalk (p=0.009), with *post-hoc* testing showing that significant differences occurred between the 1-month and 6-month EEwalk. The associated trend in reduced RER values was not statistically significant. The small number of subjects in the Faster Speed group precluded similar analysis.

Table 26. Energy expenditure during level walking at end of stage 1 of 1,2,3, and 6-month GXTs

Variable	Slower speed .35±.4 m/sec (n=19)				Faster speed .65±.2 m/sec (n=6)			
	1-mo	2-mo	3-mo	6-mo	1-mo	2-mo	3-mo	6-mo
EEwalk kcal/min	3.8±0.3	3.6±0.3	3.5±.03	3.2±0.02	3.1±0.4	2.9±0.3	2.8±0.2	2.5±0.2
$\dot{V}O_2$ l/min	.76±.13	.74±.11	.71±.08	.66±.05*	.63±.07	.59±.05	.58±.05	.52±.05
RER	.91±.07	.89±.07	.87+.06	.86±.06	.88±.06	.87+.10	.85+.09	.83+.08

Data are means ± SD, mo: month; EEwalk: energy expenditure during walking; $\dot{V}O_2$: oxygen consumption (adjusted for 15% BWS); RER: respiratory exchange ratio. *1- vs 6-mo GXTs, p<0.01.

While a clear trend of reduced EEwalk was apparent across GXTs, the EEwalk of the subjects remained significantly above the ranges reported for healthy individuals walking at comparable speeds (41) (Figure 16). Across the 1-, 2-, 3-, and 6-month GXTs, the EEwalk values of the Slower Speed subjects were, on average, about 253, 247, 240, and 220 percent, respectively, of the corresponding mean EEwalk of healthy individuals, while the

EEwalk values of the Faster Speed subjects were about 258, 241, 233, and 208 percent of the corresponding mean EEwalk of healthy individuals.
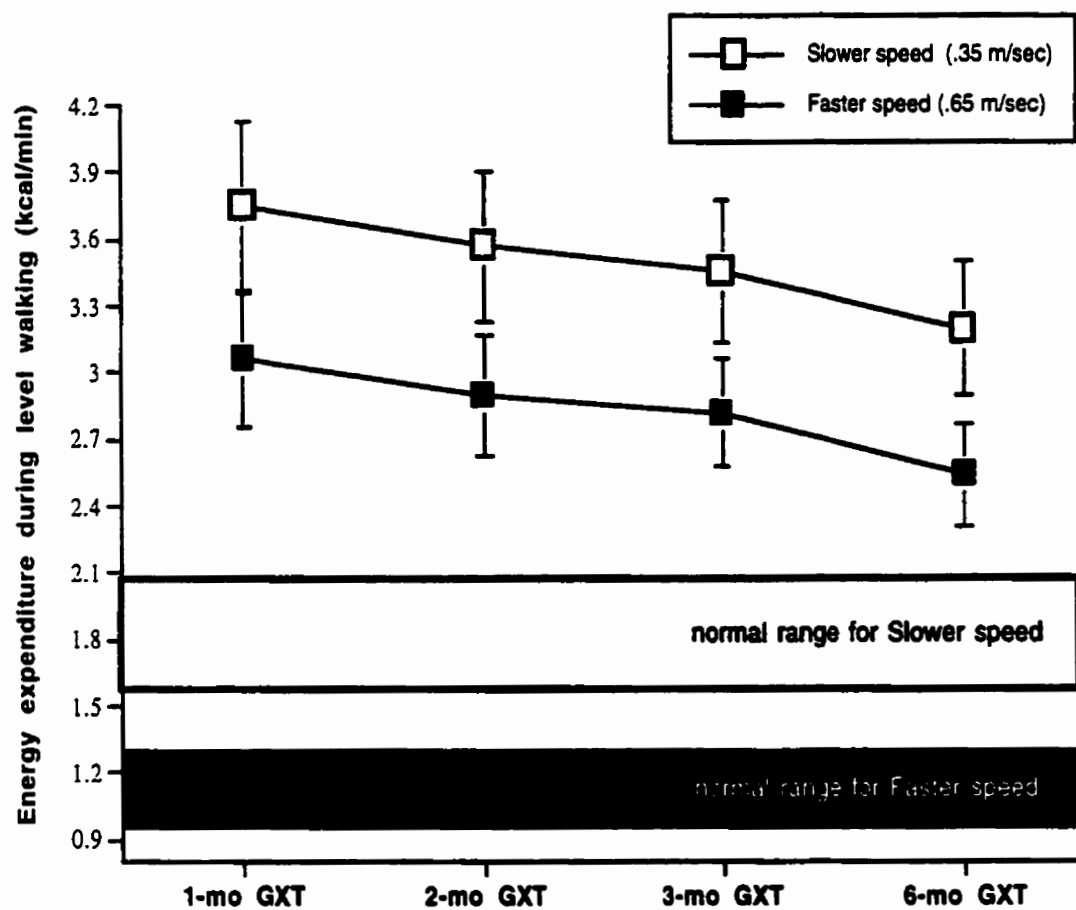
Figure 16. Energy expenditure during level walking for subgroups of Slower Speed (n=19) and Faster Speed (n=6) across GXTs with normative ranges provided for comparison. Error bars indicate 1 SD.

5.3.9   Impairment and disability status at 1,2,3, and 6 months post-stroke

All impairment and disability measures with the exception of grip strength of the more affected hand - expressed either in absolute units or as a percentage of the grip of the less involved hand - showed statistically significant improvement across tests (Figure 17). While there was a trend of improving absolute and relative grip strength over time, the extent of inter-subject variability precluded the potential for statistical significance.
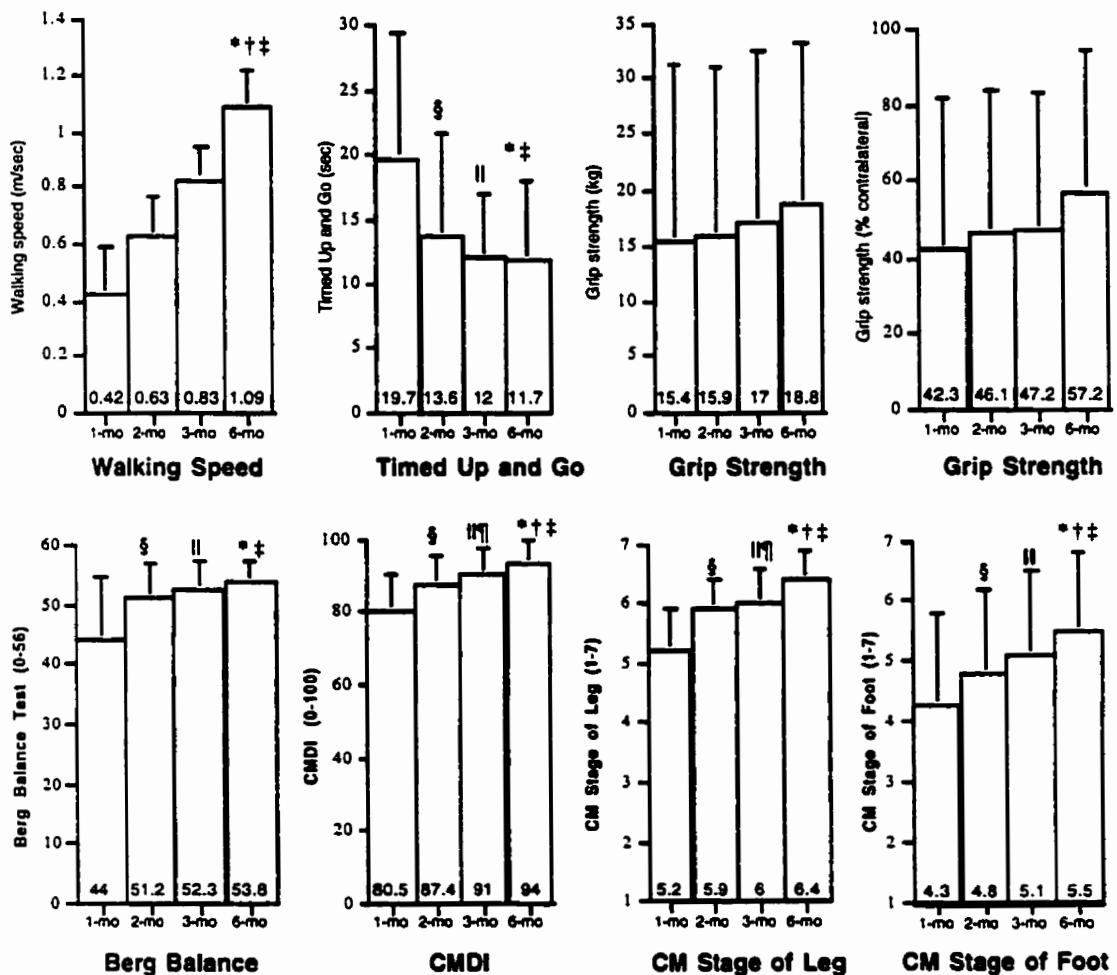
Figure 17. Impairment and disability measures across the four GXTs.   Value labels are at base of columns. Error bars indicate 1 SD. * 1- vs 6-month GXTs, p<0.001; † 2- vs 6-month GXTs, p<0.001; ‡ 3- vs 6-month GXTs, p<0.001; § 1- vs 2-month GXTs, p<0.001; || 1- vs 3-month GXTs, p,0.001; ¶ 2- vs 3-month GXTs, p<0.001.

5.3.10 Relationships among initial and percent change in $\dot{V}O_{2peak}$ and function variables

Correlation analysis of relative $\dot{V}O_{2peak}$ and functional measures at the 1-month GXT revealed significant relationships (Table 27). Relative $\dot{V}O_{2peak}$ was significantly correlated with walking speed, Berg, CMDI, and CM-leg, and also with PAQ (r = .430; p = 0.003). PAQ was not significantly correlated with any of the function variables but most of the function variables were moderately to highly correlated with each other.

Table 27. Correlation analysis of $\dot{V}O_{2peak}$ and function variables at 1-month GXT

	Speed	TUG	Berg	CMDI	CM-leg	CM-ft	Grip
$\dot{V}O_{2peak}$	.453*	-.180	.332*	.514*	.433*	.181	.278
Speed	1	-.613†	.477†	.683†	.600†	.562†	.637†
TUG		1	-657†	-.658†	-.470*	-.530‡	-.590†
Berg			1	.802†	.586†	.343*	.306*
CMDI				1	.723†	.495‡	.431*
CM-leg					1	.709†	.479‡
CM-ft						1	.671†

$\dot{V}O_{2peak}$: peak oxygen consumption (ml/kg/min); PAQ: Physical Activity Questionnaire; TUG: Timed Up and Go; CMDI: Chedoke-McMaster Disability Inventory; CM-leg: Chedoke-McMaster Stage of Recovery of the leg; CM-ft: Chedoke-McMaster Stage of Recovery of the foot. * p<.0.01; † p<0.0001; ‡ p<.0.001.

Percent change in $\dot{V}O_{2peak}$ was highly correlated with both %Δ speed (Table 28) and was also correlated with PAQ (r = .436; p = .04) but not with any of the %Δ scores of the function variables. Significant relationships were found between %Δ CMDI and %Δ CM-ft, Berg, speed and TUG. The %Δ Berg and %Δ CM-leg, %Δ Berg and %Δ TUG, and %Δ grip and %Δ CM-foot were also significantly correlated.

Table 28. Correlation analysis of $\% \Delta$ $\dot{V}O_{2peak}$ and $\% \Delta$ in function variables

	%ΔSpeed	%ΔTUG	%ΔBerg	%ΔCMDI	%ΔCM-leg	%ΔCM-ft	%ΔGrip
%Δ $\dot{V}O_{2peak}$	.758*	-.180	.140	.067	.049	.152	.054
%ΔSpeed	1	-.197	.196	.337†	.030	.060	.014
%ΔTUG		1	-.430‡	-.422‡	-.080	-.154	-.136
%ΔBerg			1	.244†	.252†	.012	.086
%ΔCMDI				1	.154	.265†	.158
%ΔCM-leg					1	.509*	.077
%ΔCM-ft						1	.276†

$\% \Delta$: percent change; $\dot{V}O_{2peak}$: peak oxygen consumption (ml/kg/min); TUG: Timed Up and Go; CMDI: Chedoke-McMaster Disability Inventory; CM-leg: Chedoke-McMaster Stage of Recovery of the leg; CM-ft: Chedoke-McMaster Stage of Recovery of the foot, * $p<0.001$; † $p<0.05$; ‡ $p<0.01$.

In the multiple regression, walking speed was the only independent variable identified that significantly predicted $\% \Delta$ $\dot{V}O_{2peak}$ between the 1- and 6-month GXT, explaining 53 percent of the variability in $\% \Delta$ $\dot{V}O_{2peak}$ across tests (Table 29). Plots of residuals suggested that the assumptions of linearity and normality were not violated. PAQ was not found to be significant predictor of $\% \Delta$ $\dot{V}O_{2peak}$ on multivariate analysis.

Table 29. Multivariate prediction of percent change in peak oxygen consumption

Significant variables	Regression coefficient	t-value	R^2	R^2 adjusted	p-value
%Δspeed	.725	4.471	.555	.528	.0004

$\% \Delta$: percentage change.

5.4 Discussion

5.4.1 Comparability of serial GXTs

For meaningful interpretation of the results of serial symptom-limited GXTs, it is critical to ensure comparable testing conditions. We used a consistent testing protocol across GXTs, despite the inevitability of improved physical function during recovery from stroke resulting in increasingly longer GXTs. Whereas only half of the 1-month GXTs were within the BWS-adjusted optimal range of 9-19.5 minutes (see Chapter 2), 68 percent of the 6-month tests were within and 22 percent exceeded this range. Values for $\dot{V}O_2$ max attained in GXTs exceeding the optimal duration may underestimate actual $\dot{V}O_2$ max values, possibly because of elevated body temperature, increased dehydration, subject discomfort or ventilatory fatigue (42). Nevertheless, consistency in attainment of $\dot{V}O_2$ max criteria (see Table 22) and in values of HR_{peak}, percentage of $HR_{max-pred}$, RER_{peak}, and RPE_{peak} across the GXTs (see Table 23) indicates that the GXTs were comparable in terms of level of exertion.

5.4.2 Changes in exercise capacity

The principal finding of this study was a significant change in $\dot{V}O_{2peak}$ from a mean of 14.8 ± 5.3 ml/kg/min at one month post-stroke to 17.3 ± 7.0 ml/kg/min at six months. Of the overall 16.9 percent change, 10.8 percent was realized between the 1- and 2-month GXTs. Although not found to be statistically significant, this magnitude of change is clinically significant. Among the healthy population the accepted variability in $\dot{V}O_2$ max on repeat testing is 2-4 percent (43). These findings of statistically and clinically significant changes did not support our first hypothesis. We had anticipated that gains in exercise capacity would be slight, an expectation that was initially based on clinical observations of contemporary stroke rehabilitation practices and later reinforced by finding a low aerobic

component to the rehabilitation program in which the present patient group participated (see Chapter 4).

There have been no other studies, to our knowledge, that have investigated longitudinal changes in exercise capacity over the course of stroke rehabilitation; hence, our ability to relate the findings of the present study to previous work is limited. Bachynski-Cole and colleagues (2) documented in eight males who were, on average, 52 years of age and 3.8 months post-stroke, a mean $\dot{V}O_{2peak}$ of 16.1 ml/kg/min, which is consistent with the mean $\dot{V}O_{2peak}$ of 16.7$\pm$6.4 ml/kg/min at the 3-month GXT in the present study. By way of comparison, a recent study reported a mean $\dot{V}O_{2max}$ of 33.2 ml/kg/min in a group of 160 healthy males over the age of 55 years (44).

Four previous studies involved longitudinal measurements of $\dot{V}O_{2peak}$ in patients in the chronic post-stroke period (Table 30). In the most recent study, Fujitani and colleagues (8) reported a mean improvement in $\dot{V}O_{2peak}$ of 19 percent in 30 ambulatory males with chronic hemiplegia after a post-rehabilitation period of 9.4 months that involved 'no special supervised training'. The mean increase in $\dot{V}O_{2peak}$ of 13 percent reported in the study by Potempa et al. (1) is comparable to the 12.8 percent mean gain made by 23 males with CAD following a 12-week walk-jog program (45). Similarly, a 15 percent mean improvement was recorded in a group of 20 patients with chronic atrial fibrillation after participation in a walking program (46). Two other intervention studies investigating changes in $\dot{V}O_{2peak}$ in patients with disability did not provide separate data for those patients with stroke, thus limiting comparability (7, 47). Santiago et al. (7) reported an overall mean change in $\dot{V}O_{2peak}$ was 27 percent. Fletcher and colleagues (47) found no change in mean $\dot{V}O_{2peak}$ of 16 patients with CAD and co-existing long-term stroke or amputation following six months of a home-based conditioning program. Discrepancies in the effects of training on $\dot{V}O_{2peak}$ in these studies could be attributed to differences in

subjects (e.g., age, severity of stroke, chronicity), mode and intensity of training, compliance with the exercise regime, and GXT testing mode and protocol. For example, the substantially lower values of $\dot{V}O_{2peak}$ reported in the study by Fletcher et al. (47) could be explained by the mode of testing - $\dot{V}O_{2\ max}$ values attained with arm ergometry have been demonstrated to be about 70 percent of the values achieved with treadmill testing (48). In contrast, the high values of $\dot{V}O_{2peak}$ reported by Santiago et al. (7) may be due to their use of an unconventional, discontinuous testing protocol that is likely to yield high $\dot{V}O_{2peak}$ values.

Table 30. Documented findings of longitudinal changes in peak oxygen consumption of individuals post-stroke

Variable	Present study	Fujitani et al. (8)	Potempa et al. (1)	Santiago et al. (7)	Fletcher et al. (47)
Subjects	25 stroke 22M:7F	30 stroke 30M	42 stroke 8M:11F(E) 15M:8F(C)	21 - 9 with stroke 2M:6F(E) 5M:8F(C)	35 M with CAD +/- stroke/amputation 16(E):19(C)
Age yr	64±14	54	56±12	40	62±8
Time post-stroke	26±9 days	mean of 10 months	chronic	not reported	chronic
Training mode	conventional rehabilitation	home exercise	cycle ergometer	aerobic exercise	arm ergometer
GXT mode	treadmill	cycle ergometer	cycle ergometer	arm/leg ergometer	arm ergometer
Pre-post test interval	5 months	9.4 months	10 weeks	12 weeks	6 months
Pre-test $\dot{V}O_{2peak}$	14.8±5.3	17.7±4.2	16.6±4.4(E) 15.1±4.8(C)	15.6±6.2(E)* 19.0±6.5(C)*	12±3(E)* 11±3(C)*
Post-test $\dot{V}O_{2peak}$	17.7±4.2	21.1±4.7	18.8±4.8(E) 15.2±4.3(C)	19.2±7.4E)* 15.7±5.7(C)*	12±4(E)* 12±3(C)*
$\Delta \dot{V}O_{2peak}$	+17%	+19%	+13%(E) +1%(C)	+23%(E) -17%(C)	+1%(E) +9%(C)

Data are means ± SD. M: male; F: female; E: experimental; C: control. *Combined data; separate data for subgroup with stroke were not provided.

In the present study, the extent of change in relative $\dot{V}O_{2peak}$ values from the 1-month to the 6-month test may have been confounded by two factors - aging and body weight. Since aging reduces $\dot{V}O_{2\,max}$ at an annual rate of as least .25 ml/kg/min, (49) (50) (44) the five-month interval between GXTs would have a subtle negative effect. More importantly, if the significant weight gain noted at the 6-month GXT were in the form of fat (which is likely), this gain would result in an underestimate of the underlying improvement in exercise capacity as reflected in $\dot{V}O_{2peak}$ changes standardized to weight. Adjusting for these potential factors, the mean percent improvement would increase from 17 percent to approximately 21 percent. Subjects who had greater disability - as determined by BI - had lower $\dot{V}O_{2peak}$ values but larger improvements in $\dot{V}O_{2peak}$. This finding is consistent with an earlier observation of those individuals with CAD who had low basal levels of exercise capacity experienced the greatest gains in cardiovascular conditioning (51).

The subjects in our study demonstrated improved aerobic capacity despite the finding that the intensity of their stroke rehabilitation program was estimated to be low (see Chapter 4). It is possible that we overestimated the minimal intensity required for this population to achieve cardiorespiratory conditioning effects. Whether the improvements in exercise capacity resulted from central or peripheral adaptations to exercise or both cannot be ascertained with the methods used in our study. It is likely that some of the mechanisms underlying the improvements are similar to those involved in training-induced adaptations of patients with CAD. This assertion is made because of the high incidence of CAD among patients with stroke (60-70 percent) as well as the comparable magnitude of improvement following training among patients post-stroke with or without CAD (as seen in the present study) or among patients with CAD and with or without stroke (45). Fergueson et al. (52) demonstrated significant increases in exercise capacity in 26 patients with CAD and exertional angina pectoris after six months of physical training, with

corresponding evidence of both skeletal muscle adaptations (e.g., increased succinate dehydrogenase activity and muscle hypertrophy) and central adaptations (e.g., reduced myocardial $\dot{V}O_2$ requirements, increased maximal coronary blood flow).

The possibility that the subjects underwent 'spontaneous' improvement in exercise capacity over the course of the study also warrants consideration. Savin et al (53) documented a 23 percent increase in mean $\dot{V}O_2$ max over an eight week period in patients with MI who underwent no formal exercise training. In the previously mentioned study by Fujitani and colleagues (8), significant improvements were noted in $\dot{V}O_2$peak in community-dwelling patients post-stroke who were not participating in supervised exercise. Bjuro and colleagues (54) showed that while patients with chronic hemiplegia performed household tasks such as vacuuming and bed making, their $\dot{V}O_2$ levels during these activities were 75-88 percent of $\dot{V}O_2$peak, almost twice that of the healthy control subjects. It appears that the aerobic requirements of many daily activities may exceed the threshold intensity for cardiorespiratory conditioning among individuals with disability, which may explain the phenomenon of 'spontaneous' improvement. In the present study the mean duration of rehabilitation was 14 weeks, leaving an average of 10 weeks of unsupervised activity prior to the 6-month GXT. We did not systematically monitor the daily activities of the subjects after discharge from rehabilitation but did record significant changes in physical activity related by the subjects at the time of the GXTs. Apart from the five who returned to work, most subjects appeared to adopt a relatively inactive lifestyle at home but there were two notable exceptions. Dramatic improvements were seen in $\dot{V}O_2$peak (42 percent and 46 percent) of the two patients who began treadmill walking after discharge (see Figure 11). This anecdotal evidence suggests that the potential to improve exercise capacity is not be fully realized using current rehabilitation strategies.

From the results of the present and previous longitudinal studies, it is apparent that significant aerobic impairment persists even when improvements in $\dot{V}O_2$peak are found over

the period of investigation. Patients in the chronic post-stroke period are left with exercise capacities between 55-75 percent of the value expected for healthy individuals of similar age, sex, and habitual activity status. $\dot{V}O_2$ max values of less than 84 percent of normative values are interpreted as being pathologic (55). The minimum exercise capacity of 15 ml/kg/min considered essential to meet the physiological demands of independent living (56) was met by the majority of subjects at the 2-month GXT in the present study. However, the mean $\dot{V}O_{2peak}$ at 6 months post-stroke (17.3 ml/kg/min) was of a magnitude that would designate the majority of subjects, at least those subjects with co-existing CAD, to be within the "high mortality group" (57). It is not surprising that in a study assessing quality of life of 224 subjects at six months post-stroke, poor energy level outranked decreased mobility, pain, emotional reactions, sleep disturbances, and social isolation as the area of greatest concern (58). This result was consistent with the findings of other qualitative studies (59) (60).

5.4.3 Changes in other indices of cardiovascular adaptation

The significant decreases in submaximal HR at several stages of the GXTs suggest a cardiovascular conditioning response. Similar findings have been documented in training studies involving patients in the chronic post-stroke period (1, 5). Reduction in submaximal HR induced by training is confined, in part, to exercise with trained muscles (61). The mechanisms underlying this bradycardic response cannot be identified from the data collected but may include increased vagal activity, reduced sympathetic-adrenergic drive, or a training-induced reduction in resting HR (HR$_{rest}$) (62) or, possibly, increased total blood volume (63).

Another indicator of cardiovascular adaptation was the reduction in submaximal RPP. Submaximal SBP values remained stable at each stage across GXTs; thus, the statistically significant decreases in submaximal RPP could be attributed more to reduction in submaximal HR values than to changes in SBP. Since RPP has been shown to be

highly correlated with measured myocardial $\dot{V}O_2$ (r=0.88) (64), it is a useful indicator of cardiac efficiency. Potempa et al (1) documented reduced submaximal SBP and RPP values following 10 weeks of conditioning. Franklin (45) demonstrated that even low to moderate exercise training intensities can reduce submaximal RPP of patients with CAD.

That HR$_{rest}$ did not change significantly over the course of the present study is not necessarily an indication of a lack of conditioning. In a recent study on the effects of 20 weeks of endurance training in 47 healthy subjects, $\dot{V}O_2$ max improved about 16 percent while HR$_{rest}$ decreased about 4.5 percent, suggesting to the authors that training had a minimal effect on either, or both, intrinsic HR and autonomic control of HR$_{rest}$ (63). In most of the training studies reviewed that involved patients with stroke, significant reductions in HR$_{rest}$ were not found (1, 4, 6). In contrast, Fletcher et al (47) reported a change in HR$_{rest}$ from 69$\pm$15 at baseline to 65$\pm$12 after a 6-month conditioning program. A lack of change in HR$_{rest}$ provides support for peripheral adaptations to exercise, which, in the case of the patients in the present study, is logical given the extent of neuromuscular recovery over the period of the study. In addition, inferences may be drawn by examining O$_2$pulse data. Quantitatively, O$_2$pulse is the product of SV and AVO$_2$difference, and therefore reflects the amount of O$_2$ extracted by the tissues from the blood ejected by each heart beat (55). Since improved peak O$_2$pulse and O$_2$pulse values at given submaximal workloads are indicators of cardiovascular adapatations to exercise (65), the lack of change in these values over the course of the study despite significant longitudinal reductions in submaximal $\dot{V}O_2$ and HR values at corresponding workloads, argues in favor of peripheral mechanisms (e.g., improved muscular efficiency, as discussed in Section 5.4.7).

Mean values of SBP$_{rest}$, DBP$_{rest}$, SBP$_{peak}$ and DBP$_{peak}$ remained stable over the period of the study. Medication changes over the same period were inconsequential. That exercise training as a sole intervention has no demonstrable effects in lowering blood

pressure levels (66) was supported by the findings of the only one other longitudinal post-stroke study that documented peak blood pressure variables (47):

5.4.4 Changes in respiratory variables

Resting and peak values of $\dot{V}E$, Vt, and RR remained relatively stable over the course of the study (see Table 25). However, the pattern of change across the GXTs in reasons for exercise termination suggests that cardiorespiratory intolerance and hemiparetic leg fatigue were important factors limiting exercise capacity in the early post-stroke period and that generalized fatigue became a more dominant factor as the post-stroke interval increased (see Table 21). Supportive evidence of a trend of decreasing respiratory stress was provided by changes in submaximal respiratory variables across GXTs. Significant decreases in submaximal $\dot{V}E$ were observed in the six stages analyzed, and were related more to reductions in submaximal Vt than to changes in submaximal RR values, particularly at the sixth stage (see Figure 15).

The mean $\dot{V}E_{peak}$ and Vt_{peak} values at the 6-month GXT remained abnormally low compared with age and sex-adjusted normative values (35). About 65 percent of the subjects had a history of smoking, and within this subgroup, each subject had, on average, a 38.4 pack-year smoking record. Also, the low Vt_{peak} values could be attributed, in part, to an iatrogenic effect. In a previous study we reported that the use of 15% BWS in the GXT protocol resulted in a small, but statistically significant, decrease in Vt_{peak} in healthy subjects (see Chapter 2). In a study of the respiratory status of 19 patients with chronic hemiplegia, Haas et al (34) found that the mean $\dot{V}E$ while walking on level ground at .25 m/sec was 1.9 times higher than in age- and sex-matched control subjects. These investigators suggested that the fatigability experienced by these patients may be partially attributed to respiratory insufficiency as indicated by decreased lung volumes, impaired mechanical performance of the thorax, and low pulmonary diffusing capacity. Annoni and

colleagues (67) suggested that the poor respiratory tolerance to effort post-stroke may be secondary to restricted thoracic excursion resulting from weakness, hypotonicity, and incoordination of the trunk musculature. This suggestion is supported by an earlier finding, based on a sample of 55 hemiplegic subjects, that the extent of ventilatory dysfunction post-stroke is related to the degree of motor impairment (68). Reduced pulmonary function was also documented in a study of 12 patients, aged 38 to 75, with a mean post-stroke interval of 11 days (69), and in a study of patients with chronic hemiplegia (70).

5.4.5   Changes in neuromuscular status and function

We encountered difficulty relating our findings of change in functional status post-stroke to those of previous studies, in part, because most studies measured function at specific events such as admission and discharge, rather than at set post-stroke intervals (19). In addition, the heterogeneity of subjects and the variety of measures used to document functional status post-stroke confound direct comparisons. Thus, the discussion is limited to comparing trends in the data. The trend of progressive and significant improvements in most of the impairment and disability measures over a 6-month post-stroke interval (see Figure 17) contradicts the findings of a plateau in functional recovery within 12.5 weeks post-stroke in 95 percent of 1,197 patients (71). In that study the BI was used as the main measure of function, and while this measure is a useful indicator of global function, it lacks sensitivity to change specifically in the domain of physical mobility. Duncan and colleagues (72) emphasized the distinction between rate of recovery of impairment-level attributes (e.g., motor control, muscle strength, muscle tone, range of motion) and rate of recovery of disability-level attributes (e.g., bed mobility, transfers, gait, self-care).

Our observation of a reduction in hemiparetic leg fatigue as a factor limiting exercise capacity across GXTs was not unexpected in view of the fact that motor function

of the lower extremity recovers most rapidly in the first three months post-stroke (20, 73). The progressive decrease in motor impairment of the paretic leg and foot noted over the course of the study (see Figure 17) concurs with previous reports of stepwise recovery in motor function (74). Magnitudes of change in the CM-leg and CM-foot, 23 percent and 29 percent, respectively, were similar to the 25 percent and 33 percent, respectively, increases reported in another Canadian study involving 113 patients over a mean post-stroke interval of 16.6 weeks (75). Our finding of no significant change in grip strength, a valid measure of upper extremity impairment (76), between one and six months post-stroke, provides indirect support for the plateau in upper extremity function observed by three weeks post-stroke (77). Similarly, Duncan and colleagues (72) found that in a cohort of 95 patients post-stroke, the most rapid improvement in motor impairment of the upper and lower extremities occurred in the first 30 days.

Since impairment variables have been found to be poor correlates of the extent of recovery (75), attention should be paid to disability-level attributes. The high correlation coefficients found between overground walking speed and other functional measures at the 1-month assessment (see Table 27) reinforce the previously reported strong relationship between speed and functional status (78). At the time of the first GXT the preferred speed of overground walking and 15% BWS-treadmill walking were similar (mean, .42 m/sec), contrary to a previous study reporting that speeds when treadmill walking with 15 percent BWS were an average of 18 percent lower than when walking overground (79). We found significant improvements in overground walking speed (mean increase of 159 percent) over the course of our study. Walking speed doubled between the 1- and 3-month assessments, in contrast to a mean increase of 71 percent reported by Goldie and et al. (80) after two months of stroke rehabilitation. The increase in speed of overground walking from a mean of .42 m/sec at one month post-stroke to a mean of 1.09 m/sec at six months to reflects a functional change from *most limited community ambulation* to *community ambulation* (81). Yet, the mean speed of our sample at six months was only about 75

percent of that of a healthy individual in the same age range (82, 83). Shiavi et al. (84) compared the gait patterns of patients at one month and one year post-stroke and documented improved speed and symmetry on post-testing. Those patients who initially walked at very slow speed (less than .28 m/sec) retained abnormal EMG patterns bilaterally at one year post-stroke. Findings of a high correlation between walking speed and CM-leg and between walking speed and CM-Foot at one-month post-stroke in our study (see Table 27) are in keeping with the results reported by Morita et al. (85) for patients in the chronic post-stroke period.

The steady improvement in functional mobility over the course of our study, as evidenced by significant changes in the CMDI, is in keeping with a previous observation of continuing progress toward independent function (e.g., sitting, walking, stair climbing) at four to six months post-stroke (86). While we documented a 28 percent change in Berg score between one and six months post-stroke, Juneja et al (87) reported a 86 percent increase within the first month, a discrepancy intimating that substantial improvement occurs in balance control in the acute phase of recovery.

5.4.6 Relationship between changes in exercise capacity and changes in functional status

Prior to the study we had anticipated significant improvements in functional measures without concomitant gains in aerobic capacity. The research hypothesis of a lack of correlation between gains in aerobic capacity and functional measures was not supported by the data although gains in most functional measures were of greater magnitude than that of exercise capacity over the course of rehabilitation. Significant correlations were found between baseline $\dot{V}O_{2peak}$ and functional measures (i.e., speed, Berg, CMDI, CM-leg) at the 1-month GXT (see Table 27) whereas similar correlations for $\%\Delta$ scores, reflecting change over time relative to baseline values, were generally low (Table 28); hence the relationship between improvements in function and in exercise capacity was weak.

Percent change in walking speed was the one functional parameter that was strongly correlated with $\%\Delta \dot{V}O_{2peak}$ (see Table 28) and that also explained a significant amount of the variability in the $\%\Delta \dot{V}O_{2peak}$ between the 1- and 6-month GXTs (see Table 29). Considering that $\dot{V}O_{2max}$ values and training-induced changes in $\dot{V}O_{2max}$ are task-specific, that is, specific to the exercise modality employed (88), or the task being trained (89, 90), finding a strong relationship between changes in these parameters was not surprising. We observed that walking was the most common activity performed in the upright position during stroke rehabilitation (see Chapter 4). Age was not a significant predictor of $\%\Delta$ $\dot{V}O_{2peak}$, in keeping with the finding that exercise trainability of older patients with CAD is comparable to that of younger patients (66). Fujitani and colleagues (8) suggested that the variability in improvements in aerobic capacity among their subjects may have been due to differences in prior history of physical activity. Although PAQ was a significant bicorrelate of $\%\Delta \dot{V}O_{2peak}$ in the present study, it was not found to be a significant predictor of $\%\Delta$ $\dot{V}O_{2peak}$ on multivariate analysis. Also, PAQ values were not significantly correlated with any of the baseline and $\%\Delta$ values of the function variables, contradicting a preliminary report of a high correlation between pre-stroke physical function and post-stroke functional outcomes (91).

5.4.7 Changes in energy expenditure during walking

The high EE_{walk} values documented in this study, in excess of twice age- and speed-related normative values (see Table 27) are consistent with the literature. In a study of patients who were six weeks post-stroke, Hash et al. (12) found that the mean EE_{walk} at a fixed velocity (.35 m/sec) was about three times higher than control values. Dasco et al. (15) determined that the mean EE_{walk} early post-stroke at a speed of 0.45 m/sec was about twice normative values whereas Corcoran et al. (15) documented that the EE_{walk} of younger

patients with chronic hemiplegia was 51-67 percent higher than control subjects walking at the same slow speed.

Discrepancies in the EEwalk post-stroke relative to normative data may be explained by differences in subjects' age (92), severity of stroke, post-stroke time interval, emotional status (93), use of orthoses (15), walking surface, method of EEwalk determination, and walking speed. The lower EEwalk values for the Faster Speed subjects than the Slower Speed subjects in our study can be explained by the profound effect of walking speed on EEwalk. Potential-kinetic energy exchange is maximized and the muscular work is minimized at speeds of 1.2-1.4 m/sec (14, 36-38). The slope of the U-shaped energy-speed curve is greater for patients with stroke than for control subjects; consequently, patients post-stroke pay a higher price in $\dot{V}O_2$ for a given increment in speed (15). The reported optimal walking speed (1.25 m/sec) for patients post-stroke in terms of energy expenditure (94) was only attained by three patients in our study by six months post-stroke.

The extent to which the protocol used to estimate EEwalk in the present study influenced the EEwalk results is difficult to ascertain. Pearce and colleagues (36) found that the energy cost of treadmill walking was about four percent less than floor walking at fixed speeds. The use of self-selected speeds, as used in our protocol, has been reported to be most efficient in terms of energy expenditure (95). Our qualitative observation that the gait pattern of most patients appeared more symmetrical and coordinated while walking on the treadmill with 15% BWS than while walking overground is supported by studies investigating the kinematic and kinetic effects of treadmill walking with BWS (79, 96, 97). Our subjects claimed to feel secure walking with BWS, thereby offsetting the concern expressed by Corcoran and Brengelman (14) that fear of treadmill walking post-stroke might increase energy costs. Thus, the use of BWS-facilitated walking may have reduced EEwalk in our study. Our use of a 150-second transition interval to reach steady-state conditions in this population is another potentially confounding factor. The time to reach

steady-state is inversely related to exercise intensity (31) (which was low in the first stage of our GXT protocol) and directly related to the level of fitness (32) (which was poor for the majority of our subjects).

The mechanisms underlying the elevated EEwalk of patients post-stroke relative to healthy individuals walking at the same speed require more investigation. Reductions in the oxidative capacity of paretic musculature could explain part of the muscular inefficiency. However, Francescato and associates (98) found that although the EEwalk of patients with chronic hemiplegia was higher than that of healthy subjects, the RER values were the same for both groups and were unaffected by speed of walking. The interpretation of these findings was that mechanical impairments are more likely than metabolic impairments to contribute to the higher energy costs of hemiparetic gait. Similarly, in the present study changes in EEwalk across GXTs were not accompanied by significant changes in RER values. Significant reductions have been noted in activity of the major muscle groups of the paretic lower extremity during walking, resulting in inefficient biomechanics (99) (100), including compensatory changes in muscle activity of the contralateral limb (e.g., prolonged muscle activation and increased coactivation) (84). In addition, decreased excursion of lower extremity joints (e.g., secondary to plantarflexor contracture) may contribute to higher energy costs of walking post-stroke.

The significant change found over the course of the study in EEwalk at a speed of .35 m/sec supports our third hypothesis. The mean reduction of 16 percent (see Figure 16) was lower than previous reports of a 23 percent decrease in EEwalk at a speed of 0.35 m/sec (12) and a 30 percent decrease in EEwalk at a speed of 0.45 m/sec (13) by the end of rehabilitation. The magnitude of these changes appears to be clinically significant; Sykes et al. (101) reported a normal biological variability in EEwalk of 5.8 percent among able-bodied subjects. In the only investigation specifically designed to study the effects of training on EEwalk post-stroke, Macko and associates (5) presented preliminary evidence of training-induced reductions in EEwalk in the order of 21 percent over a 6-month period.

These researchers determined EE$_{walk}$ after six minutes of walking at a constant speed of .44 m/sec, thus ensuring steady-state conditions. Despite using a three-minute interval in our study, the baseline EE$_{walk}$ values and the overall magnitude of changes in EE$_{walk}$ values from the 1- to 6-month GXT are consistent with the data presented by Macko et al. (5).

In their post-stroke training study, Potempa and colleagues (1) hypothesized that muscular efficiency probably improved to a greater extent than aerobic capacity because the magnitude of improvements in workload$_{peak}$ (43 percent) and exercise time (40 percent) exceeded that of $\dot{V}O_2$ max (13 percent). Indeed, the increased workload$_{peak}$ (70 percent) and exercise time (31 percent) across GXTs in the present study cannot be viewed as definitive indicators of enhanced aerobic capacity since improvements in these parameters can occur without a concomitant increase in $\dot{V}O_2$ max (102). Improved muscular efficiency was suggested in the present study by the significant reductions in submaximal $\dot{V}O_2$ values at the second and third stages between the 1-month and 6-month GXTs (see Figure 12). Similarly, Macko et al. (5) reported training-induced reductions in steady-state $\dot{V}O_2$ levels at submaximal workloads. Oxygen consumption at a given submaximal workload is not significantly altered by aerobic training in healthy subjects (103). However, in subjects with paretic limbs, improved motor function should enhance muscular efficiency, resulting in reduced energy expenditure at a given workload.

5.4.8 Study Limitations

The modest sample size, although reasonable for a clinical study, limits the ability to generalize the findings to other clinical sites. As well, the testing protocol used across the GXTs was designed to accommodate patients with significant disability at the time of the initial test. Over the course of the study, the physical status of the patients improved progressively, resulting in the increased duration of the serial tests and changes in the reasons for test termination. The influence of these avoidable changes in testing conditions

on the results is difficult to determine. The findings suggest that the serial GXTs were comparable in terms of the effort exerted by the subjects. However, the fact that during repeat testing subjects walked at a speed progressively more removed from their preferred speed could have affected the EE$_{walk}$ results. As well, three minutes of walking at a constant speed does not guarantee attainment of true steady-state conditions, a criterion for accurate energy expenditure calculations.

5.5 Conclusions

This was the first study to document the cardiovascular and metabolic responses to GXTs over the first six months following stroke. A cohort of 20 males and five females, 64±14 years of age, with first ischemic stroke performed symptom-limited, 15% BWS-facilitated treadmill tests at 1, 2,3, and 6-months post-stroke. A mean increase of 17 percent in mean $\dot{V}O_{2peak}$, together with decreased submaximal HR and RPP and improved respiratory tolerance to effort, was found between the 1- and 6-month tests. Over the same period, a significant decrease (16 percent) was noted in energy expenditure during constant speed walking at submaximal intensity. Concomitant changes were noted in several functional measures, the percent change in walking speed being predictive of the percent change in $\dot{V}O_{2peak}$. These findings provide baseline data for future intervention studies investigating the effects of cardiac rehabilitation strategies on stroke outcomes.

While progressive improvements in functional measures occurred over the course of the study, 65 percent of the 17 percent increase mean $\dot{V}O_{2peak}$ was realized between the 1- and 2-month GXTs. Moreover, at the end of the rehabilitation period low values for mean $\dot{V}O_{2peak}$ (71% of norm-referenced value), $\dot{V}E_{peak}$ (60% of normative values), and Vt_{peak} (65% of normative values) persisted. These results, together with related findings of a low aerobic component to existing stroke rehabilitation and the ability of patients early

post-stroke to exercise safely to maximal, symptom-limited intensity, suggest that aerobic conditioning might extend the period of improvement in exercise capacity and enhance the final cardiorespiratory outcomes. By applying the principles of cardiac rehabilitation early post-stroke, the magnitude of improvement in exercise capacity may approach that of the improvement in functional status. Given the incidence of mortality from cardiac complications and the high fatigability in this population, this objective should be an important priority.

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CHAPTER 6: SUMMARY AND FUTURE DIRECTIONS

6.1 Summary

It has been known for some time that most individuals with stroke have coexisting cardiac disease (4-8), a finding which is not unexpected since stroke and CAD share similar pathogenic mechanisms (9). However, what has not been adequately investigated, either under controlled laboratory conditions or during physical rehabilitation sessions, is the cardiovascular response to exercise post-stroke. Knowledge of the responses to exercise after stroke is basic to understanding the physiologic adaptation to activity, to prescribing appropriate exercise for rehabilitation, and to ensuring a reasoned approach to implementing new therapies.

The extensive neuromuscular and cardiorespiratory impairments associated with stroke are likely to adversely affect both exercise capacity (i.e., the limit in ability to respond to physiologic stresses induced by prolonged physical effort) and muscular efficiency, with consequent effects on functional mobility and resistance to fatigue. Individuals with chronic stroke identify fatigue as the area of greatest concern and a principal source of functional limitations (7-9). Nevertheless, functional recovery post-stroke is usually attributed solely to improved neurological status; thus intervention strategies are focused on improving the neuromuscular system.

The primary objective of this thesis was to investigate longitudinally the metabolic and cardiorespiratory responses to exercise over the course of post-stroke recovery. The first challenge was to design a testing protocol that would permit an objective assessment of metabolic response to exercise of individuals early post-stroke. BWS systems have been developed to mechanically offset a prescribed percentage of body mass while providing balance support, thereby facilitating safe treadmill walking for patients with motor and postural impairments. A 15% BWS-facilitated treadmill protocol was initially validated with healthy adults, using $\dot{V}O_2$ max, the definitive index of exercise capacity, as the

principal dependent variable. Seven males and eight females (55±11 yr of age) performed 3 treadmill tests with random assignment of testing condition: I) *no BWS* - standard test, ii) *0% BWS* - harness in place but no unweighting, and iii) *15% BWS* - unweighting of 15% of body mass. The use of 15% BWS did not affect the end-expiratory gas exchange variables although Vt$_{peak}$ was significantly lower in the *15% BWS* test.

To validate the protocol for patients early post-stroke, 29 subjects (65±13 yr of age) with mild to moderate disability, performed a symptom-limited treadmill GXT with 15% BWS at 26±9 days post-stroke. No complications were encountered during or following testing. $\dot{V}O_{2peak}$ was 14±5 ml/kg/min (approximately 60 percent of norm-referenced values), indicating significantly compromised exercise capacity in the early post-stroke recovery phase. This was the first study, to our knowledge, to document responses to maximal treadmill exercise in this population.

The intensity and duration of physical activity can affect the extent of adaptation to exercise. Therefore, as part of a comprehensive investigation of changes in exercise capacity after stroke, a two-phase clinical study was conducted to estimate the aerobic component of an existing stroke rehabilitation program. In Phase 1, HR responses of 20 patients post-stroke (65±13 yr of age) were continuously monitored at bi-weekly intervals during a total of 109 physiotherapy and 80 occupational therapy sessions held over the course of rehabilitation. The HR$_{target}$ zone was calculated using the Karvonen formula. Only five percent of the total time per physiotherapy session (mean, 2.8 min; median, 0.4 min) , was spent within the HR$_{target}$ zone while 23±8 minutes (42%) was spent 'inactive' (e.g., resting, talking). Similarly, two percent of the total time per occupational therapy session (mean, 0.7 min; median, 0 min) was spent within the HR$_{target}$ zone and 22±5 minutes (54%) was spent inactive. The activities that elicited HR responses within the HR$_{target}$ zone were mainly gross motor activities in standing (e.g., walking, stair climbing). No significant changes in HR responses (i.e., HR$_{rest}$, HR$_{mean}$, HR$_{peak}$) were found over the 14-week monitoring period.

Twenty-three of the cohort of patients involved in the longitudinal study described below participated in Phase 2. HR monitoring was performed during physiotherapy sessions at one, two, and three months post-stroke to coincide with the GXTs. GXT data were used to more definitively determine the HR$_{target}$ zone and to estimate the EE$_{mean}$ of the physiotherapy sessions. The results were comparable to Phase I in terms of duration of physiotherapy (54 ± 7 min/day), stable HR responses on repeat monitoring, time spent inactive (22 ± 9 min; 40%), and activities eliciting responses within the HR$_{target}$ zone. However, the time spent within HR$_{target}$ zone, determined using $\dot{V}O_{2peak}$ data, was higher than in Phase 1 - 12 percent of the session (mean, 7.3 min; median, 2.3 min). Statistically significant increases were found in EE$_{mean}$ between the 1-month and 3-months post-stroke sessions (1.8 ± 0.4 versus 2.6 ± 0.6 kcal/min, respectively). The main conclusion of this clinical study was that stroke rehabilitation, as currently delivered, does not provide sufficient cardiorespiratory stress to elicit a training effect.

The extent of change in aerobic capacity over the course of recovery post-stroke has not been documented. The main purpose of the final study was to investigate changes in exercise capacity and related GXT variables as well as EE$_{walk}$ over the course of post-stroke recovery. A cohort of 20 males and five females (64 ± 14 yr of age) with first ischemic stroke performed symptom-limited, 15% BWS-facilitated treadmill tests at 1, 2,3, and 6-months post-stroke. Between the 1- and 6-month GXTs, a 17 percent increase in mean $\dot{V}O_{2peak}$ (from 15 ± 5 to 17 ± 7 ml/kg/min) was found and mean EE$_{walk}$ at .35 m/sec decreased 16 percent (from 3.8 ± 0.3 to 3.2 ± 0.2 kcal/min). Significant decreases in submaximal $\dot{V}O_2$, HR, RPP, $\dot{V}E$, and Vt occurred over the same time period. Gains in most functional measures were of greater magnitude than that of exercise capacity and the relationships between improvements in most functional measures and in exercise capacity were weak. Percent change in walking speed explained a significant amount of the variability in the % Δ $\dot{V}O_{2peak}$ between the 1- and 6-month GXTs.

While progressive improvements in functional measures occurred over the course of the study, 65 percent of the 17 percent increase in mean $\dot{V}O_{2peak}$ was realized between the 1- and 2-month GXTs. Moreover, at the end of the rehabilitation period low values for mean $\dot{V}O_{2peak}$ (71% of norm-referenced value), $\dot{V}E_{peak}$ (60% of normative values), and Vt_{peak} (65% of normative values) persisted. These results, together with related findings of a low aerobic component to existing stroke rehabilitation and the ability of patients early post-stroke to exercise safely to maximal, symptom-limited intensity, suggest that aerobic conditioning might extend the period of improvement in exercise capacity and enhance the final cardiorespiratory outcomes. By applying the principles of cardiac rehabilitation early post-stroke, the magnitude of improvement in exercise capacity may approach that of the improvement in functional status. Given the incidence of mortality from cardiac complications and the high fatigability in this population, this objective should be an important priority.

6.2 Future directions

Research in health sciences has begun to remove the artificial boundaries that have tended to compartmentalize human form and function into neuromuscular, cardiorespiratory, and musculoskeletal systems. In the neurosciences, the historical focus on the neuromuscular system is being replaced with emphasis on how systems interact with each other and with the environment to affect functional outcomes. This broader, more holistic perspective holds promise of enhanced function and quality of life for patients with neurologic involvement.

As evidence of the paradigm shift, attention is now being paid to the previously unheeded possibility that cardiovascular adaptation to exercise may be an important determinant of outcome following neurologic insult. The BWS-facilitated treadmill exercise protocol developed as part of this thesis could be helpful in future investigations of

exercise capacity in a host of neurologic conditions (e.g. stroke, post-polio syndrome, Parkinson's disease, Guillain-Barre Syndrome, traumatic brain injury, cerebral palsy, multiple sclerosis, and spinal cord injuries). Further development of the BWS-facilitated protocol, however, is a prerequisite to its clinical application. The effects of various percentages of unweighting on respiratory gas exchange variables of individuals with and without pathology would extend the clinical usefulness of this technique. More investigation is necessary to specifically define the population who can safely undergo testing using this protocol. Another issue that needs to be addressed is the effect of harness support on respiratory function, particularly of individuals with compromised function, given evidence of reduced V_t in our preliminary testing with health adults. The interaction of handrail support and BWS on exercise capacity and the effect of BWS on energy expenditure during gait also need to be explored.

We documented low exercise capacities early post-stroke, and although a significant improvement was observed over the interval of the study, abnormally low capacities persisted. Much remains to be clarified regarding the physiologic mechanisms responsible for the poor cardiovascular adaptations to exercise post-stroke, particularly in relation to identifying factors that limit these adaptations.

The findings in this thesis have significant implications in terms of clinical practice in that the results are interpreted to be supportive of implementing aerobic conditioning strategies for patients undergoing stroke rehabilitation. However, caution should be exercised to avoid introducing therapeutic strategies prematurely or without rigorous long-term evaluation. Clear delineation of the indications, contra-indications, and efficacy is critical to assure safe and effective application of these interventions in the clinical setting.

The design of training protocols for patients with neurologic conditions can be informed by the well-developed knowledge base in the area of cardiac rehabilitation. Important components of comprehensive programs include prescription of dynamic exercise at appropriate intensities, on-going monitoring of HR, blood pressure, and RPE,

resistance training, flexibility exercises, adequate hydration, nutritional education, and counseling behavior modification.

One exciting research possibility is a controlled investigation of the effectiveness of using BWS-treadmill walking as an intervention to enhance exercise capacity, functional mobility, and energy costs of walking early post-stroke. Three-dimensional motion analysis of the changes in the kinematic parameters of gait and electromyographic analysis of changes in muscle activation patterns over the period of the trial would help elucidate the physiologic bases for the high energy expenditure of walking.

Most of the above-mentioned considerations are not aspects of contemporary neurologic rehabilitation practices. In the future we can expect substantial change in rehabilitation approaches to reduce disability and improve quality of life for stroke survivors. Investigations such as those included in this thesis will lay the foundation for such change.