Exercise training in patients with peripheral vascular disease

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For fulfilment of the degree M.Sc(Med) in Exercise Science

DECLARATION

I, Bridget Parr, hereby declare that the work on which this thesis is based is my original work and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other University.

This thesis is presented in fulfilment of the requirements for the degree of Master of Science in Medicine.

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TERMINOLOGY AND DEFINITIONS

Peripheral vascular disease (PVD)

Atherosclerosis is the most common cause of peripheral vascular disease (Weitz et al. 1996). It is the major degenerative disease of human arteries and is characterised by intimal proliferation of smooth muscle cells, with accumulation of large amounts of connective tissue matrix and lipids (Way L 1994). These lesions reduce blood flow to the leg during exercise or at rest (Weitz et al. 1996). A spectrum of symptoms results; from intermittent claudication to pain at rest (Weitz et al. 1996). It is commoner in the lower extremity vessels.

Intermittent Claudication

The Latin word "claudicare" means "to limp". Intermittent claudication is pain or fatigue in muscles of the lower extremity in patients with peripheral vascular disease, caused by walking and relieved by rest (Way L 1994). The pain is a deep-seated ache gradually progressing to a degree that forces the patient to stop walking. Patients occasionally describe "cramping" or "tiredness" in the muscle and report that it is completely relieved after 2-5 minutes of inactivity (Way L 1994).

Clinical evaluation of pulse status - ankle brachial index (ABI)

A quick screening test for PVD consists of establishing the ankle brachial index (ABI). To obtain this index two measurements are taken a) a measurement of resting systolic blood pressure at the brachial artery and b) a measurement of the ankle resting systolic pressure taken at the posterior tibial or dorsalis pedis artery. The ankle-brachial index (ABI) is determined by dividing highest pressure obtained at the ankle by the lowest brachial arterial pressure (Way L 1994).

Measurements are taken by placing standard arm blood pressure cuffs on the lower extremities just above the malleoli to obtain pressure at the ankle and a cuff of appropriate size on the right arm to obtain brachial artery pressure (Newman et al. 1993). Normally the ABI is 1.0 or greater; a value below 1.0 indicates occlusive disease proximal to the point of measurement. (Newman et al. 1993)

Pain free walking distance (PFWD)

Pain free walking distance is the distance that a patient can walk without pain in the limb(s) (Duprez et al. 1999).

Maximum walking distance (MWD)

Maximum walking distance is the greatest possible distance that a patient can walk before being forced to stop because of intermittent claudication (Duprez et al. 1999).

Ankle pressure gradient

The ankle pressure gradient (expressed as a percentage), is the percent change (fall) in ankle pressure from the resting value [(pre-post)/pre] X100. The greater the ankle pressure gradient the greater the extent of the peripheral vascular disease (Amirhamzeh et al. 1997). Calcified vessels are incompressible, thus rendering ABI inaccurate.

MET

One MET is the metabolic equivalent of using 3.5 $mlO_2 \cdot kg^{-1} \cdot min^{-1}$ (millilitres of oxygen per kilogram of body weight per minute). This is the standard resting metabolic rate.

Pack years of smoking

One pack year is one pack of cigarettes per day per year.

ABBREVIATIONS

PVD - peripheral vascular disease

CAD- coronary artery disease

ABI - ankle brachial index

BP-blood pressure

PFWD - pain free walking distance

MWD - maximum walking distance

GTET-graded treadmill exercise test

SMWT-six minute walk test

UBST-upper body strength training

CER-conventional exercise rehabilitation

CONT-control group

r - correlation coefficient

n - number of variables in group

VO_2 - oxygen consumption

VE - ventilation

RER - respiratory exchange ratio

HR - heart rate

bpm - beats per minute

ATP - adenosine triphosphate

CABG - coronary artery bypass graft

MI - myocardial infarct

ABSTRACT

Patients with peripheral vascular disease (PVD) suffer from the symptom of intermittent claudication and are walking intolerant. However, it is not clear what contributes to walking intolerance in patients with PVD. Two suggestions have been made; i) lack of absolute blood flow to the lower limb, therefore ABI (ankle brachial index) is measured to determine severity of disease and disease progression ii) an accumulation of lactate in the skeletal muscles and blood as a result of ischaemia. Exercise training mostly in the form of treadmill walking programmes of three to six months duration are usually prescribed to improve walking tolerance in patients with PVD. Recently, a pain free upper limb cycle ergometry programme has proved to be effective in increasing walking distance in patients with claudication. This is an important development in exercise prescription for patients with PVD.

The first study in this dissertation characterized 31 patients with PVD with respect to their medical history and physiological response to exercise. Patients underwent; i) standard graded treadmill exercise test (GTET) for determination of maximum walking distance (MWD), pain free walking distance (PFWD), perception of pain, heart rate, peak VO_2, VE, and RER; ii) a six minute walk test (SMWT) for determination of maximum walking distance MWD, PFWD, perception of pain and heart rate; iii) Determination of the resting ABI, post exercise ABI and resting and peak blood lactate concentrations.

Results from this study indicated that patients with PVD suffer from a variety of co-morbid conditions and risk factors for vascular disease. Patients in this study were exercise intolerant as was witnessed by their low peak oxygen consumptions (17.0 ±4.2 $mlO_2 \cdot kg \cdot min^{-1}$ [mean ±SD]) and short six minute walk distances (392 ±117 m). Patients terminated exercise at low peak RER values (0.97 ±0.13 units) and peak venous blood lactate concentrations (3.28 ±1.39 $mmol.L^{-1}$). Peak venous blood lactate concentrations did not correlate to pain

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free walking distance or total pain perceived during the graded treadmill exercise test.

ABI tended to decrease after the exercise bout (0.59 ±0.41 to 0.44 ±0.39 units; P=0.056) but resting ABI did not correlate to either MWD or PFWD or perceived pain during the exercise tests.

These data suggest that: patients with PVD suffer from a variety of co-morbidities and have a low effort tolerance as witnessed by their low peak VO_2 values, RER values and six minute walking distance. As blood lactate concentrations were low despite severe leg pain and no correlation was found between peak blood lactate concentrations and PFWD and MWD, factors other than blood lactate accumulation must be responsible for the claudication pain that leads to walking intolerance in patients with PVD. Furthermore, resting ABI does not predict functional capacity or pain in patients with PVD. The graded treadmill exercise test should be used to monitor functional capacity in these patients.

The second study in this dissertation compared the effects of a short duration (6 wk) upper body strength training programme (UBST; n=9) to conventional (walking, cycling, circuit) exercise rehabilitation (CER; n=9) in patients with PVD. A third group of patients with PVD who were given conventional medical treatment; "walk as much as possible at home," served as the control group (CONT; n=8).

At baseline, all parameters were similar between UBST, CER and CONT groups. Following the intervention period, MWD measured during the treadmill exercise test in the CER group increased from (300 ±198 to 514 ±226 m; P<0.05) but was unchanged in the UBST group (390 ±211 to 399 ±186 m; P=NS) and CONT group (460 ±200 vs. 430 ±151 m; P=NS). Similarly peak VO_2 increased after CER (14.7 ±3.0 vs. 19.4 ±5.0 $mlO_2 \cdot kg^{-1} \cdot min^{-1}$; P<0.05) but was unchanged in the UBST group (19.6 ±5 vs. 18.7 ±6 $mlO_2 \cdot kg^{-1} \cdot min^{-1}$; P=NS) and CONT groups (18.2

±4 vs. 17.6 ±3 $mlO_2 \cdot kg^{-1} \cdot min^{-1}$; P=NS) following training. Peak RER and VE, did not change in any group following intervention.

However, PFWD during the treadmill exercise test tended to increase after intervention in CER (126 ±156 vs. 256 ±187 m; P=0.07) and UBST (128 ±121 vs. 202 ±175 m; P=0.07) but was unchanged in the CONT group (175 ±123 vs. 175 ±135 m).

During the six minute walk test the CER group improved significantly in PFWD (119 ±101 to 159 ±103 m; P=0.0025) compared to the control (192 ±147 to 116 ± 72 m; P=NS) and perceived pain during the six minute walk test decreased in the CER group (359 ±126 to 292 ±152 units; P=0.009) compared to the UBST group (327 ±42 to 391 ±143; P=NS).

Heart rate at a set submaximal workload on the graded treadmill exercise test decreased significantly in the CER group (102 ±21 to 92 ±15 bpm; P<0.05) compared to the CONT group (94 ±15 to 109 ±11 bpm; P=NS).

Resting ABI (0.6 ±0.3 vs. 0.7 ±0.5; CER, P=NS; 0.9 ±.2 vs. 0.8 ± 0.1; CONT, P=NS; 0.8 ± 0.4 vs 0.9 ±0.7; UBST, P=NS) was unchanged in all groups after the intervention period. Post exercise treadmill test ABI (0.4 ± 0.4 vs. 0.4 ± 0.4; CER, P=NS; 0.6 ± 0.4 vs. 0.6 ± 0.3; CONT, P=NS; 0.6 ± 0.4 vs 0.7 ± 0.5; UBST, P=NS) was unchanged in all groups after intervention.

The results of this study suggest that although PFWD tended to improve in the UBST during the treadmill test, CER is, overall, a more effective from of treatment for patients with PVD than UBST. CER improves MWD, peak VO_2 and submaximal heart rates during the treadmill test in patients with PVD whereas UBST does not. Furthermore, PFWD and perceived pain during the six minute walk test only improved in the CER group. In addition, CER is effective in as short a time period as six weeks. These improvements occur despite an absence of improvement in ABI. Advice to exercise at home is ineffective in improving functional capacity in patients with PVD.

CONTENTS

CHAPTER 1. LITERATURE REVIEW – EXERCISE TRAINING AND PERIPHERAL VASCULAR DISEASE

Introduction

Peripheral vascular disease (PVD) is a leading cause of morbidity in the elderly in the United States where there are an estimated 5 million affected individuals (Criqui et al. 1985). The prevalence of peripheral vascular disease increases with age and it has been estimated that the biennial incidence rate is 26.6 per 1000 men and 13.3 per 1000 women in the United States (Kannel et al. 1996). In the United Kingdom it occurs in approximately 1 in 20 of the population between the ages of 55 and 74 years (Fowkes et al. 1991).

Murabito et al. (1997), using data from the Framingham Heart Study revealed that risk factors for PVD include age, gender, serum cholesterol, hypertension, cigarette smoking, diabetes and coronary artery disease. Male gender, age and smoking were associated with a 1.5-fold increased risk for PVD; diabetes and stage 2 or greater hypertension conferred a >2-fold increased risk; and coronary heart disease nearly tripled the risk for PVD (Murabito et al. 1997). These findings are similar to those reported by Newman et al. 1993 who recognised cigarette smoking as a primary risk factor for PVD (Newman et al. 1993).

Twenty five percent of patients with PVD deteriorate steadily but only 5% deteriorate to the point that they require leg amputations (Criqui et al. 1985; Dormandy et al. 1999). Intermittent claudication is the most common symptom of peripheral vascular disease, it causes severe walking intolerance and therefore impacts on the functional status and quality of life of the patient (Regensteiner et al. 1997, Breek et al. 2002). Therefore treatment has focused on alleviating the symptom of intermittent claudication and improving walking tolerance.

Exercise training as a treatment for patients with PVD

Percutaneous transluminal angioplasty (PTA), as well as vascular bypass grafting are accepted methods of treatment for limb ischaemia (Whyman et al. 1996; Chetter et al. 1999). Conservative treatment for claudication was advocated as early as 1898 when Wilhelm Erb suggested that muscular exercise increased blood flow to the ischaemic limb (Erb W 1898). Despite this recommendation, for many years passive exercise (the limb is moved by the nurse or exercise therapist through its range of motion) was the recognised therapy for these patients (Allen et al. 1955). The importance of dynamic (the patient actively performs the exercise him or herself) exercise training as a therapy for patients with intermittent claudication was rediscovered in the 1950's and 1960's (Alpert et al. 1969; Skinner and Strandess 1967; Foley WT 1957; Larsen and Lassen 1966).

Larsen and Lassen (1966) performed the first randomised controlled study comparing an exercise training group of patients to a placebo controlled group and found that pain free walking time (PFWT) increased from 1.7 minutes to 3.5 minutes after exercise training for six months. The mean maximum walking time (MWT) increased from 2.9 minutes to 8.2 minutes. In the control group no significant change was noted. Since this study a number of randomised controlled trials (Table 1.1) have shown similar results (Holm et al. 1973; Mannarino et al. 1989; Hiatt et al. 1990; Lundgren et al. 1989; Creasy et al. 1990; Parker-Jones et al. 1996; Hiatt et al. 1996; Paterson et al. 1997; Walker et al. 2000).

Table1.1 Review of the randomised controlled trials in exercise training and patients with peripheral vascular disease

Date	Treatment	n	Program length	Exercise Frequency/ duration	MWD % inc	PFWD	Protocol
Larsen et al. 1966	Walking	7	6 months	Home 1 hour 7Xweek	282%	200%	4.6km h @8%
	control	7		Placebo	N.S	N.S	
Holm et al 1973	dynamic leg exercises	6	4 months	SPVD 30 min 3Xweek	42%	26%*	
	control	6		placebo	N.S	N.S	
Mannarino et al. 1989	walk/dynamic	8	6 months	Home 1 hour 1x week SPVD 1 hour 2X week	67%	87%	2km/h@12%
	placebo	8		Placebo	NS	NS	
Hiatt et al. 1990	Treadmill	10	12 weeks	SPVD 1 hour	123%	165%	2mph at 0% and ↑3.5% per 3 min
	control	9	No treatment		N.S	N.S	
Lundgren et al. 1989	Operation	13	6months		600%	300%	4km/h 0%
	Op + Dynamic	9		SPVD 30 min 3 X week	900%	400%	
	Dynamic	11		SPVD 30 min 3 X week	200%	300%	
Creasy et al. 1990	PTA	20	6 months	PTA	N.S	N.S	3km/h@10 %
	Dynamic	16		Leg 30 min 2X week	310%		
Parker-Jones et al. 1996	Stair-master	6	12 weeks	SPVD 1 hour 2x week	N.S	↑35.5s	2mph at 0% and ↑3.5% per 3min
	treadmill	6		SPVD 1 hour 2X week	↑171.7s	↑117.7s	
Hiatt et al 1996	Walking Treadmill	10	12 weeks	SPVD 1 hour 3 X week	43%**	61.6%**	2mph at 0% and ↑3.5% per 3min
	Strength training	8		SPVD 1 hour 3X week	NS	NS	
	Control	8			NS	NS	
Patterson et al. 1997	Supex	23	12 weeks	1X week lectures + exercise	33.9%	54.5%	
	homex	23		1X week lectures + exercise instruction	N.S	N.S	
Walker et al. 2000	Arm cranking	26	6 weeks	SPVD 40 min 2X per week	47%	122%	Shuttle test
	cycling	26		SPVD 40 min 2X per week	50%	93%	
	control	15			N.S	N.S	

Abbreviations: *= taken from graph page 202, ** = increase of time in percentage, **MWD**= maximum walking distance, **PFWD**=pain free walking distance. **SPVD**=supervised. **PTA**= percutaneous transluminal angioplasty. **% inc** =percentage increase, **n**=number of subjects, **Dynamic**=dynamic leg exercises, **op**=operation, **home**=at home, **s**=seconds

In a meta-analysis by Gardner et al. (1995) of twenty one studies on exercise training in patients with PVD, PFWD increased 179% and the MWD increased 122% following exercise training. Therefore exercise training improves walking tolerance in patients with PVD.

A recent study, however, from the University of Goteborg found no value to exercise training. The effects of surgical intervention, supervised physical exercise training and no treatment on walking tolerance was studied in patients with intermittent claudication. This group found that exercise training offered no therapeutic advantage compared to untreated controls. A methodological flaw in this study was that patients, despite being recruited between 1994 and 1997 were trained using methods dating from the 1970's. Furthermore the intervention lasted for one year and no compliance was reported for the exercise training group (Gelin et al. 2001).

However earlier findings by this same group reported that surgical reconstruction (vascular bypass graft) combined with exercise training was more effective in improving maximum walking distance and pain free walking distance in patients with intermittent claudication than training alone or surgery alone (Lundgren et al. 1989). Similarly, in other studies, this group did report improvements in MWD and PFWD in patients with intermittent claudication following exercise training (Dahloff et al. 1974; Dahloff et al. 1976).

Biological adaptations to exercise training in patients with peripheral vascular disease

The mechanism by which symptomatic improvement occurs with exercise training in patients with PVD is unclear. Early work by Skinner and Strandness (1967) found a reduction in the post exercise hyperemic response with exercise training. They attributed this phenomenon to an increased collateral circulation to the ischaemic muscle with exercise training. Post exercise hyperaemia is thought to be due to blood flow increasing to the ischaemic muscle after exercise, and as a result, blood flow decreasing to the foot causing a reduction in ankle pressure. The greater the reduction in ankle pressure, the greater the extent of the underlying peripheral vascular disease (Bernstein 1993).

Alpert et al. (1969) found that training increased absolute blood flow to the lower limbs (measured by the ^{133}Xe clearance method) and also attributed this increase in absolute blood flow to the development of a collateral circulation. This method involves ^{133}Xe dissolved in saline being injected into the gastrocnemius and its rate of clearance being recorded using a rate meter (Alpert et al. 1966).

Twenty years later a study by Carter et al. (1989) also found that systolic ankle pressure recovery was more rapid after training and that an increase in walking tolerance was correlated to a reduction in the return time of the ankle pressure to pre-exercise levels but, however, not to any other hemodynamic variables (absolute ankle pressure and ABI). Similarly Jonason and Ringqvist. (1987) found that post exercise ankle pressure was higher 2-16 minutes after training however there was no change in calf blood flow at rest or post-ischaemic maximum blood flow measured by strain gauge plethysmography. Jonason and Ringqvist. (1987) attributed this reduction in post exercise hyperemia to "a more optimal distribution and utilization of available blood flow with exercise training."

Therefore neither Carter et al. (1989) or Jonason and Ringqvist. (1987) could attribute increased walking tolerance to an increased blood flow to the lower limb through an increased collateral circulation and "more optimal distribution and utilization of available blood flow" was speculated by Jonason and Ringqvist. (1987). Subsequently others have shown that blood flow to the lower limb as measured by strain gauge plethysmography increases with exercise training (Hiatt et al. 1990, Gardner et al. 2001). However neither of these studies proved that improvement in blood flow is due to an increased collateral circulation.

Recently a study in subjects with mild hypertension found that after 12 weeks of exercise training, forearm blood flow increased significantly in response to acetylcholine (an endothelium-dependent vasodilator) but not to isosorbide dinitrate (an endothelium-independent vasodilator) in the exercise group but not in the control group (Higashi et al. 1999). Studies on the elderly (Taddei et al. 2000, Rinder et al. 2000), on patients with coronary artery disease (Hambrecht et al. 2000) and on animals with chronic coronary occlusion (Griffin et al. 1999) have revealed that exercise training improves endothelium dependent vasorelaxation through an increase in the release of nitric oxide.

It has been shown in patients with PVD that endothelium-dependent dilation is impaired. This was shown by measuring maximum brachial artery diameter and flow after brachial artery occlusion with a blood pressure cuff in patients with PVD and controls (Yataco et al. 1999). Others have shown that exercise rehabilitation improves endothelial-dependent dilation in older patients with peripheral vascular disease (Brendle et al. 2001).

It is, perhaps, this improved endothelial-dependent dilation that is responsible for improvements in walking tolerance and blood flow. It is possible that improved endothelial dependent vasodilation in patients with PVD as a result of exercise training allows for a less pronounced and shorter duration post exercise hyperaemic response and decrease in ankle pressure after a bout of exercise.

Indeed, Carter et al. 1989 found that increases in walking distances after exercise training were significantly correlated with the reduction in post exercise hyperaemia, (indicated by a reduction in the time the ankle systolic pressure took to reach pre-exercise levels), but not with other hemodynamic variables (ankle pressure and ABI).

A study by Creasy et al. (1990) comparing angioplasty to exercise training as a treatment for intermittent claudication, also showed that improvements in walking tolerance were independent of changes in ABI. ABI improved by 0.21 in the angioplasty group compared to the pre-treatment values and this significant increase was sustained at the six and nine month follow up assessments (Creasy et al. 1990). The increase in blood pressure in the operated group resulted in an increase in walking tolerance at three months but this improvement was not sustained at six and nine months. In contrast, the group receiving exercise training alone for the management of PVD improved their walking tolerance at six and nine months (Creasy et al. 1990; Perkins et al. 1996). Therefore improved ABI alone does not improve walking tolerance, whereas exercise training alone, without angioplasty did improve walking tolerance.

Therefore future studies of exercise training in patients with PVD should include measurements of endothelial reactivity before and after training by measuring brachial or femoral diameters and blood flow (using vascular ultrasound).

Biochemical adaptations in skeletal muscle in patients with PVD following exercise training

Because patients with PVD have reduced blood flow to the exercising limb(s), it has been suggested that anaerobic glycolysis, resulting from ischaemia, increases the lactate concentration in the skeletal muscles and blood which leads to claudication pain (Tan et al. 2000; Lundgren et al. 1989).

This was summarised in a review article by Tan et al. (2000) who stated, "In patients with peripheral vascular disease, increasing the workload causes an inequality in the supply of and demand for oxygen. Aerobic generation of ATP becomes inadequate and anaerobic metabolism predominates. The result is an increase in lactic acid production, and a depletion of ATP and creatine phosphate, leading to pain" (Tan et al. 2000).

Support for this theory is found in studies that have shown that improvements in walking tolerance occur alongside increases in the number of oxidative enzymes found in the skeletal muscle (Holm et al. 1973; Lundgren et al. 1989; Hiatt et al. 1996) and improvements in oxygen extraction by the skeletal muscles (Zetterquist 1970; Sorlie and Myhre 1978). The theory is that these delay the onset of anaerobic glycolyis, lactate accumulation and pain. This thesis will examine the relationship between lactate accumulation in the blood during exercise and exercise tolerance in patients with PVD.

Psychological adaptations to exercise training

Some of the improvement in exercise tolerance noted with exercise training in patients with intermittent claudication may be attributed to psychological factors. This was made apparent in a review where a number of important predictors of the outcome of an exercise programme were identified (Rosfers et al. 1990). The best correlation with good outcome of the exercise programme was belief that the exercise would lead to an improvement in walking status. Moreover, patients can be influenced by the level of motivation they feel on the particular day of testing. This was made apparent in a study which noted; "The psychology involved when walking with pain was highlighted by the two-thirds of patients who said they could walk no further but then immediately walked 15-45m to the rest room..." (Watson et al. 1997).

Lastly it seems that as patients subject themselves to pain, their pain tolerance improves. Gardner et al. (1995) found in a meta-analysis that claudication pain end point used during an exercise training programme was the most important independently related predictor of the positive change in PFWD distance and MWD in patients with intermittent claudication. The longer patients "walked into" their pain during training, the more PFWD and MWD improved after training.

Therefore, factors including the belief that the exercise training will work, motivation to walk and improvements in pain tolerance can affect walking tolerance.

Measurement of the improvement in walking tolerance following exercise training in patients with intermittent claudication

To prove that exercise training is effective, walking tests are necessary. Set testing protocols on the treadmill are common tools to assess walking tolerance in patients with PVD. A wide variety of treadmill walking tests have been used to quantify improvements in walking distances and functional capacity following training in patients with intermittent claudication (Larsen and Lassen 1966; Mannarino et al. 1989; Hiatt et al. 1990; Lundgren et al 1989; Creasy et al. 1990; Walker et al. 2000) (see Table 1.1).

Two parameters are usually measured on a treadmill: pain free walking distance (PFWD) and maximum walking distance (MWD)

The use of the treadmill as a tool to measure walking distance has been criticised because the tests are not always reproducible (Ouriel et al. 1982; Johnston et al. 1987; Perakyla et al. 1998). There is disagreement about whether a graded test (a test when the speed or gradient increases at set time intervals) is more or less reproducible than a constant load test (one which does not increase in speed or gradient).

It has been suggested by some that a constant load test is fairly reproducible (Alpert et al. 1969). Others have found that both the constant load and the graded exercise test are equally well reproducible (Cachovan et al. 1999). In contrast Gardner et al. (1991) and Perakyla et al. (1998) found the progressive test to be more reproducible and Gardner et al. (1991) suggested that only one progressive test is required to obtain reliable measurements of PFWD and MWD while three tests are necessary when using constant load treadmill tests. In the present study a progressive test starting at a speed of 3.2km.h^{-1} was used. The progressive test was started using 0% inclination and the inclination was increased every 2 minutes by 2%. This test has been validated for patients with PVD (Perakyla et al. 1998).

It has also been questioned whether treadmill walking accurately assesses walking distance because it measures an "artificial" walking distance; i.e. subjects are not walking on land. This was made apparent in a study where patients were found to walk much further on a ward corridor walk test than on the treadmill, even though the treadmill was slower (Watson et al. 1997). Because of this finding, other, less artificial methods of assessing walking capacity have been explored. In a study by Montgomery et al. (1998), sixty four patients repeated two six minute walk tests a week apart. The distances walked during the two six-minute walk tests were similar, resulting in a high reliability coefficient (R= .94) and a low coefficient of variation (10.4%). Only a small non-significant 3%-4% increase in distance and steps was found on the second test (Montgomery et al. 1998).

Recently a group of researchers have used a shuttle walk test (Walker et al. 2000). Patients walk back and forth between two cones placed 10m apart. The speed at which the patients walk is controlled by audible tones recorded on a cassette. Patients begin walking on the first tone and aim to reach the second cone by the next tone. The time span between tones is decreased over time thereby increasing the speed. The patient stops walking when he/she cannot keep up with the required speed. Walker et al. (2000) found that this test offered the advantage of testing more than one patient at a time, and was also reproducible, having less than 10% variability in PFWD and MWD in patients with claudication.

Supervised hospital based exercise programmes vs home based exercise programmes in patients with PVD

Only a few studies have compared the effects of home vs hospital based exercise programmes in patients with PVD (Regensteiner et al. 1997, Savage et al. 2001, Patterson et al. 1997). Regensteiner et al. 1997 showed no improvement in MWD or PFWD in a home based exercise programme after 12 weeks of training. Patterson et al. (1997) and Savage et al. (2001) found that although the home exercise groups improved, supervised exercise programmes improved PFWD more than home based exercise programmes over a three to six month period.

Frequency and duration of exercise training in patients with PVD

The duration of most training programmes whether they are home based or hospital based is twelve weeks to six months (Table 1.1), only one study has had a shorter training period (six weeks). This study showed that training was effective in this time period (Walker et al. 2000)

The frequency of most training programmes has been three times per week usually for a period of between thirty minutes to one hour (Table 1.1).

Mode of training used in patients with peripheral vascular disease

Early studies used walking as the mode of exercise training in patients with peripheral vascular disease (Larsen and Lassen 1966; Alpert et al. 1969). Later studies included “dynamic leg exercises” (Dahloff et al. 1982; Dahloff et al. 1974; Dahloff et al. 1976). Dynamic leg exercises in a study by Creasy et al. (1990) included “walking, walking on tip toe, walking and running on the spot, static bicycling, step ups, going up and down on tip toes while on an incline and dribbling with a ball.”

In the early 1990's, treadmills became more commonplace in gymnasiums and exercise laboratories and treadmill walking replaced "dynamic leg exercises." Studies showed that training on a treadmill produced substantial increases in walking distances (Hiatt et al. 1990; Hiatt et al. 1996; Parker-Jones et al. 1996; Savage et al. 2001). Treadmill walking was established as the accepted mode of exercise training and few studies explored the effects of alternative modes of training on walking distances in patients with PVD.

Two studies did however examine the effects of stair master exercise (Parker-Jones et al. 1996) and lower body resistance training (Hiatt et al. 1994) on walking distances in patients with PVD. Neither mode of training produced improvements in walking tolerance. Therefore the researchers concluded that training effects in patients with PVD were specific to the mode of training used. Therefore it seemed logical that treadmill walking would be the most beneficial form of training for improving walking tolerance in patients with PVD.

More recently studies have again ventured to explore the effects of modes of training outside of treadmill walking on MWD and PFWD in patients with intermittent claudication. The effect of upper limb and lower limb cycle ergometry on walking tolerance in patients with intermittent claudication was assessed in the United Kingdom (Walker at al. 2000). Patients were randomised to an upper limb cycle ergometry group or a lower limb cycle ergometry group and trained twice a week for six weeks. PFWD and MWD on a graded treadmill exercise test improved similarly in both training groups. The authors suggested that central cardiovascular adaptations contributed to the increased walking tolerance in both groups because the heart rate response to submaximal work loads during the upper and lower-limb assessments was reduced after training. The authors pointed out that exercise training using lower limb weight bearing exercise can be most uncomfortable for the patient and that an upper-limb programme (using upper limb cycle ergometers) which produced similar results would be a welcome relief to patients with intermittent claudication.

However, upper limb cycle ergometers are not available in most gymnasiums. Upper body strength training apparatus is available in all gymnasiums. No study to date has assessed the effect of upper body strength training using plate loaded circuit machines, on walking distances of patients with intermittent claudication. Thus this study will address this question.

Summary of literature review and aim of this thesis

Patients with PVD develop the symptom of intermittent claudication on walking. The available evidence in this literature review indicates that exercise training improves walking tolerance in patients with PVD. However it is not clear what leads to walking intolerance in patients with PVD. The most obvious suggestion is that it is as a result of lack of blood flow to the lower limb during walking, therefore the ABI is commonly measured to determine severity of disease and disease progression in patients with PVD. Others have suggested that an accumulation of lactate in the skeletal muscles and blood during exercise as a result of ischaemia leads to claudication pain. Chapter 3 aims to document the physiological response of patients with PVD to exercise and discuss the relationship of the ABI and lactate accumulation in the blood during exercise, to exercise intolerance in patients with PVD.

A further aim of Chapter 3 of this thesis is to report the medical and demographical characteristics of 31 patients with PVD enrolled in this study. The medical history as well as risk factor profile and the medications ingested by these patients will be documented.

To quantify walking tolerance in patients with PVD, walking tests are necessary. A wide variety of tests have been used in patients with PVD to measure walking distances. In the present study a graded treadmill exercise test (Perakyla et al. 1988) and a six minute walk test were used. Chapter three aims to discuss the physiological outcome of these two exercise tests.

As has been indicated in this review, exercise training improves walking tolerance in patients with PVD and the usual mode of training in patients with PVD in the past decade has been treadmill training, usually for a minimum period of three months and two to three hourly sessions per week. However recently a upper limb cycle ergometry programme proved to be as effective as lower limb cycle ergometry in improving walking tolerance in patients with PVD. As weight bearing walking programmes are uncomfortable for the patients with PVD, this is an important development in exercise prescription for these patients. However upper limb cycle ergometers are not available in most gymnasiums. Chapter 4 aims to determine if an upper body strength training programme using plate loaded machines is effective in improving walking distances in patients with PVD. As exercise programmes of three or six months can be daunting for a patient embark on, Chapter 4 aims to determine if functional improvements occur in patients with PVD within a short term (6wk) training period of either upper body strength training or conventional exercise rehabilitation.

Studies comparing home exercise vs supervised hospital based exercise classes are few. A further aim of chapter 4 is to determine if supervised exercise training is superior to the conventional medical advice; "walk as much as possible at home," for patients with PVD.

CHAPTER 2. GENERAL METHODOLOGY

The general methodology common to the different studies detailed in Chapter 3 and 4 is described in this chapter. Methodology specific to any particular chapter is outlined in that specific chapter. All studies described in this thesis were approved by the Ethics and Research Committee of the Faculty of Health Sciences at the University of Cape Town.

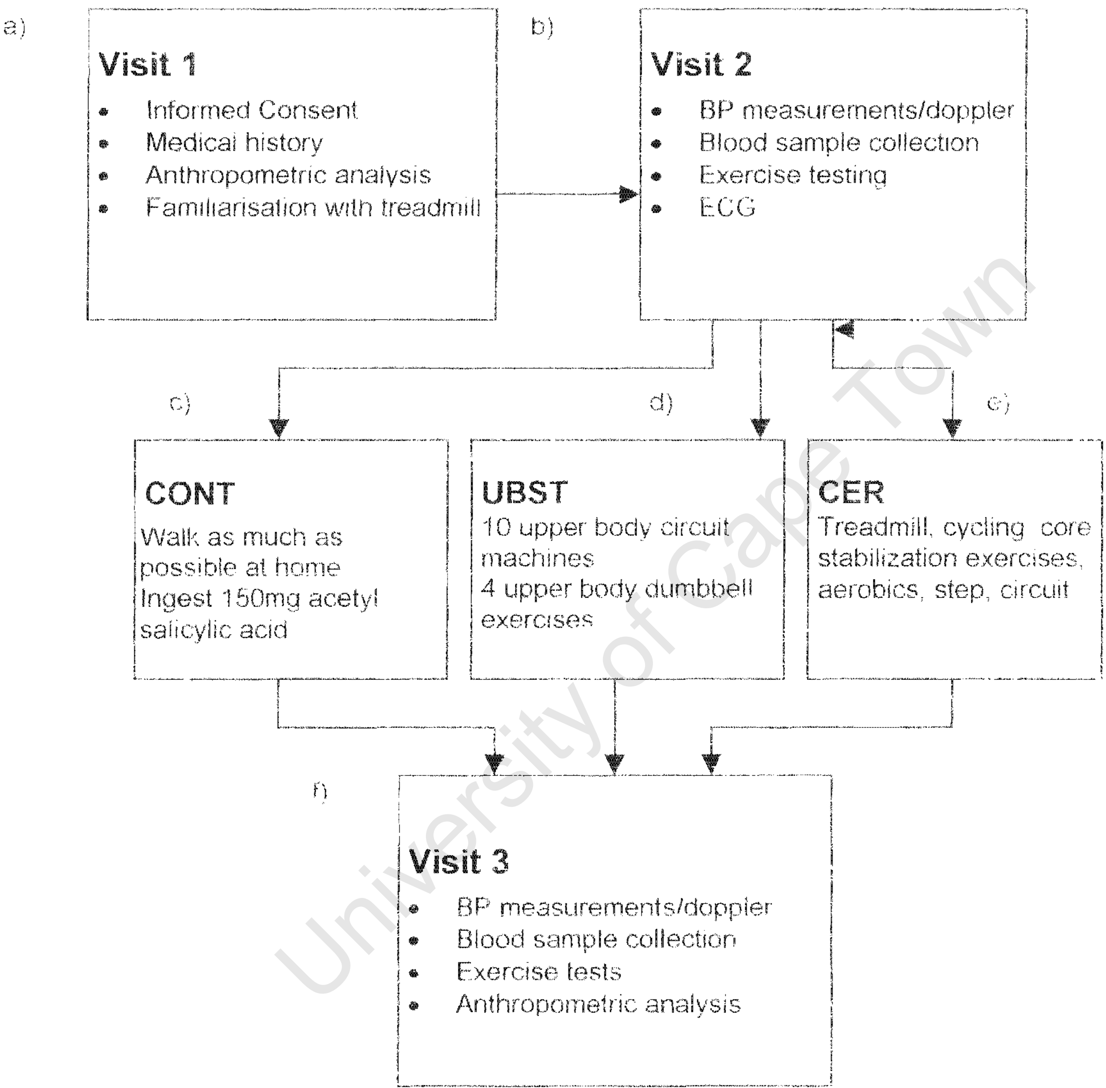
General Considerations

Thirty one patients with peripheral vascular disease were recruited from vascular surgeons from the Department of Vascular Surgery at Groote Schuur Hospital and from private practice at the Kingsbury Hospital, Cape Town, South Africa. All patients had peripheral vascular disease with intermittent claudication as diagnosed by a vascular surgeon using duplex flow Doppler and/or segmental Doppler pressures. Patients had to have intermittent claudication during a screening treadmill test and/or an ankle/brachial index at rest of less than 0.97 or a drop of ABI under 0.85 during exercise. Patients were excluded if any of the following were present: absence of PVD; rest pain or tissue loss; limitations of exercise tolerance other than claudication (ie severe coronary artery disease, dyspnea, severe arthritis that limited exercise) and active cancer, liver disease or renal disease. All patients gave their written informed consent for this study.

Study Design

The first study of this thesis described the medical characteristics and physiological response to exercise in 31 patients with PVD. The second study of this thesis compared the effects of a six week upper body strength training programme (UBST) to conventional exercise rehabilitation (CER) in patients with PVD. A third group of patients with PVD who were discharged and instructed to walk as much as possible served as the control (CONT). An overview of the study design is given in Figure 2.1. The design of the first study is listed in blocks a) and b). The design of the second study is listed in blocks a) to f).

Figure 2.1. Overview of study design



Patients visited the laboratory on at least two occasions to sign an informed consent, for recording of medical history, anthropometrical analysis, familiarisation with the treadmill, determination of ankle and brachial blood pressure, blood analysis, ECG, a six minute walk test and a graded treadmill exercise test to maximal claudication pain. A detailed medical history from the patient's vascular surgeon and/or cardiologist was obtained.

Patients then began their intervention treatment. Patients were randomized to one of three treatment groups; the conventional exercise rehabilitation group (CER), the upper body strength training group (UBST) and the control group (CONT). Intervention took place for a period of at least six weeks.

The CER group and UBST group exercised three times per week for an hour each time at the Cape Medical Rehabilitation Centre, Claremont Hospital, Cape Town. After at least six weeks of intervention, patients visited the laboratory once again for determination of ankle and arm blood pressure, blood lactate analysis, a graded treadmill exercise test to maximal claudication pain and a six minute walk test.

Anthropometrical analysis

Body mass was recorded using a scale (Healthometer professional Big Foot II H7, United Kingdom). Standing height without shoes was measured to the nearest 0.1cm. Skinfold thickness was measured to the closest 0.1mm at triceps, biceps, suprailiac and subscapula sites on the right hand side of the body using a Harpenden caliper (British Indicator HSC Body 918760, United Kingdom). Skinfolds were substituted into an equation to predict percent body fat (Brozek et al. 1963).

Ankle and arm blood pressure measurements

After subjects remained supine in a quiet environment for a period of fifteen minutes the resting brachial blood pressure (Korotkoff Phase I and IV) was measured and recorded by means of audible sphygmomanometry using a calibrated mercury column sphygmomanometer with an appropriately sized cuff.

Simultaneously, another tester measured left and right ankle pressures consecutively with a Doppler (©Huntleigh Technology PLC 1997 Dopplex ® Advanced Pocket Dopplers United Kingdom) and blood pressure cuffs affixed just above the ankles. The Doppler probe was placed over the posterior tibial or dorsalis pedis artery. The cuff was inflated until the Doppler sound disappeared. The cuff was slowly deflated until the sound returned. When the sound returned, this was recorded as the ankle systolic pressure. Ankle brachial index (ABI) was calculated for each patient by dividing the ankle pressure reading by the brachial pressure reading. An additional brachial and ankle systolic blood pressure was taken immediately post-exercise. Ankle pressure gradient was calculated for each patient (see terminology and definitions).

Graded treadmill exercise test (GTET) to maximal claudication pain

On their first visit to the laboratory, subjects were familiarized with the treadmill. They were given the opportunity to walk on the treadmill for three bouts of two minutes of walking at a speed manageable to them.

On the second visit to the laboratory the patients performed a graded treadmill exercise test. During the graded treadmill protocol (Perakyla et al. 1998), the treadmill speed was held constant at 3.2km/h with a 2% grade. The grade increased by 2% every two minutes (see appendices). If the subjects were unable to walk at this speed they were tested using the Modified Bruce protocol (see appendices). Heart rate and brachial blood pressure were monitored every two minutes. Patients were asked to report their level of perceived pain using a perception of pain scale previously used in our laboratory (Lambert et al. 2002). The scale had verbal expressions that were simple to understand and accurately describe sensations of perceived peripheral pain. Pain free walking distance (PFWD) was recorded when the patient first noticed calf pain during exercise. Maximum walking distance (MWD) was defined as the distance covered on the treadmill at which the patient could no longer continue exercise because of severe claudication pain.

During exercise total inspiratory ventilation (VE), oxygen uptake (VO_2) and respiratory exchange ratio (RER) were measured over 15-s intervals by use of a breath-by-breath Oxycon Alpha Analyzer (Oxycon Alpha®, Enrich JAEGER, Wuerzburg, Germany) previously used in this laboratory (Goedecke et al. 2000). Before each test, the gas meter was calibrated with a Hans Rudolph 3-liter syringe (Vacumed, Ventura, CA), and the analyzers were calibrated with room air and a 4% CO_2-96% N_2 gas mixture. The reliability of the Oxycon Alpha Analyzer was tested on a weekly basis by burning absolute ethanol (99% analytical reagent, Associated Chemical Enterprises (Pty), Glenvista, South Africa) as a reference. Heart rate during the graded treadmill exercise test was recorded using an electrocardiogram monitor (Cardio Perfect® 3.3, Rijswijk, Netherlands) with self-adhering electrodes placed in a modified 10-electrode (Mason-Likar) configuration (ACSM 1991).

Collection of blood for analysis of blood lactate before and after an incremental exercise test to maximal claudication pain

Prior to the start of the treadmill test, a resting venous blood sample was drawn from a subcutaneous forearm vein of each patient by a nursing sister or doctor. Two milliliters of blood was drawn directly into a sodium oxalate lined glass test tube and immediately placed on ice for later analysis of plasma lactate concentrations. An additional two milliliter blood sample was collected at minute three post exercise.

Blood sample analysis

At termination of the exercise test, the two milliliter blood samples in the sodium oxalate test tubes were centrifuged using a Sigam 302-K centrifuge (Munich, Germany) at 3000 rpm for 10 minutes at 4 C. Blood lactate concentrations were measured in plasma by means of an enzymatic kit technique (bioMerieux sa, lactate PAP 69280, Marcy l" Etoille, France).

Six minute walk test

After a rest period of twenty minutes, the patient completed a six minute walk around a track. The patient was instructed to cover as much ground as he/she could in six minutes. The tester walked behind the subject. Pain free walking time and maximum walking time were recorded as well as pain free walking distance and maximum walking distance. Heart rate was measured continuously during the six minute period by means of a Polar heart rate monitor (Polar Company, Kempele, Finland). Subjects reported perceived pain in the last ten seconds of every minute. Recovery heart rate at the end of the first minute after the six minute walk was also measured.

Intervention

To be included in the training part of this study, patients had to attend exercise rehabilitation three times per week for an hour for a period of at least six weeks.

Control subjects received conventional medical treatment. They were told to "walk as much as possible at home." All patients in the control group had been instructed by their medical doctors to ingest 150mg of salicylic acid per day. Control subjects were told that they could join the exercise programme at completion of the study.

Subjects randomised to the CER group were trained in a hospital setting three times per week for a one hour period. The CER training consisted of repetitive walking on a treadmill (Precor®, Bothell, USA) at a speed that produced claudication pain within five to ten minutes, followed by a rest period, then another series of exercise-rest periods until twenty minutes of walking was completed. The intensity of the treadmill-training programme was advanced on a weekly basis by increasing either or both the walking speed and gradient. The walking speed was increased by 0.3km/h per week or if the patient was a slow walker the gradient was increased by 1%. This is equivalent to a quarter of a MET per week (Gordon et al. 1991). After walking, the patients cycled for ten minutes (Stairmaster ® Sports/Medical products, Kirkland, USA). The next half hour of the exercise session consisted of; circuit training completing 10 machines of fifteen repetitions on the weight plated machines (Paramount Fitness Corporation ©, Los Angeles, USA) once a week, floor exercises (consisting of either step, aerobics or core stabilization exercises) once a week and a half hour spin class once a week. This CER is the programme currently used at the Claremont Hospital for coronary artery disease patients. An example of the CER programme is included in the appendices (Table 6.4) and card #1.

The UBST group completed fifteen repetitions of exercises on ten upper body weight plated machines (Paramount Fitness Corporation ©, Los Angeles, USA) and thirty repetitions of four upperbody dumbbell exercises (weight of 1.5kg). Subjects were personally trained until they could train by themselves using the correct technique. They were told to continue doing any walking they had been doing but not to start any additional exercise. The initial weight on the weight plated machines was set so the patient could comfortably complete fifteen repetitions. After two to three weeks two sets of fifteen repetitions were completed on the machines. Once the subjects could complete two sets of fifteen repetitions with ease the weights were increased an average of between four and sixteen pounds per week. An example of the UBST programme is included in Table 6.5 and in the appendices card #2.

Statistical Analysis

Data were collected and entered onto a spreadsheet (Microsoft® Windows®XP 2000). All results were analyzed using a statistical software package (Statistica©, StatSoft Inc., Tulsa, OK, USA). All data are expressed as mean ±SD. A between-subjects analysis of variance was used to detect differences between groups on entry to the study. An analysis of variance with repeated measures was used to detect differences between groups over time and changes across groups over time. The alpha level was adjusted in all statistically significant results in the repeated measures ANOVA according to the Bonferroni multiple comparisons procedure. Thereafter a LSD post hoc analysis was used to detect differences between groups from pre-treatment to post-treatment. Correlation coefficients within the patient population were calculated by means of the Pearsons product moment correlation coefficient. In the case of correlations, correlation coefficients were denoted as 'r' and the sample size as 'n'.

CHAPTER 3: PHYSIOLOGICAL RESPONSE TO EXERCISE IN PATIENTS WITH PERIPHERAL VASCULAR DISEASE

Introduction

Peripheral vascular disease is a multifaceted disease, with patients typically suffering from a variety of diseases including hypertension, diabetes and coronary artery disease (Murabito et al. 1997). Other risk factors for PVD include smoking, hypercholestrolaemia, male gender and age (Murabito et al. 1997). Men experience more claudication than women and typically patients with PVD are over the age of sixty. Therefore PVD is a multi-factorial disease. An aim of the present study is to report the demographical and medical characteristics of 31 patients with PVD enrolled in this study.

Previous studies in this laboratory have indicated that patients with chronic obstructive pulmonary disease (Coleman 1998) and patients with chronic heart failure (Derman 1995) are exercise intolerant with demonstrably low peak VO_2 values compared to age matched controls. Similarly, results from studies on patients with PVD have indicated that this population also have low peak VO_2 values (Gardner et al. 1999, Hiatt et al. 1988). An aim of the present study is to document the physiological response of patients with PVD to exercise.

It is not clear what causes walking intolerance in patients with PVD. It has been suggested that a compromised oxidative metabolism and the resultant lactate accumulation in the blood and skeletal muscles leads to claudication pain (Lundgren et al. 1989, Tan et al. 2000). Therefore researchers have studied peripheral adaptations to exercise training and found that improvements in walking tolerance occur alongside increases in oxidative enzymes found in the skeletal muscle (Holm et al. 1973; Lundgren et al. 1989; Hiatt et al. 1996) and improvements in oxygen extraction by the skeletal muscles (Zetterquist 1970; Sorlie and Myhre 1978). These findings have served to reinforce the hypothesis that lactate accumulation in the blood and skeletal muscles leads to claudication pain. Other researchers have suggested that walking intolerance is as a result of decreased blood flow to the lower limb (Alpert 1969, Jonason and Ringqvist 1987, Skinner and Strandness 1967) and therefore improvements in blood flow as a result of an increased collateral circulation (Alpert 1969, Skinner and Strandness 1967), lead to an improvement in walking tolerance. Therefore the ABI is commonly assessed.

An aim of this study is to discuss the relationship between ABI and walking tolerance in patients with PVD and the relationship between peak blood lactate and walking tolerance in patients with PVD.

To quantify walking tolerance in patients with PVD, walking tests are necessary. A wide variety of tests have been used in patients with PVD to measure walking distances (Larsen and Lassen 1966; Mannarino et al. 1989; Hiatt et al. 1989; Lundgren et al 1989; Creasy et al. 1990; Walker et al. 2000). In the present study a graded treadmill exercise test (Perakyla et al. 1988) and a six minute walk test were used. This chapter discusses the physiological outcome of these two exercise tests.

Methodology

Thirty-one patients with peripheral vascular disease were recruited from the Department of Vascular Surgery at Groote Schuur Hospital and from private practice at the Kingsbury Hospital, Cape Town, South Africa. Details of diagnostic and inclusion criteria are described in Chapter 2.

Exercise testing

All patients were tested prior to commencement of the study. All tests were conducted according to the methods detailed in Chapter Two. On the first visit to the laboratory a full anthropometrical analysis was performed for determination of body composition. Additionally a full medical history was taken from each patient and medical records were obtained from the vascular surgeon and cardiologist. The patients were familiarised with the treadmill according to the methods detailed in Chapter Two.

On the second visit each subject performed a graded treadmill test to maximal claudication pain as described in Chapter Two. The following variables were measured at regular intervals throughout the exercise bout and at peak exercise: VO_2, VE, RER, HR and perception of claudication pain.

Resting venous blood lactate concentration and brachial and ankle blood pressures were measured prior to commencement of the exercise test. Peak venous lactate concentration was measured three minutes after the treadmill exercise test and recovery brachial and ankle blood pressures were measured two minutes after the treadmill exercise test.

Each subject performed a six minute walk test on an indoor track and heart rate and perceived pain were recorded each minute. Recovery heart rate was recorded at the end of the first minute after exercise.

Statistical analysis

Data are presented as the mean ±SD. Correlation coefficients within the patient population were calculated by means of the Pearsons product moment correlation coefficient for continuous data using (Statistica©, StatSoft Inc., Tulsa, Ok, USA). Levels of significance were calculated at the 0.05 confidence levels. In the cases of correlations, correlation coefficients were denoted as r and the sample size as n. A dependent t-test was used to assess differences between pre-exercise venous lactate concentrations and post-exercise lactate concentrations. Ratings of pain taken every two minutes during the exercise tests were converted to a single variable for each patient by plotting an area under the curve for each patient. The data was normalized by expressing the pain measure (Y axis) relative to 100% of elapsed time (the X-axis).

Results

Patient characteristics on entry to the study

Location of PVD

The location of peripheral vascular disease is shown in Figure 3.1

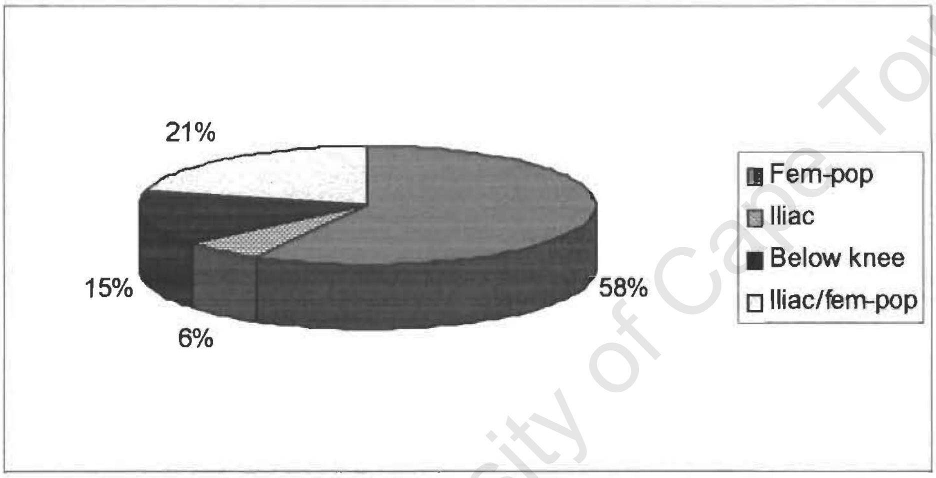


Figure 3.1 Location of disease in patients with PVD
Abbreviations: **iliac**=iliac arteries, **fem-pop**=femoral-popliteal arteries, **below knee**=peroneal, anterior tibial artery or posterior tibial artery, **Iliac/fem-pop**=femoral popliteal and iliac arteries

Thirty one patients with peripheral vascular disease were recruited for the study. Twenty two patients had bilateral disease and nine patients had unilateral disease. "Femoral-popliteal disease" in Fig 3.1 refers to disease of the femoral and popliteal arteries. "Iliac" refers to either or both the internal and external iliac arteries, and "below knee disease" constitutes disease of one or all of the peroneal artery, anterior tibial artery and the posterior tibial artery. "Iliac/fem-pop" refers to disease of both the iliac and femoral-popliteal arteries.

General characteristics of patients with PVD

Nineteen patients were male and twelve were female. Twelve were of mixed ancestral origin and nineteen were caucasian ancestral origin. Further patient characteristics are detailed in Table 3.1 and Table 3.2.

Table 3.1 Patient characteristics on entry to the study

	Mean ±SD	Range
Age (yr)	63±13	27-81
BMI (kg/m^2)	27±5.0	19-36
Mass (kg)	78±15	52-114
Height (m)	1.7±0.1	1.5-1.9
BF (%)	32±7.0	21-47
DOD (months)	26±28	3-96
Smoking (pk yrs)	23±27	0-98

Abbreviations: **Yr**=years, **Kg**=kilograms, **BMI**=body mass index, **BF**=percentage body fat, **ABI**=ankle brachial index, **DOD**=duration of disease, **Pk yrs**=pack years, **SD**=standard deviation. All Values are expressed as means ± SD and range

Table 3.2 Distribution of patients in each category of age and BMI

AGE	**Number of patients (%)**	
20-30	2 (6%)	
50-60	8 (26%)	
60-70	11 (35%)	
70-80	9 (29%)	
>80	1 (3%)	
BMI kg/m^2	**Males**	**Females**
20-24.9 (normal BMI)	3 (17%)	5 (42%)
25-29.9 (grade 1 obesity)	11 (61%)	4 (33%)
30-40 (grade 2 obesity)	4 (22%)	3 (25%)
Fat %	**Males**	**Females**
20-25	7 (39%)	1 (8%)
25-29	4 (22%)	3 (23%)
>30	7 (39%)	9 (69%)

Abbreviations: **BMI**=body mass index, **%**=percentage

Ninety percent of patients fell within the age range of fifty to eighty. The sixty to seventy year age range was the largest group (35%). Two patients were below the age of 30 years old. This was indeed unusual, but the patients did have PVD of unknown etiology as confirmed by their vascular surgeons. One patient was over eighty.

Generally patients were overweight. Sixty one percent of males and thirty three percent of females had grade 1 obesity (BMI of between 25kg/m^2 and 29kg/m^2 and twenty two percent of males and twenty five percent of females had grade 2 obesity (BMI of between 30kg/m^2 and 40kg/m^2) (Williams and Wilkins 1995). The remainder of the patients (42%) were within an acceptable range of BMI. Forty percent of males and seventy percent of females had fat percentages greater than 30%. All patients had been diagnosed with PVD for at least three months.

Medical History of patients with peripheral vascular disease

Medical history of the patients with PVD in this study is detailed in Table 3.3

Table 3.3 Medical history and risk factor profile of patients with PVD on entry to the trial

	Number of patients (%)
Peripheral vascular disease	31 (100%)
percutaneous transluminal angioplasty and stent	5 (16%)
bypass graft	2 (6%)
Coronary artery disease	14 (45%)
History of heart failure	2 (6%)
History of MI	6 (19%)
History of angina pectoris	8 (26%)
Coronary artery bypass graft	8 (26%)
Pacemaker	1 (3%)
Stent	1 (3%)
Percutaneous transluminal angioplasty	1 (3%)
Cerebral vascular disease	5 (3%)
History of transient ischaemic attack	1 (3%)
History of stroke	1 (3%)
Carotid endarterectomy	2 (6%)
Hypercholesterolaemia	15 (48%)
Hypertension	25 (81%)
Sedentary	31 (100%)
Obesity	22 (71%)
Diabetes	14 (40%)
Current smokers	5 (16%)
Former-smokers	18 (58%)
Respiratory disease	3 (10%)
Rheumatoid arthritis	1 (3%)
Osteoarthritis arthritis	7 (23%)

Abbreviations: **MI**=Myocardial infarction, **CABG**= Coronary artery bypass graft

Sixteen percent of patients with PVD had previously had peripheral vascular percutaneous transluminal angioplasty and stent procedures and only six percent had peripheral vascular bypass surgery. However, none of these procedures occurred within six months of the start of the study.

Forty five percent of patients with PVD had coronary artery disease. Twenty six percent had a history of angina. Twenty six percent of patients had undergone coronary artery bypass graft procedures and three percent had undergone percutaneous transluminal angioplasty and stent procedures. Six percent had a history of heart failure. Nineteen percent had a history of MI. However none of these procedures or incidents had occurred within six months of the start of the study. Furthermore no patients at the time of the study were in heart failure or experiencing angina.

A high percentage (80%) of patients with PVD had hypertension; almost half of the patients had hypercholesterolaemia (48%) and a similar number had diabetes (45%). All patients were sedentary at the time of entry to the study.

Fifty-eight percent of patients with PVD were ex-smokers and only twenty six percent had never smoked. Sixteen percent were smoking on entry into the study.

A small number of patients (16%) with PVD had concomitant cerebro-vascular disease. However none of the events mentioned in Table 3.3 (cerebral vascular disease) had occurred within two years of the start of the study.

A small percentage of patients with PVD had respiratory disease (9%) and twenty five percent had arthritis. Twenty two percent of the patients with PVD had osteoarthritis and three percent had rheumatoid arthritis. However the arthritis did not limit the exercise capacity of any of the patients included in the study.

Medications ingested

The medications ingested by patients with peripheral vascular disease are detailed in Table 3.4.

Table 3.4 Number of patients with PVD ingesting cardiovascular and hypoglycaemic medication

Medications ingested	Number of patients	Percentage (%)
Serum lipid reducing agents	15	48
Antihypertensives	25	81
Warfarin	5	16
Acetyl salicylic acid	26	84
Oral hypoglycaemics	14	45

A high percentage of patients were ingesting anti-hypertensive medication and 150mg tablet of acetyl salicylic acid per day. Almost half the patients were on serum lipid reducing agents and oral hypoglycaemic medication.

Exercise tolerance of patients with peripheral vascular disease

Walking distances of patients on entry to the study during the graded treadmill exercise test (GTET) and the six minute walk test (SMWT) are detailed in Table 3.5.

Table 3.5 Pain free walking distance and maximal walking distance of patients with PVD on entry to the study during the graded treadmill exercise test (GTET) and the six minute walk test (SMWT)

	(SMWT)	Range	(GTET)	Range
PFWD (m)	112 ±54	(34-270)	98 ±53	(14-262)
MWD (m)	392 ±117	(195-627)	317 ±166	(110-643)
Total pain (units)	369 ±111	(167-675)	300 ±110	(75-450)

Abbreviations: MWD=maximum walking distance, **PFWD**= pain free walking distance, **m**=meters, **SD**=standard deviation
Values are expressed as means ± SD and range

The patients walked a longer distance during the six minute walk test than on the treadmill exercise test (392 ±117 vs 317 ±166 m, SMWT vs GTET, $p=0.04$). Pain free walking distance during the six minute walk test was slightly more than pain free walking distance during the treadmill test although this was not statistically significant. Total pain perceived during the six minute walk test was significantly more than total pain perceived during the treadmill test (369 ±111 vs 300 ±110 units, SMWT vs GTET, $p=0.01$). There was a large standard deviation and range in the maximal and pain free walking distance in patients with PVD.

Physiological variables measured during the graded treadmill exercise test

Peak oxygen consumption (VO_2), peak minute ventilation (VE), peak respiratory exchange ratio (RER), peak heart rate (HR), resting venous blood lactate concentration, peak post-exercise venous blood lactate concentration and resting and post exercise ABI and ankle pressure gradient during the graded treadmill exercise test are detailed in Table 3.6.

Table 3.6 Peak oxygen consumption, peak ventilation and peak respiratory exchange ratio in patients with PVD on the graded treadmill exercise test

	Mean and SD	**Range**
Peak VO_2 ($mlO_2 \cdot kg^{-1} \cdot min^{-1}$)	17.0 ±4.2	(10-26)
Peak VE ($L.min^{-1}$)	43.0 ±14.0	(18 – 82)
Peak RER (units)	0.97 ±0.13	(0.75-1.3)
Peak HR (bpm)	114 ±22	(68-157)
Rest venous [lactate] ($mmol.L^{-1}$)	2.1 ±1.6	(0.63-7.98)
Peak venous [lacate]($mmol.L^{-1}$)	3.28 ±1.39	(1.54-7.47)
ABI rest (units)	0.59 ±0.41	(0-1.7)
ABI post exercise (units)	0.43 ±0.39	(0-1.14)
Ankle pressure gradient (%)	31 ±46	-41-(+100)

Abbreviations: VO_2=oxygen consumption, **VE**=minute ventilation, **RER**=respiratory exchange ratio, **HR**=heart rate, **SD**=standard deviation **ABI**=ankle brachial pressure index. Values are expressed as means ±SD and range

Mean peak VO_2 was 17 $mlO_2 \cdot kg^{-1} \cdot min^{-1}$, peak VE was 43 $L.min^{-1}$ and peak RER was 0.97. Peak post-exercise venous lactate concentration was significantly higher than resting values (2.08 ±1.6 vs 3.28 ±1.39 $mmol.L^{-1}$, rest vs post, $p=0.001$) however the peak venous lactate concentration was low. There was a trend for ABI to drop after the graded treadmill exercise test (0.59 ±0.41 vs 0.43 ±0.39 units, pre-exercise vs post exercise, $p=0.056$).

Exercise tolerance in patients with chronic obstructive pulmonary disease (COPD) (Coleman 1998) and in patients with chronic heart failure (CHF) and in age matched sedentary controls (Derman 1995) has been studied in this laboratory. Results of these studies in comparison to the present study are documented in Table 3.7.

Table 3.7 Peak oxygen consumption, peak ventilation, peak respiratory exchange ratio and peak venous lactate concentration in patients with CHF, COPD and PVD during a maximal exercise test

	HF (n=11)	**CHF-CONT (n=10)**	**COPD (n=13)**	**COPD-CONT (n=13)**	**PVD (n=31)**
Age (yrs)	47 ±5	39 ±3	57 ±5	55 ±7	63 ±13
Mass (kg)	85 ±6	86 ±5	65 ±14	83 ±10	75 ±15
RER	1.01 ±0.01	1.12 ±0.03	1.1 ±0.2	1.4 ±0.2	0.97 ±0.13
VO_2 ($mlO_2 \cdot kg^{-1} \cdot min^{-1}$)	12.5 ±1	34.3 ±3.5	17 ±5	26 ±6	17 ±4.2
VE ($L.min^{-1}$)	36.1 ±2.7	78.7 ±5	41.3 ±13.5	87.5 ±22.1	43 ±14.2
[Lacate] ($mmol.L^{-1}$)	4.6 ±0.5	7.3 ±0.3	5.1 ±2.7	9.7 ±2.7	3.3±1.4

Abbreviations: yrs=years, **kg**=kilogram, **RER**=respiratory exchange ratio, **VO_2**=oxygen consumption, **VE**=minute ventilation, **HF**=heart failure, **CHF-CONT**=chronic heart failure controls, **COPD**=chronic obstructive pulmonary disease, **COPD-CONT**=chronic obstructive pulmonary disease controls, **PVD**=peripheral vascular disease. Values are expressed as means ±SD

Patients in the present study had lower RER values in comparison to patients with CHF and COPD and controls. Similarly, in comparison to patients with COPD and CHF and to the controls in these studies, peak lactate levels in the present study were lower. Patients with PVD in the present study had similar peak VO_2 values to patients with COPD and higher peak VO_2 values than patients with CHF.

Relationships between walking tolerance, demographic data, physiological variables and performance variables of patients with PVD

To determine if any relationship existed between the observed walking tolerance on the treadmill exercise test and selected demographic data and physiological variables in patients with PVD, a correlation analysis was performed. Results are detailed in Table 3.8

Table 3.8 Results of a correlation analysis between measures of walking tolerance on the graded treadmill exercise test and demographic data and physiological variables of thirty one patients with PVD.

	MWD (GTET) (m)	PFWD (GTET) (m)
Age (yrs)	NS	NS
Mass (kg)	NS	r=0.39 n=31 P=0.031
BMI (kg/m^2)	NS	NS
Fat %	NS	NS
DOD (months)	NS	NS
Smoking (pk yrs)	NS	NS
Pk VE (L/min)	r=0.5 n=31 P=0.005	NS
Pk VO_2 ($mlO_2 \cdot kg^{-1} \cdot min^{-1}$)	r=0.68 n=31 P=0.001	NS
Pk RER (units)	NS	NS
p-e venous lactate (mmol/L)	NS	NS
Total pain (units)	NS	NS
ABI (units)	NS	NS
peABI (units)	NS	NS
Pr gradient (%)	NS	NS

Abbreviations: yrs=years, **kg**=kilogram, **BMI**=body mass index, %=percentage, **DOD**=duration of disease, **Pk yrs**=pack years, **pe**=post-exercise, **Pk**=peak, **VE**=minute ventilation, **VO_2**=oxygen consumption, **RER**=respiratory exchange ratio, **ABI**=ankle brachial index, **peABI**=post exercise ankle brachial index, **Pr**=pressure, **MWD**=maximum walking distance, **PFWD**=pain free walking distance, **m**=meters, **GTET**=graded treadmill exercise test, **r Value**=correlation coefficient, **NS**=non significant

As expected maximum oxygen consumption and maximum ventilation correlated positively and significantly to maximum walking distance during the treadmill exercise test. This is illustrated in Figure 3.2 and Figure 3.3.

No significant correlations were found between age, BMI, fat percentage, duration of disease, pack years of smoking and total pain, and walking tolerance on the treadmill exercise test. There was however a weak but significant correlation between mass and pain free walking distance on the treadmill exercise test.

Of significance is that there was no correlation between peak post-exercise venous lactate concentrations and pain free walking distance or maximum walking distance during the treadmill exercise test (Figure 3.4)

Similarly, resting ABI did not correlate to maximal walking distance or pain free walking distance on the treadmill exercise test (Figure 3.5 and 3.6), nor was there any relationship between post exercise ankle brachial index or ankle pressure gradient and walking tolerance on the treadmill exercise test.

In addition to Table 3.8, a correlation analysis was formed between total pain perceived on the GTET and peak venous blood lactate concentration and total pain perceived on the GTET and ABI. No correlation was found between these variables.

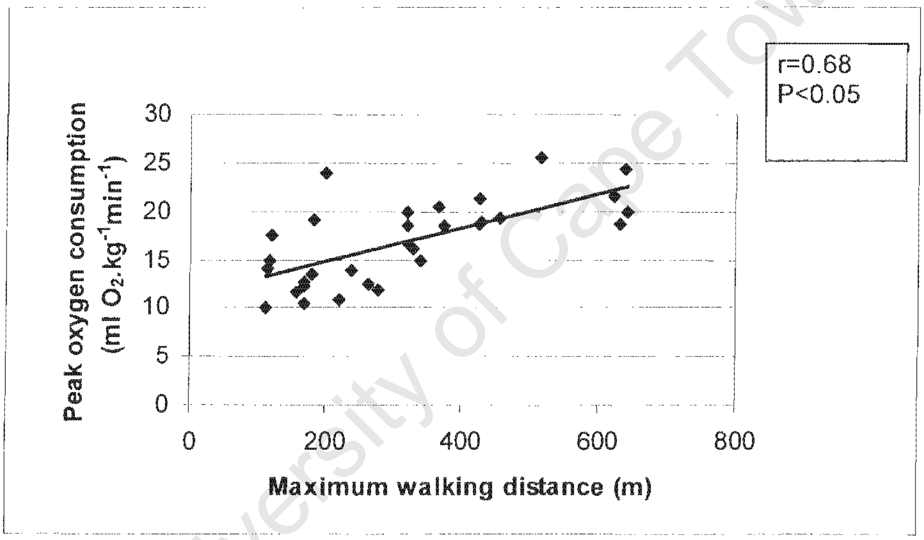


Figure 3.2 Relationship between maximum walking distance and peak oxygen consumption on the graded treadmill exercise test (GTET) (n=31).

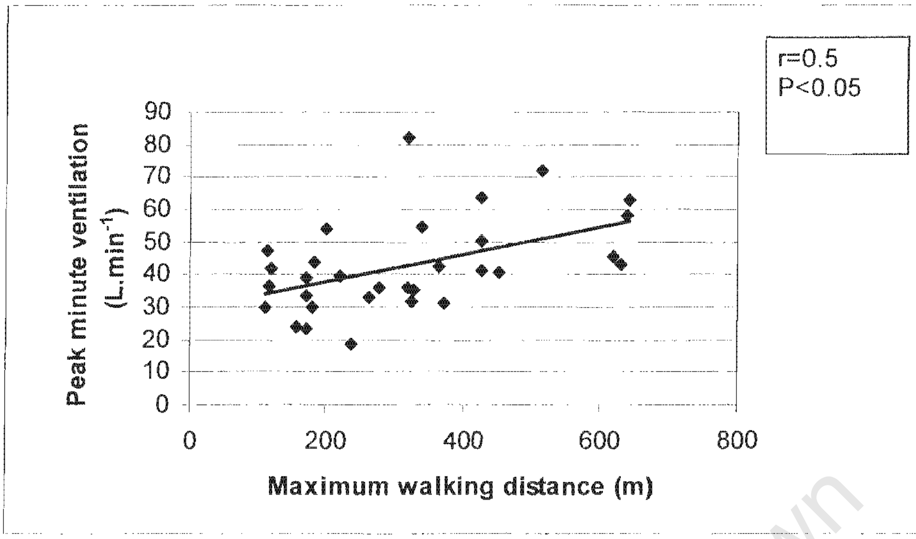


Figure 3.3 Relationship between maximum walking distance and peak ventilation on the graded treadmill exercise test (GTET)(n=31).

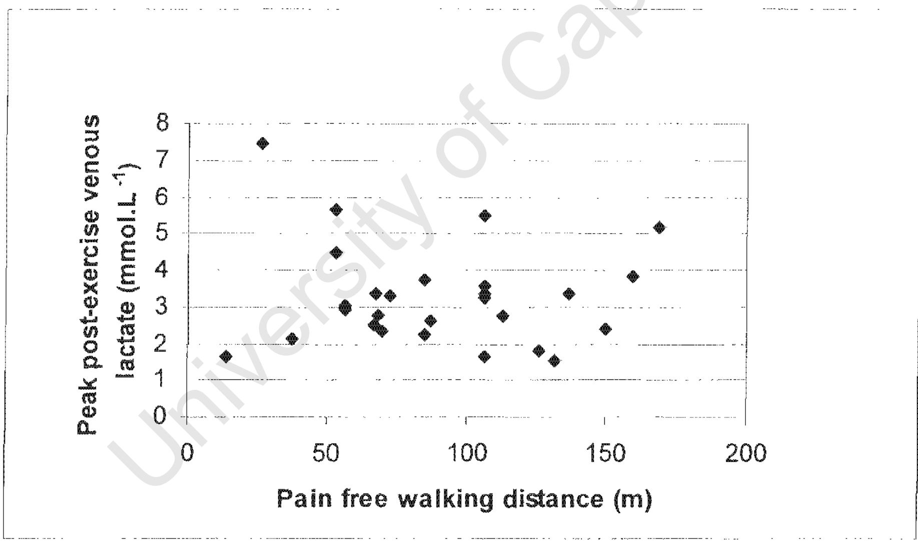


Figure 3.4 Relationship between peak post-exercise venous lactate concentration and pain free walking distance on the graded treadmill exercise test (GTET) (n=26)

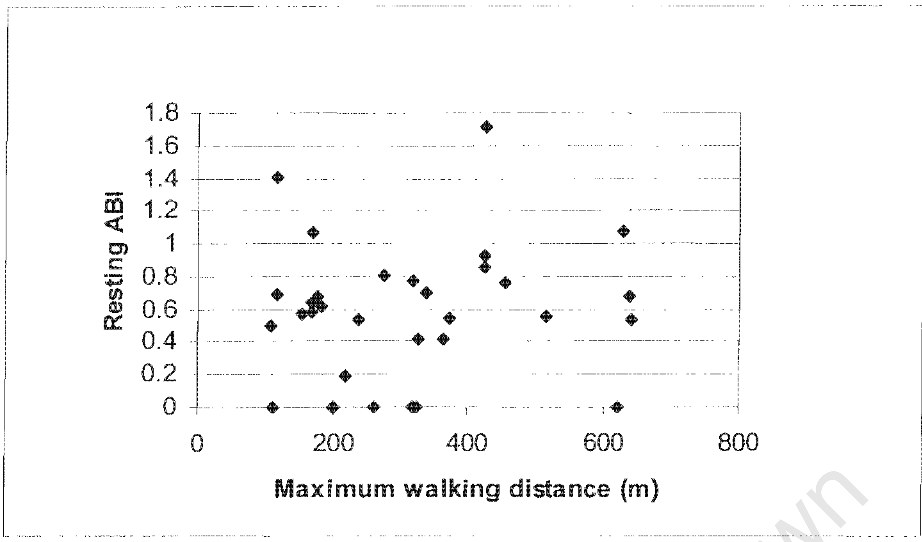


Figure 3.5 Relationship between resting ABI and maximum walking distance on the graded treadmill exercise test (GTET) (n=31)

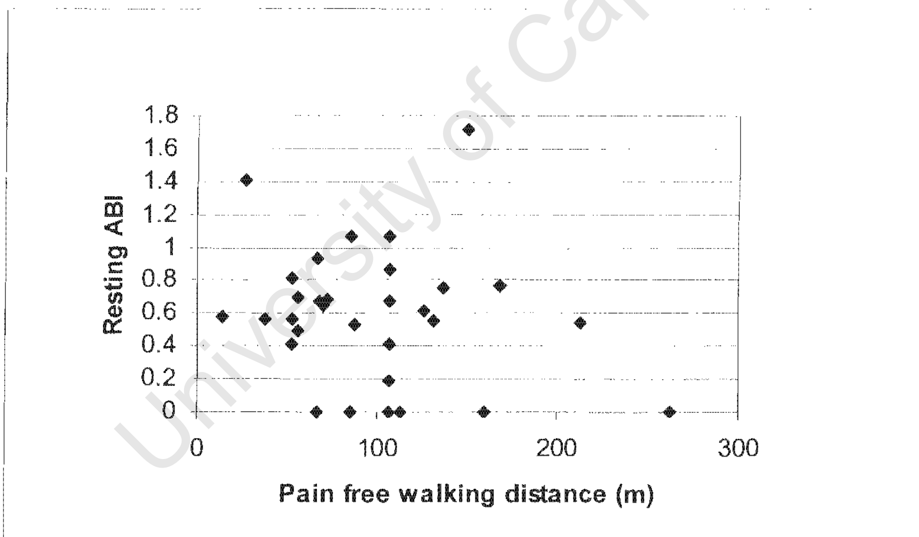


Figure 3.6 Relationship between resting ABI and pain free walking distance on the graded treadmill exercise test (GTET) (n=31)

To determine if any relationship existed between the observed walking tolerance during the six minute walk test and selected demographic data and physiological variables in patients with PVD, a correlation analysis was performed. Results are detailed in Table 3.9

Table 3.9 Results of a correlation analysis between measures of walking tolerance on the six minute walk test and demographical data and physiological variables of thirty one patients with PVD

	MWD (six minute walk test)	PFWD (six minute walk test)
Age (yrs)	NS	NS
Mass (kg)	NS	r=0.51 n=31 P=0.003
BMI (kg/m^2)	NS	NS
Fat %	NS	NS
DOD (months)	r=0.36 n=31 P=0.049	
Smoking (pk years)	NS	NS
p-e venous lactate (mmol/L_	NS	NS
Total pain (units)	NS	NS
Peak VO_2 ($mlO_2 \cdot kg^{-1} \cdot min^{-1}$)	r=0.52 N=31 P=0.003	r=0.4 N=31 P=0.034
Peak VE (L/min)	NS	NS
Peak RER (units)	NS	NS
ABI (units)	NS	NS
peABI (units)	NS	NS
Pr gradient (%)	r=-0.53 n=26 P=0.006	NS
Max HR (bpm)	NS	NS
Rec HR (bpm)	r=-0.33 n=31 P=0.073	NS
MWD(GTET)	r=0.54 n=31 P=0.002	r=0.58 n=31 P=0.001
PFWD (GTET)	NS	r=0.39 n=31 P=0.033

Abbreviations: yrs=years, **kg**=kilogram, **BMI**=body mass index, %=percentage, **DOD**=duration of disease, **Pk yrs**=pack years, **pe**=post-exercise, **Pk**=peak, **VE**=minute ventilation, **VO_2**=oxygen consumption, **RER**=respiratory exchange ratio, **ABI**=ankle brachial index, **peABI**=post exercise ankle brachial index, **Pr**=pressure, **HR**=heart rate, **bpm**=beats per minute, **MWD**=maximum walking distance, **PFWD**=pain free walking distance, **m**=meters, **GTET**=graded treadmill exercise test, **r Value**=correlation coefficient, **NS**=non significant

Maximum walking distance and pain free walking distance correlated significantly to peak VO_2 (Table 3.9). There was a significant correlation between the maximal walking distance during the treadmill test and the maximal walking distance during the six minute walk test. This is shown in Figure 3.7. Similarly a significant correlation was found between maximum walking distance during the treadmill test and pain free walking distance during the six minute walk test (Figure 3.8). A weaker but significant correlation was found between pain free walking distance during the treadmill test and pain free walking distance during the six minute walk test (Figure 3.9).

There was a weak but significant correlation between maximum walking distance during the six minute walk test and the ankle brachial pressure gradient (Figure 3.10). The greater the reduction in ankle pressure after the treadmill exercise test, the less the MWD during the six minute walk test.

Pain free walking distance during the six minute walk test correlated significantly to body mass (Table 3.9). Duration of PVD correlated weakly but significantly to MWD on the six minute walk test (Table 3.9). No significant correlations were found between age, BMI, fat percentage, smoking and walking tolerance on the six minute walk test.

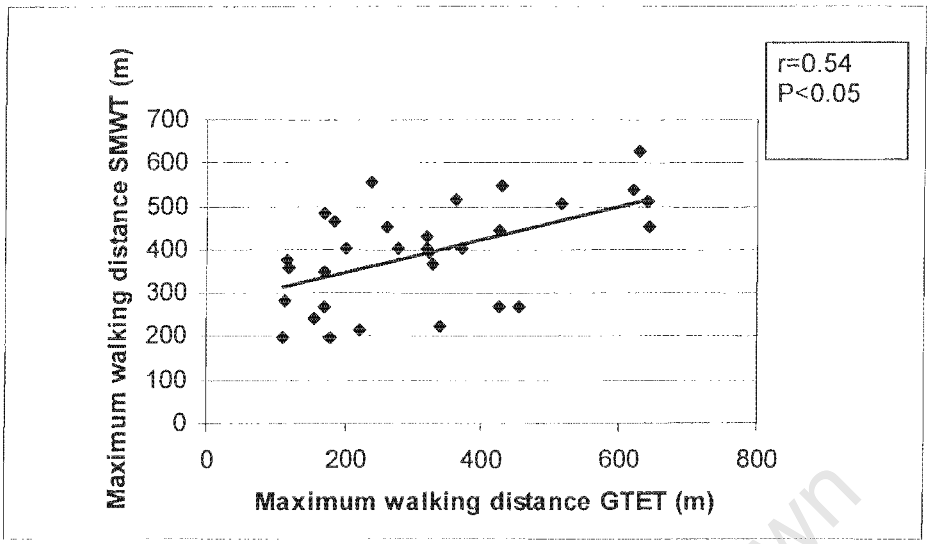


Figure 3.7 Relationship between maximum walking distance on the graded treadmill exercise test (GTET) and maximum walking distance on the six minute walk test (SMWT) (n=31)

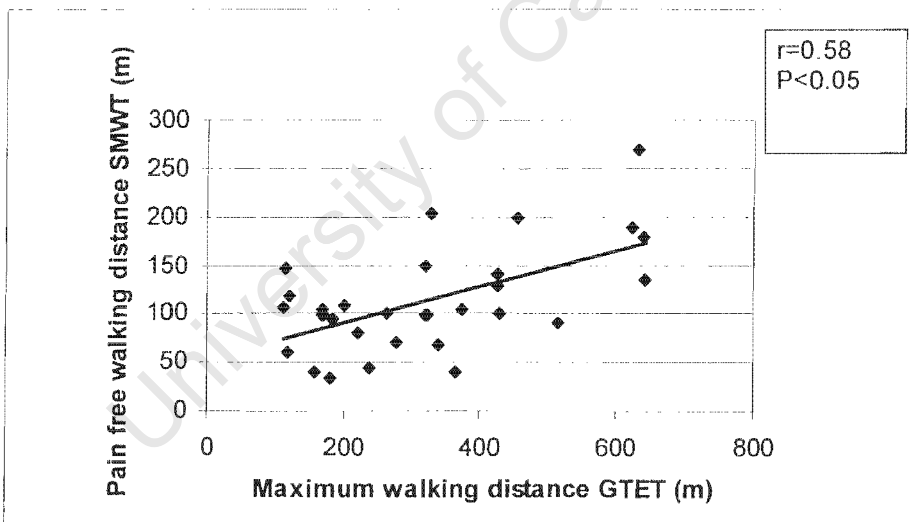


Figure 3.8 Relationship between maximum walking distance on the graded treadmill exercise test (GTET) and pain free walking distance on the six minute walk test (SMWT) (n=31)

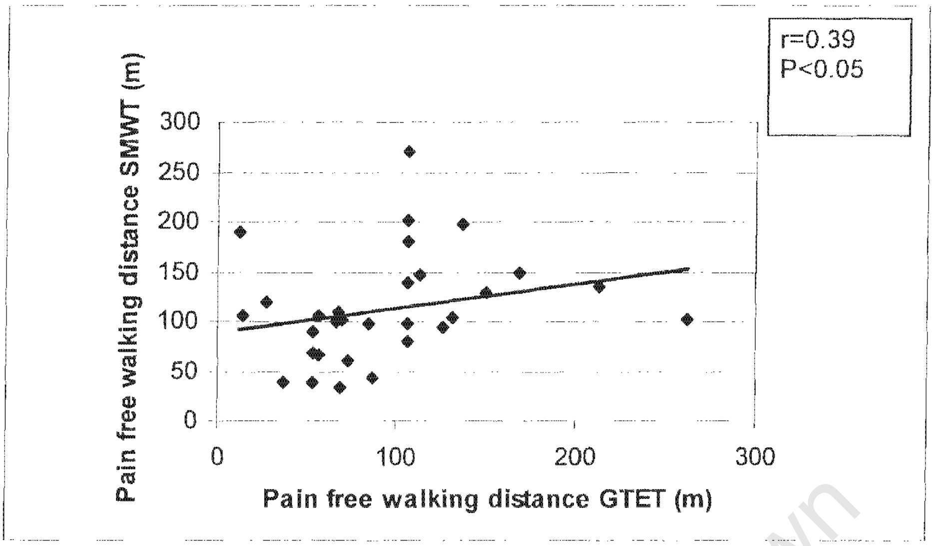


Figure 3.9 Relationship between pain free walking distance on the graded treadmill exercise test (GTET) and pain free walking distance on the six minute walk test (SMWT) (n=31).

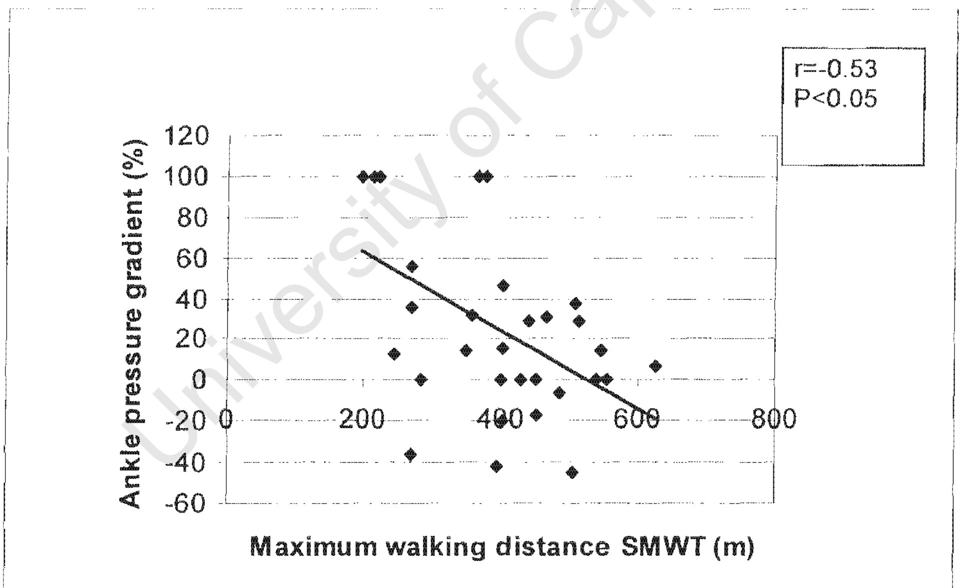


Figure 3.10 Relationship between ankle pressure gradient and maximum walking distance on the six minute walk test (SMWT) (n=26).

Discussion

Results from this study confirm that peripheral vascular disease exists as part of a vascular disease affecting multiple organs. Almost half of the patients had coronary artery disease; twenty six percent had undergone coronary artery bypass surgery (CABG) and nineteen percent had a history of myocardial infarction (MI). Six percent had a history of heart failure. Almost half the patients had diabetes and a small number had cerebrovascular disease, respiratory disease and arthritis.

Moreover this group of patients displayed the typical risk factor profile for PVD as described by Murabito et al. (1997). Murabito et al. (1997) found that typically patients with PVD are usually over the age of sixty years (mean age 64 years old) and men experience nearly double the rate of claudication that women experience. Serum cholesterol concentrations, hypertension, cigarette smoking, diabetes and coronary artery disease were associated with increased risk for intermittent claudication (IC). Smoking was associated with a 1.5-fold increased risk for IC; diabetes and stage 2 or greater hypertension conferred a >2-fold increased risk; and coronary artery disease nearly tripled the risk for IC.

In the present study, the average age was sixty-three years and 61% of the population was male and 39% was female. As mentioned previously patients in the present study had coronary artery disease, diabetes and hypertension. Only twenty six percent were non-smokers. These results show that the population with peripheral vascular disease in this study displayed a risk factor profile similar to the profile found in the study by Murabito et al. (1997). A similar risk profile was found in another study on exercise and patients with PVD with a coronary artery disease incidence of 41% and hypertension occurrence of 77% (Izquierdo-Porrera et al. 2000).

These findings indicate that patients with peripheral vascular disease should participate in regular physical activity. Regular physical activity reduces all cause mortality (Paffenbarger et al. 1986) and has a beneficial effect in reducing the risk of cardiovascular disease (Powell et al. 1987; Paffenberger et al. 1984). Furthermore, habitual exercise reduces blood pressure (Kelley & McClellan 1994) and exercise rehabilitation has a favourable effect on lipid profile (Lavie et al. 1994; Pasquali et al. 2001).

Obesity was not identified as a risk factor for PVD in the study by Murabito et al. (1997). However patients in the present study were, according to standards set out by the Panel on Energy, Obesity, and Body Weight Standards, obese (Jaequier E 1987). The average BMI was 27±4.7. According to the Panel this value falls in the category of Grade 1 obesity. Mean percent body fat for males and females in this sample group indicated that 69% of females and 39% of males were obese (body fat percent greater than 30%). Weight, BMI and fat percentage values of patients in this study compared similarly to samples of PVD patients in other studies (Womack et al. 1997; Gardner et al. 1999; Montgomery et al. 1998). Therefore obesity may be a risk factor for patients with PVD.

A limitation of the present study was an absence of a control group. However studies from this laboratory have assessed exercise tolerance in patients with chronic heart failure (Derman 1995) and patients with chronic obstructive pulmonary disease (Coleman 1998) and controls (Table 3.7). These data will assist in discussing the physiological response of patients with PVD to exercise.

Patients with PVD in the present study were exercise intolerant. This was demonstrably apparent, firstly, by their low mean peak oxygen consumption values during exercise. Values indicated in other studies on patients with PVD are similarly low (Gardner et al. 1999, Hiatt et al. 1988). In comparison to patients with COPD (Coleman 1998), the patients in the present study had similar peak VO_2 values but shorter six minute walking distances. Therefore it would seem that claudication pain, not the ability to attain peak VO_2 limits walking tolerance in patients with PVD.

Patients in the present study had low RER values indicating that they terminated exercise at an early stage in their maximal exercise test. Patients therefore in the present study did not fulfil the criteria of a maximal exercise test as stipulated by the ACSM guidelines (ACSM 1991). Moreover when comparing the RER values found in the present study to values found in patients with chronic heart failure (Derman 1995) or COPD (Coleman 1998), patients in the present study had lower RER values. This is again indicative that pain in the peripheral skeletal muscle, inhibits patients from reaching their maximal exercise capacity.

Patients in the present study had low peak venous lactate concentrations. In comparison to patients with COPD (Derman 1995) and chronic heart failure (Coleman 1998), and to the controls in these studies, peak lactate concentrations in the present study were lower.

This is an interesting finding because it is common belief amongst exercise physiologists studying peripheral vascular disease that anaerobic glycolysis and the resultant increase in lactate concentration in the ischaemic muscles and blood leads to claudication pain in patients with PVD (Lundgren et al. 1989, Tan et al. 2000). A review article by Tan et al. (2000) stated, "In patients with peripheral vascular disease, increasing the workload causes an inequality in the supply of and demand for oxygen. Aerobic generation of adenosine triphosphate (ATP) becomes inadequate and anaerobic metabolism predominates. The result (of exercise) is an increase in lactic acid production, and a depletion of ATP and creatine phosphate (CP), leading to pain" (Tan et al. 2000).

This theory of walking intolerance in patients with PVD stems from the popular cardiovascular/anaerobic theory of fatigue which suggests that fatigue develops when the exercising skeletal muscles fail to get enough oxygen to them and as a result have to rely on anaerobic glycolysis to produce enough ATP to continue exercising (Noakes 1999). A by-product of anaerobic glycolysis is lactate accumulation in the skeletal muscles and blood.

Therefore much research in patients with PVD has revolved around investigating peripheral adaptations which may delay the onset of anaerobic glycolysis and therefore contribute to increases in walking tolerance. These adaptations include increase in the number of skeletal oxidative enzymes (Holm et al. 1973; Lundgren et al. 1989; Hiatt et al. 1996) and improved oxygen extraction by the skeletal muscles (Zetterquist 1970; Sorlie and Myhre 1978). Indeed Lundgren et al. (1989) cited above stated that "the results of the present study (his study) support the contention that an improved oxidative capacity is beneficial in improving PFWD. But as long as there is blood flow restriction, there will be a point when flow becomes the limiting factor producing hypoxia, lactate accumulation and pain."

In the study that Tan et al. (2000) sited above, venous and arterial lactate concentrations are indeed higher in patients with PVD at maximal exercise capacity than in age-matched controls at maximal exercise capacity (Pernow et al. 1975) and lower after surgical reconstruction or physical training in these patients (Pernow et al. 1975, Ruell et al. 1984). However, patients in the above two studies and the present study, failed to show elevated blood lactate concentrations at maximal exercise. Concentrations of blood lactate never reached higher than $4mmol.L^{-1}$ in either study. Values in a normal population at maximal exercise capacity reach far greater values than this ($7.59mmol.L^{-1}$) and the subjects never experience claudication (Nichols et al. 1997, Beneke et al. 1996).

Despite venous and arterial lactate concentrations being higher in PVD patients than controls at maximal exercise capacity (Pernow et al. 1975) and lower after surgical reconstruction or physical training in patients with PVD (Pernow et al. 1975, Ruell et al. 1984

Moreover, lactate in skeletal muscle was assessed from muscle biopsies in patients with PVD and controls at maximal exercise capacity (Pernow et al. 1975), there was no difference between the two groups in skeletal muscle lactate concentrations at maximal exercise. Therefore it cannot be said that lactate "leads to pain" (Tan et al. 2000) as the control group in the study by Pernow et al. (1975) did not experience claudication at maximal exercise. Also much higher blood lactate concentrations in healthy athletes does not cause the symptom of intermittent claudication.

Finally, in the present study peak post exercise venous lactate concentrations did not correlate to pain free walking distance. We found that patients with the highest venous lactate concentrations did not have the shortest pain free walking distances. Moreover, as mentioned earlier, patients in the present study, in comparison to studies in this laboratory on patients with chronic heart failure (Derman 1995) and chronic obstructive pulmonary disease (Coleman 1998), had low peak venous lactate concentrations and similar peak VO_2 values. Therefore it would seem that it was more likely that the pain in the periphery limited walking performance and therefore blood lactate concentration was low, rather than an accumulation of blood lactate limiting walking performance.

Therefore, the suggestion that accumulation of lactate in the skeletal muscles and blood leads to claudication pain, (as has been suggested by Lundgren et al. 1989 and Tan et al. 2000), is unlikely. There has to be some other mechanism for the pain that patients with PVD experience. Unfortunately the mechanism for patients with PVD experiencing pain is beyond the scope of this thesis. Recently however, it has been suggested that fatigue in the normal population develops when muscle recruitment is reduced by the motor cortex causing exercise to terminate. This happens because inhibitory reflexes arise from the exercising muscles and feedback to the spinal cord and motor cortex reducing skeletal muscle recruitment. This theory has been reviewed by (Noakes 1999, Davis and Bailey 1991). It is possible that pain in the peripheral muscles may also act centrally in this manner to reduce muscle recruitment by the motor cortex causing patients to terminate exercise.

It is widely believed that improvements in walking distance are related to increased blood flow following exercise training in patients with PVD (Alpert et al. 1969, Gardner et al. 2001). Therefore, the ABI is commonly measured.

Results of the clinical evaluation of the pulse status before and after exercise in the present study were as expected. Resting ABI was less than one in the patients in the present study, this is as expected for these patients and is indicative of peripheral vascular disease (Newman et al. 1993). Post exercise ABI was lower than resting ABI. This is known as the post exercise hyperaemic response and is thought to be caused by blood flow being directed towards the ischaemic muscle and away from the ankle vessels causing the ankle pressure to drop (Bernstein 1993). Patients in the present study had an ankle pressure gradient of around thirty percent. The ankle pressure gradient is a measure of the degree the ankle pressure decreases after exercise and it is accepted that the steeper the gradient the more prolific the disease (Amirhamzeh et al. 1997). The results of the ankle pressure gradient in the present study were similar to the results found in another study in patients with peripheral vascular disease measuring the percent change in ankle pressure after a bout of exercise (Amirhamzeh et al. 1997).

However, in this study resting ABI did not correlate to pain free or maximum walking distances measured during the graded treadmill exercise test. Therefore functional capacity was independent of ABI in patients with PVD in this study. This finding is in agreement with a study by Creasy et al. (1990) who reported that improvements in walking performance were not accompanied by improvements in ABI in patients with PVD. If ABI is not indicative of functional capacity, the use of a graded treadmill exercise test to monitor functional capacity in patients with PVD is superior to using the ABI. An important limitation in this study was that 14 of the patients had diabetes which could have affected their ankle pressure measurements. However only in four of the diabetic patients did this seem to be the case. As patients were very hard to recruit, no diabetic patients were excluded from the study.

In this study there was no correlation between perception of pain during the six minute walk test and maximum walking distance or pain free walking distance measured during this test. Neither was there a correlation between total pain perceived during the treadmill test and maximum walking distance or pain free walking distance measured during this test. This means that some patients, even though they perceive pain, will persevere; others will terminate exercise because of the pain experienced. This may depend on the individual's ability to tolerate pain which may be affected by past experiences of pain, and on the determination of the patient to proceed despite pain. The decision to terminate exercise is a conscious one that can be influenced by psychological beliefs.

Finally maximum walking distance on the treadmill exercise test correlated weakly but significantly with maximum walking distance on the six minute walk test with a r value of 0.54 ($p<0.005$). This is similar to the result of Montgomery et al. (1998) which reported a "r" value of 0.53 ($p<0.001$). Moreover in the present study PFWD on the treadmill test correlated weakly to PFWD on the six minute walk test.

It is concluded from this that only 29% of the variance in MWD during the treadmill test can be explained by the variance in MWD during the six minute walk test and only 15% of the variance in PFWD during the treadmill test can be explained by the variance in PFWD during the six minute walk test. Therefore the six minute walk test can be used as a tool for measuring MWD and PFWD in patients with peripheral vascular disease. Treadmills are not always available and are expensive so an alternative test to measure maximum and pain free walking distance is needed. However, this data suggests that the treadmill test and the six minute walk test may measure walking distances quite differently. This may be because during the treadmill test the speed is kept constant whereas during the six minute walk test, the subject chooses his/her walking speed. In addition the six minute walk test is restricted to six minutes whereas the treadmill test can continue indefinitely. In the present study, MWD during the six minute walk was significantly different to MWD during the treadmill test (392 ±117 vs 317 ±166 m, SMWT vs GTET, p=0.04) and PFWD during the six minute walk test was slightly more than PFWD during the graded treadmill exercise test (112 ±54 vs 98 ±53 m, SMWT vs GTET, p=NS) although this was not statistically different.

Conclusion

In conclusion this study confirmed that PVD is part of a multi-organ vascular disease. Patients with PVD in the present study had a variety of co-morbid conditions (CAD and diabetes) and recognised risk factors (hypertension, smoking history, hypercholesterolaemia, older age, male gender) for peripheral vascular disease.

Patients with PVD terminate exercise at low peak VO_2 values and short six minute walking distances, they are therefore exercise intolerant. Furthermore, patients with PVD terminate exercise at low peak RER values and low peak venous lactate concentrations. In this study patients with the highest venous lactate concentrations did not have the shortest pain free walking distances or maximum walking distances. Therefore this study demonstrated that peak post exercise venous lactate concentrations cannot predict pain free walking distance on the treadmill in patients with peripheral vascular disease.

This study found that resting ABI's do not predict maximum or pain free walking distances in patients with peripheral vascular disease. Therefore the use of a graded treadmill exercise test to monitor functional capacity in patients with PVD is superior to using the ABI.

Furthermore the perception of pain did not correlate to MWD or PFWD in either the GTET or the SMWT in patients with PVD. Even though patients perceive pain, it is their ability to tolerate pain that allows them to walk further.

Finally MWD and PFWD during the six minute walk test correlated weakly but significantly to MWD and PFWD on the treadmill exercise test. Therefore although the six minute walk test can be used as a clinical tool for measuring maximum walking distances in patients with PVD, the six minute walk test and the treadmill exercise test measure walking distances quite differently. The six minute walk test allows the patient to walk at his or her own speed for a fixed time period and the treadmill test is set at a fixed speed but allows the patient to walk indefinitely. Therefore one cannot expect similar walking distances from the two tests in patients with PVD.

CHAPTER 4: EFFECTS OF UPPER BODY STRENGTH TRAINING VS CONVENTIONAL EXERCISE REHABILITATION IN PATIENTS WITH PERIPHERAL VASCULAR DISEASE (PVD)

Introduction

As described in chapter 1, patients with peripheral vascular disease (PVD) develop the symptom of intermittent claudication on walking.

Since 1898 exercise training has been advised as a therapy for intermittent claudication when Wilhelm Erb suggested that muscle work increased blood flow to the ischaemic limb (Erb W 1898). A number of randomised controlled trials have indeed shown that exercise training improves walking tolerance in patients with PVD (Walker et al. 2000, Creasy et al. 1990, Mannarino et al, 1989, Hiatt et al. 1990, Patterson et al. 1997, Parker-Jones et al. 1996, Price et al. 1997, Holm et al. 1973, Hiatt et al. 1996).

Typically exercise training programmes for patients with PVD have included walking as the mode of exercise training (Hiatt et al. 1990, Hiatt et al. 1996, Parker-Jones et al. 1996, Mannarino et al. 1989).

Exercise programmes that involve instructing the patient to walk to near maximal pain have shown to incur greater improvements in MWD and PFWD in patients with PVD than programmes which instruct the patient to walk to the onset of pain (Gardner et al. 1995). Forcing patients with peripheral vascular disease to walk, (especially to near maximal pain) is problematic. Claudication is very painful and the patient may dread the exercise training which in turn may lead to poor attendance of training sessions. Recently, a group in the United Kingdom compared the effects of a six week pain free upper limb cycle ergometry exercise programme using arm cranks to a lower limb cycling exercise programme, and a control group. Their findings were that MWD and PFWD improved equally in both training groups in patients with PVD (Walker et al. 2000). Therefore it was concluded that increases in MWD and PFWD occur despite the mode of exercise training used. A pain free exercise programme was an important development for exercise prescription for patients with PVD.

However, arm cranks are not regular gym apparatus, whereas upper body strength training equipment is found in most gymnasiums. Furthermore only one study has ever examined the effects of strength training on patients with PVD (Hiatt et al. 1996). Therefore the principle aim of this study was to compare the effects of a 6 wk upper body strength training programme (UBST) to conventional (walking, cycling, circuit) exercise rehabilitation (CER) in patients with PVD. A third group of patients with PVD who were given conventional medical treatment; "walk as much as possible at home," served as the control group. Patients in the control group had also been told by their medical doctors to ingest 150mg of salicylic acid.

The duration of most of the training programmes in the randomized controlled trials discussed in the literature review were either three months or six months (Larsen and Lassen 1966, Holm et al. 1973, Mannarino et al. 1989, Hiatt et al. 1990, Lundgren et al. 1989, Creasy et al. 1990, Parker-Jones et al. 1996, Hiatt et al. 1996, Paterson et al. 1997). However to embark on a three or six month training programme can be quite daunting for the patient, however a six week programme may be more manageable for the patient to commit to initially, and therefore it is important to determine if improvements in physiological parameters occur during this period.

Therefore this study was designed to determine if a short duration (6 wk) upper body strength training programme improved walking tolerance in patients with PVD. A secondary aim of this study was to determine if a short duration (6 wk) conventional exercise rehabilitation programme is superior to the standard advice given to patients by their doctors ie "walk as much as possible at home," in patients with PVD.

Methods

Patient characteristics on entry to the study

31 patients with peripheral vascular disease were recruited from vascular surgeons at the Department of Vascular Surgery at Groote Schuur Hospital and from the Kingsbury Hospital, Cape Town, South Africa. Details of diagnostic and inclusion criteria are described in Chapter Two. Patients were randomly assigned to one of three treatment groups. Randomisation was carried out before patients entered the programme, numbers were given to each "potential" patient, the numbers were randomized to one of three treatment groups. When the first patient arrived, he/she was told which group she (number 1) had been randomized to. Only one patient randomized to the control group refused this treatment and was placed in the CER group.

Twenty six patients completed the study, nine in the CER group, nine in the UBST group and eight in the control group. Five patients dropped out of the study: one suffered a stroke, two underwent peripheral vascular angioplasty before they could be re-tested, one suffered a ruptured biceps tendon and one was diagnosed with cancer.

Exercise testing prior to intervention treatment

All three groups were tested prior to commencement of the study. All tests were conducted according to the methods detailed in Chapter Two. On the first visit to the laboratory, a full anthropometrical analysis was performed for determination of body composition. Furthermore, a full medical history was taken from each patient and medical records obtained from the vascular surgeon and cardiologist. The patients were familiarised with the treadmill according to the methods detailed in Chapter Two.

On the second visit, each subject performed a graded treadmill exercise test to maximal claudication pain. The following variables were measured at regular intervals throughout the exercise bout and at peak exercise: oxygen consumption (VO_2), minute ventilation (VE), respiratory exchange ratio (RER), heart rate (HR), and perception of claudication pain.

Resting venous blood lactate concentration and brachial and ankle blood pressures were measured prior to commencement of the treadmill exercise test. Post-exercise peak venous blood lactate concentration was measured at minute three of recovery and recovery brachial and ankle blood pressures were measured two minutes after the treadmill exercise test.

Twenty minutes after completion of the graded treadmill exercise test, each subject performed a six minute walking test on an indoor track and heart rate and perceived claudication pain were recorded each minute. Recovery heart rate was recorded at the end of the first minute after exercise.

Intervention Treatment

The UBST group and the CER group participated in exercise rehabilitation at the Cape Medial Rehabilitation Centre, Claremont Hospital, Cape Town, South Africa according to the methods detailed in Chapter Two. Patients had to complete a minimum period of 6 weeks of training before re-testing took place. Details of the training regime are included in Chapter 2 and in the Appendices section.

Statistical analysis

Data were collected and results analyzed as detailed in Chapter 2.

Pain ratings for each patient were converted to a single variable by plotting an area under the curve for each patient. The data were normalized by expressing the pain measure (Y axis) relative to 100% of elapsed time (the X-axis). Thereafter an analysis of variance with repeated measures was used to detect differences between groups over time in this variable.

The Kruskall Wallis anova was used to detect differences between groups in Δ (delta) pain free walking distance on the treadmill exercise test (pre-treatment to post-treatment) and Δ (delta) pain free walking distance on the six minute walk test (pre-treatment to post-treatment) as these data were not normally distributed.

A Fishers exact test was used to assess differences between groups in morbidity, gender, race and the medications ingested by each group.

A dependent t-test was used to assess changes in strength in the UBST group before and after treatment. An independent t-test was used to assess differences in compliance to training sessions between the UBST group and the CER group.

A between subjects analysis of variance was used to assess differences in the length of the intervention period between groups.

Results

General characteristics and medical history of patients with PVD in the UBST, CER and CONT group on entry to the study

General characteristics of the treatment groups and the control group on entry to the study are detailed in Table 4.1.

Table 4.1 General characteristics of patients with PVD in the treatment groups and the control group on entry to the study

GROUP	UBST (n=9)		CER (n=9)		CONT (n=8)	
Age (yr)	66 ±13		58 ±13		62 ±10	
Mass (kg)	79 ±19		77 ±14		84 ±14	
BMI (kg/m2)	27 ±5		27 ±6		30 ±3	
DOD (months)	34 ±33		24 ±30		29 ±30	
Smoke(pk yr)	34 ±26		15 ±32		16 ±21	
Male (nr) (%)	7	(77%)	5	(55%)	5	(63%)
Female	2	(22%)	4	(44%)	3	(38%)
Mixed	4	(44%)	3	(33%)	1	(13%)
Caucasian	5	(55%)	6	(67%)	7	(88%)

Abbreviations: Yr=year, **kg**=kilograms, **BMI**=body mass index, **m^2**=meter squared, **DOD**=duration of disease, **nr**=number of patients in each group, **pk yr**=pack year, **%**=percentage of patients in each group, **mixed**=mixed ancestral origin, **SD**=standard deviation, **UBST**=upper body strength training group, **CER**=conventional exercise rehabilitation group, **CONT**=control group. Values are expressed as means ±SD

All the groups were similar in mean age, mass, BMI and months of PVD (duration of disease) and pack years of smoking. There was no difference between groups in the number of males and females in each group, and people of mixed ancestral origin or caucasian origin in each group.

The medical history of the treatment groups and the control group are listed in Table 4.2

Table 4.2 Medical history of patients with PVD in the two treatment groups and the control group on entry to the study

	UBST (n=9)	CER (n=9)	CONT(n=8)
Peripheral vascular disease	9 (100%)	9 (100%)	8 (100%)
Percutaneous transluminal angioplasty and stent	2 (22%)	2 (22%)	2 (25%)
Bypass graft	0 (0%)	1 (11%)	1 (11%)
Coronary artery disease	3 (33%)	4 (44%)	4 (50%)
History of heart failure	0 (0%)	2 (22%)	0 (0%)
History of MI	2 (22%)	2 (22%)	0 (0%)
History of angina pectoris	1 (11%)	2 (22%)	2 (25%)
Coronary artery bypass graft	2 (22%)	1 (11%)	2 (25%)
Pacemaker	1 (11%)	0 (0%)	0 (0%)
Stent	0 (0%)	1 (11%)	0 (0%)
Percutaneous transluminal angioplasty	0 (0%)	1 (11%)	0 (0%)
Cerebral vascular disease	3 (33%)	0 (0%)	1 (13%)
History of transient ischaemic attack	1 (11%)	0 (0%)	0 (0%)
History of stroke	0 (0%)	0 (0%)	0 (0%)
Carotid endarterectomy	1 (11%)	0 (0%)	0 (0%)
Risk factors for PVD: Hypercholesterolaemia	2 (22%)	5 (56%)	4 (50%)
Hypertension	6 (67%)	5 (56%)	8 (100%)
Sedentary	9 (100%)	9 (100%)	8 (100%)
Obesity	3 (33%)	6 (67%)	8 (100%)
Diabetes	2 (22%)	5 (56%)	4 (50%)
Current smokers	2 (22%)	1 (11%)	1 (13%)
Former-smokers	7 (78%)	3 (33%)	4 (50%)
Respiratory disease	1 (11%)	1 (11%)	0 (0%)
Rheumatoid arthritis	2 (22%)	0 (0%)	1 (13%)
Osteoarthritis arthritis	2 (22%)	0 (0%)	3 (38%)

Values are expressed as number of patients in each group and the percentage of patients in each group

The medical history of the patients in this study has been described in Chapter 3. Therefore the medical history of this population will not be described here. However, it is important to note that none of the procedures or events listed above took place within a year of the start of the study, no patients had angina at the time of entry to the trial and there was no statistically significant difference in the medical history of each group in any of the procedures, events or diseases listed above. Because there was no difference between groups in Table 4.1 and Table 4.2 the groups were comparable and the randomization techniques adequate.

Medications ingested by the patients with PVD in the treatment groups and the control group during the study are listed in Table 4.3

Table 4.3 Patients ingesting medication in the two treatment groups and the control group during the course of the study

	UBST (n=9)	CER (n=9)	CONT (n=8)
Medications ingested			
Serum lipid reducing agents	2 (22%)	4 (44%)	4 (50%)
Antihypertensive agents	6 (67%)	4 (44%)	8 (100%)
Warfarin	1 (11%)	2 (22%)	0 (0%)
Acetyl salycilic acid	7 (78%)	5 (56%)	6 (75%)
Oral hypoglycaemic agents	1 (11%)	5 (56%)	4 (50%)
Insulin	0 (0%)	1 (11%)	0 (0%)

Abbreviations: UBST=upper body strength training group, **CER**=conventional exercise rehabilitation group, **CONT**=control group. Values are expressed as number of patients in each group and the percentage of patients in each group ingesting the medication

There was no statistically significant difference between groups with respect to the medications ingested.

Intervention period and compliance to exercise in patients with PVD in the treatment groups and the control group

Table 4.4 details the compliance to exercise training of the two treatment (UBST and CER) groups.

Table 4.4 Compliance to exercise training sessions during intervention in the two treatment groups

Group	UBST (n=9)	CER (n=9)
% attendance at training sessions	89±14	90±13

UBST=upper body strength training group, **CER**=conventional exercise rehabilitation group. Values are expressed as means ±SD

Compliance with training sessions was high. There was no statistically significant difference in percentage compliance to the exercise training sessions between the UBST group and the CER group.

Training response in patients with PVD in the UBST, CER and CONT groups after the six week intervention period

Improvements in strength before and after training in the UBST group are detailed in Table 4.5

Table 4.5 Improvement in strength (lb) from entry to exit of the training programme in the UBST group

Plate loaded machine	Strength before training (lbs)	Strength after training (lbs)	% change	P value
Lower back	54 ±7	84 ±21	56	P=0.002*
Abdominal	49 ±3	66 ±9	35	P=0.0003*
Rotary chest	22 ±7	43 ±13	49	P=0.0003*
Rotary upper back	14 ±2	29 ±16	107	P=0.02*
Rotary lat	41 ±6	58 ±15	41	P=0.009*
Rotary shoulder	12 ±3	16 ±5	33	P=0.08
Pec-dec	31 ±7	41 ±11	32	P=0.001*
Tricep extension	22 ±7	34 ±12	55	P=0.002*
Bicep curl	17 ±9	32 ±17	88	P=0.02*
Lat pull down	42 ±7	60 ±10	43	P=0.001*

Abbreviations: lb=pounds. * =p<0.05 strength entry vs strength exit. Values expressed as mean ±SD

There was a statistically significant improvement in strength in the UBST group after six weeks of training on all but one (rotary shoulder) of the upper body strength plate loaded machines (Table 4.5).

Table 4.6 lists the peak cardiovascular measurements (peak VO_2, peak VE, peak RER and peak HR) measured during the graded treadmill exercise test on entry to the study and after training in the treatment groups (UBST and CER) and the control group (CONT).

Table 4.6 Peak VO_2, peak VE, peak RER and peak HR during the graded treadmill exercise test on entry to the study and after the six week intervention period

	UBST (n=9)		CER (n=9)		CONT (n=8)	
	O wks	6 wks	O wks	6 wks	O wks	6 wks
Pk VO_2 $mlO_2 \cdot kg^{-1} \cdot min^{-1}$	19.7 ±4.6	18.7 ±6.1	14.8 ±3.4	19.4±4.6*	18.2 ±3.9	17.6 ±3.4
Pk VE $L.min^{-1}$	47.6 ±20	47.0 ±19	37.9 ±10	45.0 ±12	48.0 ±14	51.0 ±15
Pk RER (units)	0.93 ±0.1	0.95 ±0.7	0.94 ±0.1	0.99 ±0.1	1.02 ±0.2	1.0 ±0.2
Pk HR bpm	107 ±25	110 ±26	118 ±17	122 ±19	122 ±15	128 ±10

Abbreviations: **Pk**=peak, **VO_2**=oxygen consumption, **VE**=ventilation, **RER**=respiratory exchange ratio, **HR**=heart rate, **wks**=weeks, **bpm**=beats per minute, **UBST**=upper body strength training, **CER**=conventional exercise rehabilitation group, **CONT**=control group. *=$p<0.05$ CER vs CONT and CER vs UBST. All values expressed as mean ± SD.

There was no significant difference between the groups with respect to peak VO_2, peak VE, peak RER, and peak HR on entry to the study

Peak VO_2 in the CER group increased significantly more after training than the control group (29% vs -1%, CER vs control, p=0.008) (Fig 4.1) and the UBST group (29% vs -6%, CER vs UBST, p=0.002) (Fig 4.1), indicating a training response in the CER group.

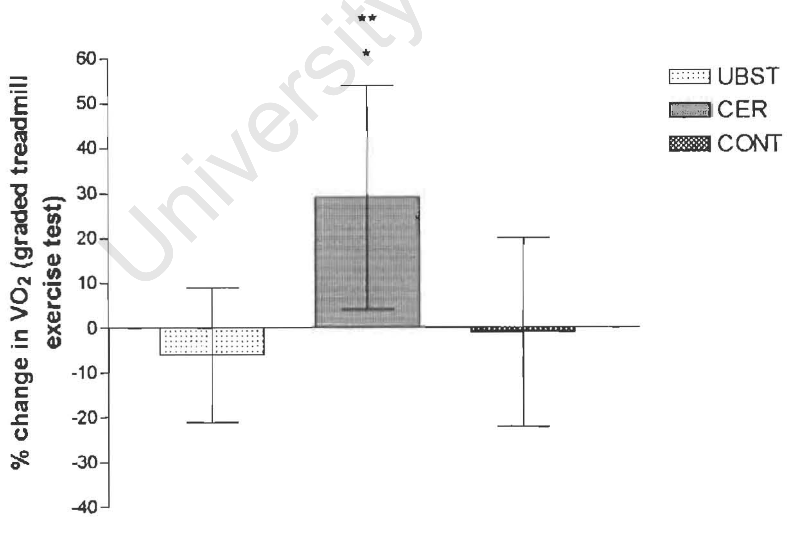


Figure 4.1 Percentage change in maximum oxygen consumption after six weeks of intervention. ** =p<0.05 CER vs UBST * =p<0.05 CER vs CONT. All values expressed as mean ± SD

However there was no significant difference between groups with respect to peak RER or peak HR and peak VE after six weeks of training although there was a trend for VE to increase in the CER group after training (37.9 ±10 to 45.0 ±12 $L.min^{-1}$, pre vs post, P=NS).

Table 4.7 lists the submaximal cardiovascular measurements achieved during the graded treadmill exercise test on entry to the study and after the six week intervention period in the treatment groups (UBST and CER) and the CONT group.

Table 4.7 Submaximal VO_2, VE, RER and heart rate measurements during the graded treadmill exercise test in the treatment groups and the control group on entry to the study and after the six week intervention period

	UBST (n=9)		CER (n=9)		CONT (n=8)	
Weeks	**O wks**	**6 wks**	**O wks**	**6 wks**	**O wks**	**6 wks**
VO_2 2min $mlO_2 \cdot kg^{-1} \cdot min^{-1}$	14.4±5	14.2±5	11.6±3	13.1±3	11.3±2	13.1±4
VO_2 4min $mlO_2 \cdot kg^{-1} \cdot min^{-1}$	15.8±4	14.0±5	13±3.2	14.3±3	14.5±3	14.3±4
VE 2min $L.min^{-1}$	30.2±11	32±13	25.3±7	25.6±5	24.9±3	31.5±10
VE 4min $L.min^{-1}$	35.1±18	33.2±12	33±6	31.9±6	34±9	35.6±14
RER 2min	0.77±0.07	0.79±0.08	0.79±0.13	0.75±0.09	0.85±0.09	0.82±0.08
RER 4min	0.84±0.09	0.88±0.07	0.9±0.15	0.86±0.14	0.89±0.11	0.89±0.10
HR 2min (bpm)	92±20	94±21	102±21	92±15*	94±15	109±11
HR 4min (bpm)	96±23	102±24	111±20	104±14 Ŧ	103±14	115±10

Abbreviations: **VO_2**=peak oxygen consumption, **VE**=minute ventilation, **RER**=respiratory exchange ratio, **HR**=heart rate **%**=percentage, **bpm**=beats per minute, **min**=minute, **wks**=weeks, **UBST**=upper body strength training group, **CER**=conventional exercise rehabilitation group, **CONT**=control group, All values expressed as mean ± SD * =P<0.05 CER vs CONT. Ŧ= p<0.05 CER vs CONT and CER vs UBST.

Heart rate at minute two during the graded treadmill exercise test was significantly lower in the CER group compared to the CONT group (-9% vs 18%, CER vs CONT, p=0.003) (Fig 4.2). Similarly, heart rate at minute four on the graded treadmill exercise test was significantly lower in the CER group compared to the CONT group (-6% vs 14%, CER vs CONT, p=0.003) (Fig 4.3) and the CER group compared to the UBST group (-6% vs 6%, CER vs UBST, p=0.004) indicating a training response in the CER group.

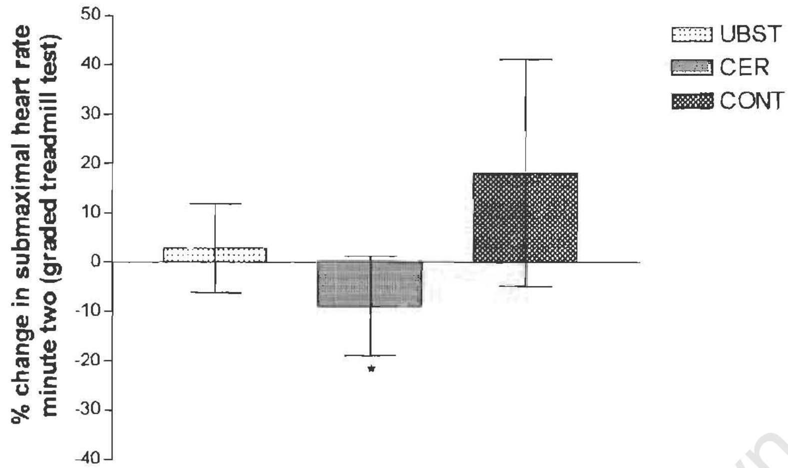


Figure 4.2 Percentage change in submaximal heart rate at minute two after six weeks of intervention. * =p<0.05 CER vs CONT. All values expressed as mean ± SD

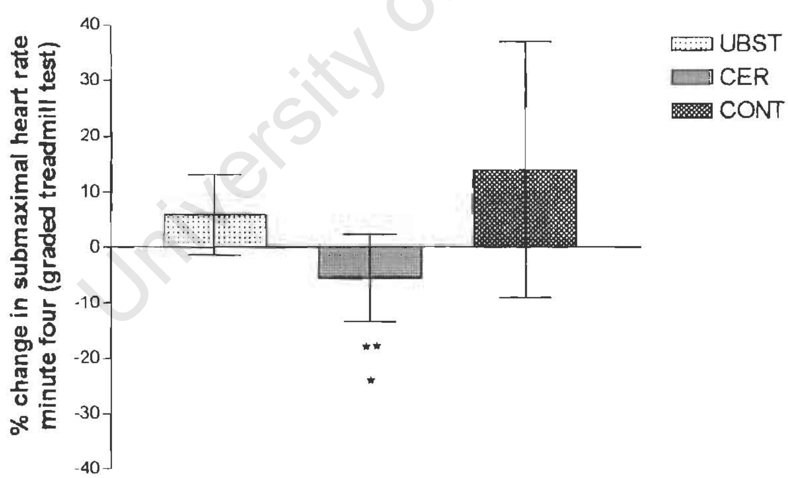


Figure 4.3 Percentage change in submaximal heart rate at minute four after six weeks of intervention. * =p<0.05 CER vs CONT and **=P<0.05 CER vs UBST. All values expressed as mean ± SD

There was no difference in percentage change in submaximal VO_2, submaximal VE or submaximal RER values between the three groups after six weeks of training.

Maximum and recovery heart rate achieved during the six minute walk test on entry to the study and after intervention in the treatment groups (UBST and CER) and the CONT group are detailed in Table 4.8.

Table 4.8 Maximum heart rate and recovery heart rate in the six minute walk test in the treatment groups and the control group on entry to the study and after six weeks of intervention

	UBST (n=9)		CER (n=9)		CONT (n=8)	
Weeks	**O wks**	**6 wks**	**O wks**	**6 wks**	**O wks**	**6 wks**
Max HR (bpm)	98±24	99±21	112±19	111±16	117±21	116±13
Rec HR (bpm)	92±25	93±19	103±22	94±18	94±23	97±23

Abbreviations: Max=maximum, **HR**=heart rate, **Rec**=recovery, **wks**=weeks, **UBST**=upper body strength training group, **CER**=conventional exercise rehabilitation group, **CONT**=control group. All values expressed as mean ± SD

On entry to the study there was no difference between groups with respect to maximum or recovery heart rate during the six minute walk test. However, recovery heart rate after the six minute walk test tended to be reduced in the CER group after training but this trend was not statistically significant. Furthermore, there was no difference between groups with respect to maximum heart rate during the six minute walk after six weeks of training.

Table 4.9 lists the anthropometric data on entry to the study, and after six weeks of intervention, in the treatment groups (UBST and CER) and the CONT group.

Table 4.9 Body mass, BMI and fat percentage of treatment groups and the control group on entry to the study and after six weeks of intervention

	UBST (n=9)		CER (n=9)		CONT (n=8)	
Weeks	**O wks**	**6 wks**	**O wks**	**6 wks**	**O wks**	**6 wks**
Mass(kg)	78.9 ±19	78.5 ±17	76.7 ±14	76.7 ±13	84 ±14	85.4 ±14
BMI(kg/m^2)	26.9 ±5.3	26.8 ±4.8	26.7 ±5.6	26.6 ±5.0	29.8 ±3.2	30.3 ±3.6
Fat %	29.7 ±5.1	28.4* ±5.6	30.6 ±5.18	30.06 ±7.3	33.6 ±6.9	34.6 ±7.5

Abbreviations: BMI=body mass index, **kg**=kilogram, **m^2**=meters squared, **%**=percentage, **wks**=weeks, **UBST**=upper body strength training group, **CER**=conventional exercise rehabilitation group, **CONT**=control group * =p<0.05 UBST vs CONT. All values expressed as mean ± SD

There was no significant difference between groups in mass, BMI or fat percentage on entry to the study. The UBST group decreased in fat percentage more than the CONT group (-8 vs +2.6 %, UBST vs CONT, p=0.006). There was no significant difference in mass or BMI among the treatment groups after six weeks of intervention.

Effect of exercise training on walking tolerance and perceived pain in patients with PVD in the UBST, CER and CONT groups

Maximum walking distance and pain free walking distance on the graded treadmill exercise test (GTET) and six minute walk test (SMWT), on entry to the study and after training in the treatment groups (UBST and CER) and the CONT group is detailed in Table 4.10

Table 4.10 Maximum walking distance, pain free walking distance and total pain during the graded treadmill exercise test and the six minute walk test in the treatment groups and the control group on entry to the study and after six weeks of intervention

	UBST (n=9)		CER (n=9)		CONT (n=8)	
weeks	**0 wks**	**6 wks**	**0 wks**	**6 wks**	**0 wks**	**6 wks**
MWD GTET (m)	390±211	399±186	300±198	514±226* Ŧ	460±200	430±151
PFWD GTET (m)	128±121	202±175	126±157	256±187	175±123	175±136
MWD SMWT (m)	441±128	484±122	373±116	425±117	415±144	408±125
PFWD SMWT (m)	170±165	169±99	119±101	157±103#	192±147	116±75
Total pain GTET (units)	302±12	271±56	284± 117	251± 162	257± 153	251± 173
Total pain SMWT (units)	327±42	391±134	359 ±126	292± 152*	359± 108	392± 150

Abbreviations: MWD=maximum walking distance, **m**=meters, **PFWD**=pain free walking distance, **GTET**=treadmill exercise test, **SMWT**=six minute walk test, **UBST**=upper body strength training group, **CER**=conventional exercise rehabilitation group, **CONT**=control group, **wks**=weeks * = p<0.05 CER vs UBST; Ŧ = P<0.05 CER vs CONT. #=p<0.05 CER vs CONT. Values are expressed as means ±SD

There was no significant difference between the groups in maximum walking distance or pain free walking distance on the treadmill exercise test or the six minute walk test on entry to the study.

Maximum walking distance on the treadmill exercise test increased in the CER group after treatment significantly more than in the CONT group (95% vs 7%, CER vs CONT, P=0.002) and the UBST group (95% vs 7%, CER vs UBST, P=0.002) (Fig 4.4).

There was no significant difference between groups in maximum walking distance during the six minute walk test after training although all groups tended to increase in MWD (Fig 4.5).

There was no significant difference after intervention between the groups with respect to pain free walking distance during the treadmill exercise test. There was however a trend (p=0.07) towards statistical significance for pain free walking distance to increase in both UBST and CER groups (157% vs 156% vs

14%, UBST vs CER vs CONT, P=0.07) during the treadmill exercise test (Fig 4.6).

Pain free walking distance during the six minute walk test increased significantly in the CER group compared to the CONT group after training (42% vs -30%, CER vs CONT, p=0.0025) (Fig 4.7). PFWD during the six minute walk test decreased by 30% in the control group after the intervention period.

On the treadmill exercise test total pain perceived after six weeks of training decreased slightly in the CER and CONT group following training and increased by 1% in the UBST group (Fig 4.8). The results were however not significant.

Total pain perceived during the six minute walk test after six weeks of training decreased significantly in the CER group compared to the UBST group (-22% vs 27% CER vs UBST, p=0.009, Fig 4.9). Total pain increased slightly in the CONT group. Therefore the CER group was the only group to improve in PFWD and total pain perceived on the six minute walk test.

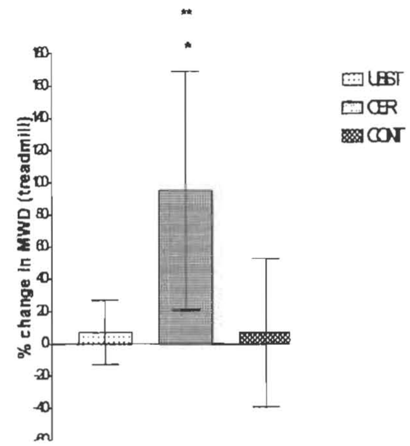


Figure 4.4

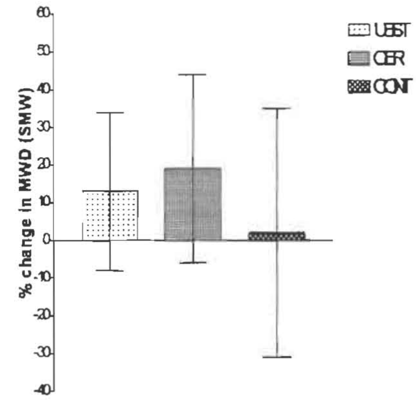


Figure 4.5

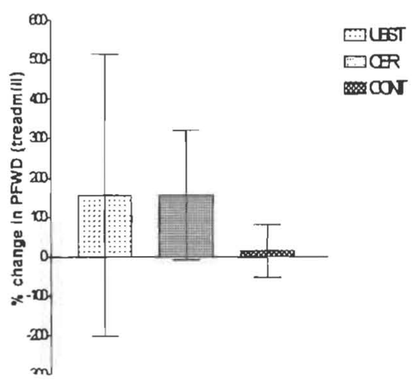


Figure 4.6

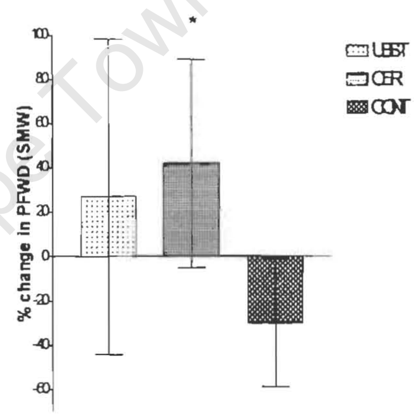


Figure 4.7

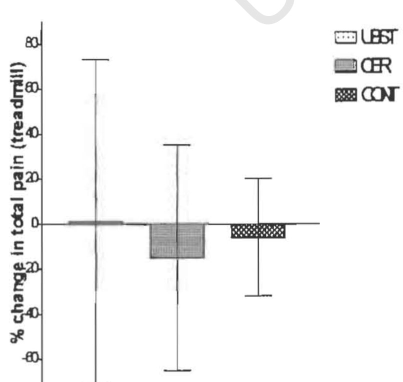


Figure 4.8

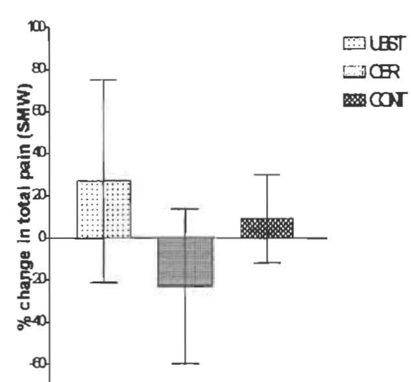


Figure 4.9

Effect of exercise training on resting and peak venous blood lactate concentrations in patients with PVD in the UBST, CER and CONT groups

Resting and peak post exercise venous blood lactate concentrations in the treatment groups and the control group on entry to the study and after intervention are detailed in Table 4.11

Table 4.11 Resting and peak post-exercise venous lactate concentrations in the treatment groups and the control group on entry to the study and after six weeks of intervention

	UBST (n=9)		**CER (n=9)**		**CONT (n=8)**	
Weeks	**0 wks**	**6 wks**	**0 wks**	**6 wks**	**0 wks**	**6 wks**
lactate rest (mmol. l^{-1})	2.4 ±2.2	1.7 ±0.7	1.7 ±0.6	1.5 ±.0.4	1.9 ±0.9	1.8 ±0.3
Peak lactate post exercise (mmol. l^{-1})	3.9 ±1.9	3.0 ±1.2	2.8 ±1.2	2.9 ±1.3	2.9 ±1.0	3.0 ±0.8

Abbreviations: lactate=venous lactate concentration, **wks**=weeks **UBST**=upper body strength training group, **CER**=conventional exercise rehabilitation, **CONT**=control group,. All values expressed as mean ± SD

There was no significant difference between groups with respect to resting blood lactate concentration and peak post-exercise blood lactate concentration on entry to the study.

Furthermore there was no significant difference between groups in post exercise venous blood lactate concentrations after six weeks of intervention.

Effect of exercise training on resting and post exercise brachial and ankle blood pressures in patients with PVD in the UBST, CER and CONT groups

Systolic brachial blood pressure, ankle brachial pressure index (ABI), post exercise ABI and ankle pressure gradient in the treatment groups and the control group on entry to the study and after training are detailed in Table 4.12

Table 4.12 Systolic blood pressure, resting ABI, post exercise ABI and ankle pressure gradient in the treatment groups and the control group on entry to the study and after six weeks of intervention

	UBST (n=9)		**CER (n=9)**		**CONT (n=8)**	
Weeks	**0 wks**	**6 wks**	**0 wks**	**6 wks**	**0 wks**	**6 wks**
Systolic blood pressure (mmHg)	147±18	142±19	151±27	134±22	161±25	146±12
Resting ABI (units)	0.8±0.4	0.9±0.7	0.6±0.3	0.7±0.5	0.9±0.2	0.8±0.1
Post exercise ABI (units)	0.6±0.4	0.7±0.5	0.4±0.4	0.4±0.4	0.6±0.4	0.6±0.3
Ankle pressure gradient (%)	30.5±49	10.4±61	32.2±48	39±41	22.6±40	22.5±38

Abbreviations: ABI=ankle brachial pressure index, **wks**=weeks, **UBST**=upper body strength training group, **CER**=conventional exercise rehabilitation group, **CONT**=control group. All values expressed as mean ± SD

There was no significant difference between groups in systolic blood pressure, resting ABI, post exercise ABI and ankle pressure gradient on entry to the study. Moreover there was no significant difference in all pressure measurements at rest or after peak exercise in any of the three groups after intervention. The systolic blood pressure measurements indicate that patients in all three groups were hypertensive, however there was no difference between groups in the number of hypertensive patients in each group or the number of hypertensive patients on antihypertensive medication in each group.

Discussion

Whilst exercise rehabilitation programmes lasting three to six months in the form of walking and dynamic leg exercises have previously been studied in patients with peripheral vascular disease (see Table 1.1), the effects of a shorter duration (6 week) conventional exercise rehabilitation programme (walking, cycling, circuit weight training) or upper body strength training programme has not been assessed in patients with peripheral vascular disease. Therefore in this study the effects of a short duration (6 wk) upper body strength training (UBST) programme was compared to a conventional exercise rehabilitation (CER) programme in patients with PVD. A third group of patients with PVD who were discharged and instructed to "walk as much as possible at home" served as the control group.

Training sessions were well attended by the CER and the UBST group and there was evidence of a training effect in both of the training groups in the six week period. The training effect was evident through changes in a number of physiological parameters.

After six weeks of training the UBST group had significantly increased their strength and had lost fat percentage compared to the control group. The UBST group did not improve in functional capacity, there was no change in peak VO_2 or MWD during the treadmill test and submaximal heart rates during the treadmill test did not change in this group after training.

The CER group improved more than the UBST group and the CONT group with respect to peak VO_2 as well as MWD after six weeks of training. Thus the CER group showed improvement in functional capacity to a greater extent than the UBST group or the CONT group.

Further evidence that there was a training effect in the CER group was that this group achieved lower submaximal heart rates than the UBST group and the

CONT group during the treadmill exercise test after six weeks of training, and recovery heart rate measured during the six minute walk test tended to be reduced in the CER group after training. Therefore, there was evidence of a cardiovascular training effect in the CER group but not in the CONT group and the UBST group.

These findings are in keeping with the results of the only other study which has examined the effects of strength training (albeit lower body strength training) and treadmill walking training on walking tolerance in patients with PVD (Hiatt et al. 1996). This study used resistive isotonic training of five specific muscle groups in each leg. Peak VO_2 improved significantly along with MWD in the walking training group but the lower body strength training group did not improve with respect to either parameter.

PFWD during the treadmill exercise test tended to increase in the UBST group. However no significant changes were noted in PFWD during the six minute walk test in this group. The treadmill test is an artificial walking test. The speed of the treadmill test is constant, only the grade increases, so the patient is forced to walk at a particular speed. This does not simulate walking during every day activities. Moreover the subject has a mask attached to his/her face and three research assistants in the room for the testing procedure. There may be positive psychological motivation when performing the treadmill test in this environment. Indeed Gardner et al. (1995) said that pain is a perception and can be affected by a variety of factors, including pain tolerance and motivation (Gardner et al. 1995).

The six minute walk test simulates walking during activities of daily living. The tester walks behind the subject and the subject chooses his or her own speed and just informs the tester when claudication sets in. Perhaps the SMW test allows the patient to perceive pain more accurately and does not create an environment in which the patient's pain may be affected by factors such as external motivation.

A limitation in this study is that there is the possibility of a type I error occurring due to small sample size. Had the group sample sizes been bigger, PFWD during the six minute walk and during the treadmill test may have improved significantly after UBST in patients with PVD. However MWD during the treadmill test did not improve in the UBST group and MWD during the six minute walk only improved slightly (not significantly) in the UBST group. Moreover in this group there were no improvements in peak VO_2 or submaximal heart rate values.

Improvements in PFWD in the UBST group could, however, be attributed to psychological factors. Rosfers et al. (1990) identified a few important predictors of an exercise programme. The best predictor of a good outcome of an exercise programme was belief that the exercise would lead to an improvement in walking status. In the present study, one subject in the UBST group improved in pain free walking distance during the treadmill test by 1100%. He reported that he was no longer experiencing pain. As a group the UBST group improved by 157%. Since this group did not improve with respect to functional capacity, or with respect to ABI or peak blood lactate concentrations as discussed later, improvements in the UBST group could have been due to psychological factors, such as belief that the programme would work, or feeling more in control of their disease, and therefore perceiving the onset of pain at a later stage than they would have before training.

The CER group also tended to increase in PFWD during the treadmill test and was the only group to improve significantly in PFWD and total pain perceived during the six minute walk test.

No physiological improvement in any of the parameters measured in this study were noted in the control group. In fact PFWD during the SMWT decreased significantly in comparison to the CER group. Since doctors do not conventionally ask patients to keep a log book of their walking when they advise patients to walk at home, patients in this study were not asked to keep a log book of their walking at home. Therefore we do not know that this group did not improve because they did not walk, however it is assumed that patients in this group did not follow the advice to exercise at home as submaximal and maximal heart rates increased in this group and peak VO_2 was lower in this group after the intervention period.

Some authors have attributed increases in walking tolerance after training to an increase in oxidative metabolism of the lower leg (Holm et al. 1973, Lundgren et al. 1989, Hiatt et al. 1996). The increase in oxidative capacity is as a result of an increase in succinic oxidase activity of the gastrocnemius muscle. The result of this is that venous lactate concentrations are lower because pyruvic acid is no longer converted to lactic acid but broken down in the oxygen dependent Krebs cycle (Dahloff et al. 1974, Sorlie and Myhre 1978). Therefore in this study resting and peak venous lactate concentrations were measured. Unlike the studies cited above, increases in walking tolerance in the CER group were not accompanied by lower peak venous lactate concentrations. Therefore the mechanism of the training response may not be an increase in the oxidative metabolism of the lower leg as was suggested by these authors. Also lacate concentrations at exercise termination were too low for this mechanism to be probable.

Many authors have attributed improvements in walking to changes in blood flow with exercise training (Skinner and Strandness 1967, Alpert et al. 1969, Hiatt et al. 1990, Gardener et al. 2001). Therefore in this study the ABI was assessed. There was no significant change in resting ABI, post exercise ABI or ankle pressure gradient after training between treatment groups. Therefore improvements in walking tolerance in the CER group and the UBST group cannot be attributed to improvements in any of the above parameters. Improvements in maximum walking distance and pain free walking distance in the CER group and the UBST group occurred independently of changes in resting ABI, post exercise ABI and ankle pressure gradient.

Conclusion

The results of this study suggest that although UBST produces improvements in fat percentage and strength and tends to increase PFWD during the treadmill exercise test, it is not as effective as CER in producing functional improvements in patients with PVD. CER improves MWD, peak VO_2 and submaximal heart rates during the treadmill exercise test and during the six minute walk test, only conventional exercise rehabilitation significantly improved PFWD and total pain perceived.

The control group who were given conventional medical treatment; "walk at home as much as possible," showed no improvement in functional capacity or walking distance after the intervention period.

Improvements in walking tolerance and functional capacity in the CER group occurred independently of changes in ABI. Therefore the graded treadmill exercise test should be used to monitor functional capacity.

Increases in walking tolerance in the CER group were not accompanied by lower peak venous lactate concentrations. Therefore the mechanism of the training response may not be an increase in the oxidative metabolism of the lower leg.

Therefore, although UBST does produce improvements in fat percentage, strength and tends to increase PFWD in patients with PVD, CER programmes are, overall, more effective in producing improvements in MWD, PFWD, peak VO2, submaximal heart rates and perceived pain in patients with PVD. A short term (6 wk) conventional exercise rehabilitation programme is time enough to affect functional improvements in patients with PVD. Advice to exercise at home did not improve functional capacity in patients with PVD and is an ineffective form of treatment for these patients with PVD.

CHAPTER 5: SUMMARY AND CONCLUSIONS

The principle aim of this study was to compare the effects of a six week UBST programme to conventional exercise rehabilitation or advice to exercise at home in patients with PVD. A second aim of this thesis was to describe the medical characteristics and physiological response to exercise of 31 patients with PVD.

The first study of this thesis reported in Chapter 3 established that this sample group of patients with PVD had a variety of co-morbid conditions (CAD and diabetes) and displayed typical risk factor profiles (hypertension, hypercholesterolaemia, smoking, older age and male gender) for patients with PVD.

Secondly, this study established that patients with PVD are exercise intolerant and have low peak VO_2 values and short six minute walk distances.

Thirdly, patients in this study terminated exercise at low peak RER values and peak venous lactate concentrations. Furthermore, patients with the highest venous lactate concentrations did not have the shortest pain free walking distances. Therefore peak post exercise venous lactate concentrations in this study did not predict pain free walking distance on the treadmill in patients with peripheral vascular disease. Therefore factors other than blood lactate accumulation must be responsible for the claudication pain that leads to walking intolerance in patients with PVD.

Fourthly, this study reported that resting ABI's do not predict maximum or pain free walking distances in patients with peripheral vascular disease. Therefore the graded treadmill exercise test should be used to monitor functional capacity in patients with PVD.

The second study of this thesis, reported in Chapter 4, showed that although UBST produces improvements in fat percentage and strength and tends to increase PFWD during the graded treadmill exercise test in patients with PVD, conventional exercise rehabilitation (CER) is more effective in improving maximum walking distance, peak oxygen consumption and submaximal heart rate values during the graded treadmill exercise test in patients with PVD. Moreover only CER significantly improves PFWD during the six minute walk test and total pain perceived during the six minute walk test. Advice to exercise at home is totally ineffective in improving functional capacity in patients with PVD.

Improvements in the CER group in walking tolerance occurred independently of changes in ABI. Therefore the treadmill exercise test may be a better measure of functional capacity than the ABI. Increases in walking tolerance in the CER group were not accompanied by lower peak venous lactate concentrations. Therefore the mechanism of the training response may not be due to an increase in the oxidative metabolism of the lower leg.

In conclusion, this dissertation confirms that PVD is a complex disease rendering the patient with PVD exercise intolerant. An accumulation of lactate in the blood is not responsible for walking intolerance in these patients and resting ABI's do not predict walking tolerance in patients with PVD. The graded treadmill test should be used to monitor functional capacity in patients with PVD

As a treatment, UBST is not as effective as CER in producing functional improvements and improving walking distances in patients with PVD. The conventional medical treatment; "walk as much as possible at home," is an ineffective form of treatment for these patients. A short term (6 wk) conventional exercise rehabilitation programme is time enough to affect significant improvements in functional capacity in patients with PVD and should be prescribed as a treatment for this patient population.

CHAPTER 6: APPENDICES

The following section includes tables which compliment the text. Table 6.1 and 6.2 depict the testing protocols used in this study. Patients who were unable to walk at 3.2km/h in the protocol by Perakyla et al. 1998 walked at 1.7km/h on the Bruce protocol.

Table 6.1 Graded treadmill exercise test protocol (Perakyla et al. 1998)

STAGE	SPEED	GRADE	MINUTES
I	3.2km/h	2%	1 2
II	3.2km/h	4%	1 2
III	3.2km/h	6%	1 2
IV	3.2km/h	8%	1 2
V	3.2km/h	10%	1 2
VI	3.2km/h	12%	1 2
VII	3.2km/h	14%	1 2

Table 6.2 Modified Bruce treadmill exercise test

STAGE	SPEED	GRADE	MINUTES
I	1.7km/h	0%	1 2 3
II	1.7km/h	5%	1 2 3
III	1.7km/h	10%	1 2 3
IV	2.5km/h	12%	1 2 3
V	3.4km/h	14%	1 2 3
VI	4.2km/h	16%	1 2 3

Table 6.3 depicts the pain scale which was shown to the patients every minute during the six minute walk and every two minutes during the graded treadmill test. Patients were asked to score their perceived pain.

Table 6.3 Rating of pain scale (Lambert et al. 2000)

0	**no pain at all**
1	**Very very slight**
2	**Very slight**
3	**Slight**
4	**Mild**
5	**Moderate**
6	**Moderate to severe**
7	**Severe**
8	**Very severe**
9	**Very very severe**
10	**maximum**

Table 6.4 depicts the training programme of the conventional exercise rehabilitation group and Table 6.5 the training programme of the upper body strength training group. An original programme of the walking and cycling part of the programme is included in card # 1

Table 6.4 Content of the exercise training sessions scheduled for each week for the CER group

	Monday	**Wednesday**	**Friday**
30 minutes	Walking, cycling	Walking, cycling	Walking, cycling
30 minutes	Circuit 10-12 upper and lower body machines, 15 reps on each machine	Aerobics, step, pelvic stabilization exercise	Spinning

An original programme for the upper body strength training group is included in card # 2.

Table 6.5 An example of the UBST programme for one of the members of the UBST group

Plate loaded machine	Strength before training (lbs)
Lower back	50
Abdominal	50
Rotary chest	25
Rotary upper back	15
Rotary lat	40
Rotary shoulder	15
Pec-dec	35
Tricep extension	30
Bicep curl	30
Lat pull down	40
Dumbells	1.5kg
Lateral raises	15 x2 reps
Frontal raises	15 x2 reps
Bicep curls	15 x2 reps
Tricep extensions	15 x2 reps

CARD # 1

EX SHEET

Exercise log for CER group

Name	Jane Smart	DR	Marley
Diagnosis	PVD.	DOB	11/4/37
Symptoms	claudication	Biokineticist	BP
Medication		Payment Code	1431/ 2002 (0001-)

HR =   RPE =

	Pre exercise				Exercise				Post Exercise		
	Date	BP	HR	Gluc	Tread	Bike	HR	BP	HR	BP	Gluc
1	7/12				assess						assess
2	10/12	145/80			assess						
3	12/12	135/80			3.2 (15)	(10)		circuit			
4 (Wed)	14/12				3.4 (15)	(10)		Floor			
5	19/12	120/80			3.4 - 3.8 (15)	(10)		circuit			
6	21/12	110/70						Floor			
7	4/01				3.4 (15)	10		circuit			
8	16/01	110/80			3.6 (15)	(10)		Floor			
9	18/01	120/70			3.6 (15)	(10)		SPIN			
10	21/01	130			4.2 (17)	(10)		circuit			
11	23/01	128/80			4.2 (17)	10		Floor			
12	25/01	130/80			4.2 (20)	10		SPIN			
13	28/01	120/70			4.4 (25)	10	circuit				120/70
14	[illegible]	120/80			4.4 (25 35)	(10)		Floor			
15	4/02	[illegible]			4.4 (30)	(10)		SPIN			
16	6/02	110/70			4.4 (30)	(10)		Floor			
17	8/02	130/80			4.4 (30	10		SPIN			
18	11/2	120/80			4.6 (30)	10		circuit			
19	13/2	120/80			4.6 (30)	10		Floor			
20	15/2				4.6 (30)	10		140/85	SPIN		
21	18/2	120/80			4.8 (30)	(10)		circuit			
22	20/2				5.0 (30	10		Floor		110/80	
23	22/2	120			5.0 (30)	10		SPIN		120/85	
24	25/2				5.0 (30)	10		circuit		110/70	
25	27/2				REASSESS			120/80			
26	1/3	110/80			5.0 -						
27	4/3									100/70	
28	6/3									110/80	
29	8/3				5.2 (	18 km					
30	11/3	135/80									
31	13/3	130/80									
32	15/3									120/80	
33	18/3										
34	20/3					(10MIN)				120/85	
35	22/3					18 km				135/80	
36	25/3	120/80			5.4	30					

3/4   120/80

CARD # 2

EXERCISE LOG FOR 6 WEEKS FOR GROUP2 – STRENGTH TRAINING

NAME A. Eglinton CODE: PVD 223

DATE	27/2	—	1/3	—	4/3	—	6/3.		8/3		11/3	
HR EXER												
BP	50/90				130/80		130/90		120/75	165/90	140/95	
CIRCUIT	W	R	W	R	W	R	W	R	W	R	W	R
1	15	50	50	15	50	15/15	50	15/15	60	15/15	60	15/15
2	15	50	50	15	50	15/15	50	15/15	50	15/15	50	15/15
3	15	25	25	15	25	15/15	25	15/15	25	15/15	25	15/15
4	15	15	15	15	15	15/15	15	15/15	15	15/15	15	15/15
6	15	40	40	15	40	15/15	40	15/15	45	15/15	45	15/15
* 8	15	15	15	15	15	15/15	15	15/15	25	15/15	15	15/15 ?
? 10	15	35	35	15	35	15/15	35	15/15	35	15/15	35	15/15
11	15	25	25	15	25	15/15	25	15/15	25	15/15	25	15/15
12	15	15	15	15	15	15/15	15	15/15	15	15/15	15	15/15
13	15	50	50	15	50	15/15	50	15/15	50	15/15	50	15/15
SIDE RAISES	10			15		15		15		15		20
FRONT RAISES	10			15		15		15		15		20
BICEPS	10			15		15		15		15		20
SHOULD	10			15		15		15		15		20
TRICEPS	10			15		15		15		15		20
					100/90.		125/85			165/90	170/80.	

DATE	13/3		15/3		18/3		20/3		22/3		25/3	120/80
HR EXER												
BP	120/80	[illegible]	120/80		120/80		130/80		100/70			
CIRCUIT	W	R	W	R	W	R	W	R	W	R	W	R
1	60	15/15	60	15/15	60	15/15	60	15/15	60	15/15	60	15/15
2	50	15/15	50	15/15	50	15/15	50	15/15	50	15/15	50	15/15
3	25	15/15	25	15/15	25	15/15	25	15/15	25	15/15	25	15/15
4	15	15/15	15	15/15	15	15/15	15	15/15	15	15/15	15	15/15
* 6	45	15/15	45	15/15	45	15/15	50	15/15	50	15/15	50	15/15
8	15	15/15	15	15/15	15	15/15	15	15/15	15	15/15	15	15/15
* 10	35	15/15	35	15/15	35	15/15	40	15/15	40	15/15	40	15/15
* 11	30	15/15	30	15/15	30	15/15	40	15/15	40	15/15	40	15/15
12	20	15/15	20	15/15	20	15/15	20	15/15	20	15/15	20	15/15
* 13	50	15/15	50	15/15	50	15/15	60	15/15	60	15/15	60	15/15
SIDE RAISES	10	15		15		15		15		15		15
FRONT	10	15		15		15		15		15		15
BICEPS	10	15		15		15		15		15		15
SHOULD	10	15		15		15		15		15		15
TRICEPS	10	15		15		15		15		15		15
	130/80		110/70			120/80	140/90.		130/75			128/80

	Wed 3		Fri 5		mon 8		wed 10		Fri 12		mon 15	
DATE					8/4		10/4		12/4		15/4	
HR EXER	3/4		5/4.									
BP	120/80		128/80		135/85			140/90	120/80			110/80
CIRCUIT	W	R	W	R	W	R	W	R	W	R	W	R
1	60	15/15	60	15/15	60	15/15	70.	15/15	70	15/15	70	15/15
2	50	0/0	50	15/15	50	15/15	60.	15/15	60	15/15	60	15/15
3	25	15/15	25	15/15	25	15/15	40.	15/15	40	15/15	40	15/15
4	15	15/15	15	15/15	15	15/15	15	15/15	15	15/15	15	15/15
6	50	15/15	50	15/15	50	15/15	60.	15/15	60	15/15	60	15/15
8	15	15/15	15	15/15	15	15/15	15	15/15	15	15/15	15	15/15
10	40	15/15	40	15/15	40	15/15	40	15/15	40	15/15	40	15/15
11	40	15/15	40	15/15	40	15/15	40	15/15	40	15/15	40	15/15
12	20	15/15	20	15/15	20	15/15	20	15/15	20	15/15	20	15/15
13	50	15/15	50	15/15	50	15/15	60	15/15	60	15/15	60	15/15
SIDE RAISES	10	15		15		15		15	~~15~~	15		15
FRONT	10	15		15		15		15		15		15
BICEPS	10	15		15		15		15		15		15
SHOULD	10	15		15		15		15		15		15
TRICEPS	10	15		15		15		15		15		15
		125/85		140/85	130/70			125/85		120/80		100/80

EXERCISE OUT OF GYM HOURS

26/2 16/4

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