

1-1-2005

The effects of combined creatine monohydrate supplementation and physical training on body composition and muscular function in patients with inflammatory myopathies

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**THE EFFECTS OF COMBINED CREATINE
MONOHYDRATE SUPPLEMENTATION AND
PHYSICAL TRAINING ON BODY COMPOSITION
AND MUSCULAR FUNCTION IN PATIENTS WITH
INFLAMMATORY MYOPATHIES**

By

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Frank Mastaglia and Dr. Peter Hamer

This thesis is presented for the degree of Master of Science
(Sports Science) from the School of Exercise, Biomedical
and Health Sciences, Edith Cowan University, Perth,
Western Australia.

Date of submission: 7th June 2005

ABSTRACT

Patients with neuromuscular disorders such as idiopathic inflammatory myopathies experience a loss of muscular strength and a deficiency in intra-muscular creatine and phosphocreatine levels. Inflammatory myopathies affect people of all ages, and little is known about which therapy is optimal. In many cases patients become resistant to the prescribed therapies causing performance to decline. Creatine monohydrate has been proposed as an alternative natural treatment to the currently available drug therapies.

Recent long- and short-term supplementation studies involving patients with various neuromuscular disorders have reported increases in muscular strength and enhances in body composition. These improvements are possibly due to an increased intra-muscular creatine store and rate of phosphocreatine resynthesis.

The purpose of this investigation was to examine the effects of a twelve-week program of creatine monohydrate supplementation, combined with a resistance-training programme, on muscular mass and strength in knee extensors and flexors in patients with inflammatory myositis by restoring intra-muscular creatine and phosphocreatine levels.

Patients ($n = 3$) received $20 \text{ g}\cdot\text{d}^{-1}$ of creatine monohydrate for the first two weeks followed by $5 \text{ g}\cdot\text{d}^{-1}$ for the remaining period. A control group ($n = 7$) of similar demographics was tested for comparison between disease and non-disease. In conjunction with the supplementation the subjects participated in a resistance-training program. The training involved knee flexor and extensor exercises $3 \text{ d}\cdot\text{wk}^{-1}$. The subjects were allocated a limb to exercise whilst the untrained limb rested, serving as a within-subject control.

Measurements of neuromuscular performance, isometric and isokinetic strength and a fatigue test were assessed throughout the study at given angles and velocities. Body composition was performed pre- and post-supplementation, using a dual energy x-ray absorptiometer, as well as fingertip blood samples to test for creatinine.

After twelve-weeks of supplementation and training, there were no signs of increased disease activity. The patients all noted a considerable improvement in their general wellbeing, resulting in reduced medications being reported.

No significant changes occurred for any of the parameters. However isometric peak torque increased for both the patient (30.7% and 2.2%) and control group (6.7% and 0.5%) at an angle of 60° for trained and untrained limbs respectively. Isokinetic peak torque also increased in the trained limbs of the patient (7.8%, 23.3%, 7.3% and 8.8%) and control group's extensors (24.8%, 14.7%, 0.6% and 8%) at 60, 120, 180 and 240° s⁻¹. The fatigue index for the patient group decreased for the trained limb (-8%) although increased for the untrained limb (1%) and the control group increased slightly (0.3% and 5%) for both trained and untrained limbs.

Lean body mass increased (2.1% and 4.3%) and fat mass decreased (2.9% and 1.7%) for patient and control groups respectively. There were no significant changes in creatinine concentrations, increasing by 14.8% and 15% for the patient and control group with the controls being 11% higher than the patient group at baseline and week twelve.

The results indicate that a low intensity, home-based resistance-training programme can be safely employed for patients with stable, inactive inflammatory myopathies, with small non-significant improvements in muscle function and endurance.

Keywords: Idiopathic inflammatory myopathy; Polymyositis; Dermatomyositis; Weight training; Creatine monohydrate supplementation; Muscle strength; Muscle mass; Muscle endurance; Body Composition.

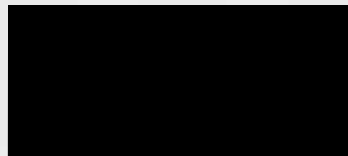
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ACKNOWLEDGEMENTS

There are many people I would like to thank for their support and guidance in (finally) completing this thesis.

Firstly, my supervisors, to Dr Paul Sacco who helped me start. To Mike Newton, who alongside his own heavy workload motivated and encouraged me despite many set backs. To Dr Mike McGuigan, who helped me finish, for all your attention to detail and prompt returns.

To Professor Frank Mastaglia, Dr Paul Zilko and Sue Walters at Sir Charles of Gairdner Hospital for giving me this opportunity and to Peter Hamer, formally of the University of Western Australia, for your help in allowing me to complete my testing.

To the staff at Metabolic Medicine, in particular David Reed, who helped with the DEXA scanning.

To Nadija and the staff at Edith Cowan University. Thank you for helping me, distracting me and putting up with me stressing all day long. The afternoons of M & M's and jellybeans (and the occasional joke) were rare comforts during my data analysing and thesis writing.

To my fellow postgraduates, thank you for helping me maintain a level head throughout the writing of this thesis.

To Stefan Underwood, my practicum student, thank you for all your efforts in helping me with the pilot study. I hope I have not put you off any further studies.

I would also like to acknowledge the efforts and support that I received from the individuals who volunteered in the study. Especially those that took part in my gruelling protocol and those who surrendered a lot of time, I really do appreciate your involvement.

Lastly, I would like to extend my thanks to my family and friends for your invaluable support and encouragement even when you thought I would never finish. To my parents, Fran and Dennis, for your time proofreading, editing and of course financially supporting me. Now that I have finished I guess its time to find a real job (we can only hope).

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CHAPTER ONE

1. INTRODUCTION

1.1 Background

Myopathy is derived from the Greek phrase “disease of muscle”. Myopathies are diseases that cause abnormal conditions with the tone and contraction of skeletal (voluntary) muscle. Myositis, Greek for “muscle inflammation”, is a form of muscle disease known as Idiopathic inflammatory myopathy (IIM) (cited in 1995). Idiopathic inflammatory myopathies are a heterogenous group of systemic diseases that fall into three categories, Polymyositis (PM), Dermatomyositis (DM) and Inclusion Body Myositis (IBM) (Brouwer et al., 2001; Lampa, Nennesmo, Einarsdottir & Lundberg, 2001).

Inflammatory myopathies (IM) affect one in every 100 000 individuals with a prevalence rate in PM of six in every 100 000 (Chen, Wu & Shen, 2001; de Oliveira Karnikowski, Costa, Osella & de Tolêdo Nóbrega, 2002). The incidence rates of PM and DM in the United Kingdom vary between an estimated 1.9 and 7.7 per million each year (Choy & Isenberg, 2002). Oddis, Conte, Steen and Medsger (1990) performed a twenty year study on hospital diagnosed cases of PM and DM in the United States of America and found an annual incidence rate of 5.5 in every million between 1952 and 1963. However it is believed that these figures are underestimated due to the number of IIM going undiagnosed (Choy & Isenberg, 2002).

Polymyositis and DM are the most common type of IIM with PM being the most misdiagnosed due to its similarities with other diseases (Hilton-Jones, 2003). The aetiology of the disease remains to be fully elucidated. Although it has previously been suggested that PM is caused by various autoimmune disorders and immunodeficiencies, as supported by the presence of T cell-mediated myocytotoxicity, the complement-mediated microangiopathy and the existence of various autoantibodies to nuclear and cytoplasmic antigens are frequently found in the system (Hirakata, 2000; Rosenkranz, 2002; Hara et al., 2003). It is also increasingly apparent that these diseases develop in genetically vulnerable individuals after exposure

to environmental agents that stimulate immune activation and inflammation (Miller, 1993).

Polymyositis rarely affects people under the age of twenty however cases of childhood and infant PM have been reported (Rosenkranz, 2002). Polymyositis is commonly found in adults aged between 30 and 60 years (Belostocki & Paget, 2002; Wortmann, 2002), DM, on the other hand, exhibits a peak initially in childhood (5 – 15 years of age) and again in adulthood (45 – 65 years) (Belostocki & Paget, 2002; Figarella-Branger, Civatte, Bartoli & Pellissier, 2003). More females are afflicted with PM and DM than males, with the ratio of female to male being two to one (Choy & Isenberg, 2002; Rosenkranz, 2002).

The literature is replete with gender and age related studies highlighting the effects of creatine (Cr) and the creatine kinase (CK) reaction in healthy and diseased populations (Wyss & Kaddurah - Daouk, 2000). The majority of research focuses on Cr monohydrate (CrM) supplementation as a disease preventer and a form of non-steroidal, or natural treatment in already diagnosed populations (Willer, Stucki, Hoppeler, Bruhlmann & Krahenbuhl, 2000). Recently, CrM supplementation has been used in select patient populations (e.g. patients with neuromuscular disorders) in an attempt to inhibit the progression and severity of the disease (Terjung et al., 2000).

Muscle weakness, atrophy and fatigue are common impairments in neuromuscular diseases (Tarnopolsky & Martin, 1999; Persky & Brazeau, 2001). Recent evidence suggests that these patients have the potential to benefit from CrM supplementation based on the hypothesis that increasing the intramuscular Cr concentrations increases the Cr levels in the blood, the transport of Cr in the cells, the availability of phosphocreatine (PCr) and enhances muscle mass (Benzi, 2000; Persky & Brazeau, 2001).

It has been reported in studies of elderly subjects that the greatest benefits from CrM ingestion are seen in people with initially low levels of intramuscular Cr (Volek, 1999). Patients with IM, muscular dystrophy, mitochondrial cytopathies and other neuropathies are reported to have lower intra-muscular levels of adenosine triphosphate (ATP) and PCr when compared with that of normal populations (Tarnopolsky & Parise, 1999).

Therefore, it is believed that these patients stand to derive the greatest benefits from CrM supplementation regimens (Spector et al., 1997), without resulting in severe physical disabilities and suffering many of the deleterious side effects associated with various prescribed drug therapies (i.e. steroid myopathy) (Lundberg & Chung, 2000; Hara et al., 2003; Bromberg & Carter, 2004). Creatine monohydrate supplementation in conjunction with a strength training program has also been reported to provide further benefits in these patient populations by delaying the onset of muscular weakness and atrophy (Spector et al., 1997).

1.2 Purpose of the Study

The aim of the study was to determine whether CrM supplementation and physical training leads to an increase in exercise performance, muscle mass and strength in patients with PM and DM.

1.3 Significance of the Study

Creatine monohydrate supplementation has been shown to increase strength and muscular performance in several studies of young healthy subjects (Balsom, Ekblom, Soderlund, Sjodin & Hultman, 1993; Bermon, Venembre, Sachet, Valour & Dolisi, 1998; Tarnopolsky & Martin, 1999) and in studies of elderly individuals (Rawson, Wehnert & Clarkson, 1999; Chrusch, Chilibeck, Chad, Davison & Burke, 2001). In these cases CrM supplementation is not only aimed at enhancing muscular performance in young subjects, but the ability to carry out daily tasks, such as cleaning the house, or participating in various physical activities for the elderly.

In addition to the positive influences of CrM supplementation in muscular performance, the therapeutic value of exercise training has also shown to enhance muscular strength and muscular endurance in the elderly (Chrusch et al., 2001; Fatouros et al., 2002; Ferri et al., 2003) and for patients with various neuromuscular disorders (Spector et al., 1997; Tarnopolsky, Roy & MacDonald, 1997; Louis et al., 2003). Exercise has been shown to reduce the risk of cardiovascular disease (Alexanderson, Stenstrom & Lundberg, 1999) and slow down the unavoidable loss of

muscle mass and muscular function associated with ageing and more importantly with muscle diseases (Wiesinger et al., 1998a).

Due to the disease aetiology of PM and DM not being entirely understood and the positive outcomes of CrM and exercise with healthy and elderly individuals, further investigation is warranted as to the effectiveness of the two regimens on PM and DM.

A better understanding of the disease will be extremely useful when considering natural therapies. Non-pharmacological therapies have received little attention concerning muscle diseases. The few studies available concerning alternative treatments often include small numbers of patients with a variety of diseases. There is a lack of studies primarily targeting PM and DM. Gaining a deeper understanding of non-steroidal therapies, such as CrM and exercise, and any effects on muscular function may be extremely useful for doctors when prescribing treatments for individuals suffering with muscular diseases.

By developing a safe and effective regimen, other researchers may also benefit from this study by reproducing the study with other populations. The information obtained will hopefully, prove valuable for other patient populations that suffer with similar symptoms.

1.4 Research Questions

1. Will three months of CrM supplementation and resistance training (RT) cause an increase in muscle mass, strength, and endurance of patients with PM and DM?
2. Will three months of CrM supplementation combined with RT improve muscle mass, strength or endurance of the trained limb versus non-trained limb?

1.5 Abbreviations

ADP	Adenosine Diphosphate	IM	Inflammatory Myopathy
ANOVA	Analysis of Variance	IVIg	Intravenous Immunoglobulin
ATP	Adenosine Triphosphate	JDM	Juvenile Dermatomyositis
BL	Baseline	LBM	Lean Body Mass
BWR	Best Work Repetition	MCG	Matched Control Group
B2	Biodex System 2	MVC	Maximal Voluntary Contraction
B3	Biodex System 3 Pro	p	Probability
CG	Control Group	PCr	Phosphocreatine
CGT	Control Group Trained	PG	Patient Group
CGU	Control Group Untrained	PGT	Patient Group Trained
CK	Creatine Kinase	PGU	Patient Group Untrained
Cr	Creatine	PM	Polymyositis
CrM	Creatine Monohydrate	PT	Peak Torque
Crn	Creatinine	ROM	Range of Movement
DEXA	Dual Energy X-ray Absorptiometry	RT	Resistance Training
DM	Dermatomyositis	SCGH	Sir Charles of Gairdner Hospital
ECU	Edith Cowan University	SD	Standard Deviation
FFM	Fat Free Mass	SEM	Standard Error of the Mean
FM	Fat Mass	STW	Set Total Work
IBM	Inclusion Body Myositis	TCr	Total Creatine
ICC	Interclass Correlation Coefficient	TW	Total Work
IIM	Idiopathic Inflammatory Myopathy		

1.6 Definitions

Adenosine Diphosphate	A compound consisting of adenosine and two phosphates
Adenosine Triphosphate	A compound consisting of adenosine and three phosphates
Atrophy	Decrease in cell/tissues associated with pathological conditions
Coefficient of Variation	A measure of the deviation of a variable from the mean
Concentric Contraction	A contraction in which the muscle shortens
Creatine Kinase	An enzyme that catalyses formation of PCr from ATP and Cr
Creatine	A natural nitrogenous compound serving as an energy reserve
Creatinine	A by-product of Cr metabolism
Dermatomyositis	An inflammatory disease of connective tissue marked by swelling, dermatitis and proximal muscle weakness
Dry Weight	The weight of material remaining after the removal of water
Endurance Ratio	The average of PT in the last five contractions divided by the average of the first five contractions expressed as a percentage
Fat Free Mass/ Fat Mass	Lean soft tissue/ Fat soft tissue
Idiopathic Inflammatory Myopathy	A group of muscle diseases, DM, PM and IBM, characterised by the inflammation of skeletal muscle
Correlation Coefficient	The degree to which two variables are related
Isokinetic	Maximum contraction to an accommodating resistance
Isometric	Muscle tension/contraction without any change in muscle length
Myositis	Inflammation of muscle tissue
Microangiopathy	Any disease of the capillaries
Myocytotoxicity	Destruction of muscle fibres
Phosphocreatine	An endogenous substance found in striated muscle. Synthesised and broken down to buffer ATP concentration, and acts as an immediate energy reserve for muscles
Polymyositis	An inflammatory condition characterised by progressive symmetrical weakening of the skeletal muscles
Power	The amount of work done
Standard Deviation	The degree of deviation from the central tendency
Standard Error of the Mean	A statistical index of the probability that a given sample mean is representative of the mean of the population used
Torque	A force which causes something to rotate
Work	A measure of the energy used by muscles under test conditions

CHAPTER TWO

2. LITERATURE REVIEW

2.1 Creatine

Creatine was first discovered in meat products in 1835 by a French scientist Chevreul (Silber, 1999). It was termed Cr coming from the word 'kreas' which is Greek for 'flesh' (Wyss & Kaddurah - Daouk, 2000). In 1847, Liebig showed that Cr could be extracted from several muscles of the body but not from the organs he thought to be involved (Greenhaff, 1995). Work by Eggleton and Eggleton (1927) as well as Fiske and Subbarow (1927) saw the discovery of PCr (cited in Wyss & Schulze, 2002). Due to its unstable nature PCr was also termed 'phosphagen' (Wyss & Schulze, 2002). Lohmann discovered ATP in 1929 (Silber, 1999), shortly after Lundsgaard (1930) examined the PCr breakdown and its importance in supplying energy for muscle contraction, the two discoveries saw the discovery of the CK reaction later revealed by Lohmann in 1934 (Wyss & Schulze, 2002).

Creatine is an amino acid derivative that is synthesised to form acetic acid - (α - methylguanidine) (Bemben, Bemben, Loftiss & Knehans, 2001a). Creatine is produced in the liver (hepatocytes), pancreas (islet alpha cells) and the kidneys (cortex and the proximal tubule) (Maughan, 1995; Feldman, 1999). It is a non-essential dietary element found primarily in meat (preferably raw), eggs, fish and poultry (Bemben, Tuttle, Bemben & Knehans, 2001; Metzl, Small, Levine & Gershel, 2001). For an average male weighing 70 kilograms the nutritional requirement of Cr is approximately $2 \text{ g}\cdot\text{d}^{-1}$, but for most individuals the average intake of Cr through diet is $1 \text{ g}\cdot\text{d}^{-1}$ (Harris, Soderlund & Hultman, 1992; Bird, 2003). This value is much lower for vegetarians and other individuals who consume little or no meat (Andres, Sacheck & Tapia, 1999).

Creatine is transported from its primary site of synthesis through the bloodstream in the plasma at a concentration of 50 – 100 micromols per litre (mol/L) (Andres et al., 1999). A sodium dependent neurotransmitter transporter on the muscle membrane helps to facilitate its uptake for storage in various tissues (Volek, 1999; Willoughby & Rosene, 2001). The total Cr (TCr) found in humans' ranges between 120 – 150 grams (Bemben et al., 2001). About 60% of this is found in skeletal muscle in the form of free Cr

and PCr (Stout, Eckerson, May, Coulter & Bradley-Popovich, 2001). These values tend to vary slightly between each study due to individual variability and differences in diet and muscle fibre composition (Maughan, 1995).

2.1.1 Creatine Kinase

Creatine kinase is an enzyme that catalyses biochemical reactions that occur intra-muscularly. The primary role of CK is to convert a phosphate group to Cr, resulting in a high-energy molecule PCr. Creatine kinase is also used in many research and clinical studies, as it is an imprecise indication of skeletal muscle microtrauma (Lundberg, 2001). Creatine kinase is normally found in muscle, when the muscle is damaged due to injury, unaccustomed exercise or increases in the intensity or volume of exercise. Muscle cells start to breakdown and the components start circulating through the bloodstream. A rise of CK levels in the blood is a sign that muscle damage is occurring or has occurred (Raastad & Hallén, 2000; Schwane, Buckley, Dipaolo, Atkinson & Shepherd, 2000). This peak can occur anywhere from six hours to five days after exercise (Raastad & Hallén, 2000). Measures of CK is also used as an indicator of existing muscle disease severity in the assessment and management of PM and DM (Kiely, Bruckner, Nisbet & Dagher, 2000; Chung, Wassif, Bell, Hurley & Scott, 2003).

2.1.2 Creatine Kinase Reaction

Creatine is often termed as an 'ergogenic', Greek phrase meaning 'work production', as it has a positive effect on muscle metabolism (Pepping, 1999). Muscles need energy to be able to function, they obtain this energy through the intracellular breakdown of ATP to adenosine diphosphate (ADP) (Maughan, 1995). Creatine is primarily responsible for the ATP re-synthesis in skeletal muscle (Walter et al., 2000). When ATP is stripped of a phosphate molecule to form ADP free energy is released to perform mechanical work. Creatine is known to have a high phosphate transfer potential and therefore, is very efficient in phosphorylating ADP (Volek et al., 1997).

During high intensity exercises that last up to five seconds, muscle ATP remains fairly constant as PCr, the primary fuel reserve during

anaerobic exercise, levels drop almost to zero (Biwer, Jensen, Schmidt & Watts, 2003). The decrease of PCr during exercise is due to its involvement in replenishing ATP and ADP reserves (Andres et al., 1999). This is done via the CK reaction ($\text{PCr} + \text{ADP} + \text{Hydrogen} \leftrightarrow \text{ATP} + \text{Cr}$) by which ADP is re-phosphorylated back into ATP (Metzl et al., 2001; Bemben et al., 2001a). The energy released from ATP in this reaction can generate enough power for four seconds of muscle contraction (Feldman, 1999; Bird, 2003). During recovery after strenuous exercise, the CK reaction is reversed to produce PCr and ADP.

The importance of the PCr system is its buffering ability of ATP use (Bemben et al., 2001). Phosphocreatine also facilitates energy translocation from the mitochondria to various sites of ATP utilisation, this is referred to as the PCr energy shuttle (Bemben et al., 2001a). This process helps to secure the availability of energy for work (Maughan, 1995; Edwards, Rhodes, McKenzie & Belcastro, 2000).

2.1.3 Creatinine

Creatine metabolism and production results in a waste product called creatinine (Crn) (Benzi, 2000). The daily requirement of Cr supplied by one's diet can be measured by the renal excretions of Crn or in blood samples. Normal plasma Crn values for males range between 44 – 97 $\mu\text{mol/l}$ and values for females range between 44 – 80 $\mu\text{mol/l}$ (Borner, Szasz, Bablok & Busch, 1979). Values outside these ranges can be due to age, varying pH levels and certain illness, which can cause the levels to be depressed or elevated. Like CK, Crn can be found in muscle and a rise in the levels of Crn in the blood is also an imprecise indicator of muscle damage.

In the absence of CrM supplementation, muscle Cr stores breakdown at a constant rate of approximately $2 \text{ g}\cdot\text{d}^{-1}$ into Crn (Volek, 1999). This amount must be replenished from dietary sources or by endogenous synthesis to maintain the constant body pool of intra-muscular Cr and PCr (Feldman, 1999).

Creatinine does not remain in the muscle it diffuses out of the cells into the blood stream. From here it enters the kidneys where it is removed by glomerular filtration and to a minor degree by tubular secretions.

Creatinine is not reabsorbed back into the body by the renal tubules and is rapidly excreted in urine via the kidneys (Wyss & Kaddurah - Daouk, 2000).

Muscles normally become saturated with Cr at $160 \text{ mmol}\cdot\text{kg}^{-1}$ of dry muscle, close to a 30% increase from resting values (Andres et al., 1999). Previously any extra Cr, due to supplementation, that was not used by the muscles was thought to be converted to Crn and readily excreted by the kidneys, as there is no renal threshold for the urinary excretion of Crn (Feldman, 1999). However one recent study by Chung, Wassif, Bell, Hurley and Scott (2003) claimed that in healthy individuals kidneys have a Cr excretion threshold of about 0.05 mM/L and that any extra circulating Cr can lead to a condition called creatinuria. However, no evidence of Cr biosynthesis was found by Chung et al. (2003), therefore suggesting the creatinuria observed was caused by other means.

Creatine uptake and use is regularly measured by the amount of Crn found in urine samples; for example, urinary excretion have previously indicated that the greatest Cr uptake usually occurs within the first two days of supplementation (Odland, MacDougall, Tarnopolsky, Elorriaga & Borgmann, 1997). This method, however, is also a very imprecise measurement as endogenous Crn excretion varies among individuals due to physical activity, maturity, metabolic state and gender (Lukaski, 1997).

2.2 Creatine Supplementation

Creatine monohydrate supplementation has been shown to increase pre-exercise intra-muscular stores of PCr improving muscular performance during exercise (Rossiter, Cannell & Jakeman, 1996; Armsey & Green, 1997). Casey, Constantin-Teodosiu, Howell, Hultman and Greenhaff (1996) stated that the 30% decrease in muscle ATP as a result of short high intensity exercise together with the increased work performed indicated that ADP rephosphorylation improved as a result of CrM supplementation.

In healthy subjects, several studies have demonstrated ergogenic benefits of CrM supplementation on muscular mass and strength. Harris, Soderlund and Hultman (1992) performed one of the first studies on CrM supplementation. They investigated the absorption rates of short term CrM

supplementation on intramuscular levels, as well as the effects exercise may have on CrM uptake. Harris et al. (1992) demonstrated that supplementation of CrM ($20 - 30 \text{ g}\cdot\text{d}^{-1}$) for two or more days resulted in a significant increase in TCr levels of the quadriceps femoris muscle in 17 subjects (Females = 5; Males = 12). The greatest of these increases (up to 50%) were seen in subjects with initially lower intramuscular TCr pools (Harris et al., 1992).

In another study, men aged 19 – 60 years were found to have elevated their muscle Cr stores by 20% with as much as 20% stored in the form of PCr after ingesting $20 \text{ g}\cdot\text{d}^{-1}$ of CrM for five days or $3 \text{ g}\cdot\text{d}^{-1}$ for thirty days (Hultman, Soderlund, Timmons, Cederblad & Greenhaff, 1996). They showed that muscle Cr levels increased as a result of CrM supplementation ($25 \text{ g}\cdot\text{d}^{-1}$ for five days) and intra-muscular Cr was shown to increase by 20%, reaching a TCr pool of about $150 - 160 \text{ mmol}\cdot\text{kg}^{-1}$ of dry weight (Hultman et al., 1996). The TCr levels were also shown to increase by about $20 - 40 \text{ mmol}\cdot\text{kg}^{-1}$ of dry weight in a study conducted by Urbanski, Loy, Vincent and Yaspelkis (1999), after the subjects ingested $20 \text{ g}\cdot\text{d}^{-1}$ of CrM for five days.

Stout, Eckerson, May, Coulter and Bradley-Popovich (2001) demonstrated that CrM supplementation during RT resulted in greater increases in fat free mass (FFM), muscular strength and training volume compared with training alone. Various studies, such as Tarnopolsky and Parise (1999), suggest that low muscle PCr levels contribute to fatigue in daily activities and that this may be avoided by increasing the PCr levels through CrM supplementation.

Ingesting CrM is thought to decrease the dependency on anaerobic glycolysis, a process that promotes the onset of fatigue by the build up of lactate and hydrogen ions. Creatine monohydrate supplementation also enhances the CK reaction and allows for greater training through increases in FFM (Andres et al., 1999). The increase in body mass and FFM may also be due to the increase in total body water, muscle fibre size and protein synthesis.

Haussinger, Roth, Lang and Gerok (1993) view Cr as an osmotically active substance that can change the intra-cellular levels of Cr, including

cellular swelling which is believed to lead to increased protein synthesis (Andres et al., 1999). This idea is supported by reports of lowered urinary output and an increase in body mass during CrM supplementation as a result of water retention (Hultman et al., 1996).

In addition, Preen, Dawson, Goodman, Lawrence, Beilby and Ching (2001) have reported findings that suggest CrM supplementation is associated with increased protein synthesis, which may also be responsible for the elevations in body mass observed in the Cr groups. Other authors report this increase in body mass to be due to an increase in dry mass growth in association with normal fluid levels in the body and not that of water retention (Francaux, Demeure, Goudemant & Poortmans, 2000).

Possible mechanisms responsible for the ergogenic effect of CrM supplementation include increased intramuscular PCr, improved buffering, enhancement of Mitochondrial CK activity and stimulated biosynthesis of muscle myosin (Bermon et al., 1998). These mechanisms accelerate the rate of ATP re-synthesis, enhancing recovery and resulting in an improved muscular performance (Schilling et al., 2001).

2.2.1 Long and Short-term Supplementation

Short-term (five – seven days) CrM supplementation studies have been shown to increase both lean body mass (LBM) and intra-muscular TCr stores (Balsom et al., 1993; Kreider, 1998). Kreider et al. (1998) reported a 0.6 – 1.1 kilogram increase in body mass. However, numerous authors suggest that the increases are the result of increased total body water content rather than an increase in myofibrillar protein synthesis (Rawson & Clarkson, 2000).

Long-term (> four weeks) CrM supplementation studies of healthy individuals show greater gains in strength and LBM (Kreider, 1998) than studies that last only five to fourteen days (Volek et al., 1997). Long-term supplementation of CrM (25 g·d⁻¹ for five – seven days and 2 – 5 g·d⁻¹ for up to twelve-weeks), is known to promote significant gains in strength, LBM and FFM in conjunction with a training program in comparison to placebo controls (Kreider, 1998). Pepping (1999) suggested that these improvements be mainly due to the uptake of amino acids into contractile

muscle proteins thus stimulating protein synthesis. However, not all studies have found the same enhanced performance with supplementation (Stevenson & Dudley, 2001).

2.2.2 Loading

There is a vast variation in the required dosage of many studies, which leads to dispute as to what dosage is the safest and most effective. Loading phases of $20 \text{ g}\cdot\text{d}^{-1}$ is popular in many research studies of older individuals and people with diseases (Schilling et al., 2001). This dose has been shown to increase TCr and intramuscular PCr levels by up to 30% and Cr levels from $50 - 100 \mu\text{mol/L}$ to over $500 \mu\text{mol/L}$ (Ziegenfuss, Lowery & Lemon, 1998). However, similar effects can be found in younger and healthier subjects with lower doses of CrM ($3 \text{ g}\cdot\text{d}^{-1}$) by extending the supplementation period (Juhn, 1999; Terjung et al., 2000).

It can take approximately two days for supplementation to increase levels of muscle Cr and PCr above baseline (BL) levels and four – seven days for muscle performance to be increased (Andres et al., 1999; Yquel, Arsac, Thiaudiere, Canioni & Manier, 2002). The Cr levels in muscle can increase as much as 20 – 50% after initial loading, this is dependant on pre-existing levels (Feldman, 1999).

Volek et al. (1999) have shown that as little as $2 \text{ g}\cdot\text{d}^{-1}$ of CrM ingested can maintain intra-muscular Cr levels in men who are not exercising vigorously. Harris et al. (1992) found that four to six doses of $5 \text{ g}\cdot\text{d}^{-1}$ of CrM for two days produced a significant increase in TCr stores in the quadriceps femoris muscle of seventeen subjects. Again the greatest improvements were seen in subjects with an initially low TCr content (Harris et al., 1992).

It has been suggested that the lower the supplement dose the less likely it is to develop side effects (Schilling et al., 2001). However, it is possible that dosage for the elderly needs to be extended and measured above the standard dosage of younger healthier subjects due to older individuals' displaying a lower absorption rate.

2.2.3 Wash Out Period

After CrM supplementation muscle Cr concentrations can remain elevated for weeks, even months depending on the initial dosage ingested (Maughan, 1995). The period it takes for BL values to return is often referred to as the wash out period.

After a brief period of supplementation TCr levels and Cr synthesis have been found to return to pre-existing values (Terjung et al., 2000). Andres, Sacheck and Tapia (1999) reported that after one week most of the ingested CrM was excreted as Crn. Feldman (1999) and Wyss and Kaddurah - Daouk, (2000) stated that Cr and PCr concentrations returned to BL levels approximately thirty days after brief CrM ingestion ceased. On the other hand, Vandenberghe et al. (1997) found that muscle PCr and urinary Cr and Crn excretion returned to normal values after four weeks of long-term CrM supplementation was stopped.

In contrast, Rawson, Persky, Price and Clarkson (2004) found that thirty days washout was insufficient in returning muscle PCr levels to BL following short term CrM supplementation of $20 \text{ g}\cdot\text{d}^{-1}$ for five days. It did however report that plasma and urine Cr levels returned to BL levels within this period (Rawson et al., 2004).

2.2.4 No Ergogenic Effect

Many reports have indicated that CrM supplementation does not improve exercise performance (Yquel et al., 2002). Creatine monohydrate supplementation has shown to be less ergogenic when the supplementation regimens are short term and involve supplementing less than $20 \text{ g}\cdot\text{d}^{-1}$ or with regimens that do not have an initial loading phase (Kreider, 1998).

Edwards, Rhodes, McKenzie and Belcastro (2000) found no improvements in the repeated, anaerobic running performance of eleven moderately active males ingesting $20 \text{ g}\cdot\text{d}^{-1}$ of CrM for six days. A study by Stevenson and Dudley (2001) reported that CrM supplementation did not increase levels of PCr use or recovery during maximum voluntary contractions (MVC's) and dynamic muscle strength or endurance measurements. Stevenson and Dudley (2001) performed this double-blinded

placebo experiment on a group of resistance trained males and females. They concluded that CrM loading did not provide an ergogenic effect for unilateral knee extension exercises or electrically stimulated isometric knee extensions and suggested that CrM loading may even slow PCr replenishment (Stevenson & Dudley, 2001). These negative findings may be due to a CrM loading phase of only one week with no maintenance phase to ensure adequate Cr uptake.

Failure to produce ergogenic effects of CrM supplementation may be due to the inadequate muscle Cr accumulation in subjects (Volek, 1999). Other causes could be due to the familiarisation of the subject with the equipment prior to testing, time of day when testing occurs, number of subjects involved, drug and nutrient intake prior to the trial, the length of supplementation and the type of exercise evaluated (Kreider, 1998; Tarnopolsky & MacLennan, 2000).

2.2.5 Side Effects

Creatine monohydrate is known as a relatively 'safe' supplement due to its low molecular weight (149.15) which allows for its non-toxic removal by the kidneys via diffusion (Bemben et al., 2001a). However, there have been negative reports, although few, of potential health implications in connection with CrM supplementation (Terjung et al., 2000). Anecdotal reports suggest that CrM supplementation is a potential hazard to the human body as it is believed to promote the incidence of muscle strains and pulls (Waldron et al., 2002). It is believed that supplementation places large amounts of stress on bones, joints and ligaments because of the rapid gains in strength and body mass. Other reported side effects include nausea and skin rashes (Rawson et al., 1999; Schilling et al., 2001).

Long-term effects of CrM supplementation on the liver, heart and kidneys have recently been of concern (Benzi, 2000). Poortmans and Francaux (1998) found that CrM ingestion increased the susceptibility of an individual to gastrointestinal dysfunction and cardiovascular problems. Chrusch, Chilibeck, Chad, Davison and Burke (2001) reported minor side effects as a result of CrM supplementation (i.e. loose stools, cramping, pulls or strains). However, these negative effects were not serious enough to

impair performance measured in the study and have been considered as isolated incidences (Persky & Brazeau, 2001). Given the little evidence in the literature of harmful side effects to date, further research into the long term side effects of CrM supplementation are needed (Andres et al., 1999; Lehmkuhl et al., 2003).

A recent study by Brenner, Rankin and Sebolt (2003) found no indications of liver or kidney trouble with CrM supplementation (20 g·d⁻¹ for one week followed by 2 g·d⁻¹ for four weeks) in women over a five week supplementation period. Kreider et al. (2003) examined the effects of long term CrM supplementation on blood and urinary markers in college football players (n = 98) in conjunction with intense exercise. Subjects (n = 54) ingested 15.75 g·d⁻¹ of CrM for five days and an average of 5 g·d⁻¹ thereafter in 5 – 10 g·d⁻¹ doses for the remainder of the study. The effects of 0 – 6 months (mean 4.4 ± 1.8 months, n = 12), 7 – 12 months (mean 9.3 ± 2.0 months, n = 25), and 12 – 21 months (mean 19.3 ± 2.4 months, n = 17) were compared with subjects who did not take CrM (n = 44). No significant relationships were found among any of the groups for blood or urinary markers. Kreider et al. (2003) concluded that CrM supplementation (of up to 21 months) showed no adverse effects in the health status of college football players.

Controlled studies of CrM supplementation have not shown any evidence of side effects (Vandenbergh et al., 1997; Benzi, 2000; Waldron et al., 2002). Therefore, causes other than CrM ingestion have been proposed, e.g., the co-ingestion of other supplements (Terjung et al., 2000), and problems associated with hydration and dietary problems (Schilling et al., 2001).

The structure of Cr has both a positive and a negative charge and it is believed that the water retention is related to the additional water uptake when Cr ions enter the muscle. This increase within the cells can induce muscle oedema, cramps and other symptoms (Benzi, 2000). This is supported by other studies showing that muscle cramps are associated with hydration or dietary inconsistencies as increased total body water dilutes electrolytes, leading to cramps. Intracellular swelling has also been found to be one of the causes of muscle tightness and stiffness (Feldman, 1999).

Thus, it has been suggested that CrM should be administered only when properly hydrated and to avoid vigorous training during the primary stages of CrM ingestion (Benzi, 2000). This is very important, as the elderly are more at risk of dehydration due to a decreased fluid consumption rate and a reduced water content in the body (Davidhizar, Dunn & Hart, 2004).

As the recognition and safe use of CrM increases researchers are starting to target possible uses for the supplement in a variety of disciplines such as treatment alternatives as well as the documented athletic improvements (Bemben et al., 2001).

2.3 Supplementation for Athletes

Differences in the performance of elite athletes, is often very small and any slight improvement in one's ability may change the outcome of the competition (Hopkins, Hawley & Burke, 1999). In order to achieve this additional gain, athletes are regularly in search of and consuming supplements that can potentially result in an ergogenic effect (Andres et al., 1999).

Creatine monohydrate is readily available for use in the international sporting community (Becque, Lochmann & Melrose, 2000). The athletic population willingly consumes CrM because of its perceived ability to increase muscular performance (Nelson, Arnall, Kokkonen, Day & Evans, 2001). Athletes often take supplements to promote rapid increases in FFM, muscular strength and to accommodate extra training (Kreider et al., 1999; Brenner et al., 2003).

A team of twenty five college football athletes (males aged 18 – 22 years) were studied by Bemben, Bemben, Loftiss and Knehans (2001a) over a period of nine weeks. 20 g·d⁻¹ of CrM or placebo was ingested for the first five days followed by 5 g·d⁻¹ for the remaining period. Along side the supplementation an RT program (4 d·wk⁻¹) was also implemented. On completion strength and power were improved in the Cr group in comparison to the placebo group, this was believed to be due to the increase in resynthesis of ATP and ADP (Bemben et al., 2001a).

A study by Rico-Sanz and Marco (2000) found highly trained cyclists ingesting 20 g·d⁻¹ of CrM for five days increased both time to exhaustion

and oxygen consumption whilst performing three minute intervals of 30% and 90% maximal power output to the point of exhaustion. Grindstaff et al. (1997) performed a double-blinded randomised study on both male and female competitive swimmers. They were required to ingest $21 \text{ g}\cdot\text{d}^{-1}$ of CrM or placebo for nine days. The findings found that not only did the subjects tolerate the CrM supplementation, but their sprint performance was also improved (Grindstaff et al., 1997).

Not all individuals, however, experience this improvement (Terjung et al., 2000). The data obtained from Biwer, Jensen, Schmidt and Watts (2003) revealed that soccer athletes ingesting $0.3 \text{ g}\cdot\text{kg}^{-1}\cdot\text{d}^{-1}$ of CrM for six days did not experience any enhanced performance during a sub-maximal protocol combined with high-intensity intervals using a treadmill ergometer.

Delecluse, Diels and Goris (2003) also found a negative response to CrM supplementation with nine highly trained sprinters. Following one week of CrM supplementation at a dose of $0.35 \text{ g}\cdot\text{kg}^{-1}\cdot\text{d}^{-1}$, no ergogenic effects on single or repeated sprint times were observed even with varying rest periods. Delecluse et al. (2003) believe the negative response was due to the insufficient increase of intramuscular PCr and Cr content as a result of CrM supplementation and the fact that the subjects were highly trained athletes and had already trained their bodies to cope with vigorous training.

2.4 Supplementation for Non-athletes

Several authors have reported significant increases in LBM with CrM supplementation in younger subjects (Balsom et al., 1993; Greenhaff, Bodin, Soderlund & Hultman, 1994). Young subjects have been known to portray increases in LBM of about one – three kilograms and intra-muscular levels of PCr following supplementation have also been reported to improve by 15% (Rawson, Clarkson, Price & Miles, 2002). Volek et al. (2004) investigated the effects of short term CrM supplementation in conjunction with an RT program on performance, body composition and resting hormone concentrations. Seventeen males (aged 20.7 ± 1.9) were randomly allocated to a supplementation ($n = 9$) or placebo ($n = 8$) group. Supplementation consisted of $0.3 \text{ g}\cdot\text{kg}^{-1}\cdot\text{d}^{-1}$ of CrM while both groups performed RT exercises $5 \text{ d}\cdot\text{wk}^{-1}$ for four weeks followed by two weeks

reduction phase. They found that short term CrM supplementation was effective in maintaining muscular performance and body composition during the initial phase of RT however these changes were not related to the changes in hormone concentrations in the resting or the post absorptive state (Volek et al., 2004).

Vandenbergh et al. (1997) examined the effects of CrM supplementation and RT on intramuscular PCr levels, muscular strength and body composition on sedentary females (n = 19) aged 19 – 22 years. The double blind study involved the females ingesting 20 g·d⁻¹ for four days of CrM or placebo followed by 5 g·d⁻¹ for ten weeks during which the RT program commenced (Vandenbergh et al., 1997). After the four loading days PCr levels increased 6% in the Cr group and during the low dose phase, muscular strength, body composition and muscular PCr levels all remained higher in the Cr group compared with the placebo group (Vandenbergh et al., 1997).

In contrast, Bemben et al. (2001), also conducted a double blind study on sedentary males (n = 19) aged 18 – 25 years. Subjects ingested 20 g·d⁻¹ of CrM or placebo for five days (loading phase) followed by 5 g·d⁻¹ for five days (maintenance phase) (Bemben et al., 2001). The study demonstrated no ergogenic effect of CrM supplementation in the untrained adult male but did indicate a possible advantage in increasing the endurance potential of larger muscle groups (Bemben et al., 2001).

Smith et al. (1998) studied age and the differences in CrM supplementation on muscle metabolism. They found that CrM supplementation of 0.3 g·kg⁻¹·d⁻¹ for five days had a greater influence with middle-aged (>50 years) individuals than younger (<40 years) subjects (Smith et al., 1998). After performing single leg knee extension the results indicated that CrM supplementation enhanced muscular endurance in both groups, however, muscle PCr availability, hydrolysis and resynthesis was greatly improved in the middle-aged individual (Smith et al., 1998).

2.4.1 Elderly

Mature populations experience a loss of muscular strength after the age of 50, accelerating at the age of 70 years and above (Aniansson,

Hedberg, Henning & Grimby, 1986). This loss can be attributed to muscle atrophy, as a result of reduced TCr levels, a sedentary lifestyle, a decline in muscle force-generation as well as impaired neurological function and mobility (Aniansson et al., 1986; Fiatarone et al., 1994; Bassey, 2002; Degens & Alway, 2003). It has been reported that approximately 0.5 kilograms of muscle is lost per annum in adults that do not perform regular exercise and a further 50% loss of type II muscle fibres in adults over the age of 80 years (Elliott, Sale & Cable, 2002). It has also been reported in the elderly that there is a 2.5% and 2% annual loss of strength for knee flexion and knee extension (Frontera et al., 2000).

This loss of muscle size and strength as well as changes in the sarcoplasmic reticulum and motor neurons contribute to a decreased ability to perform daily activities (Frontera et al., 2000). Decreases in the functional ability of the respiratory, cardiovascular and neuromuscular systems further result to this decrease in strength and aerobic power (Izquierdo et al., 2003). Aging is also associated with a decrease in FFM, a reduced metabolic rate and a lower capillary to fibre ratio (Campbell et al., 1999; Laguno, Miro, Perea, Picon & al., 2002), this loss of muscle is normally replaced with connective and fatty tissues contributing to various age related disorders (Ferri et al., 2003).

Rawson and Clarkson (2000) found that elderly people have lower intra-muscular TCr concentrations. Elderly individuals have also been reported to experience a greater increase in muscle Cr and PCr, and PCr re-synthesis due to CrM supplementation compared with healthy subjects (Rawson & Clarkson, 2000). The reduced TCr concentration, due to a lower Cr uptake in the muscles, could also contribute to the decrease seen in type II muscle fibres (Bermon et al., 1998).

Chrusch et al. (2001) performed a CrM supplementation experiment, using a double-blinded placebo design with thirty-three men aged 60 – 84 years old over twelve-weeks. A CrM loading phase of five days at a dosage of $3 \text{ g}\cdot\text{kg}^{-1}\cdot\text{d}^{-1}$ of body weight, followed by a maintenance phase of $0.07 \text{ g}\cdot\text{kg}^{-1}\cdot\text{d}^{-1}$ of body weight thereafter, resulted in enhanced muscular strength, endurance and power of the lower body as well as LBM (Chrusch et al., 2001).

Chrusch et al. (2001) found that PCr availability was an important factor for preventing fatigue during exercise. The men were able to train at higher volumes (31% higher than initial volumes) as a result of both the training program and CrM supplementation (Chrusch et al., 2001). Rawson, Wehnert and Clarkson (1999) also performed a double-blinded placebo experiment involving elderly males aged 60 – 78 years old and found that their results also supported the notion that CrM supplementation and RT allows for a greater improvement of strength performance.

In contrast to these findings, Eijnde et al. (2003) investigated the effects of CrM supplementation and exercise on males (n = 46) aged between 55 and 75 years old. The Cr group were instructed to ingest 5 g·d⁻¹ of CrM while both groups performed two – three sessions per week of moderate RT and cardio-respiratory endurance training for six months. They concluded that long term CrM supplementation and RT did not improve the physical fitness of males aged 55 to 75 years old (Eijnde et al., 2003).

Rawson, Clarkson, Price and Miles (2002) found that CrM ingestion in older subjects had no effect on intra-muscular PCr levels, also that elderly subjects had significantly higher blood Cr and muscle PCr levels initially when compared with younger adults. Bermon, Venembre, Sachet, Valour and Dolisi (1998), also found that CrM supplementation failed to show any ergogenic effects towards dynamic strength or isometric endurance performances in sedentary elderly men and women following an eight week training program. They also demonstrated that CrM ingestion did not extend the time to fatigue nor did it induce additional strength gains in the latter stages of exercise. These contradictions could possibly be due to a poor RT program design and/or insufficient supplement levels (Bermon et al., 1998).

There are many potential reasons as to why CrM appears to have no ergogenic effect in older individuals. Elderly people are believed to have a decreased Cr absorption rate in the gut, slow transport in the blood, and inappropriate rate of Cr uptake into muscles after supplementation (Rawson et al., 2002). To obtain similar performance increases to younger individuals, older individuals require a longer supplementation period or a higher CrM supplement dosage (Rawson & Clarkson, 2000).

2.5 Myopathy

Idiopathic inflammatory myopathies was first documented in three patients by Wagner and Unverricht in 1887 (Bronner, Linssen, van der Meulen, Hoogendijk & de Visser, 2004). At first the three cases were termed PM, after realising the occurrence of cutaneous irregularity together with the disease, Unverricht changed the name to DM a few years later (Hashmat & Daud, 2004). After this discovery the terms PM and DM were loosely used and over many decades it was alleged the dermatological irritation was a part of the disease. The status of PM remained vague until the late 20th century where Walton and Adams started to classify the symptoms in 1958. This was later completed in 1975 by Bohan and Peter who documented the well known diagnostic criteria for PM and DM that are still used today (Callen, 2002; Bronner et al., 2004). Diagnosis included (1) a symmetrical weakening of the limb girdle muscles declining over several weeks even months, (2) elevated CK levels, (3) electromyographic triad, muscle response to nerve stimulation, of small amplitude, short duration polyphasic motor unit action potentials, positive Harp waves and increased insertional irritability and impulsive high frequency discharges and (4) muscle biopsy abnormalities (i.e. necrosis, phagocytosis, perifascular atrophy, interstitial infiltrates of mononuclear cells and degeneration and regeneration) (Launay et al., 2001; Cleland & Venzke, 2003). The skin rashes according to Bohan and Peter (1975) were the only distinguishing feature between PM and DM. In 1991, Dalakas refined the diagnostic foundation that Bohan and Peter provided by including specific histopathological abnormalities in its description (Bronner et al., 2004).

2.5.1 Polymyositis

Polymyositis is a cell-mediated autoimmune disorder, the abnormalities begin with a group of cells called lymphocytes, known as CD8+ T-lymphocytes (Dalakas, 2001; Hilton-Jones, 2003; Komiya et al., 2004). These lymphocytes continuously migrate back and forth between the bloodstream and peripheral tissue. In healthy individuals, lymphocytes act as a defence mechanism against invading pathogens, bacteria and viruses, or

against abnormal body cells and cancerous cells, by physically attacking or using chemical discharges to attack the foreign agents (Martini, 1998).

In patients with PM, CD8+ T-lymphocytes and reactive macrophages surround, invade and destroy normal muscle fibres which express Major Histocompatibility Complex class I antigens, also known as Human Leukocyte Antigen, as though they were foreign or abnormal to the body (Buchbinder, Forbes, Hall, Dennett & Giles, 2001; Hara et al., 2003; Vianna et al., 2004). Other cells start to aid lymphocytes by producing antibodies to attack the tissue, these misguided antibodies are referred to as autoantibodies, causing architectural and functional damage, known as autoimmunity (Martini, 1998), resulting in the loss of cross-striations in targeted muscle fibres (Buchbinder et al., 2001).

Diagnosis of DM can be made through electromyography and serological data, however the “gold standard” for diagnosis is through muscle biopsy samples (Cleland & Venzke, 2003). Due to the disease muscle membranes start degenerating and releasing muscle enzymes from the muscle fibre. Creatine phosphokinase, muscle enzyme, can be found in significantly high concentrations above normal levels. Due to muscle damage, changes can also be found with low amplitude short acting firing potential and fibrillations (Cleland & Venzke, 2003). Muscle biopsies taken in the study by de Oliveira Karnikowski, Costa, Osella and de Tolêdo Nóbrega (2002) of the biceps brachii and quadriceps muscles from a PM patient showed a degeneration and disorganisation of striated muscle fibres. High counts of endomysial infiltrates of polymorphonuclear cells were also found with rare signs of regeneration, phagocytosis and endomysial fibrosis throughout the muscle. Examples of this can be seen in Figure 1 from Hashmat and Daud (2004).

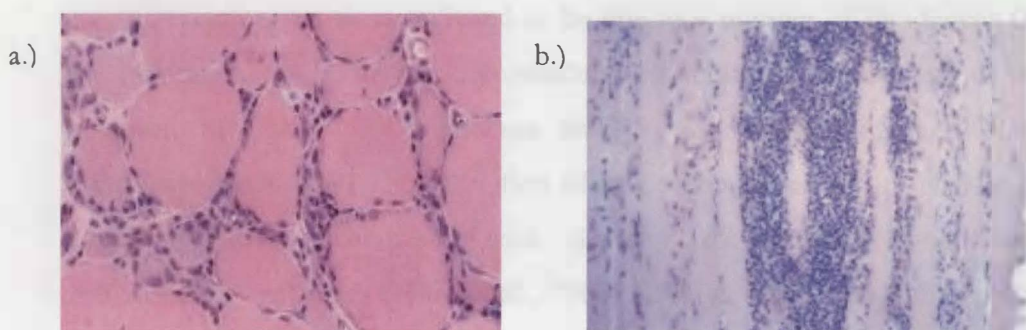


Figure 1. PM. a.) Muscle biopsy showing an infiltration of inflammatory cells within the muscle. b.) A longitudinal view of the inflammatory infiltrate within a muscle sample (Hashmat & Daud, 2004).

As well as the degeneration of muscular tissue PM involves persistent inflammation (Dalakas, 2001). Muscle weakness is usually symmetrical and develops slowly over a few months, even years (Lampa et al., 2001). Early signs of PM include difficulty rising from a chair, climbing a flight of stairs, self grooming or lifting the arms above head level (Hilton-Jones, 2003). Other symptoms include: weight loss, pain, fatigue, shortness of breath, fever, tenderness within the muscle, skin changes, arthritis (Wortmann, 2002), frequent gastrointestinal, pulmonary and cardiac dysfunction (Joffe et al., 1993). Difficulty in swallowing, dysphagia, and choking incidents are very common, affecting more than 60% of patients especially in the later stages of the disease (Dalakas, 2001).

Diagnosis is normally based upon the presence of proximal muscle weakness, an increase in serum levels of enzymes derived from skeletal muscle, abnormal electromyography and the presence of an inflammatory infiltrate in muscle biopsy (Brouwer et al., 2001; Belostocki & Paget, 2002). These diagnostic measures should be cautiously examined as serum enzyme levels such as CK are influenced by many factors such as race, prior exercise performed, fitness levels, disease activity and general physical activity (Chung et al., 2003). Electromyography abnormalities differ between individuals and in more than 20% of cases can show no abnormalities, as affected muscles can contain areas of normal muscle (Chung et al., 2003).

2.5.2 Dermatomyositis

Dermatomyositis is believed to be due to a number of incidences (1) the binding of antibodies to microvascular components, (2) damage of the complement C5b – C9 membrane and (3) the opening of the classic complement pathway. The activation of this pathway results in the loss of capillaries and ischemia-induced damage of muscle fibres with inflammatory infiltrates (Hara et al., 2003; Komiya et al., 2004). Diagnosis of DM is similar to that of PM in reference to muscular responses to the disease however DM is actually quite different from PM. Dermatomyositis is a humorally mediated auto-immune disorder (Hilton-Jones, 2003). It involves the presence of a distinctive skin rash on the eyelids, cheeks and hands as well as a flat red rash on the knees, chest, neck and back (Dalakas, 2001; Figarella-Branger et al., 2003) seen Figure 2 by Callen (2002). The major feature of DM is the saturation of inflammatory cells into the perivascular and interstitial regions surrounding the myofibrils (Dalakas, 2001). Dermatomyositis is also characterised by vasculopathy, disease of the blood vessels, and the deposition of membrane attack complexes (Hara et al., 2003; Komiya et al., 2004).

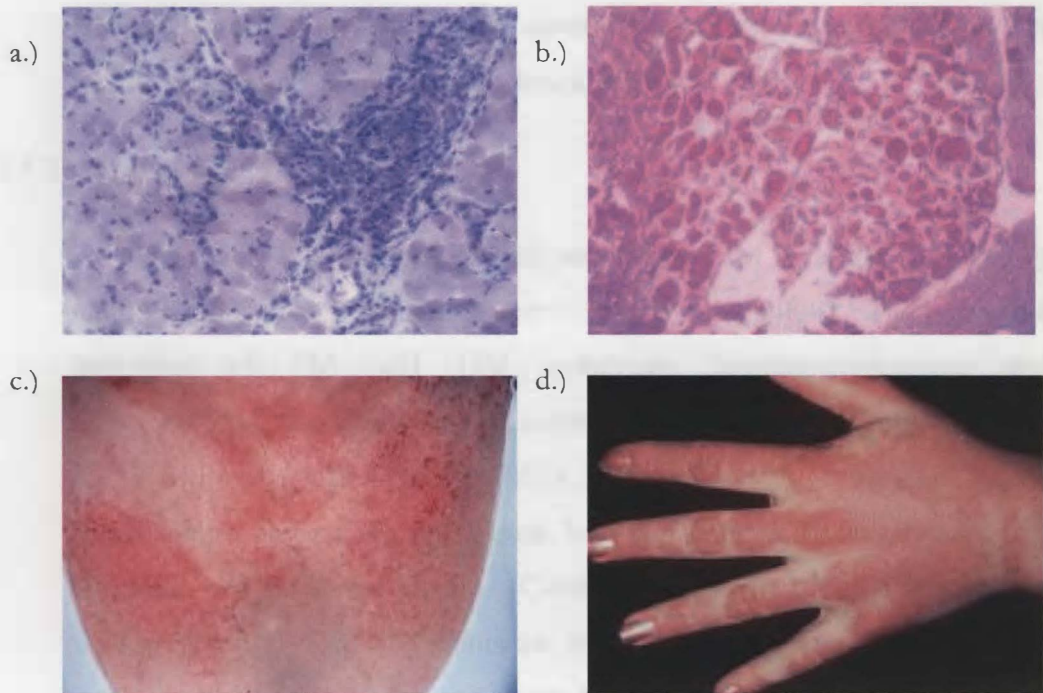


Figure 2. DM. a.) Juvenile type DM portraying a large infiltrate of inflammatory cells within the perimysium. b.) Adult DM characterised by a group of degenerative fibres within a fascicle (Figarella-Branger et al., 2003) c.) The typical rash associated with DM. d.) Lesions on the hand of a patient with DM (Callen, 2002).

Dermatomyositis is also characterised by a form of capillaropathy (loss of capillaries numbers), muscle hypoxia, muscle fibre death and perifascicular myofibril atrophy (Dalakas et al., 1993; Hilton-Jones, 2003). The activation of the complement system is believed to be the sole cause of capillary depletion, one of the initial signs of the disease seen in muscle biopsies (Komiya et al., 2004). Another uniqueness to DM is the association of malignancies with the disease (Dalakas, 2001) however this is not observed in Juvenile DM (JDM) (Figarella-Branger et al., 2003).

Dermatomyositis is a disease also found in children. Lymphocytes and macrophages invade and destroy capillaries in JDM as it does in adult DM, shown by Figarella-Branger, Civatte, Bartoli and Pellissier (2003) in Figure 2, however JDM does differ (Rider et al., 2002). Subcutaneous calcifications are more common in JDM, muscular weakness is not seen as much, the emotional state of the child is usually affected, the face tends to look flushed, the rash is not always as visible and the bowel may become

involved. On the other hand distal weakness can occur in adult DM. Adult DM also progresses slowly over several weeks and in severe cases can include respiratory failure (Hilton-Jones, 2003).

2.5.3 Treatment and Prevention

The prospects of a patient with any form of IM is reliant on the early identification and treatment (Vencovský et al., 2000). The effective treatment of PM and DM comprises immunosuppressive and immunomodulating agents, these current therapies are generally identical for all IIM's (Choy & Isenberg, 2002). Prednisone or its primary metabolite Prednisolone, an immunosuppressant, has been found to be an effective first line treatment for many patients (Cleland & Venzke, 2003). Patients start with a high oral dose of Prednisone or Prednisolone daily for four to six weeks until there is an improvement in symptoms and a decrease in the serum CK levels. The dose is tapered down to a maintenance dosage with improvements, which is continued for at least twelve months (Mastaglia, Phillips & Zilko, 1999).

Most medical practitioners use steroids as a first line treatment as most believe it improves the disease among the majority of patients (Choy & Isenberg, 2002). However, steroids have been associated with the re-appearance and morbidity of certain diseases (Danieli et al., 2002). About 32% to 41% of patients also suffer from increased disability as well as other various side effects as a result of steroids and with long term prescription of the drug, osteonecrosis and osteoporotic vertebral fractures are common (Lundberg & Chung, 2000; Dalakas, 2001; Choy & Isenberg, 2002). Therefore non-steroidal immunosuppressants, such as Azathioprine and Methotrexate, are more commonly prescribed (Mastaglia et al., 1999; Vencovský et al., 2000).

Azathioprine is commonly used as the preferred steroid-sparing agent in PM and DM (Choy & Isenberg, 2002). It can be slow acting, however it is still popular as it is suggested to allow for a lower dose of Prednisone or Prednisolone with time (Hilton-Jones, 2003). Oral Methotrexate is a second-line treatment most commonly used for patients with rheumatoid arthritis. It was first reportedly used in the treatment of childhood and adult DM, as it is

known to suppress inflammation and improve function. However, Methotrexate has also been associated with side-effects such as pulmonary and liver dysfunction, haematological disorders and hair loss requiring regular blood tests to monitor progression (Choy & Isenberg, 2002; Cleland & Venzke, 2003).

Intravenous immunoglobulin (IVIg) therapy is effective for patients who do not respond well to Prednisone or Prednisolone. Intravenous immunoglobulin therapy is the last drug treatment administered and it is believed to be effective for patients who suffer from severe flares of the disease and whose conditions are declining (Mastaglia et al., 1999; Danieli et al., 2002).

Dermatomyositis responds to these therapies more positively than PM. Most patients make a full recovery back to initial strength, which is sustained by maintenance doses of the treatments (Dalakas, 2001). A study by Dalakas et al. (1993) found that IVIg therapy enhanced muscular strength in patients with DM, cleared the rash, restored the capillary network and improved the structure and function of tissues in muscle biopsies. However, the effectiveness of IVIg is usually short-lived as repeated treatments are needed for long term results and the drug is very expensive to obtain (Dalakas et al., 1993).

2.5.4 Problems Associated with Current Drug Therapies

In some cases of PM and DM, patients can continue to demonstrate reduced muscular strength despite the disappearance of inflammation due to the disease or in extreme cases even intense treatment of IVIg (Lundberg & Chung, 2000). There are a number of factors that can describe an individuals' poor response to these drug therapies, including the duration of muscular weakness prior to diagnosis, the severity of the weakness and an individuals association with malignancy or cardiac disease (Joffe et al., 1993). Also the duration of treatment and inadequate dose prescribed can also affect ones response to particular treatments (Hilton-Jones, 2003). It can take several weeks for mixed treatments like corticosteroid and immunosuppressive treatment to have an effect therefore early treatment is essential (Vencovsky et al., 2000).

A decrease in CK concentrations normally is associated with increased strength, however, with many immunosuppressive treatments a decrease in CK concentration does not always mean an increase in muscular strength (Dalakas, 2001). A reason for this is that patients who have been suffering with the IM for a long period have noticeably less muscle fibres due to atrophy than those patients recently diagnosed. In contrast CK levels can be promoted by some medications, like Methotrexate, as well as trauma and unaccustomed exercise (Komiya et al., 2004). Furthermore, as there is strict criteria for identifying PM (Rosenkranz, 2002) the clinical diagnosis of PM can vary between General Practitioners. Another factor is age, as elderly patients have a less favourable response to drug therapy when compared with younger patients (Belostocki & Paget, 2002).

The same fate seen in the elderly population is common in the patient population. They are both associated with reduced intra-muscular ATP, Cr and PCr (Wiroth et al., 2001). Multiple studies by Tarnopolsky and others (1997; 1999; 1999; 2001) when investigating numerous diseases including IIM, found significantly lower PCr concentrations for all patients when compared with normal controls. It has been reported that the amount of TCr is 14% lower for patients with IIM (Tarnopolsky & Beal, 2001).

2.5.5 Natural Therapies

Tarnopolsky and Martin (1999) demonstrated that a ten-day CrM supplementation program could significantly increase strength and LBM in patients with a variety of neuromuscular diseases. Studies by Tarnopolsky and Parise (1999) have found that short-term (fourteen days) CrM supplementation can increase PCr concentrations by 15% to 20% in both healthy humans and patients with myopathies. They have also found that individuals with the lowest initial muscle PCr concentrations show the greatest increase in response to CrM supplementation. Tarnopolsky and Martin (1999), suggest that the possible mechanisms responsible for the increased LBM and strength is possibly due to a significant increase in PCr content, allowing for an increased training volume and increases in protein synthesis.

Although most studies suggest a beneficial effect of CrM supplementation there are a few studies that show no ergogenic effect. One such study is by Tarnopolsky, Roy and MacDonald (1997), yet they support CrM use for patients with mitochondrial cytopathies even though their results do not support it. They found that CrM ingestion had a slight effect on high-intensity anaerobic and aerobic performance but did not affect body composition, aerobic cycle ergometry performance or the ability to complete daily activities (Tarnopolsky et al., 1997).

In addition to these findings Vorgerd et al. (2002) found CrM supplementation to be detrimental to patients with McArdle Disease, one of the most common metabolic myopathies. It was previously reported that short-term low doses of CrM supplementation ($60 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{d}^{-1}$) had positive effects such as increasing the exercise capacity of patients. In the study by Vorgerd et al. (2002) a higher dose of CrM ($150 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{d}^{-1}$) was ingested during a double-blinded placebo controlled trial. The dose actually worsened the clinical symptoms of exercise intolerance despite the positive neurophysiological findings (Vorgerd et al., 2002).

However, the reductions in muscle Cr and PCr in patients with neuromuscular disorders provide theoretical support for the use of CrM as a therapeutic intervention. Strength training in conjunction with the CrM ingestion may also provide further benefits, possibly delaying the onset of muscle weakness and atrophy (Spector et al., 1997).

2.6 Exercise

When the blood flow is restricted, the availability of Cr for active muscles to absorb is also reduced. Due to this reduction, there is a further decrease in ATP availability and PCr re-synthesis, as this process is oxygen dependant, reducing the contractile force of each muscle (Urbanski et al., 1999; Yquel et al., 2002). Previous research by Harris et al. (1992) have found that exercise promotes blood flow to the active skeletal muscles, thus increasing the amount of available Cr and ATP and restoring PCr re-synthesis.

Exercise has numerous health benefits. Apart from cardiovascular improvements exercise has been known to improve and maintain physical

performance, hindering the unavoidable loss of muscle mass and neurological function found with aging (Bennell et al., 1997; Bassey, 2002; Elliott et al., 2002). This gain in muscular strength and mass is thought to be the result of neural adaptations and muscle hypertrophy (Kreider et al., 1999; Augustsson et al., 2003).

2.6.1 Adaptations to Exercise

As a result of exercise, adaptations can be seen in muscles as a result of structural, neural and mechanical changes (Abernethy & Jurimae, 1996). Muscle hypertrophy is the result of an increase in individual muscle fibre, whole muscle cross-sectional area and possibly hyperplasia, the abnormal increase of normal cells in tissue (Chesnut & Docherty, 1999). Higbie, Cureton, Warren and Prior (1996) illustrated that after heavy RT changes in strength were not only due to hypertrophy but also to increased neural activation within the muscle.

Changes in the recruitment of muscle fibres, discharge frequency and synchronisation of the motor unit, as well as reflex responses, increased excitability of the alpha motoneurone pool and/or motor end plates, a decrease in Golgi tendon organ inhibition and in the activation of the antagonistic muscles have all been suggested as possible neural adaptations to heavy resistance exercise (Staron et al., 1994). Although muscle fibre characteristics are determined to a large extent by genetics, training the recruitment process can enhance the synchronisation of muscle fibre discharge frequencies (McLaughlin, 2001). It has also been suggested that training creates new neural pathways, increasing the neural flow to motor neurons in turn increasing the activation of muscle groups involved in the contraction (Evetovich et al., 2001).

Neural adaptations have also been proposed as the main principle for any increase in performance seen in the first few weeks of resistance exercise (Staron et al., 1994; Evetovich et al., 2001). However it has become increasingly more aware that intramuscular changes are also evident during this period (Staron et al., 1994). After six weeks of training muscle hypertrophy, an increase in cross-sectional area of the muscle being employed, mainly contributes to the strength increases (Chesnut & Docherty, 1999).

Earlier work by Staron et al. (1991) and Staron and Johnson (1993) show significant hypertrophy in all major muscle fibre types (I, IIa and IIb) as well as the fibre type conversions between type IIb and IIa. Increases of 15.6%, 17.3% and 28% for the fibre types I, IIa and IIb were seen in the vastus lateralis muscle of females after six weeks of high intensity RT, as well as a significant decrease in type IIb fibres (pre 24.9%; post 6.7%) (Staron et al., 1991). Larger increases of 15%, 45% and 57% for the muscle fibre types I, IIa and IIb were demonstrated in the vastus lateralis muscle of females after 20 weeks of high intensity RT (Staron & Johnson, 1993).

It is still not known to what extent this remodelling of intramuscular structure has on strength, however gradual increases in the number and/or size of the myofibrils as well as the decrease of IIa fibres to the conversion to IIb has been postulated to contribute to these strength increases (Staron et al., 1994). The study by Chestnut and Docherty (1999) states that untrained subjects adapt more generically to exercise than trained subjects. Therefore neural changes can also be seen with light resistance exercise performed on sedentary individuals.

2.6.2 Contralateral Limb

Several authors have reported contralateral strength increases due to unilateral exercises (Housh, Housh, Weir & Weir, 1996; Evetovich et al., 2001; Munn, Herbert & Gandevia, 2004; Munn, Herbert, Hancock & Gandevia, 2005) where as others have reported no strength changes (Narici, Roi, Landoni, Minetti & Cerretelli, 1989; Garfinkel & Cafarelli, 1992; Housh, Housh, Johnson & Chu, 1992). The latest review of existing studies showed that the untrained limb produces a small yet statistically significant increase of up to 8% from initial strength due to unilateral training (Munn et al., 2005).

Narici, Roi, Landoni, Minetti and Cerrettelli (1989) and a study by Krotkeiwski et al. (1979) (cited in Housh et al., 1992) examined the effects of unilateral training on the cross section area of the contralateral limb using various techniques, neither found a cross-training effect in relation to hypertrophy. Housh, Housh, Johnson and Chu (1992) study was also consistent with these findings, however, although no significance was reported ($p > 0.0008$) increases in cross sectional area of the contralateral muscles increased (0.1 to 14.0%) as well as PT measurements (6.7 to 14.8%) of the contralateral side of the body during testing. Munn, Herbert, Hancock and Gandevia (2005) revealed a significant relationship between strength gains for the trained and untrained limbs. However, the circumference measures of the tested upper limb may have been too impervious to detect any changes in cross sectional area, Munn et al. (2005) stated that it was unlikely to be caused by muscle hypertrophy.

The mechanisms behind the increase in contralateral strength remains unclear (Munn et al., 2004). Two possible mechanisms for the explanation of the cross-training effect have been proposed 1) motor impulses circulating to the contralateral side of the body and 2) contraction of the contralateral side of the body in an effort to maintain stability and assume the appropriate posture for the unilateral testing (Housh et al., 1992; Evetovich et al., 2001). It has also been suggested that a learning effect following unilateral RT may cause increased strength results in the contralateral limb due to the activation of both the contralateral and ipsilateral sensorimotor cortex (Munn et al., 2005). In the absence of muscle hypertrophy an increased ability to recruit motor units and the firing rate of these units through central neural mechanisms may be part responsible for the increases in strength as well as other neural changes involving spinal and supraspinal pre-motor networks has also been proposed (Munn et al., 2005).

It is believed that with a longer training period or a greater magnitude of strength gained in the trained limb, statistically significant increases in strength and cross sectional area of the contralateral side could be recorded (Housh et al., 1992; Munn et al., 2005). Since training volume, duration and training speed are thought to have an effect on the degree of strength adaptations seen in the trained limb, it is probable that they could also influence changes in the contralateral limb (Munn et al., 2005).

2.6.3 Therapeutic Exercise

The benefits of exercise for health related purposes are now widely accepted as a means of rehabilitation and as this is applicable across all ages its popularity has excelled (Bassey, 2002). The therapeutic value of exercise training in the enhancement of muscular strength and muscle mass has been well documented for healthy and elderly individuals (Tracey et al., 1999). A study by Ferri et al. (2003) supports the use of exercise with elderly patients over the age of 65 years as it was found to increase strength and power, in addition to producing further gains in performing daily activities. Rhodes et al. (2000) investigated the effects of one-year progressive RT in forty four elderly women (mean age 68.8 years). The study proved beneficial as significant changes were found in muscle strength for the bench press (>29%), bilateral leg press (>19%) and unilateral leg press (>20%) as well as

improvements in biceps curl, triceps extension and quadriceps extension. The overall strength increases over the one-year period ranged from 19 – 53%. These changes also found associated increases to bone density in lumbar and femoral regions (Rhodes et al., 2000).

No recent published data supports rest or the use of restricted exercise for the rehabilitation of patients with PM and DM. There is some positive evidence, supporting exercise training as beneficial for patients with various neuromuscular disorders (Alexanderson et al., 1999; Alexanderson, Stenström, Jenner & Lundberg, 2000; Cleland & Venzke, 2003). It is often believed that the use of an exercise regime for a person with various inflammatory myopathies is dangerous because exercise, mainly eccentric, can cause increases in CK levels and muscle fibre inflammation, which can induce muscle fibre death. It has previously been reported that even after five days of exercise, cytokine levels are high which can result in muscle fibre damage (Spector et al., 1997). Furthermore exercise induces lymphocytes and neutrophils migration and increases the number of killer T-cells and cytotoxic T-cells that result in further inflammation (Spector et al., 1997).

However, Mastaglia, Phillips and Zilko (1999) suggested that exercise can improve muscular strength in patients with PM and DM when prescribed appropriately. A study conducted by Spector et al. (1997) showed that a twelve-week high-resistance strength training program significantly improved dynamic muscle strength without any evidence of muscle damage in patients with IBM. DeBolt and McCubbin (2004) examined the effects of an eight week home-based RT program on balance, power, and mobility in adults with multiple sclerosis. Twenty-nine women (age, 50.3 ± 8.5 years) and eight men (age, 51.1 ± 7.1 years) were randomly assigned into an exercise ($n = 19$) and a control ($n = 17$) group. The control group maintained their exercise levels while the exercise group performed three sessions of lower extremity exercises a week. Although measurements of balance and mobility did not significantly change a significant improvement in leg extensor power (an increase of 30%) was seen. The home-based program was tolerated well by the individuals as it did not

cause any additional injuries or enhance any of the symptoms as a result of the disease (DeBolt & McCubbin, 2004).

Wiesinger et al. (1998) performed a training program for six months on a group of eight patients suffering from either PM or DM. Their results were compared with a group of five patients that also suffered from the disease that did not undergo the training. The long term physical training did not result in any significant increases in disease activity and it improved both the patients' muscular strength and cardiorespiratory fitness (Wiesinger et al., 1998).

After twelve-weeks of moderate exercise, a study by Alexanderson, Stenstrom and Lundberg (1999) also found no signs of increased disease activity in a group of ten PM adults aged 27 – 60 years. Upon completing the whole body exercise regimen every patient showed improvements in muscle function of the upper and lower limbs as a result their medication was reduced (Alexanderson et al., 1999).

The same exercise program was employed again in eleven patients with PM and DM. These patients were aged between 23 – 80 years old and were recently diagnosed with IM. After twelve-weeks of exercise training no signs of increased inflammation were detected and significant improvements in muscle function and quality of life were also evident (Alexanderson et al., 2000).

Arnardottir, Alexanderson and Lundberg (2003) performed a twelve-week home-based training programme adapted from Spector et al. (1997) with seven IBM patients (aged between 45 – 78 years old) with an additional 20 minutes walk or a five minutes stationary cycle five days a week. No signs of increased inflammation were found and the home-based training program was well tolerated with all except one experiencing improved muscle function (Arnardottir et al., 2003).

Exercise is very important in that not only does it maintain the remaining strength, but also aids the muscles' recovery following damage due to the inflammatory process (Hilton-Jones, 2003). Exercise may also help reverse or to some extent prevent the side effects of steroid myopathy (Mastaglia, Garlepp, Phillips & Zilko, 2003).

It is unclear as to when the optimal time is to introduce exercise as a form of therapy, however it is recommended that patients are gradually eased into physical activity as their disease subsides (Lundberg & Chung, 2000). The patients' current physical ability and disease status should determine the balance between physical exercise and rest (Cleland & Venzke, 2003). It has been suggested that the exercise should be in the form of a light to moderate home-based exercise program for the whole body or a low intensity aerobic program on a bicycle or in a pool (Lundberg & Chung, 2000). Both passive and active exercise has been suggested to improve muscular performance as well as reduce the risk of developing contractures (Hilton-Jones, 2003). It is also recommended that the training consist mainly of concentric muscle contractions due to the ultra structural damage resulting from eccentric muscle contractions (Wiesinger et al., 1998). Creatine kinase levels should therefore be used as a guide for the exercise program as it is an indicator of the sensitivity of the disease (Cleland & Venzke, 2003).

2.7 Implications of the Literature Review

There are a large number of studies investigating different training regimens and their role in increasing muscular strength and mass in a variety of populations (Folland, Irish, Roberts, Tarr & Jones, 2002). However, there is little experimental evidence documenting beneficial effects of exercise in patient populations suffering from PM and DM and even less incorporating CrM supplementation into the program. There are also limited studies examining the effects of exercise on the non-trained limbs (Evetovich et al., 2001). This investigation is the first study to incorporate contralateral findings in this particular patient population.

This study was therefore designed to examine the effects of a twelve-week home-based exercise program and CrM supplementation on trained and untrained limbs in patients with PM and DM. It is hypothesised that training and supplementation will lead to an increase in muscular mass and strength for each individual involved in the study.

CHAPTER THREE

3. MATERIALS AND METHODS

3.1 Subjects

The participants in the study were recruited from the Neuromuscular Clinic within the Australian Neuromuscular Research Institute at Sir Charles of Gairdner Hospital (SCGH). The study targeted patients with PM or DM between the ages of 20 and 60 years due to the low numbers of patients available. A group with similar demographics to the patients were also recruited from the local community (see Appendix A). Edith Cowan University (ECU) Ethics Committee and SCGH Human Research Ethics Committee both approved the study.

Ten subjects (3 = patients, 7 = controls) participated in the study. However, one patient withdrew due to the disease flaring as a result of a cold after the loading phase and one control withdrew after the 5th week due to time restrictions and nausea as a result of the supplementation. The two patients (one = male, one = female) that completed the study were matched with two controls of the same gender and similar physical characteristics. The male patient (197 cm, 81 kg) aged 24 years was matched with a control (197 cm, 78 kg) aged 20 years. The female patient (159 cm, 101 kg) aged 42 years was matched with another female (158 cm, 79 kg) aged 41. The patient that withdrew after the second week (164 cm, 54.5 kg) aged 60 years was matched with a female control (155 cm, 58 kg) aged 51 years who completed the study.

Patient One was a 24-year-old male student who was diagnosed with DM in December 2001. Prior to diagnosis, he was a fulltime student and exercised regularly, swimming at a state level when younger. Six weeks prior to diagnosis, he was bed bound. Tests showed a history of pulmonary infiltrates whilst physical tests showed severe muscle weakening in the left vastus lateralis and joint stiffness. He began taking Methotrexate ($10 \text{ mg}\cdot\text{wk}^{-1}$) and Prednisolone ($50 \text{ mg}\cdot\text{d}^{-1}$). Prednisolone was dropped 4 months later to $7.5 \text{ mg}\cdot\text{d}^{-1}$, this was not well tolerated and both Methotrexate and Prednisolone were increased to 20 mg. During this time a distinct rash started to appear and Plaquenil ($400 \text{ mg}\cdot\text{d}^{-1}$) was introduced shortly after. In the first eight months the muscle disease was mildly active and Imuran ($150 \text{ mg}\cdot\text{d}^{-1}$) was also prescribed. Within the year, after no relapse, he started to stabilise and began tapering off the medications.

Patient Two was a 43-year-old woman whom began displaying symptoms of PM in early 1999 when she was three months postpartum. Tests showed increased activity within myelinated fibres consistent with early active IM. The onset of PM was thought to be triggered by an episode of fever and malaise. The fever eventually passed but the malaise continued to a certain degree. By April 2000 she complained of increased muscle aching in the thigh and weakness in the shoulder and hip girdles. A month later she recorded an elevated CK reading and was prescribed $75 \text{ mg}\cdot\text{d}^{-1}$ of Prednisolone, only to relapse resulting in the addition of Methotrexate ($15 \text{ mg}\cdot\text{wk}^{-1}$). A case of erythema, possibly induced by steroids was seen in January 2001. A bone density scan in June showed femoral osteopaenia, there was also evidence of patellofemoral osteoarthritis in both knees, the left being the worst affected. By April she was taking Prednisolone ($50 \text{ mg}\cdot\text{d}^{-1}$), Methotrexate ($20 \text{ mg}\cdot\text{wk}^{-1}$) and Imuran ($150 \text{ mg}\cdot\text{d}^{-1}$) from which the disease started to stabilise and Prednisolone was slowly dropped. The characteristics of all 10 subjects can be seen in Table 1.

Table 1.*Characteristics for the Study Participants*

Group		Age (yrs)		Height (cm)		Weight (kg) (pre)		Weight (kg) (post)
Control	Male (n = 3)	43.7	±	183	±	77.9	±	77.5
		21.2		12.1		7.2		11.2**
	Female (n = 4)	42.8	±	162.8	±	68.4	±	69.3
		7.1		8.0		9.0		8.2
Patient	Total (n = 7)	43.1	±	171.4	±	72.5	±	72.0
		13.3		14.1		9.1		9.1**
	Male (n = 1)	24.0*		197.0*		81.0*		81.5*
	Female (n = 2)	51 ±		161.5 ±		77.8 ±		100.0*
Patient		12.7		3.5		32.9		
	Total (n = 3)	42.0	±	173.3	±	78.8	±	90.8
		18.0		20.6		23.3		13.1

Note. Values are mean ± SD * one subject therefore no SD. ** excludes the male that withdrew.

Subjects were required to attend a health screening with a General Practitioner in order to ensure subjects were medically fit to participate. This reduced the chance of participants experiencing adverse side effects due to the training or testing protocol. The subjects then commenced the study after reading and signing a consent and medical form (Appendix B & C).

Subjects engaging in any form of RT in the past six months or who had previous back complaints or other musculoskeletal injuries inhibiting their performance in the test were asked not to participate in the study. Sedentary subjects were preferred because it has been proven difficult to isolate the improvements in performance related to the CrM supplementation with that from any training currently performed (Bemben et al., 2001).

3.2 Experimental Protocol

3.2.1 Design

Subjects were split into two groups, a patient group (PG) and a control group (CG). The CG was later further split into a matched control group (MCG) for the comparison between disease and non-disease. All groups ingested CrM throughout the duration of the study in conjunction with a twelve-week home-based training protocol in which the groups were divided into subgroups of trained (PGT and CGT) and untrained limbs (PGU and CGU).

The CG was included for comparison purposes between diseased and non-diseased individuals as well as providing a basis for eliminating extraneous variables. The untrained limb was also included to act as a within-subject control for the trained limb in both groups. For example, if an increase in strength and endurance parameters were seen in the CG but not in the PG then the lack of improvement would be due to the disease and not the age of the individual.

3.2.2 Supplementation

In healthy, active subjects, five to ten-days of 20 to 25 g·d⁻¹ of CrM has been demonstrated to increase intra-muscular Cr levels resulting in the ability to cope with extra training. A study by Rawson, Wehnert and Clarkson (1999), found that studies that employed older subjects did not allow sufficient time for CrM loading to occur. Therefore, a loading phase of fourteen days was employed to enable the older subjects to effectively utilise the extra CrM ingested.

All participants ingested 20 g·d⁻¹ of CrM during the loading phase (two weeks) and 5 g·d⁻¹ of CrM during the maintenance phase (ten weeks) (Appendix D). The CrM (Aussie Bodies – Victoria, Australia) was measured out using an electronic chemical balance scale (Mettler PM 4600 Deltarange). The CrM was in powder form and administered by the subject with the aid of a measuring scoop, one to three times a day. Subjects were asked to mix the supplement powder with water to make sure the subject stayed hydrated whilst ingesting CrM.

A dietary questionnaire (see Appendix F) was used, as certain foods are known to affect the consumption of CrM. In a diet loaded with carbohydrates the response to CrM intake and use is enhanced due to the presence of insulin (Andres et al., 1999). High caffeine consumption has been suggested to have an adverse effect to the ergogenic potential of CrM (Andres et al., 1999). Therefore the subjects were asked to restrain from caffeine intake for 24 hours prior to testing.

3.2.3 Training Protocol

Both groups participated in a twelve-week home-based light-resistance training protocol (Appendix D). Training sessions were performed three times per week throughout the entire study (36 total exercise sessions). The training sessions were carried out on the knee extensors and knee flexors using an adjustable ankle cuff and weights (Australian Barbell Company – Victoria, Australia). The session consisted of one set of twelve repetitions of knee extension and knee flexion exercises, building up to two sets of twelve repetitions after the first two weeks. Each session lasted no more than five minutes, as only one leg was trained. The training limb was chosen randomly.

The weights were set and equivalent to 30% of the subjects' maximal isometric force as determined from isokinetic dynamometry. The loads were examined regularly via the training diary with an increase every two weeks by an extra set or by 250 - 500 grams when they have reached the third set. Extra care was taken with the PG and if difficulty arose, weights/sets were dropped. The increases took place when subjects were able to perform the training sessions without any muscle soreness lasting more than one day.

An exercise questionnaire (see Appendix E) was provided to evaluate the activity habits of the subjects. Activity levels were assessed to gain information on the fitness of the subject normal activity levels of the subjects. All subjects were contacted on a regular basis to ensure that they were continuing the program as outlined and that they had not encountered any problems.

If the subject could not cope with the discomfort they were instructed to take a day off training, however they were strictly informed to keep supplementing. Each subject was given a simple training diary (see Appendix F) to complete, which was used to quantify the volume of training as a product of repetitions and weight.

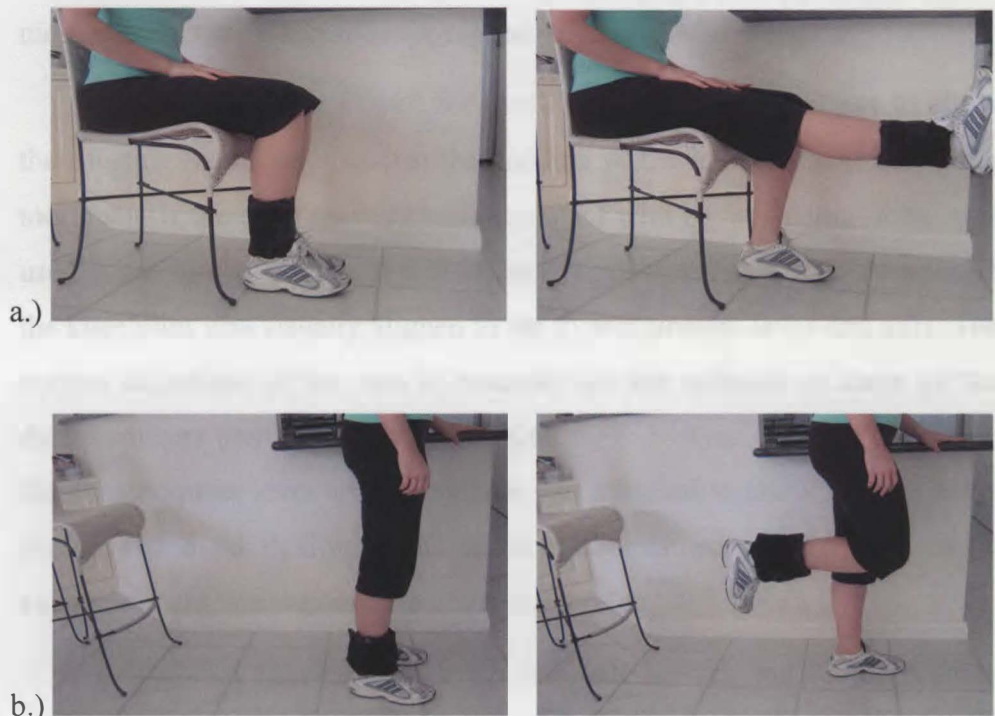


Figure 3. Extension and flexion training exercises. a.) Extension exercises
b.) Flexion exercises.

3.2.4 Isokinetic Dynamometer

Strength tests were completed on a Cybex 6000 Extremity Testing and Rehabilitation System (Ronkonkoma, NY), Biodex (B3) Multi Joint System 3 Pro (Shirley, NY) or a Biodex (B2) System 2 (Shirley, NY) computer controlled isokinetic dynamometer. Three isokinetic dynamometers were operated throughout the study as the Cybex became unavailable due to over booking. Subjects also refused to travel to the Joondalup campus for testing and therefore the B2 was utilised at the University of Western Australia. As a result, a pilot study was performed on each dynamometer with 22 subjects (11 = male; 11 = female) employing both isometric and isokinetic exercises. Interclass correlation coefficients (ICC) ranged from 0.66 – 0.92 and 0.77 – 0.97 for isometric and isokinetic extension exercises respectively (see Appendix H).

Each dynamometer was calibrated prior to commencing the study. The first session started with a verbal explanation of the aims and practical procedures of the study to each subject. The subject's height and weight measurements were recorded with a height scale and an electronic weight scale (Mettler ID1 Multirange). With these anthropometric measurements, the dynamometer was adjusted to each subject individually. These measurements were recorded for reproduction on each testing day.

The backrest was moved forward depending on the subject to allow their testing leg to push against the padding of the lever without extending too much. If the chair was not well equipped with back padding, foam was used in the lumbar region to ensure correct posture. The axis of rotation in the knee joint was visually aligned to the dynamometers lever arm axis. The correct alignment of the two is essential for the analysis of force as the dynamometers arm acts as the limb (Keating & Matyas, 1996). Padding on the dynamometer lever arm attachment was adjusted to allow for free ankle plantar and dorsi flexion. If the subjects complained of shin soreness an extra piece of foam was used to cover the foreleg.

A diagonal shoulder and a lap seat belt secured the subject's trunk against the chair. A velcro strap positioned firmly at the distal thigh secured the test leg to the chair. These straps help stabilise the upper body and upper limb preventing unwanted movements (Evetovich et al., 2001). The non-test leg was left to hang free at about 90°- knee flexion. The operator moved the subject's leg through the entire range of movement (ROM), limits of motion of a limb, to ensure that the lever arm and the subject's leg follow the same rotation and gravitational corrections was then calculated at 45°- knee flexion on both the Cybex and B2, whereas the leg was placed in full knee extension for B3. An extendable goniometer (Lafayette Instrument Company) was needed to acquire this angle on the B2.

A practice test was employed to familiarise each subject to the testing velocities used. Two repetitions were performed at submaximal effort, the last repetition was performed at full maximal effort to familiarise the subject. After the subject felt comfortable with the different tasks, the actual exercise was started.

The test session lasted no more than one hour and included three isometric contractions of the knee extensors and knee flexors at two different angles (45° and 60°) with a 30-second rest period between each angle. An Ambassador stopwatch (Accusplit, USA) was used to measure the rest period. The short rest was chosen as it is known to show increased torque production by an average of 5% when compared with a protocol with no rests which is shown to portray more of a declining trend (Keating & Matyas, 1996).

The subjects were then instructed to exert four extension and flexion MVC's as rapidly and as hard as possible over four constant angular velocities 60°, 120°, 180° and 240° s⁻¹ (slow to fast) with a 30-second rest between each velocity. Two minutes after the exercise test was performed and recorded the endurance test begun. This consisted of five sets of fifteen repetitions at a velocity of 180° s⁻¹ with a 30-second rest between sets. The subject was instructed to concentrate on extension repetitions, as flexion was not measured in this test. For this reason the flexion velocity was set at 450° s⁻¹ on the B2 to prevent any torque production. The subject then rested for five minutes and the protocol was repeated with the non-trained leg for comparison. The procedure was repeated at the end of weeks two, seven and twelve (Appendix C). All sessions were performed under the supervision of the same investigator. All testing was performed while receiving strong and frequent encouragement both verbally and visually on screen. Measurements of torque, work and power were assessed in each exercise.

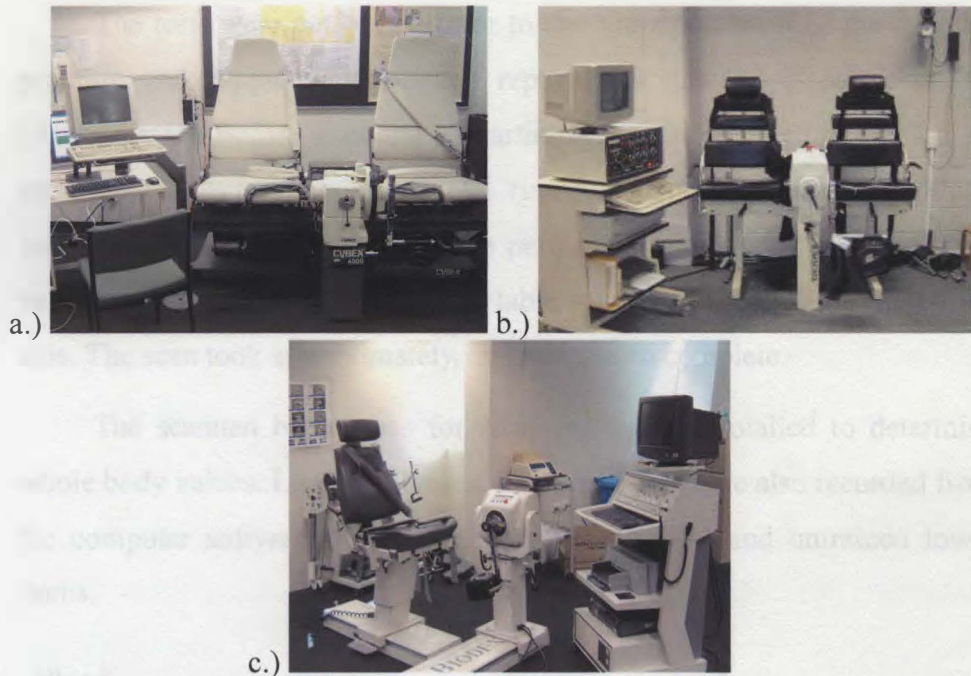


Figure 4. Isokinetic dynamometers. a.) Cybex 6000 Extremity Testing and Rehabilitation System (Ronkonkoma, NY). b.) Biodex System 2 (Shirley, NY). c.) Biodex Multi Joint System 3 Pro (Shirley, NY).

3.3.5 Body Composition (DEXA)

Body composition measurements were assessed using a Norland XR – 46 Dual Energy X-ray Absorptiometer (DEXA) via pencil beam technology. The DEXA scans are used to measure bone and soft tissue composition in vivo, also permitting the assessment of whole-body and regional body composition (Lukaski, 1997). Dual energy x-ray absorptiometer scanning is a very reliable ($r = 0.99$) and accurate means (Coefficient of Variation = 0.5 - 1%) of quantifying body composition for regional as well as whole body parameters (Maud & Foster, 1995; Kreider et al., 1996).

The DEXA scans separate the body tissue into three chemical components, lean soft tissue, fat soft tissue, and bone (Kreider et al., 1998). Scans were taken of the whole body with the left and right upper legs singled out after to quantify the mass of the limb segment (see Appendix G). The upper leg data was achieved by repositioning the cursor from individual DEXA scans to the most superior point of the greater trochanter to the lateral epicondyle of the femur.

The tests were performed prior to the commencement of the exercise program and supplementation and repeated at the end of week twelve (Appendix D). Before scanning all participants were required to take off all removable objects containing metal (i.e. jewellery, glasses, and clothing with buttons or zippers). Scans were performed with the subject lying in a supine position along the scanning table's centre line of the longitudinal axis. The scan took approximately five minutes to complete.

The scanned bone mass for each region, was totalled to determine whole body values. Lean body mass, FM, and FFM were also recorded from the computer software for whole body, and trained and untrained lower limbs.

3.3.6 Blood

The serum Crn level was measured in the first week before supplementation and at the end of week twelve using a portable Reflotron Spectrophotometer (Boehringer-Mannheim – Pöde, Czech Republic) (Appendix D). A site on the fingertip was cleaned using an alcohol swab where the lancet (Boehringer-Mannheim – Pöde, Czech Republic) was to puncture the skin and draw blood into a heparinized capillary tube. The blood was then placed on a Crn assay strip (Roche Diagnostics – Mannheim, Germany) in which the Reflotron Spectrophotometer analysed the circulating Crn levels.

3.3 **Data Analysis**

Torque (peak and low values), work and power were recorded for each isometric, isokinetic and endurance test. However not all tables were displayed in the results section due to the large amount of data recorded. Isometric data for the first angle, 45°, and isokinetic data at predetermined speeds of 120° s⁻¹ and 240° s⁻¹ were not included as they showed little or no variation in comparison to data obtained from the second isometric angle, 60°, and velocities of 60° s⁻¹ and 180° s⁻¹.

The fatigue index was determined as the measurement of PT for the last five repetitions (last third) divided by the first five PT values (first third) and expressed as a percentage decline in work performance (Westblad, Svedenhag & Rolf, 1996). Total training volume was measured by firstly multiplying the amount of weight lifted by the numbers of repetitions performed, then by the number of sets performed in one session. The training volume for each session was added together to obtain the total training volume.

These variables were compared in the patient population group prior to the training program and at the end of week twelve. In addition, the results obtained from the trained leg were compared with the non-trained leg. The patient data were then compared with the healthy subject's data, which was analysed the same way. In line with similar research in this area values in the results section are expressed as mean \pm standard error of mean (SEM) unless otherwise stated.

3.4 Statistics

Differences between exercise parameters obtained at given velocities and angles were tested for significance using a one-way analysis of variance (ANOVA) with repeated measure design. Standard statistical methods were used to calculate the mean, standard deviations (SD) or SEM. Serum Crn levels and DEXA scans were analysed using a t-test with repeated measures. Differences were considered significant if the p value was < 0.05 (Fenter, Bellew, Pitts & Kay, 2003).

3.5 Limitations

The major limitation of the study was the variability between patients and the lack of numbers. An individuals' response differed as well as their physical abilities due to the progression of their disease. Another limitation was that the control subjects were sought out through advertisements in the local community therefore it is difficult to say whether the participants were a true representation of the general population.

Further limitations with the study were that supplementation and the training exercises were performed in the subject's home not directly supervised by the investigator. A considerable amount of trust was placed on the subject to ensure both the supplementation and the training was being followed as instructed. An additional limitation to training was that no between-group comparisons of the contralateral limb were tested. Due to the low subject numbers only within-group comparisons were conducted and it has been known with this design that contralateral strength increases may be due to familiarisation with the test exercise and procedures (Munn et al., 2004). Another major limitation was that three dynamometers were used to test the subjects due to transport and other unforeseen problems, which may also account for the variability between results. Lastly, in regards to the training volume, a low training intensity was implemented based on previous work with CrM supplementation and training in elderly males. The muscular weakness of the patient population was also kept in mind when the training intensity was employed. Due to the lack of studies in this area and the unknown responses to heavy RT, a lowered intensity was instigated.

To control most of the above limitations the training was monitored through the completion of a training diary and supplementation was pre-packed and a reliable measuring tool was implemented for the subject to calculate the proper dosage needed. A pilot study was also conducted (n = 22) to compare the data output of PT and TW between all three isokinetic dynamometers (see Appendix H) however, this showed that for the three isokinetic dynamometers, reliability was low for some measures, accounting for the majority of variability seen between results.

CHAPTER FOUR

4. RESULTS

4.1 Exercise Training

Figure 5 below shows the average training volumes for the CG and PG calculated from their training diaries. The CG ($n = 6$) performed an estimated mean total volume of 3070 ± 280 J (\pm SEM) compared with the PG [$n = 2$ (one female, one male)] who averaged 4241 ± 2234 J over the twelve-weeks. The MCG [$n = 2$ (one female, one male)] measured a mean total volume of 3047 ± 374 J, a 39% difference from the PG pairs.

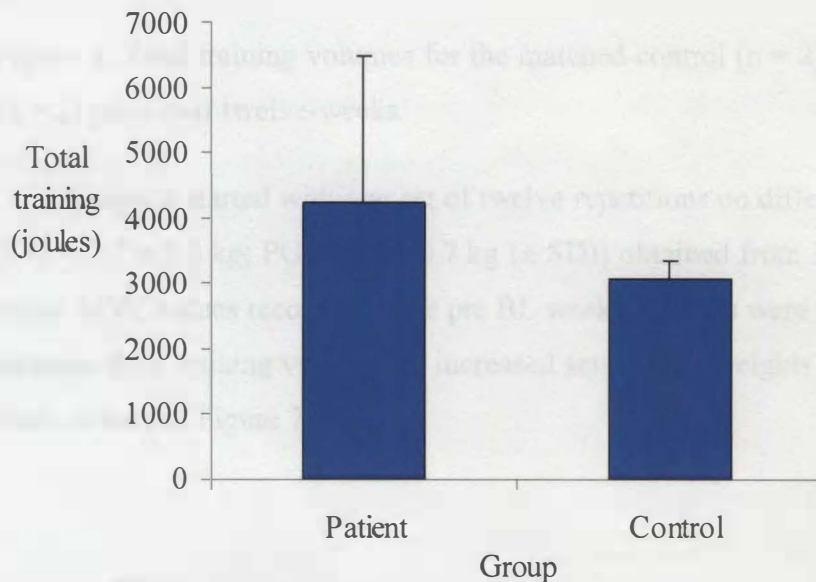


Figure 5. Total training volumes for control group ($n = 6$) and patient group ($n = 2$) for twelve-weeks (Mean \pm SEM).

The total volume of training for the two pairs can be seen in Figure 6. The total training for the female pair was 2673 J and 2007 J for the control and patient respectively. As for the male pair the control's total training was 3420 J compared with 6476 J of the patient.

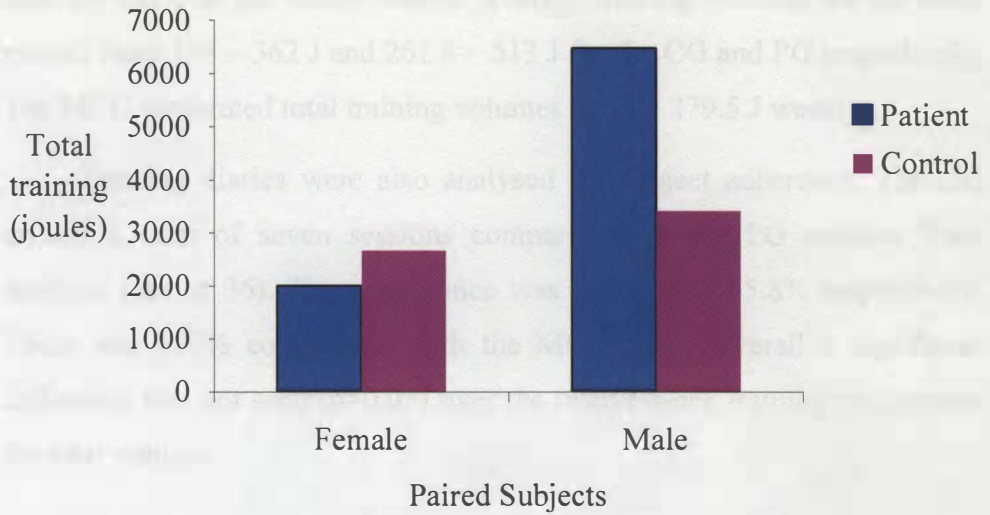


Figure 6. Total training volumes for the matched control (n = 2) and patient (n = 2) pairs over twelve-weeks.

Subjects started with one set of twelve repetitions on different weights [CG = 2.7 ± 0.3 kg; PG = 2.5 ± 0.7 kg (\pm SD)] obtained from 30% of their initial MVC values recorded in the pre BL week. Subjects were instructed to increase their training volume via increased sets and/or weights on a regular basis as seen in Figure 7.

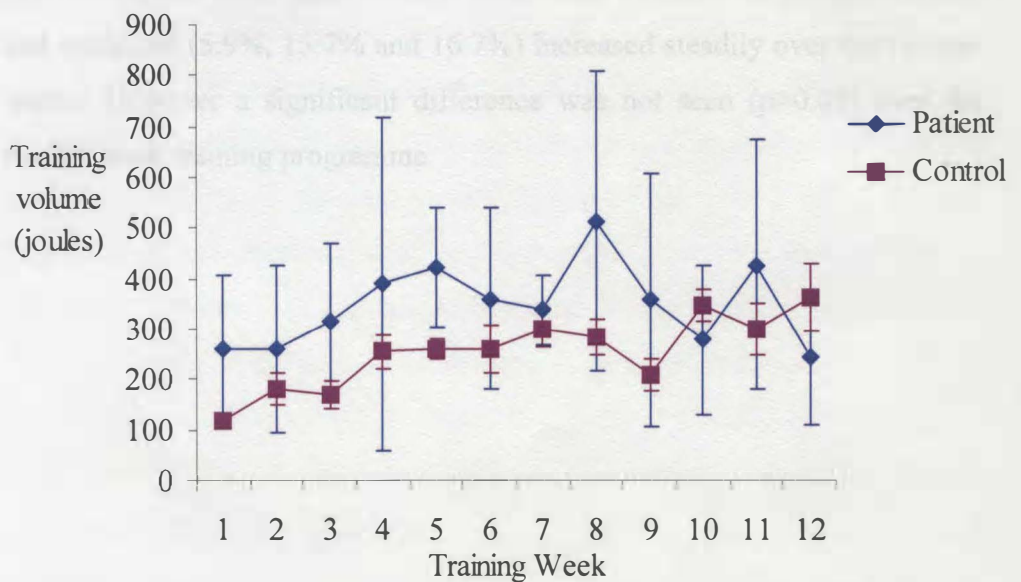


Figure 7. Weekly training volumes for control (n = 6) and patient (n = 2) groups over twelve-weeks (Mean \pm SEM).

On average the PG performed slightly higher weekly training loads than the CG over the twelve-weeks. Average training volumes for the week ranged from 118 – 362 J and 261.8 – 513 J for the CG and PG respectively. The MCG performed total training volumes of 99 – 379.5 J weekly.

Training diaries were also analysed for subject adherence. The CG missed a total of seven sessions compared with the PG missing three sessions (out of 36). The compliance was 98.6% and 95.8% respectively. There was 100% compliance with the MCG pairs. Overall a significant difference was not seen ($p>0.05$) over the twelve-week training programme for total volume.

4.2 Strength Testing

The isometric PT responses of the CG and PG at 60° for knee flexion can be seen in Figure 8. Baseline strength started at 49 ± 27 Nm and 63 ± 36 Nm for the trained and untrained leg of the PG. The CG averaged a BL strength of 57.8 ± 8 Nm and 53.1 ± 9.4 Nm for the trained and untrained limb respectively. The trained limb of the patients decreased in Week 2 (-18.4%) then increased by 16.3% and 12.2% in Week 7 and Week 12 compared with BL values. The untrained limb decreased (-9.5% and -17.5%) in Week 2 and Week 7 respectively, finally increasing in Week 12 (5.6%). On the other hand the CG both trained (7.6%, 16.2% and 20.8%) and untrained (5.9%, 15.7% and 16.7%) increased steadily over the twelve-weeks. However a significant difference was not seen ($p>0.05$) over the twelve-week training programme.

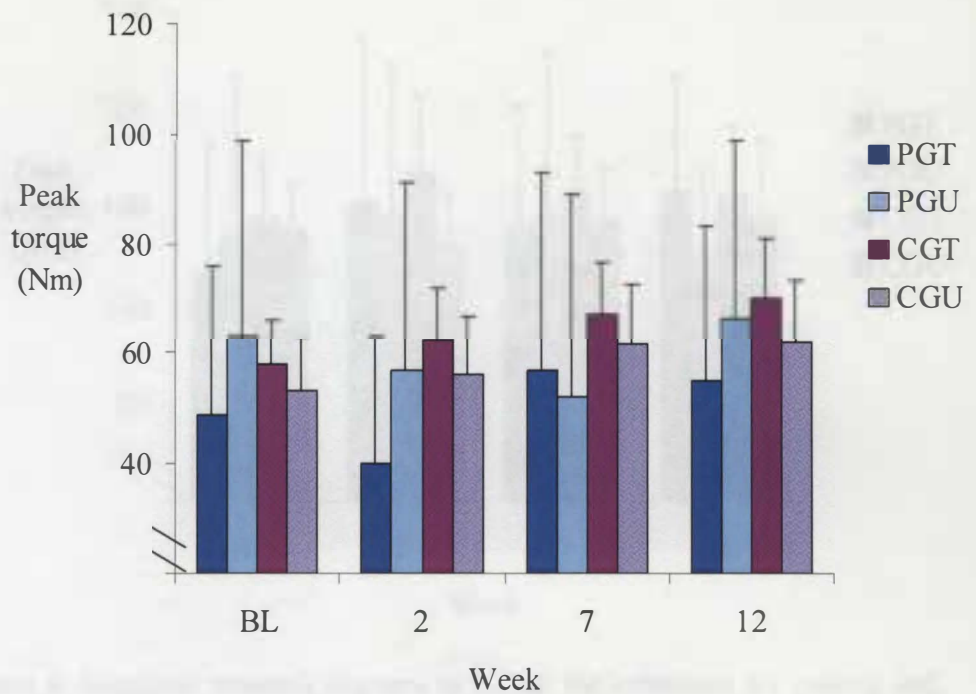


Figure 8. Isometric strength changes at 60° of the flexors for trained and untrained limbs in the control (n = 6) and patient (n = 2) groups (Mean ± SEM).

Figure 9 shows the responses of the CG and PG over time for isometric PT values at 60° for the knee extension. Baseline strength for the trained and untrained limbs of the PG were 133.5 ± 52.5 Nm and 148.5 ± 65.5 Nm. The CG averaged an initial strength of 155.8 ± 25 Nm and 151.1 ± 18.8 Nm for the trained and untrained limb respectively. The PGT limb increased strength by 21.8% in the second week, slightly decreased in the seventh (14.2%) and increased to 24.3% by the final week compared to BL figures. Both the untrained limb of the PG and the trained limb of the CG increased in Week 2 (6.1% and 11.8%) and slowly declined over Week 7 (5.1% and 6.6%) and Week 12 (-6.4% and 6.1%). The untrained limb for the CG decreased in Week 2 (-4.2%) until increasing in Week 7 (2%) and again in Week 12 (3.2%). A significant difference was not seen (p>0.05) over the twelve-week training programme.

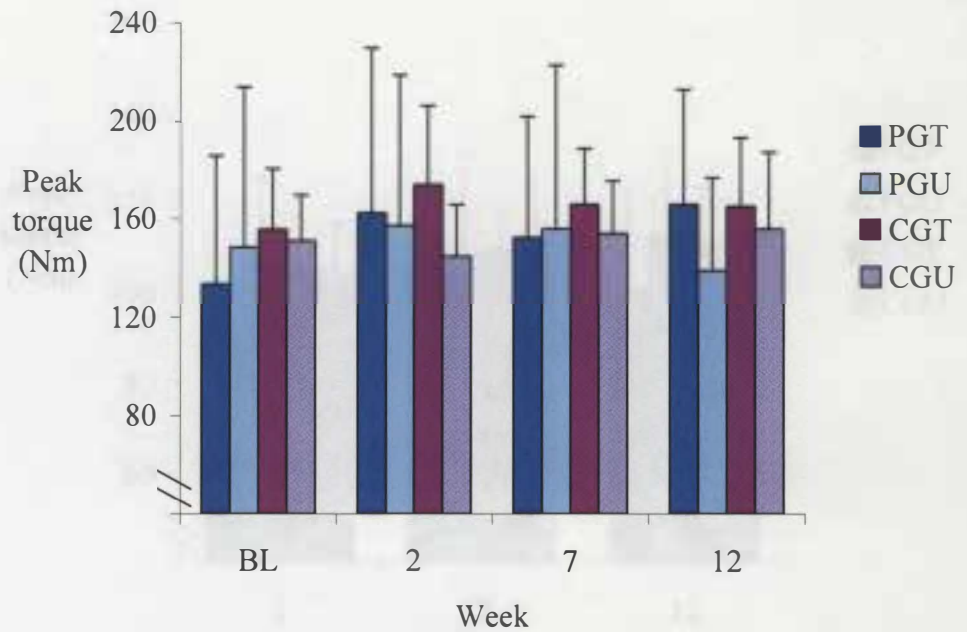


Figure 9. Isometric strength changes at 60° of the extensors for trained and untrained limbs in the control (n = 6) and patient (n = 2) groups (Mean ± SEM).

Figure 10 shows the responses of the CG and PG over time for isokinetic PT values at 60° s⁻¹ for the knee flexors. By Week 2 PGT had decreased by 10.4% whilst PGU (6.4%), CGT (4%) and CGU (4.4%) increased. The PGT, PGU, CGT and CGU limbs all increased by the seventh week (11.8%, 8.6%, 9.2% and 13.1% respectively). Both PGU and CGT again by Week 12 (12.3% and 10.9%), PGT and CGU on the other hand tended to decrease (0.1% and 5%) in Week 12 compared with BL values. A significant difference was not seen (p>0.05) over the twelve-week training programme.

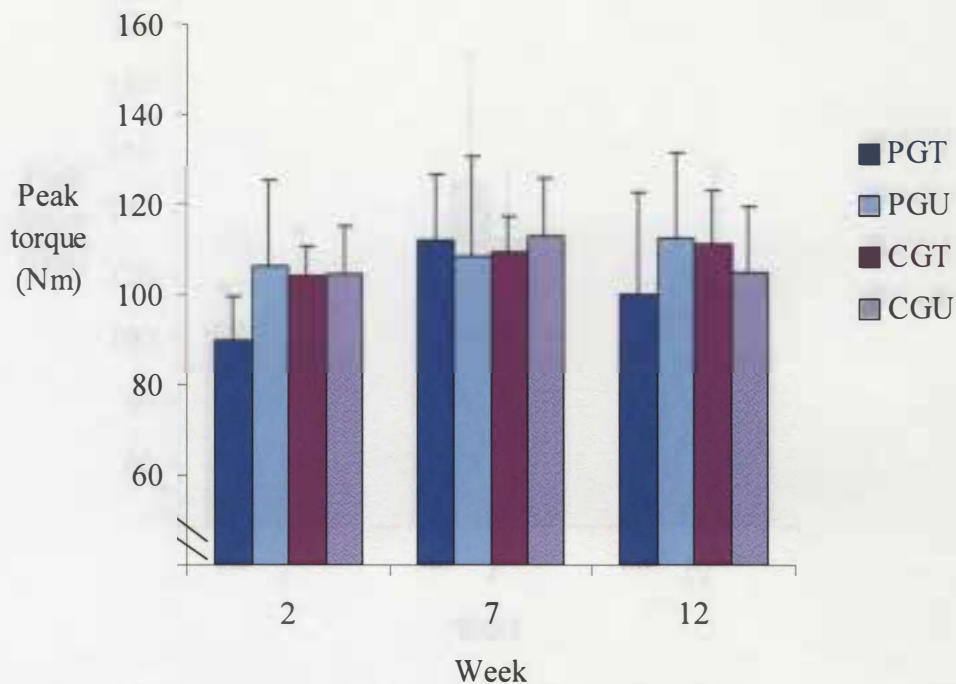


Figure 10. Isokinetic strength changes at $60^{\circ} \text{ s}^{-1}$ of the flexors expressed as a mean percentage from BL values for trained and untrained limbs in the control ($n = 6$) and patient ($n = 2$) groups (Mean \pm SEM).

Figure 11 shows the responses of the CG and PG over time for isokinetic PT values at $180^{\circ} \text{ s}^{-1}$ for the knee flexors. Over the twelve-weeks CGU slowly declined below BL values (Week 2 = -3.7%; Week 7 = -5.3%; Week 12 -5.8%). The PGU limb started below BL levels (-12.6%) in Week 2. By Week 7 and 12 the limb had improved (48.8% and 24.9%) from BL. As for PGT the limb increased over the twelve-weeks (4.5%, 11.6% and 7.8%) just like CGT (17.2%, 31.1% and 24.8%). A significant difference was not seen ($p > 0.05$) over the twelve-week training programme.

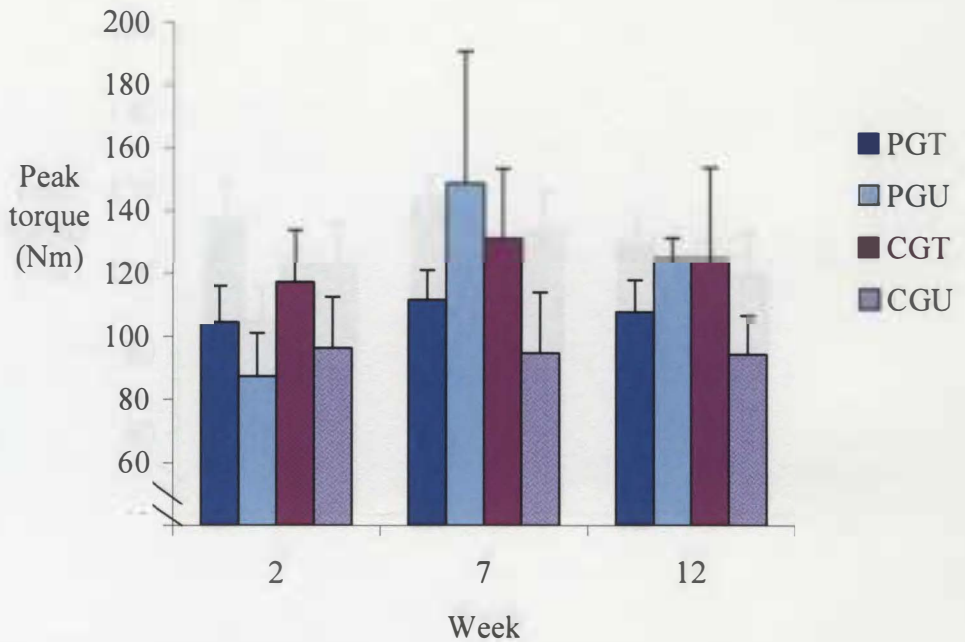


Figure 11. Isokinetic strength changes at $180^{\circ} \text{ s}^{-1}$ of the flexors expressed as a mean percentage from BL values for trained and untrained limbs in the control ($n = 6$) and patient ($n = 2$) groups (Mean \pm SEM).

Figure 12 shows the responses of the CG and PG over time for isokinetic PT values at $60^{\circ} \text{ s}^{-1}$ for the knee extension. In Week 2 both PG and CG trained limb and the CG untrained limb increased (13.1%, 2.2% and 2.2% respectively). The PGU limb decreased (-12.3%) from BL values. By Week 7 PGT, PGU and CGU increased again (18.5%, 1.5% and 10.1%) whilst CGT decreased slightly (1.4%). Towards the end PGT, CGT and CGU also started to decline (7.3%, 0.6% and -0.8%) where as the untrained limb of the PG increased to 2.5%. A significant difference was not seen ($p > 0.05$) over the twelve-week training programme.

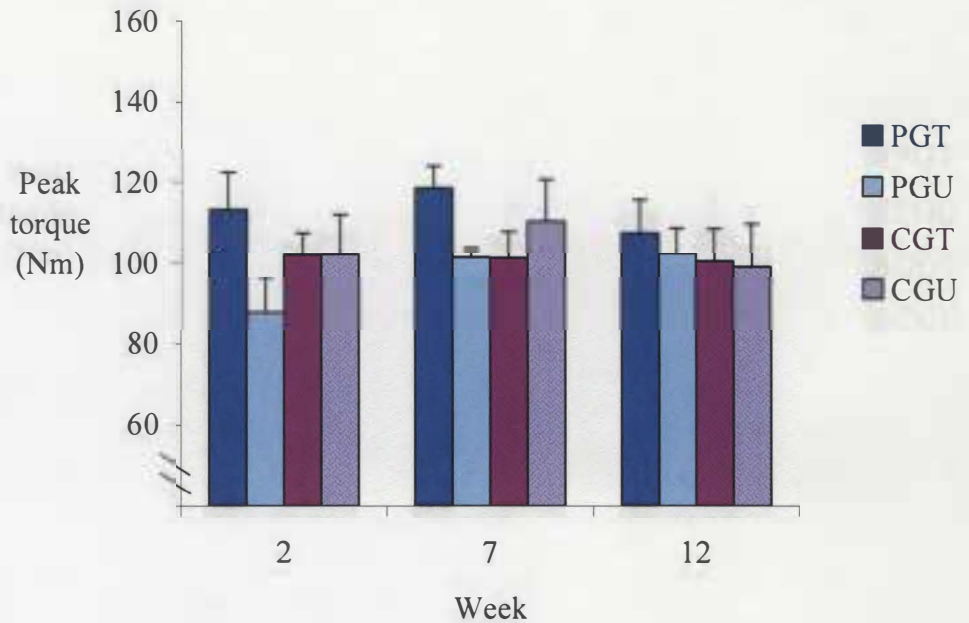


Figure 12. Isokinetic strength changes at $60^{\circ} \text{ s}^{-1}$ of the extensors expressed as a mean percentage from BL values for trained and untrained limbs in the control ($n = 6$) and patient ($n = 2$) groups (Mean \pm SEM).

Figure 13 shows the responses of the CG and PG over time for isokinetic PT values at $180^{\circ} \text{ s}^{-1}$ for the knee extension. PGU started below BL figures in Week 2 (-11.5%) and slowly started to increase (Week 7 = -4.1% and Week 12 = -0.8%). The CGT limb kept increasing above BL values (Week 2 = 4.6%; Week 7 = 6.4%; Week 12 = 8.3%). Both PGT and CGU started off increasing in Week 2 (6.8% and 6.9%) and Week 7 (12.7% and 8.7%) dropping off in Week 12 (12.3% and 3.9% respectively). A significant difference was not seen ($p > 0.05$) over the twelve-week training programme.

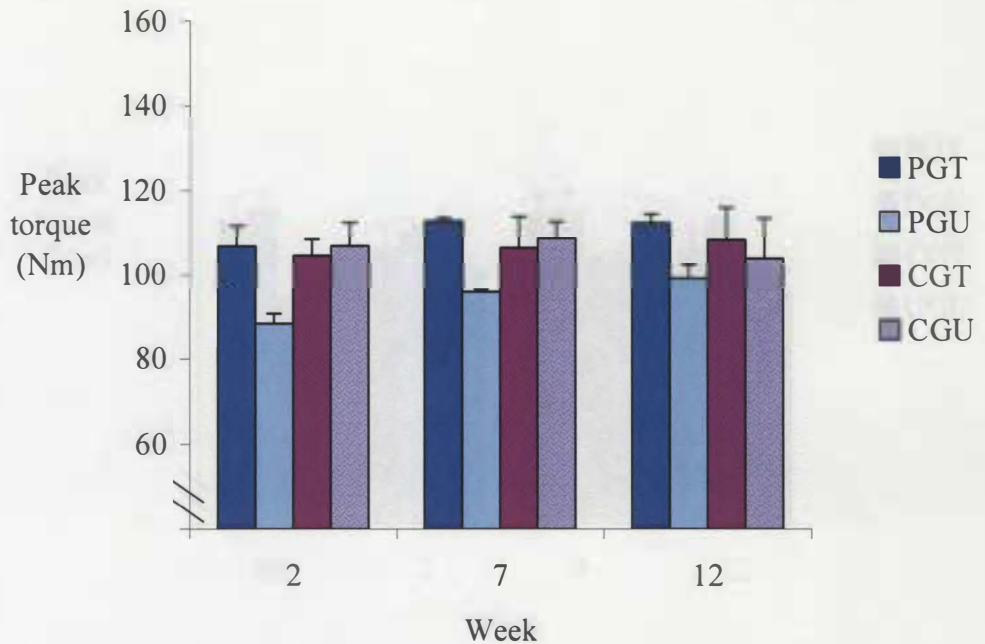


Figure 13. Isokinetic strength changes at $180^{\circ} \text{ s}^{-1}$ of the extensors expressed as a mean percentage from BL values for trained and untrained limbs in the control ($n = 6$) and patient ($n = 2$) groups (Mean \pm SEM).

Figure 14 shows the responses of the CG and PG over time for the endurance protocol performed at $180^{\circ} \text{ s}^{-1}$. It represents the PT changes for the untrained and trained knee extensors. At BL both PGT and PGU were higher ($112.4 \pm 5.8 \text{ Nm}$; $115.1 \pm 4.8 \text{ Nm}$) than the CG (Trained = $92.2 \pm 1.6 \text{ Nm}$; Untrained = $94 \pm 1.8 \text{ Nm}$). By Week 2 the CG (Trained = $98.3 \pm 2.3 \text{ Nm}$; Untrained = $101.5 \pm 2.5 \text{ Nm}$) had increased whereas the PG both trained and untrained declined ($105.9 \pm 5.6 \text{ Nm}$; $109.6 \pm 2.5 \text{ Nm}$). By Week 7 PGT, CGT and CGU increased their PT values above BL levels ($114.2 \pm 5 \text{ Nm}$; $101.8 \pm 1.7 \text{ Nm}$; $103.2 \pm 1.8 \text{ Nm}$), the PGU limb fell slightly short ($115 \pm 4.8 \text{ Nm}$). Over the twelve-weeks the CG had increased its strength from BL levels (Trained = $101.9 \pm 1.9 \text{ Nm}$; Untrained = $96.7 \pm 1.7 \text{ Nm}$) compared with the PG (Trained = $105 \pm 4.7 \text{ Nm}$; Untrained = $113.2 \pm 4.9 \text{ Nm}$). A significant difference was not seen ($p > 0.05$) over the twelve-week training programme.

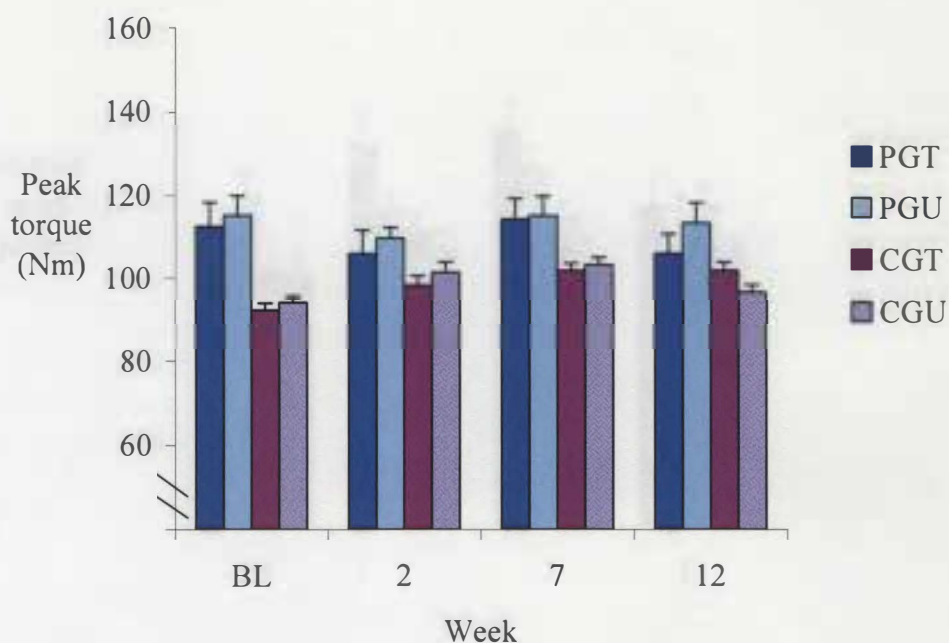


Figure 14. Strength changes of the extensors in the endurance protocol at $180^{\circ} \text{ s}^{-1}$ for trained and untrained limbs in the control ($n = 6$) and patient ($n^{\circ} = 2$) groups (Mean \pm SEM).

Figure 15 shows the responses of the CG and PG over time for the endurance protocol performed at $180^{\circ} \text{ s}^{-1}$. Representing the STW generated for the untrained and trained knee extensors. The CGT limb increased throughout the twelve-weeks (BL = $1030.6 \pm 25.6 \text{ J}$; Week 2 = $1126 \pm 41.3 \text{ J}$; Week 7 = $1156 \pm 35.8 \text{ J}$; Week 12 = $1189.8 \pm 44.3 \text{ J}$) where as the untrained limb started to drop off at Week 7 only to improve by Week 12 (BL = $1017 \pm 40.2 \text{ J}$; Week 2 = $1079 \pm 42.9 \text{ J}$; Week 7 = $1066 \pm 39.2 \text{ J}$; Week 12 = $1082.9 \pm 27.2 \text{ J}$). The PGU limb decreased overall (BL = $1206.7 \pm 66.5 \text{ J}$; Week 2 = $1178.6 \pm 40.9 \text{ J}$; Week 7 = $1275.9 \pm 52.6 \text{ J}$; Week 12 = $1106.9 \pm 101.7 \text{ J}$) where as PGT increased up until Week 7 dropping in Week 12, staying above BL figures (BL = $1112.6 \pm 65.8 \text{ J}$; Week 2 = $1340.5 \pm 74.9 \text{ J}$; Week 7 = $1370.3 \pm 69.6 \text{ J}$; Week 12 = $1181.4 \pm 73.9 \text{ J}$). A significant difference was not seen ($p > 0.05$) over the twelve-week training programme.

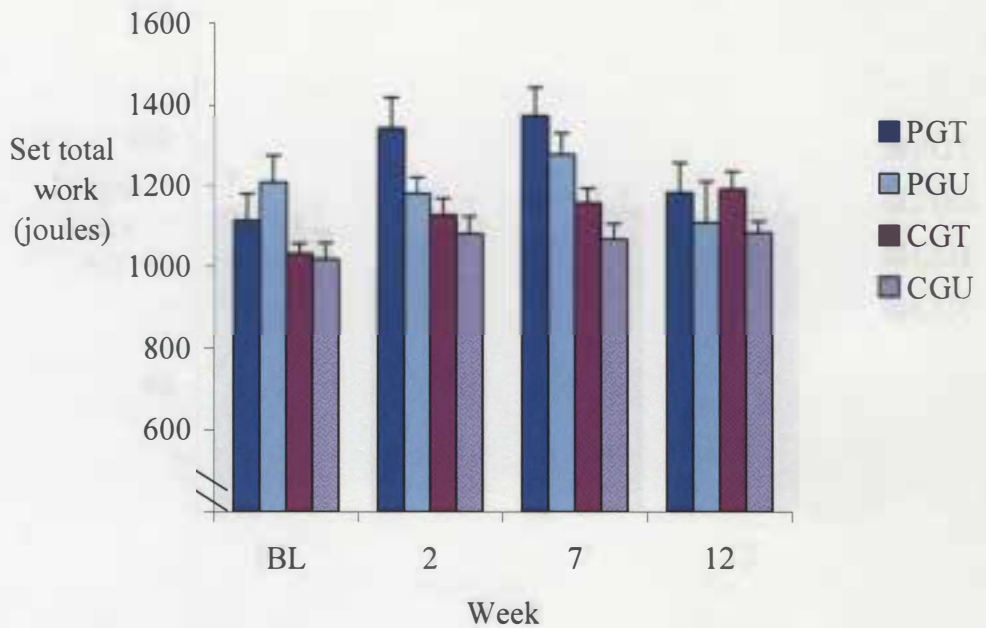


Figure 15. Set total work changes of the extensors in the endurance protocol at $180^{\circ} \text{ s}^{-1}$ for trained and untrained limbs in the control ($n = 6$) and patient ($n = 2$) groups (Mean \pm SEM).

Figure 16 represents the fatigue index of the CG and PG over time for the untrained and trained knee extensors. Fatigue index for the PG declined from BL to Week 2 for trained ($88.4 \pm 5.9 \%$; $78.3 \pm 2.3 \%$) and untrained ($84.5 \pm 4.2 \%$; $84 \pm 2.9 \%$). From BL the fatigue index increased in Week 2 for the CGT ($87.9 \pm 2.6 \%$; $88 \pm 3.4 \%$) and CGU ($83.3 \pm 3.4 \%$; $86.6 \pm 3.3 \%$ respectively). By Week 7 all groups continued increasing (PGT = $80.8 \pm 3.4 \%$; PGU = $87.2 \pm 1.2 \%$; CGT = $89.1 \pm 3 \%$; CGU = $88.3 \pm 3.2 \%$), although PGT was still below BL values. This trend continues into Week 12 where PGT was still below BL ($81.5 \pm 3.9 \%$). Although PGU, CGT and CGU stayed above BL values they had decreased slightly from Week 7 (PGU = $85.3 \pm 2.8 \%$; CGT = $88.2 \pm 3.2 \%$; CGU = $87.5 \pm 3 \%$). A significant difference was not seen ($p > 0.05$) over the twelve-week training programme.

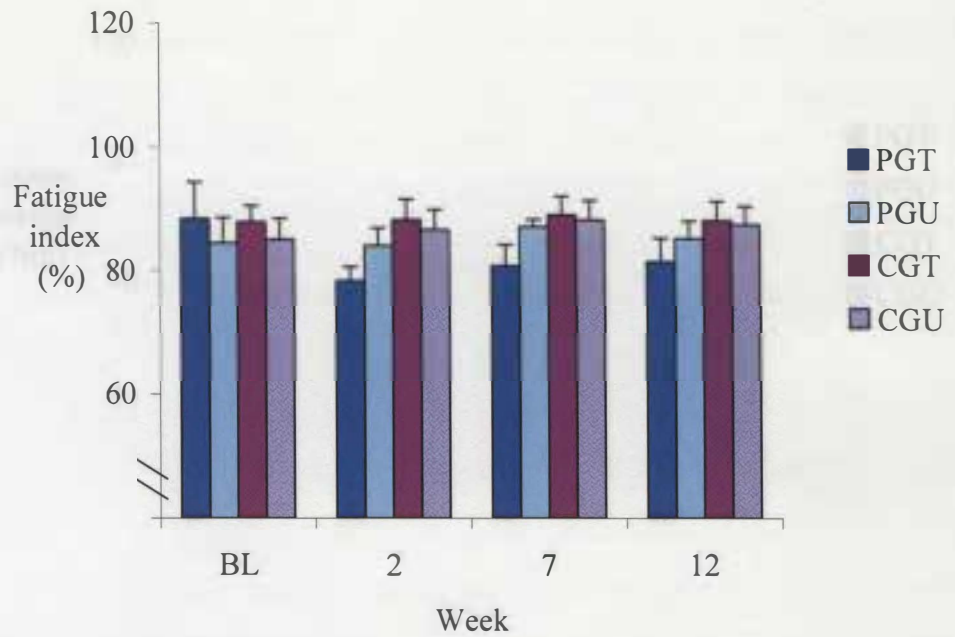


Figure 16. Changes in the fatigue index of the extensors at $180^{\circ} \text{ s}^{-1}$ for trained and untrained limbs in the control ($n = 6$) and patient ($n = 2$) groups (Mean \pm SEM).

Figure 17 represents the lowest torque generated by the trained and untrained extensors during the endurance protocol for the CG and PG over time. The CGT and the CGU limbs improved values of lowest torque throughout the twelve-weeks (BL = $58.9 \pm 2.6 \text{ Nm}$, $60 \pm 3 \text{ Nm}$; Week 2 = $67.1 \pm 3.8 \text{ Nm}$, $63.5 \pm 3.2 \text{ Nm}$; Week 7 = $70.1 \pm 2.5 \text{ Nm}$, $66 \pm 3.9 \text{ Nm}$; Week 12 = $70.5 \pm 3.5 \text{ Nm}$, $67.2 \pm 3.9 \text{ Nm}$ respectively). The PGT limb decreased below BL levels by Week 12 (BL = $59.6 \pm 6.1 \text{ Nm}$; Week 2 = $52.3 \pm 4.5 \text{ Nm}$; Week 7 = $58.8 \pm 4.4 \text{ Nm}$; Week 12 = $52.4 \pm 4.6 \text{ Nm}$) whereas PGU improved (BL = $54.2 \pm 6.2 \text{ Nm}$; Week 2 = $52.5 \pm 6.6 \text{ Nm}$; Week 7 = $62.1 \pm 3.9 \text{ Nm}$; Week 12 = $57.4 \pm 3.5 \text{ Nm}$). A significant difference was not seen ($p > 0.05$) over the twelve-week training and CrM supplementation period.

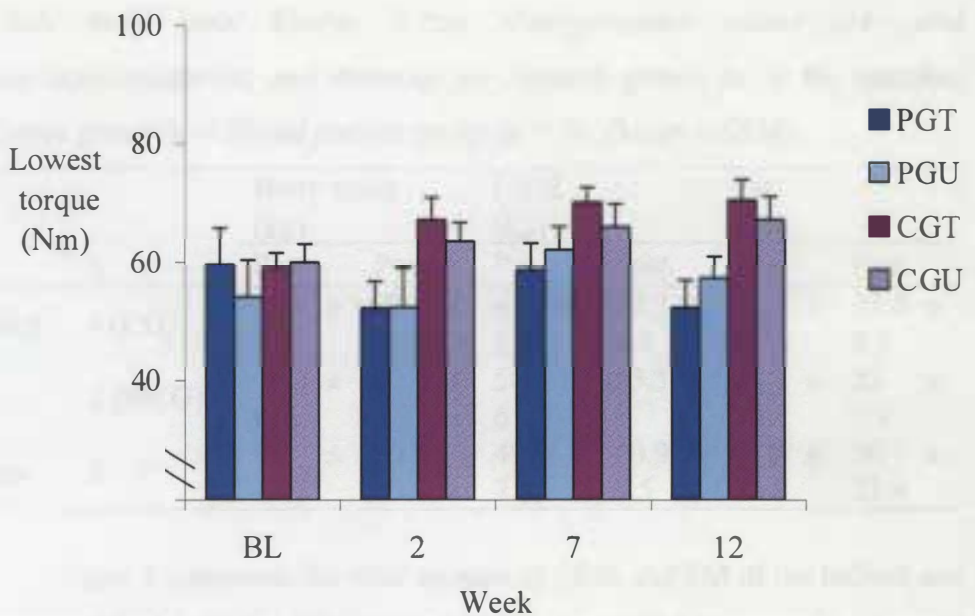


Figure 17. Changes in the lowest torque generated by the extensors at $180^{\circ} \text{ s}^{-1}$ for trained and untrained limbs in the control ($n = 6$) and patient ($n = 2$) groups (Mean \pm SEM).

4.3 Body Composition (DEXA)

Table 2 represents the total amount of body mass, LBM and FM of the whole body for all groups. Body mass increased for the CG and MCG (2.3% and 5% respectively) and decreased for the PG (-0.3%). The LBM increased for all groups (CG = 4.4%; MCG = 4.7%; PG = 2.2%) and FM decreased for both CG and PG (-1.8% and -3% respectively) but increased for the MCG (4.2%). No significant difference was seen ($p > 0.05$) in any group over the twelve-week training programme for body mass, LBM or FM.

Table 2.

Whole body Dual Energy X-ray Absorptiometer values pre- and post-supplementation and training for control group (n = 6), matched control group (n = 2) and patient group (n = 2). (Mean ± SEM).

	n	Body mass (kg)		LBM (kg)		Fat (kg)	
		Pre	Post	Pre	Post	Pre	Post
Control	6 (CG)	70.4 ± 8	72 ± 9.1	45.2 ± 3.8	47.2 ± 4.6	22.1 ± 4.2	21.7 ± 3.9
	2 (MCG)	78.5 ± 0.7	82.4 ± 4.2	50.9 ± 6	53.3 ± 8	24 ± 8.8	25 ± 7.9
Patient	2	91 ± 14.1	90.8 ± 13.1	49.8 ± 7.8	50.9 ± 8.5	37.2 ± 21.8	36.1 ± 21.4

Table 3 represents the total amount of LBM and FM of the trained and untrained limbs for the PG, CG and MCG. The LBM increased by a small amount for both trained (CG = 5.4%; MCG = 9.3%; PG = 6.3%) and untrained (CG = 3.1%; MCG = 9.5%; PG = 6.2%) limbs across all groups. Fat mass decreased in the trained (CG = -2.4%; MCG = -5.9%) and untrained (CG = -5.9%; MCG = -6%) limbs of the CG and MCG and the untrained limb of the PG (-3.2 %) while increasing for the trained limb (1.9%). No significant difference was seen ($p > 0.05$) over the twelve-week training programme for LBM or FM.

Table 3.

Limb segment DEXA values pre and post supplementation and training for control group (n = 6), matched control group (n = 2) and patient group (n = 2). (Mean ± SEM).

	n	LBM (kg)		Fat (kg)		
		Pre	Post	Pre	Post	
Control	CGT	6 (CG)	5.6 ± 0.6	5.9 ± 0.7	4.2 ± 0.8	4.1 ± 0.7
		2 (MCG)	6.4 ± 1	6.6 ± 1.3	5.1 ± 1.5	4.8 ± 1.1
	CGU	6 (CG)	5.4 ± 0.6	5.9 ± 0.8	4.2 ± 0.8	4.1 ± 0.7
		2 (MCG)	6.3 ± 0.9	6.9 ± 1.4	5 ± 1.5	4.7 ± 1
Patient	PGT	2	6.3 ± 2	6.7 ± 2	5.2 ± 2	5.3 ± 2.4
	PGU	2	6.5 ± 1.2	6.9 ± 1.6	6.1 ± 3	6 ± 3.1

4.4 Creatinine

Figure 18 below shows the Crn values of CG, MCG and PG, pre and post the training and supplementation programme. Creatinine levels at BL were $55.8 \pm 11.6 \mu\text{mol/l}$ for the PG and $62.2 \pm 5.3 \mu\text{mol/l}$ for the CG. A slight increase was seen in the both CG ($71.5 \pm 6.4 \mu\text{mol/l}$) and PG ($64.1 \pm 19.9 \mu\text{mol/l}$) by the final week. The MCG also increased ($65.7 \pm 16.2 \mu\text{mol/l}$ to $72.2 \pm 21.7 \mu\text{mol/l}$). No significant difference was seen ($p > 0.05$) over the twelve-week programme, for neither time nor group in serum Crn values.

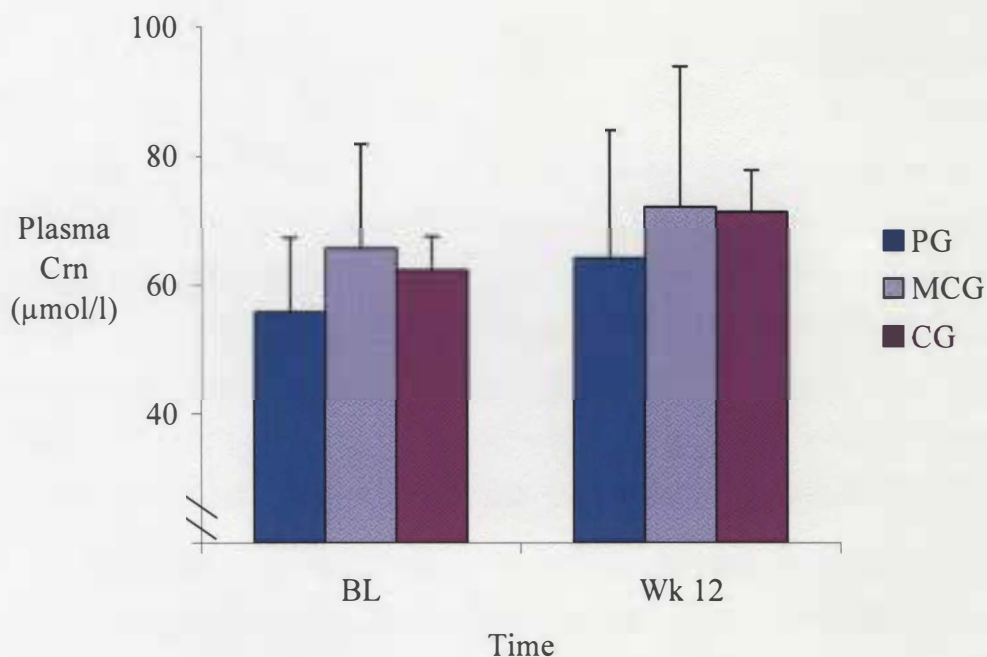


Figure 18. Serum creatinine values pre and post supplementation and training for control ($n = 6$), matched control ($n = 2$) and patient ($n = 2$) groups. (Mean \pm SEM).

CHAPTER FIVE

5.1 Exercise Training

In the present study both the CG and MCG trained at a volume 28% lower than that of the PG due to the patients being 14.3% and 1.74% weaker than the CG for trained and untrained limbs in isometric exercises. As all subjects ingested CrM throughout the twelve-weeks no data can be described for improvements of exercise training alone. However, studies involving neuromuscular disorders support the role of RT, providing that the training is progressive and supervised (Spector et al., 1997).

A study by Alexanderson et al. (1999) demonstrated significant improvements in six out of ten patients for the upper and lower limbs compared with BL values. Spector et al. (1997) found that almost all patients encountered some degree of improvement in PT production for each muscle group tested, although increases seen as a result of the training implemented showed no statistical significance (Spector et al., 1997). A study by Wiesinger et al. (2000) also showed significant progress in muscular strength, oxygen uptake and the overall health of the patients with no rise in disease activity due to the RT programme performed.

There are many possible reasons as to why the strength increases may not be statistically significant. The first could be due to the low numbers involved in both the CG ($n = 6$) and PG ($n = 2$) group and the insufficient training volume and intensity applied in the home-based RT programme (Ahtiainen, Pakarinen, Alen, Kraemer & Hakkinen, 2003; Arnardottir et al., 2003). The training volume was chosen based on the work of a previous researcher and with the muscular weakness of the patient population in mind. Low participation numbers were unavoidable in this study due to the extended waiting period prior to recruitment and testing. This was further delayed as a result of equipment failure, taking one year for experts to realise that the isokinetic dynamometer was not repairable. Also testing location and the duration of testing played a big role as many of the patients lived an hour away, planing holidays and/or starting full time work, which would have interrupted testing. Initial numbers for participation were 18 controls and 16 patients.

Another reason could be that certain muscles may be affected differently due to muscle degeneration as the disease progresses. These affected muscles are less likely to respond to the RT as well as nonaffected muscles or muscles with a smaller amount of affected fibres (Spector et al., 1997). An additional reason could be due to the prescribed drugs effect on capillary numbers and myofibril mass (Cherin et al., 2002). Prednisone and Prednisolone have been known to decrease the amount of capillaries and reduce the size of myofibrils (Wiesinger et al., 2000). Steroid therapy can also cause atrophy in selected muscles (especially in muscles with prevalence for type II muscle fibres) (Bromberg & Carter, 2004). It has been suggested that this reduction could be due to the inhibition of protein synthesis and/or as a result of reduced myofibril mass (Wiesinger et al., 2000). It is also likely that a more sedentary lifestyle may result in some degree of disuse (Spector et al., 1997).

The subjects were informed during the first few weeks of training that they might encounter slight muscle soreness. This was not seen in the CG and the PG reported only slight fatigue and mild soreness post exercise which disappeared after a few hours or at the latest the following day. Overall, previous studies involving strength training emphasise the importance of physical exercise and the possible improvements that could be achieved with patients suffering from different myopathies (Spector et al., 1997; Wiesinger et al., 2000).

5.2 Creatine Supplementation

In the present study all subjects were required to ingest CrM over the twelve-weeks, whilst training one leg and resting the other. The effects of CrM supplementation alone can be seen in the strength changes of the untrained limb for PGU (2.5%) and for CGU (9.3%) in isokinetic extension exercises. No significant increases were reported and it was not known whether the 20 g.d⁻¹ of CrM ingested in the initial loading phase increased the intramuscular stores of Cr, as these measurements were not assessed.

As previously stated ingestion of CrM has found to be advantageous in numerous studies conducted with young and elderly individuals. It can increase intramuscular stores of TCr and PCr, increasing muscular strength and muscular functional capacity (Casey et al., 1996; Smith et al., 1998; Eijnde et al., 2003; Louis et al., 2003).

Several studies by Tarnopolsky et al. (1997), Tarnopolsky and Martin (1999), Tarnopolsky and Parise (1999), Tarnopolsky and Beal (2001) and Tarnopolsky, Parshad, Walzel, Schlattner and Wallimann (2001) have studied the effects of CrM supplementation with individuals diagnosed with various muscle diseases including IM. It is believed that these patient populations would benefit from CrM supplementation due to their low intramuscular Cr concentrations, similar to that found in elderly individuals (Rawson et al., 1999; Tarnopolsky & Parise, 1999).

Louis et al. (2003) showed increases in muscle mass and muscle endurance with PT strength for knee extension increasing by 37% and knee flexion by 12.4%. After three months of CrM ingestion, the patients were able to maintain 75% of their MVC for twice the time. These improvements were maintained after the two month wash out period, even when the intramuscular Cr levels were restored to BL values (Louis et al., 2003). However, Lambert et al. (2003) found that CrM ingestion did not significantly increase intramuscular stores of TCr or PCr nor did it improve TW during the exercises. A slight increase was seen in the knee extension exercises however a decline was present for knee flexion (Lambert et al., 2003).

In the present study isometric strength in the untrained leg increased over the twelve-weeks of supplementation at 60° by 13% and 16.1% for flexion of the PGU and CGU limbs respectively and 2.2% and 0.5% for the extension exercises. No significant differences were found. Flexor muscles seemed to benefit more from CrM than extensor muscles and the PG improved more than the CG.

Isokinetic flexion strength also increased over time except for the CGU limb at 180° s⁻¹. Flexion strength changes ranged from 12.3 – 24.9% and -5.8 – 5.3% for the PGU and CGU limbs over 60° s⁻¹ and 180° s⁻¹. Extension strength decreased for the PGU limb at the faster velocities and

the CGU limb decreased at the slower velocities. Extension strength varied from -0.8 – 2.5% (PGU) and -0.8 – 3.9% (CGU). The lack of significant strength increases could be due to the light intensity of the training employed and possibly insufficient loading of CrM to influence changes in muscle mass and strength.

No significant changes were seen in the endurance protocol. Strength values for the untrained limb varied from -3.5 – 2.7% (PGU) and -3.2 – 0.9% (CGU). The STW changed between -23.3 – 15.3% and -2.2 – 8.7% for the PGU and CGU limbs overtime. Differences in the fatigue index ranged from -6.3 – 8.5% and -0.8 – 7.2% for the PGU and CGU limbs. A greater difference was seen in the lowest torques generated in each set for the PGU (-5.9 – 38.1%) compared with the CGU limb (1.7 – 12.6%).

Another encouraging characteristic of the CrM ingested was that no major health problems were reported as a result of CrM ingestion in this study. Only four of the ten subjects complained of minor discomforts such as bloating with one complaint of an irritable stomach.

Improvements in the untrained limb, despite no significance, could be due to the improved endurance capability of the muscles and its ability to recover more readily between bouts. There are a number of potential reasons why CrM ingestion did not significantly affect muscular strength. Firstly the loading period may not have been long enough. Secondly the amount of CrM ingested may have been insufficient to elicit an increase in intramuscular Cr stores that would normally be effective in healthy individuals (Chetlin, Gutmann, Tarnopolsky, Ullrich & Yeater, 2004). This would have required the use of muscle biopsies to determine the amount of Cr uptake into the muscles. Thirdly it is not known whether the functioning of the Cr transporter within the cells of patients functions normally or that it can synthesis large amounts of oral CrM. Lastly the subjects may not have complied with the instructions given by the investigator in regards to the daily dose of CrM (Chetlin et al., 2004), however this was not reported during the study as the containers used to store the CrM were reviewed by the investigator.

No study to the writers knowledge has demonstrated the effects of RT on strength in the trained and untrained limbs of patients with PM and DM. It has been suggested that neural adaptation due to exercise can cross over

from the limb being trained to the untrained limb, which may result in increases in PT values (Housh et al., 1992; Evetovich et al., 2001; Munn et al., 2005).

A study by Evetovich et al. (2001) found significant increases over time in both the trained (15.5%) and untrained (5.5%) limbs of the trained group however no significant difference were seen in the controls, or in the electromyography amplitude of either group. They concluded that in the absence of electromyography changes, increases in PT were due to hypertrophic factors and/or changes with the muscle or surrounding muscles involved in knee extension training (Evetovich et al., 2001).

However, neural adaptations are considered more likely for any changes in the untrained limb and are possibly related to increases in the stimulation of motor units, increasing the flow of impulses to the untrained muscle and/or the ability of the untrained muscles to adopt a structural support or balance to cope with the trained limb producing maximal strength measures (Housh et al., 1992; Evetovich et al., 2001; Munn et al., 2005).

5.3 Strength Training

The present study found no significant changes in any of the exercises performed, however, both flexion and extension strength increased over the twelve-week supplementation and training period. Isometric strength in the trained limb increased at an angle of 60° by 30.7% and 6.7% for extension of the PGT and CGT limbs respectively and 16% and 21.1% for flexion. Isokinetic flexion strength increased with time for both trained limbs over velocities of 60° s⁻¹ and 180° s⁻¹. Flexion strength ranged from 0.1 – 7.8% and 10.9 – 24.8% for the PGT and CGT limbs respectively. Extension strength also increased by 7.3 – 12.3% and 0.6 – 8.3% for the PGT and CGT limbs. Again no statistically significant differences were found.

It is possible that there was sufficient uptake of Cr into the muscles to show slight improvements in strength without observing any increases in lower limb muscle mass. A placebo group would have been needed to prove this, however the overall strength increases and recovery at the end of each set in the endurance protocol could possibly relate the improvements to CrM supplementation and its ability to prolong fatigue.

The increases could also be due to neural adaptations in the muscles, however, this was not measured.

In the endurance protocol, strength values decreased with every set as expected due to fatigue. However, over time strength improved for all groups slowing slightly by the final week for both trained and untrained limbs. Changes in strength ranged from -6.9 – 5.5% and 5.5 – 11.8% for the trained limbs of the PG and CG. The STW varied from 11.2 – 18.2% and 10.2 – 18.6% for PGT and CGT limbs. Differences in the fatigue index ranged from -15.1 – 5.5% and from no change to 8.9% in the PGT and CGT limbs respectively. Lowest torques varied from -19.8 – -1.8% (PGT) and 9.7 – 26.8% (CGT) over twelve-weeks of supplementation and training.

The slight decreases seen in most exercises between Week 7 and Week 12 in the present study could be due to reasons other than the absence of an ergogenic effect. The patients may have lost motivation due to the insufficient intensity and volume of the RT program and that it was home-based therefore being rarely supervised, this was not indicated in the training diaries. However, lower intensities and volumes were used in the RT because it was not known what weights would have been suitable for the diseased population. There is a possibility that the maintenance doses of CrM became ineffective over time. If there were insufficient uptake of Cr into the muscles any improvements would not have been sustained by the maintenance phase. Also the recovery time between protocols and endurance sets may not have been long enough for the groups to recover, possibly suggesting that the individuals were partially fatigued before even commencing the endurance protocol.

Chetlin, Gutmann, Tarnopolsky, Ullrich and Yeater (2004) performed a twelve-week RT program combined with CrM supplementation with 20 patients diagnosed with Charcot Marie Tooth disease. No benefits were found for adding CrM to RT however increases were reported for knee extension strength (3.3 and 2.4 Nm) and for knee flexion strength (2.1 and 2.5 Nm of the left and right limbs respectively). The patients were unable to lift the reported intensities of healthy studies (67 – 80% max strength) yet they were able to perform the same volume by performing more repetitions using lower weights. Chetlin et al. (2004)

suggested that if higher weights were used the increases in strength may have been statistically significant. However, due to moderate intensity exercises being associated with increasing the risk of performance decrements in neuromuscular patients a lower intensity was assumed.

The lack of significant effects as a result of combined CrM and RT are also seen in studies involving healthy individuals. Bermon et al. (1998) found no benefits in six weeks of heavy RT and CrM supplementation in older individuals. Eijnde et al. (2003) tested forty-six men aged 55 – 75 years over a six month period in a double blinded fashion and found no benefit to combining two – three session of RT a week with five^og.d⁻¹ of CrM over six months in older individuals. Possibly a different supplementation programme and/or training regimen need to be developed along with intensity, frequency and duration of the exercises performed.

However not all studies show nonsignificant increases in strength. Chrusch et al. (2001) reported significant increases in muscular strength of men aged >60 years old after twelve-weeks of RT and CrM supplementation. Brose, Parise and Tarnopolsky (2003) also found significant increases in muscular strength after fourteen weeks of RT and supplementation. Isometric PT values for knee extension, increased by 25% by the final week as a result of the exercise and supplement combination.

It is believed that these small strength increases could be due to changes in the neural functioning of different muscles involved. It has also been stated that neural adaptations are a result of strength increases in novice lifters opposed to hypertrophy, which accounts for major gains in trained individuals (Volek et al., 2004). It is not exactly known how these changes in protein expression elicit strength gains however it is possible that the intramuscular restructuring could be a contributing factor (Evetovich et al., 2001).

Insignificant strength increases could also be due to a learning effect (Gilliam, Hohzorn, Martin & Trimble, 2000). Once the muscles adapt to the type of training fairly small increases, if any, are reported (Evetovich et al., 2001). Another reason for insignificant increases could be due to the low subject numbers and the type of training employed, especially in the case of isometric strength gains.

Training normally incorporates lifting free weights at low intensities making it possible for the strength measures in patients to benefit from isokinetic testing greater than isometric training as this can induce strength changes at higher and/or lower angles than the angles tested (Chetlin et al., 2004). Another explanation for the small increases could be due to the comparison of data between three different isokinetic dynamometers. The ICC's of a comparative study (see Appendix H) involving 22 individuals (11 males and 11 females) on all three isokinetic dynamometers used were not reliable for isometric (Cybex = 0.64 – 0.89; B2 = 0.80 – 0.90; B3 = 0.84 – 0.92) and isokinetic (Cybex = 0.81 – 0.92; B2 = 0.77 – 0.93; B3 = 0.92 – 0.97) extension exercises. Therefore, the differences between machines could also be the cause of insignificant values.

In addition CrM has been shown not to increase muscular function due to the actual training workloads being insufficient (i.e. 20 – 30 RM). It's previously been reported that higher, more demanding workloads (5 – 10 RM) are necessary to produce muscle changes in elderly individuals (Eijnde et al., 2003). Therefore if subject numbers, training volumes (possibly the number of repetitions for the patients), training intensity and the loading phase of CrM were increased, greater changes may have been detected. However, considering the target population low training intensities and volumes were adapted to suit the nature of the IM.

5.4 Body Composition (DEXA)

In the present study whole body mass and limb segment mass did not differ greatly. The LBM increased (CG = 2 kg; MCG = 3.4 kg; PG = 1.1 kg) for the whole body data as well as for the trained (CG = 0.3 kg; MCG = 0.5 kg; PG = 0.4 kg) and untrained (CG = 0.2 kg; MCG = 0.6 kg; PG = 0.4 kg) limb. Whole body FM increased for the MCG (1 kg) and decreased for the CG and PG (-0.4 kg and -1.1 kg respectively). Small decreases were also seen in the FM for the trained limb of the CG and MCG (-0.1 kg) and untrained (-0.3 kg). The PGU limb also decreased slightly (-0.2 kg) however the PGT limb increased (0.1 kg).

Increases in body mass of approximately 0.7 – 1.6 kilogram are reported in most studies using CrM supplementation (Grindstaff et al., 1997). It has been suggested that the circulation of total body water between

the intracellular and extracellular spaces can induce both protein and glycogen production (Ziegenfuss et al., 1998; Bembien et al., 2001a). Therefore DEXA procedures for the measurement of body composition are becoming more desirable in clinical practices as it can detect even the slightest changes in LBM and FM (Diessel et al., 2000).

Volek et al. (2004) found that the Cr group gained more LBM than the placebo group, with results being significant in the increases of LBM for the legs (+1.6 kg). Over the four weeks LBM increased for total body measurements by 3.4 kilogram as a result of CrM supplementation and training. This increase above normal reported values could be due to the subjects having five years RT experience. As previously stated in experienced lifters the majority of strength gains can be attributed to hypertrophy of the muscles (Volek et al., 2004). Francaux and Poortmans (1999) found no changes in body mass for either the control or placebo groups, while a two kilogram increase in body mass was seen in the CrM group. Due to the absence of changes in extracellular and intracellular compartments the increases were attributed to LBM expansion (Francaux & Poortmans, 1999).

Huso, Hampl, Johnston and Swan (2002) studied the effects CrM supplementation on substrate utilisation during twelve-weeks of RT and within three weeks of CrM supplementation, body mass increased 1.6 ± 0.5 kilograms with no significant changes in the placebo trial. Significant increases in LBM were found after CrM and placebo ingestion (1.9 ± 0.8 and 2.2 ± 0.7 kg, respectively) however FM did not change significantly with CrM supplementation and decreased significantly after placebo ingestion (2.4 ± 0.8 kg) (Huso et al., 2002). Stout et al. (2001) also performed a study on a patient with Myasthenia Gravis (age 26 yrs) to determine the effects of RT and CrM supplementation on body composition, training volume and PT strength. Increases in body mass (6.8%) and FFM (4.3%) were found with 15 weeks of CrM supplementation and RT (Stout et al., 2001).

The increase in body mass observed as a result CrM supplementation could be due to muscle hypertrophy, the structural change in the myofibrils, possibly due to increased protein synthesis or an increase in total body water (Balsom et al., 1993; Becque et al., 2000; Bembien et al., 2001a). Creatine is

believed to enter the intracellular space of a cell and by osmosis, a process by which a liquid is drawn from a weak solution to a more concentrated solution through a semi-permeable membrane, draws water within the cell (Lambert et al., 2003). Thus leading to increases in intracellular water, with little or no change to extracellular fluid, and total body water enhancing muscle volume (Ziegenfuss et al., 1998; Bembien et al., 2001a; Lambert et al., 2003).

Body mass increases of up to two kilograms can normally be found with a CrM supplementation period of five to seven days. Due to the short period of supplementation and the sudden increase in body mass, increases in intracellular water are thought to be the cause rather than increases in protein synthesis, which is thought to be the case in studies with a long supplementation period. However exact confirmation of this speculation is not presently accessible and other studies involving short term supplementation have suggested increases in LBM as a result of protein synthesis (Andres et al., 1999).

Although there were increases in serum Crn values in the present study, these increases may not have been adequate enough to influence muscle mass. A longer supplementation and training period, increased subject numbers, the employment of whole body RT as opposed to lower body exercises and diet restrictions throughout the entirety of the study could have seen greater differences and possibly even significant differences in body composition of the patient populations. However this study was implemented for use in specific patient populations in which no true set of exercise guidelines or knowledge of the effects of diet restrictions are available. It was also designed to test the simplicity and practicality of use at home, so that it could be performed safely without supervision and without expensive equipment.

5.5 Creatinine

In the present study serum Crn values increased for the PG (14.9%), the MCG (9.9%) and for the CG (15%) over the twelve-weeks. Baseline figures only differed by 11.5% between the PG and CG and 17.7% between the PG and MCG. In Week 12 the PG differed by 11.5% and 12.6%

between the CG and MCG respectively. Elevated serum Crn values in both the PG and CG suggest that intramuscular Cr concentrations were increased.

Chetlin et al. (2004) found increases of 10 mmol.kg^{-1} in patients with Charcot Marie Tooth disease did not improve performance however increased intramuscular concentrations of Cr by 7%. Volek et al. (2004) reported significant increases of 5.8% in plasma Crn in a Cr group compared with no changes in a placebo group of healthy subjects.

Following CrM supplementation, intramuscular Cr is broken down into Crn. Increases in Crn values post loading have been suggested to be the result of enhanced Cr turnover and/or an ability to maintain improved training volumes (Kreider et al., 2003). Increase of 20 mmol.kg^{-1} of muscle Crn is said to be due to CrM supplementation, which can provoke increases in exercise performance (Greenhaff, 1997).

The small increases seen in each study is likely due to the larger concentrations of muscle Cr levels after supplementation (Volek et al., 2004). Increases in Crn levels suggest that the CrM ingested was absorbed and metabolised. Again the lack of subject numbers and the absence of muscle biopsies reduce the possible significant effects that could have been seen.

5.6 Limitations

The major limitation of this study is that only a small number of subjects were obtained, reducing the potential power and statistical significance of the results. In addition there is a limited number of controlled studies available for PM and DM, and those that have been reported also used insignificant numbers (Choy & Isenberg, 2002). Therefore the results of this study could not be compared with a large number of statistically significant studies.

A further limitation was that both urinary Cr measurements and muscle biopsies were not analysed. Urinary Cr measurements were not attained and therefore the uptake of Cr into the body was not assessed. Muscle biopsies were not performed therefore the extent of muscle fibre depletion and regeneration could not be measured.

A restriction in the recruiting process was also a limitation. The study was limited to a selected population and the patients were in a dormant phase of their disease. The study also targeted subjects without a heavy RT background or recent CrM use in the last six months.

However, despite these limitations the rationale behind the present study is very important and should be re-emphasised. There are not many reports of the benefits of exercise and CrM supplementation in special populations like PM and DM. The study shows that patient populations can exercise without fear of their disease flaring up as a result of activity. It also shows that supplementation with CrM was well tolerated and had no serious side effects that would have inhibited any improvements. Due to a lack of CrM supplementation and RT studies with PM and DM, the study was designed based on previous work with elderly individual so that training and supplementation could be easily followed and performed at home without supervision and the need for expensive equipment. For this reason, weights were employed at a low intensity and the subjects were allowed to progress individually. Overall, despite the lack of statistical significance in strength changes and the low participation numbers the study provides an encouraging foundation for future studies in this area.

5.7 Conclusion

The present study has shown that a light home-based RT programme performed in conjunction with CrM supplementation can have a positive effect on muscle mass and muscular strength. Although the increases in strength were minimal, further research with a larger population and possibly a longer study period could potentially show greater significance in muscle function. Overall, the study showed that the employment of a safe exercise programme and the ingestion of CrM was not detrimental to the health or well being of individuals with PM and DM.

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APPENDIX A: ADVERTISEMENT FOR VOLUNTEERS



The Effects of Combined Creatine Monohydrate Supplementation and Physical Training on Body Composition and Muscular Function in Patients with Inflammatory Myopathies

Volunteers needed!!!

Aim: -

This exercise program has been developed to ascertain whether supplementation of Creatine Monohydrate, linked with appropriate muscular training, will lead to an increase in lower leg muscle mass and strength in patients with Polymyositis and Dermatomyositis.

Participants must be: -

- Healthy individuals and patients with Polymyositis or Dermatomyositis
- Aged 30 – 80 years both males and females
- With no previous history of any heart conditions or joint instability

All information obtained throughout the study is confidential. If you are interested in participating or want to find out more regarding the study, please do not hesitate to contact me on:

Lynda Murray

Phone (W): 6304 5073

E-mail: l.murray@ecu.edu.au

Creatine Strength Study Lynda Murray Phone (W): 6304 5073 E-mail: l.murray@ecu.edu.au	Creatine Strength Study Lynda Murray Phone (W): 6304 5073 E-mail: l.murray@ecu.edu.au	Creatine Strength Study Lynda Murray Phone (W): 6304 5073 E-mail: l.murray@ecu.edu.au	Creatine Strength Study Lynda Murray Phone (W): 6304 5073 E-mail: l.murray@ecu.edu.au	Creatine Strength Study Lynda Murray Phone (W): 6304 5073 E-mail: l.murray@ecu.edu.au	Creatine Strength Study Lynda Murray Phone (W): 6304 5073 E-mail: l.murray@ecu.edu.au	Creatine Strength Study Lynda Murray Phone (W): 6304 5073 E-mail: l.murray@ecu.edu.au
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APPENDIX B: INFORMED CONSENT FORM



EDITH COWAN
UNIVERSITY

PERTH WESTERN AUSTRALIA
JOONDALUP CAMPUS

Lynda Murray B.Sc (Sports Science)
Exercise Physiology Masters Candidate
School of Biomedical & Sport Science
Telephone: +61 8 6304 5073
E-mail: l.murray@ecu.edu.au

Informed Consent Form

The Effects of Combined Creatine Monohydrate Supplementation and Physical Training on Body Composition and Muscular Function in Patients with Inflammatory Myopathies

Thank you for your recent interest in participating in an exercise study looking into muscular strength. My name is Lynda Murray and I am a Masters student at Edith Cowan University. The purpose of this study is to investigate the responses of muscle to strength training while taking a dietary supplement under the supervision of Mike Newton. Please take a few minutes to read the following.

A twelve-week program has been developed to ascertain whether supplementation of Creatine Monohydrate (CrM), linked with appropriate muscular training, would lead to an increase in muscle mass and strength in knee extensors and flexors in patients with Polymyositis and Dermatomyositis.

During the twelve-weeks you will be asked to ingest CrM. Creatine (Cr) is a form of amino acid produced in the liver, pancreas and kidneys, which can be found in meat, eggs, fish and poultry. A loading phase (first two weeks) and a maintenance phase (10 weeks) will be employed to maintain Cr levels throughout the twelve-weeks. The CrM will be packed in sealed bags and proper instructions will be given to you on how to use and measure the supplement at home.

Training will also be home-based and consist of you lifting one leg (this will be determined by the examiner) with an ankle cuff to provide weighted resistance. As an increase in the ease of your training is noticed, the amount of reps and/or weight will be increased slightly. Training will last no more than five minutes and be conducted three times a week for twelve-weeks.

Strength of your lower leg will be measured using a Cybex 6000 or a Biodex isokinetic dynamometer. There are three main tests. The first test involves you pushing against an immovable object at two varying angles. The second test involves you extending (lifting) and flexing (lowering) your lower leg as hard as you can four times at four different angles. These two tests last only a few seconds each, with adequate rest stops between them. The last test is an endurance test lasting about three minutes. In each of these tests, strength of the lower leg will be recorded. The entire procedure will take no more than one hour if everything goes to plan. There will be five testing sessions taking

place over the twelve-weeks (baseline, 1st week, 2nd week, 7th week and in the last week). During this time if you wish to stop the session for any reason, we will stop without prejudice. Testing will be carried out in Building 19 room 150 at Edith Cowan University in Joondalup and/or at UWA.

Finger prick blood samples will be obtained as well as x-rays from a machine called a Dual energy x-ray absorptiometry (DEXA). The DEXA scan is a non-invasive technique, which exposes your body to a very low level of radiation (1.5 - 5 millirems) to determine your body composition. These x-rays will be taken of each thigh and will take approximately 20 minutes to obtain. Both the x-rays and the blood samples will be carried out before the supplementation and training program begins and again in week 12.

I hope that this research will help reduce the severity of the disease, improve muscular function in older populations and improve the lifestyle of this population by making physical pursuits more enjoyable. For the purposes of this study, you will receive a free strength assessment. On completion of the study, you will be reimbursed \$40 for the time spent training at home and for any travelling cost incurred.

You should be aware that this study is not part of your clinical treatment and you should not stop any medication or any other treatment as a result of participation. Please refrain from any physical exercise and alcohol consumption at least 24 hours before commencing each test, refrain from caffeine drinks at least 4 hours before each test and please keep to your normal activity level throughout the entire time you are involved in the study. If you have any history of claustrophobia, heart conditions, joint instability or muscle strain, please volunteer for this study however you may be excluded from participating.

As a result of participation, a few side effects may or may not occur. Temporary bloating or the feeling of fullness may result as a consequence of the supplement, temporary soreness from the fingertip pinprick blood sample may also occur. If you follow the correct dosage and maintain your hydration levels the risk of these side effects occurring is very low. Muscular soreness and/or fatigue may result as a consequence of the training program and strength testing. In the incidence of muscle soreness, the tenderness should only last one day and be very minimal. However, should you suffer from any muscle soreness beyond this period or any other problems please notify the principle researcher and the appropriate steps will be taken as you are covered by the ECU School of Biomedical and Sport Science Medical Insurance Policy.

All written documents will be kept in a secure place and electronic documents will be backed up on disc and kept under lock and key in a secure room at SCHG and/or at ECU Joondalup. One copy of the original data will be archived in a secure storage area at ECU Joondalup for a period of at least five (5) years. Access to codes that may identify individuals and/or results will be restricted to my supervisors (Mike Newton & Prof. Frank Mastaglia) and myself. This study will also comply with the principles set out by the National Health and Medical research Council.

NB: Please wear appropriate clothes for physical activity (shorts) and make sure you wear a pair of long socks.

For Further questions or information about the study please feel free to contact me, Lynda Murray on (08) 6304 5073 or l.murray@ecu.edu.au or my supervisor Mike Newton on (08) 6304 5961.

If you would like to contact an independent person:

Assoc. Prof. Barry Gibson
Faculty of Computing, Health and Science
Edith Cowan University
100 Joondalup Drive,
Joondalup, Western Australia 6027
(08) 6304 5037

OR

Dr Susan Walters
Centre of Neuromuscular and Neurological Disorders,
University of Western Australia, QEII Medical Centre,
Nedlands, Western Australia 6009
(08) 9346 3980 or Susan.Walters@health.wa.gov.au

Consent Form

The Effects of Combined Creatine Monohydrate Supplementation and Physical Training on Body Composition and Muscular Function in Patients with Inflammatory Myopathies

I (the participant) have read and understand the above information form, which explains the nature of the study, the risks and advantages of participating. Any questions I had have been explained to my full satisfaction.

I agree to take part in this study, however, I understand that I am free to withdraw at any time without prejudice to my medical treatment, if any.

I understand that all information provided is treated as confidential and will not be released by the investigator unless required to do so by law. I agree that the research data obtained from the result of the study may be published and held for a period of time provided I am not identifiable.

I _____, agree to participate as a subject in this study.

(Please Print)

Signature: _____ Date: _____

Witness: _____

(Please Print)

Witness Signature: _____ Date: _____

Investigator: _____ Date: _____

APPENDIX C: HEALTH SCREENING QUESTIONNAIRE

Health Screening Questionnaire

The Effects of Combined Creatine Monohydrate Supplementation and Physical Training on Body Composition and Muscular Function in Patients with Inflammatory Myopathies

To assist us with this check up please complete this health-screening questionnaire. Read the questions carefully and answer each one honestly: Tick yes or no.

- | | Yes | No |
|---|--------------------------|--------------------------|
| 1. Are you currently suffering from any illness? If so provide details, (type and severity)
_____ | <input type="checkbox"/> | <input type="checkbox"/> |
| 2. Has your doctor ever said you have a heart condition <u>and</u> that you should only do physical activity recommended by a doctor? | <input type="checkbox"/> | <input type="checkbox"/> |
| 3. Do you feel pain in your chest when you do physical activity? | <input type="checkbox"/> | <input type="checkbox"/> |
| 4. Do you lose balance because of dizziness? Do you ever lose consciousness? | <input type="checkbox"/> | <input type="checkbox"/> |
| 5. Do you currently have any (upper/lower limb) injuries? If so provide details:
_____ | <input type="checkbox"/> | <input type="checkbox"/> |
| 6. Do you have symptoms of (bone / joint / muscle) (stiffness / swelling / pain), which may limit your physical activity? If so provide details:
_____ | <input type="checkbox"/> | <input type="checkbox"/> |
| 7. Are you a vegetarian? | <input type="checkbox"/> | <input type="checkbox"/> |
| 8. Do you drink coffee or tea? How much? ___ Cups/day. | <input type="checkbox"/> | <input type="checkbox"/> |
| 9. Do you drink alcohol? How much? ___ Drinks/day. | <input type="checkbox"/> | <input type="checkbox"/> |
| 10. Is your doctor currently prescribing drugs for your blood pressure or heart condition? If so please comment, (supplement and dosage):
_____ | <input type="checkbox"/> | <input type="checkbox"/> |
| 11. Are you currently taking any other medication? If so please comment:
_____ | <input type="checkbox"/> | <input type="checkbox"/> |
| 12. Do you know of any other reason why you shouldn't do any physical activity?
_____ | <input type="checkbox"/> | <input type="checkbox"/> |

I have read, understood and completed this questionnaire. Any questions I had were answered to my full satisfaction.

Name.....

Date.....

Signature.....

Investigator.....

Date.....

Doctor's Name.....

Date.....

Signature.....

(If applicable)

The Sir Charles Gairdner Hospital Human Research Ethics Committee and Edith Cowan University Ethics Committee have given ethics approval for the conduct of this project. If you have any ethical concerns regarding the study you can contact the secretary of the SCGH Human Research Ethics Committee on (08) 9346 2999 or ECU Ethics Committee on (08) 9273 8492.

APPENDIX D: PARTICIPANT'S TIMETABLE

Timetable

Week	Supplementation	Training	Data obtained
0			Meeting with the campus Doctor <u>Pre Baseline:</u> Cybex
1	Loading phase (20 g.d ⁻¹)	5 minutes per day / 3 times a week	<u>Baseline:</u> Cybex <u>Pre Values:</u> Blood Crm & DEXA
2	Loading phase (20 g.d ⁻¹)	5 minutes per day / 3 times a week	<u>Week 2:</u> Cybex
3 - 6	Maintenance Phase (5 g.d ⁻¹)	5 minutes per day / 3 times a week	
7	Maintenance Phase (5 g.d ⁻¹)	5 minutes per day / 3 times a week	<u>Week 7:</u> Cybex
8 - 11	Maintenance Phase (5 g.d ⁻¹)	5 minutes per day / 3 times a week	
12	Maintenance Phase (5 g.d ⁻¹)	5 minutes per day / 3 times a week	<u>Week 12:</u> Cybex <u>Post values:</u> Blood Crm & DEXA

APPENDIX E: EXERCISE AND DIET QUESTIONNAIRE



Exercise & Diet Questionnaire

*The Effects of Combined Creatine Monohydrate Supplementation and Physical Training on
Body Composition and Muscular Function in Patients with Inflammatory Myopathies*

For the completion of this study and to assist us with your results please complete the following questionnaire. **Please read the questions carefully and answer each one honestly.**

1. Evaluate your motivation throughout the study.

Poor Satisfactory Good Excellent

2. Describe an example of the exercise you normally performed in one week. Please record all types physical activity and for how long, e.g. Two hours heavy/light gardening, one hour house cleaning, 30 min slow/fast walking.

Monday: _____

Tuesday: _____

Wednesday: _____

Thursday: _____

Friday: _____

Weekend: _____

3. Evaluate your diet during your participation in the study.

Poor Satisfactory Good Excellent

4. Describe an example of the foods you normally eat in one week. Please record all types of meals, snacks and drinks, e.g. one glass of OJ, two slices of toast with butter and jam for breakfast. Evaluate your diet during your participation in the study.

Monday: _____

Tuesday: _____

Wednesday: _____

Thursday: _____

Friday: _____

Weekend: _____

I have read, understood and completed this questionnaire.

Name: _____

Date: _____

(Please Print)

Signature: _____

APPENDIX F: PARTICIPANT'S TRAINING DIARY

Training Diary

Name: Joe Citizen

ID: LMTEST#

Week 1			
	REP	Set	Weight
Monday Date:			
Tuesday Date:			
Wednesday Date:			
Thursday Date:			
Friday Date:			
Saturday Date:			
Sunday Date:			

Comments:


APPENDIX G: DUAL ENERGY X-RAY ABSORPTIOMETRY SCANS

METABOLIC MEDICINE

Name [REDACTED]
ID 311282
Age 21

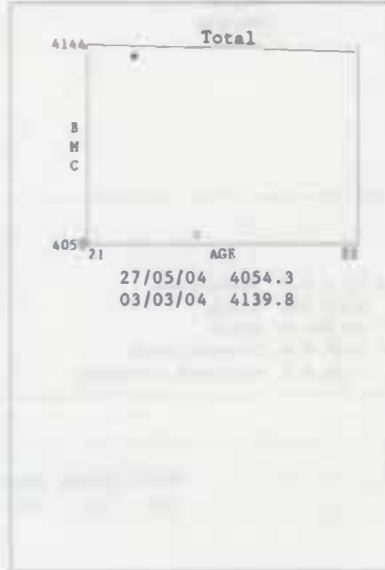
Sex Male

Ethnic caucasian
Height
Weight

L  H Body on 03/03/04 14:04



Bone image not for diagnosis



Total BMC (g) ± 4140

STD CV for Total BMC: 0.9 See Guide for other CVs.
6.5 x13.0 mm, 260 mm/s, 65.65 cm Rev. 3.9.6b/2.3.1 Calib. 03/03/04

COMMENTS



METABOLIC MEDICINE

<i>Name</i>	██████████	<i>ID</i>	311282
<i>Address</i>	██████████	<i>Ethnic</i>	caucasian
		<i>Age</i>	21
<i>Telephone</i>		<i>Menopause</i>	
<i>History</i>	<i>days</i>	<i>Sex</i>	Male
		<i>Height</i>	
<i>Treatment</i>		<i>Weight</i>	
		<i>Armspan</i>	
<i>Medications</i>			
<i>Comments</i>			

SCAN INFORMATION

<i>Type</i>	Body	<i>Resolution</i>	6.5 x 13.0 mm
<i>Scan Date</i>	██████████	<i>Speed</i>	260 mm/s
<i>Analysis Date</i>	██████████	<i>Width</i>	65.65 cm
<i>Calibration Date</i>	27/05/04	<i>Host/Scanner</i>	3.9.6b/2.3.1
<i>Technician</i>	TF	<i>Analysis Revision</i>	3.9.6b
<i>Physician</i>	AS		

DETAILED RESULTS

	BMD	BMC	AREA	LENGTH	WIDTH
	g/cm ²	g	cm ²	cm	cm
Head		374.9			
Trunk		1457			
Abdomen		647.7			
Arms		644.6			
Legs		1578			
Total		4054			
right		454.3	50.70	20.80	
left		510.0	53.30	21.45	



APPENDIX H: PILOT STUDY

H.1 Pilot Study

H.1.1 Background

Isokinetic dynamometry is extensively used in the rehabilitation fields for training and research (Iossifidou & Baltzopoulos, 1998). Hislop and Perrine were one of the first to introduce the concept of isokinetic contractions in the late 1960's (Pincivero, Lephart & Karunakara, 1997; Ling, Chen & McDonough, 1999). The Cybex was the first model to be made, since then difference manufacturers have developed other devices for muscular testing and rehabilitation (Ling et al., 1999).

Isokinetic dynamometry allows for a predefined speed during exercise, speeds from 5 - 500° s⁻¹ can be performed (Dickhuth, 1994). Isokinetic dynamometers also provide the ability to test isolated muscle groups and data such as torque, work, power and endurance can be recorded through a built-in software database (Wilson, 1994).

Establishing the reliability of the isokinetic dynamometer is very important as it determines the consistency and credibility of the data it produces (Drouin, Valovich-mcLeod, Shultz, Gansneder & Perrin, 2003). To obtain true measures, dependable and consistent measurement techniques, such as the dynamometer itself, the protocol implemented, the procedure to which it is carried out and the constancy of the individuals participating need to be employed (Lund et al., 2005).

Previous studies have found measures of torque to be reliable for various kinds of isokinetic dynamometers, such as the Cybex (Gross, Huffman, Phillips & Wray, 1991; Kannus, 1992; Li, Wu, Maffulli, Chan & Chan, 1996; Dolny, Collins, Wilson, Germann & Davis, 2001), B2 (Feiring, Ellenbecker & Derscheid, 1990; Gross et al., 1991; Brown, Whitehurst, Bryant & Buchalter, 1993; Pincivero et al., 1997; Iossifidou & Baltzopoulos, 1998) and the B3 (Drouin et al., 2003; Lund et al., 2005) isokinetic dynamometers. Few studies comparing data information between different isokinetic dynamometers expose problems in relation to the design of the dynamometer or the differences in the computer software (Drouin et al., 2003; Lund et al., 2005). As a result, a comparison between isokinetic dynamometers is necessary when reporting measures from more than one dynamometer (Lund et al., 2005).

H.1.2 Purpose of the Study

The aim of the study was to evaluate the reliability of the Cybex 6000, B2 and B3 isokinetic dynamometers and compare flexion and extension of the knee with isometric and isokinetic exercises between dynamometers.

H.1.3 Subjects

22 healthy volunteers (11 = males, 11 = females) were recruited from the student population at ECU. Both males and females were required to read and sign a consent and medical form before commencing the study. Subject characteristics can be seen in Table 1.

Table 1.

Characteristics for the Pilot Study Participants

Group	Age (yrs)	Height (cm)	Weight (kg)
Male (n = 11)	23.9 ± 2.7	178.2 ± 4.5	75.3 ± 9.2
Female (n = 11)	22.0 ± 2.4	166.0 ± 8.1	66.5 ± 8.2
Total (n = 22)	23.0 ± 2.6	172.1 ± 8.9	70.9 ± 9.6

Note. Values are mean ± SD

H.1.4 Isokinetic Dynamometer Protocol

Each dynamometer was set up and calibrated prior to commencing the test, similar to the main study. The subjects were instructed verbally of the aims and practical procedures of the test in the first session and anthropometric measurements were measured and recorded. The dynamometer was then adjusted to ensure each subject was individually aligned with the dynamometer. These measurements were noted for reproduction at their next test. Practice tests were again employed until the subject was comfortable with the different tasks. A similar protocol to the master study was used although the endurance test was not applied. Each subject had to perform three isometric contractions at two different angles (45° and 60°) with a 30-second rest period between each angle. To account for any familiarisation within the short period of testing a second exercise at 45° was included two minutes following the isometric test.

The subjects were then instructed to perform four MVC's from slow to fast at constant angular velocities 60°, 120°, 180° and 240° s⁻¹ with a 30-second rest intervals and again at 60° s⁻¹ following a two minute rest. After a short break the protocol was repeated with the other leg. The procedure was repeated twice on each isokinetic dynamometer within a period of three weeks. The dynamometer sequence was randomly chosen for each subject, as was their first testing leg, to help eliminate extraneous variables.

H.1.5 Statistics

Torque was recorded for isometric exercises. Torque, TW and ROM were recorded for isokinetic exercises and were tested for significance in a similar fashion to the master study. A t-test design was used and standard statistical methods were used to calculate the mean, SD or SEM and ICC.

Differences were considered significant if the p value was < 0.05. The results were classed highly reliable with an ICC of $r > 0.90$ and reliable with an r-value of > 0.80 . An r-value of 0.69 or less meant that the results were poor (Fenter et al., 2003).

H.1.6 Results

Figure 1 below represents the isometric PT values for the extensors (left and right) at 45° and 60° for each isokinetic dynamometer. The B2 dynamometer produced slightly lower PT values for both left and right limbs at 45° (Left = 129.7 ± 7.4 Nm; Right = 118.1 ± 6.4 Nm) and 60° (Left = 142.9 ± 8.8 Nm; Right = 140.5 ± 8.5 Nm). The B3 however recorded similar PT values to the Cybex, in relation to angle and legs. The Cybex averaged 168.1 ± 9.2 Nm for the left and 159 ± 9.2 Nm for the right at 45°, and 208.6 ± 12.5 Nm and 188.7 ± 11.1 Nm respectively at 60°. The B3 was slightly more reliable at 45° (Left = 170.1 ± 8.7 Nm; Right = 170.1 ± 9.4 Nm) and 60° (Left = 202.6 ± 11 Nm; Right = 197.7 ± 10.6 Nm). Overall the B2 was found to be more consistent (lower SEM's) however produced lower PT than the Cybex and B3.

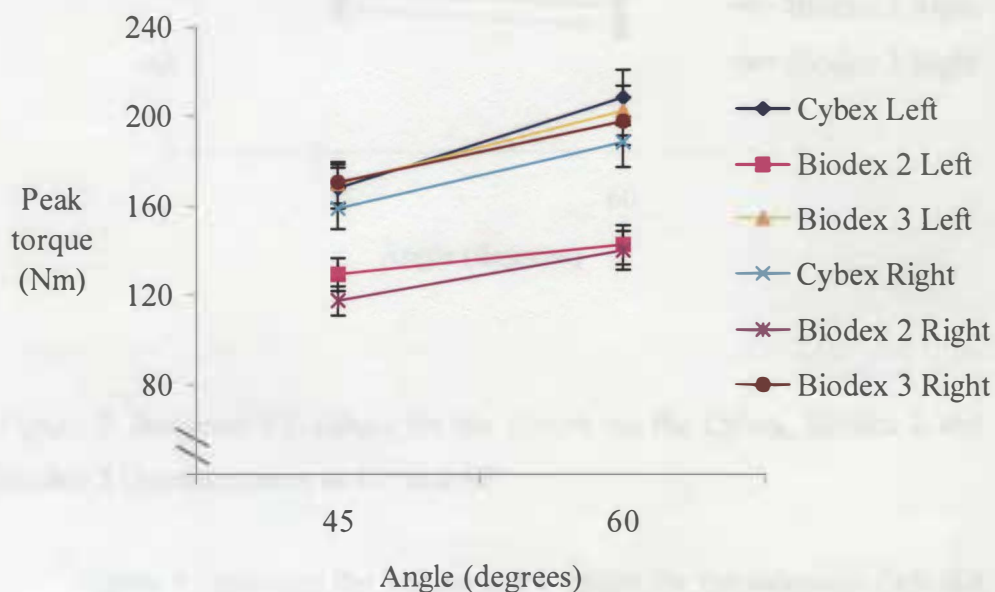


Figure 1. Isometric PT values for the extensors on the Cybex, Biodex 2 and Biodex 3 Dynamometers at 45° and 60°.

Figure 2 represents the isometric PT values for the flexors (left and right) at 45° and 60° for each isokinetic dynamometer. At 45° isometric the Cybex produced similar PT (Left = 102.4 ± 7.2 Nm; Right = $103.4 \pm$

7.2 Nm) to the B3 dynamometer (Left = 102.2 ± 7.2 Nm; Right = 100.6 ± 6.2 Nm). However, B2 produced lower PT values (Left = 67.1 ± 4.9 Nm; Right = 76 ± 4.6 Nm). There was a larger variation between the three machines at 60° isometric. The Cybex produced the highest and most reliable PT (Left = 91.1 ± 6.7 Nm; Right = 93.1 ± 6.5 Nm) followed by B3 slightly lower. The B3 tended to generate lower torques than the Cybex in this case. Again the B2 (Left = 57.9 ± 4.3 Nm; Right = 67.9 ± 4.3 Nm) was more constant (lower SEM's) however produced lower torques than the Cybex and B3.

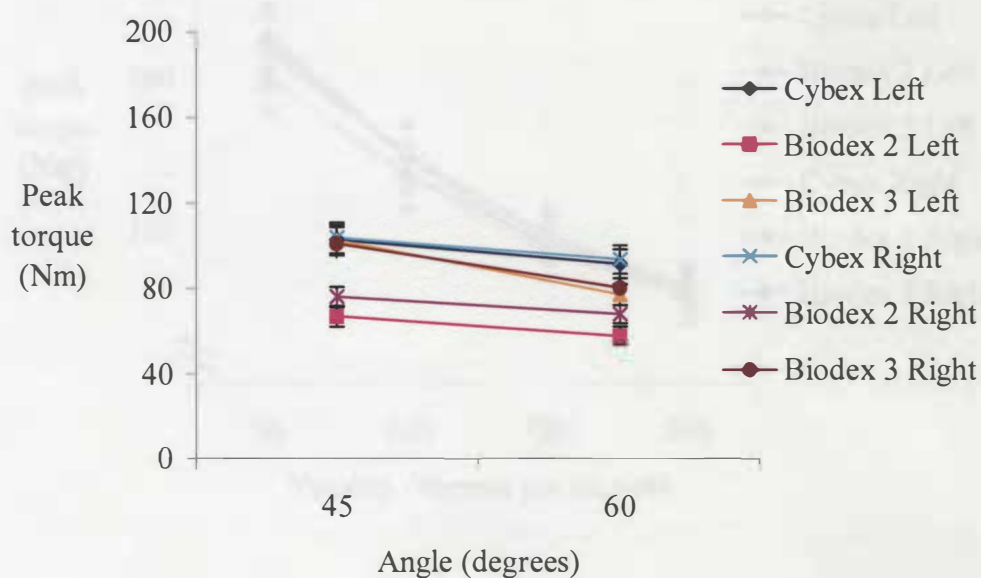


Figure 2. Isometric PT values for the flexors on the Cybex, Biodex 2 and Biodex 3 Dynamometers at 45° and 60°.

Figure 3 represents the isokinetic PT values for the extensors (left and right) at 60, 120, 180 and 240° s⁻¹ for each isokinetic dynamometer. A more consistent trend was seen in the isokinetic MVC's at 240° s⁻¹ than at 60° s⁻¹. Similar findings were found in the left leg as in the right leg, across the velocities and machines. At 60° s⁻¹ the Cybex produced closer PT (Left = 170.7 ± 8.5 Nm; Right = 169.3 ± 10 Nm) to B2 (Left = 167 ± 8.5 Nm; Right = 167.3 ± 10 Nm). At 120° s⁻¹ both the Cybex (Left = 140.4 ± 8.5 Nm; Right = 138.7 ± 8.7 Nm) and B2 (Left = 139.6 ± 8.5 Nm; Right = 138.7 ± 8.7 Nm) increased. The B3 was slightly lower at 60° s⁻¹ (Left = 160.5 ± 8.5 Nm;

Right = 160.1 ± 9.6 Nm) and 120° s^{-1} (Left = 133.8 ± 7.7 Nm; Right = 134.3 ± 8.8 Nm). The higher the velocity the more constant the PT became for the left (Cybex = 117.2 ± 6.4 Nm; B2 = 117.5 ± 6.8 Nm; B3 = 113.7 ± 7 Nm) and right legs (Cybex = 115 ± 7.1 Nm; B2 = 119.2 ± 7.3 Nm; B3 = 116.5 ± 7.9 Nm) at 180° s^{-1} , and again for the left (Cybex = 101.5 ± 6.6 Nm; B2 = 105.2 ± 6.1 Nm; B3 = 102.6 ± 6.7 Nm) and right (Cybex = 103 ± 7.2 Nm; B2 = 104.1 ± 6.4 Nm; B3 = 104.4 ± 7.1 Nm) legs at 240° s^{-1} .

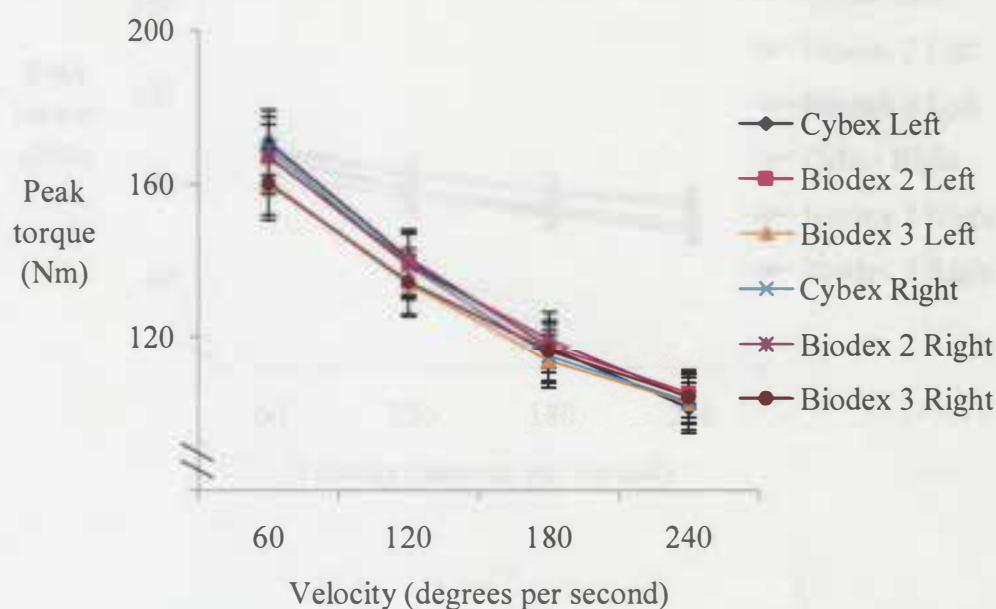


Figure 3. Isokinetic PT values for the extensors on the Cybex, Biodex 2 and Biodex 3 Dynamometers at 60, 120, 180 and 240° s^{-1} .

Figure 4 represents the isokinetic PT values for the flexors (left and right) at 60, 120, 180 and 240° s^{-1} for each isokinetic dynamometer. The B3 performed the greatest PT at 60, 120, 180 and 240° s^{-1} for the left ($60^\circ \text{ s}^{-1} = 97.1 \pm 5.4$ Nm; $120^\circ \text{ s}^{-1} = 86.4 \pm 5.3$ Nm; $180^\circ \text{ s}^{-1} = 79.51 \pm 5.1$ Nm; $240^\circ \text{ s}^{-1} = 73.5 \pm 4.7$ Nm) and the right legs ($60^\circ \text{ s}^{-1} = 95.2 \pm 5.4$ Nm; $120^\circ \text{ s}^{-1} = 84.2 \pm 5.3$ Nm; $180^\circ \text{ s}^{-1} = 76.5 \pm 4.5$ Nm; $240^\circ \text{ s}^{-1} = 71.2 \pm 4.4$ Nm). The Cybex and B2 generated lower torques than the B3. The Cybex performed slightly better on average (Left = 91.3 ± 6.35 Nm; Right = 93.3 ± 6.9 Nm) compared with B2 (Left = 85.5 ± 6 Nm; Right = 91.9 ± 6.6 Nm) at 60° s^{-1} and at 120° s^{-1} (Cybex Left = 78.2 ± 6.3 Nm; Right = 78.3

± 6.3 Nm; B2 Left = 74.8 ± 6 Nm; Right = 77.2 ± 5.9 Nm). At 180° s^{-1} both Cybex and B2 were fairly similar (Cybex Left = 66.6 ± 5.3 Nm; Right = 68.4 ± 6 Nm; B2 Left = 66.3 ± 5.4 Nm; Right = 70.3 ± 5.3 Nm). At 240° s^{-1} B2 was slightly higher (Left = 60.5 ± 5.1 Nm; Right = 63.8 ± 4.9 Nm) than the Cybex (Left = 59.3 ± 5.2 Nm; Right = 60.4 ± 5.7 Nm).

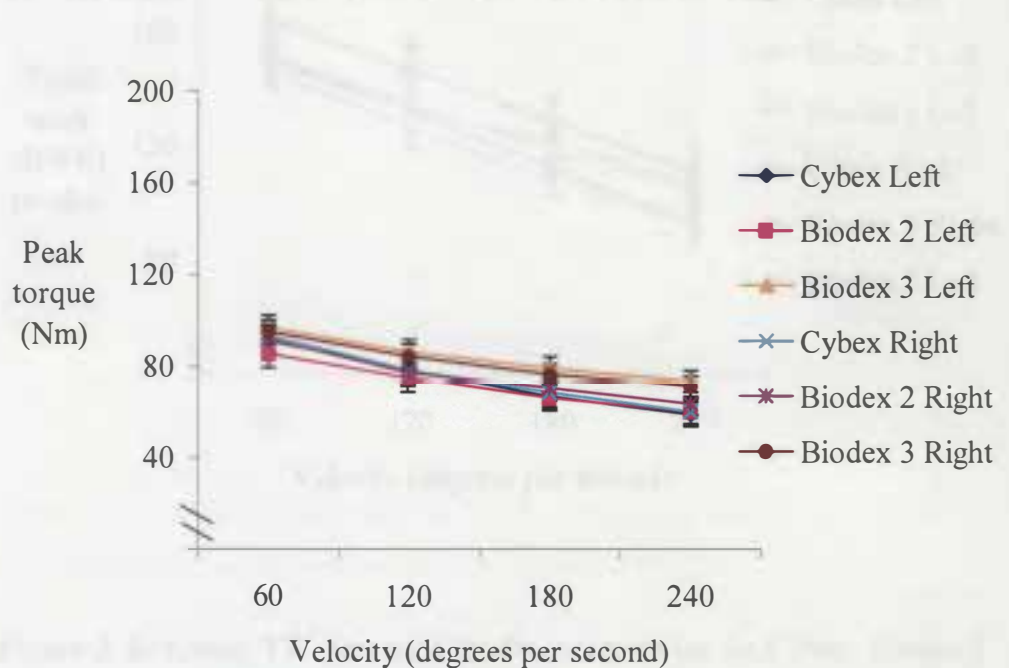


Figure 4. Isokinetic PT values for the flexors on the Cybex, Biodex 2 and Biodex 3 Dynamometers at 60 , 120 , 180 and 240° s^{-1} .

Figure 5 represents the isokinetic TW values for the extensors (left and right) at 60 , 120 , 180 and 240° s^{-1} for each isokinetic dynamometer. The B3 generated higher TW at 60 , 120 , 180 and 240° s^{-1} for the left ($60^\circ \text{ s}^{-1} = 162.8 \pm 7.8$ J; $120^\circ \text{ s}^{-1} = 146.5 \pm 7.5$ J; $180^\circ \text{ s}^{-1} = 127.5 \pm 7.4$ J; $240^\circ \text{ s}^{-1} = 110.7 \pm 7.3$ J) and the right ($60^\circ \text{ s}^{-1} = 164.8 \pm 8.5$ J; $120^\circ \text{ s}^{-1} = 146.2 \pm 9.1$ J; $180^\circ \text{ s}^{-1} = 128.6 \pm 8$ J; $240^\circ \text{ s}^{-1} = 111.3 \pm 7.4$ J) legs. The B2 generated slightly lower TW values for left ($60^\circ \text{ s}^{-1} = 151.8 \pm 7.9$ J; $120^\circ \text{ s}^{-1} = 134.7 \pm 7.6$ J; $180^\circ \text{ s}^{-1} = 117.3 \pm 6.7$ J; $240^\circ \text{ s}^{-1} = 104.7 \pm 6.1$ J) and right ($60^\circ \text{ s}^{-1} = 149.1 \pm 8.2$ J; $120^\circ \text{ s}^{-1} = 132 \pm 7.6$ J; $180^\circ \text{ s}^{-1} = 121.3 \pm 7.1$ J; $240^\circ \text{ s}^{-1} = 106.8 \pm 6.4$ J) legs. Overall the Cybex had the lowest TW values at 60° s^{-1} (Left = 151.1 ± 8.3 J; Right = 145.8 ± 6.6 J), 120° s^{-1} (Left = 131.9 ± 7.1 J;

Right = 125.9 ± 6.3 J), 180° s^{-1} (Left = 111.9 ± 6.2 J; Right = 108.7 ± 5.9 J) and 240° s^{-1} (Left = 92.9 ± 6.4 J; Right = 91.7 ± 5.8 J).

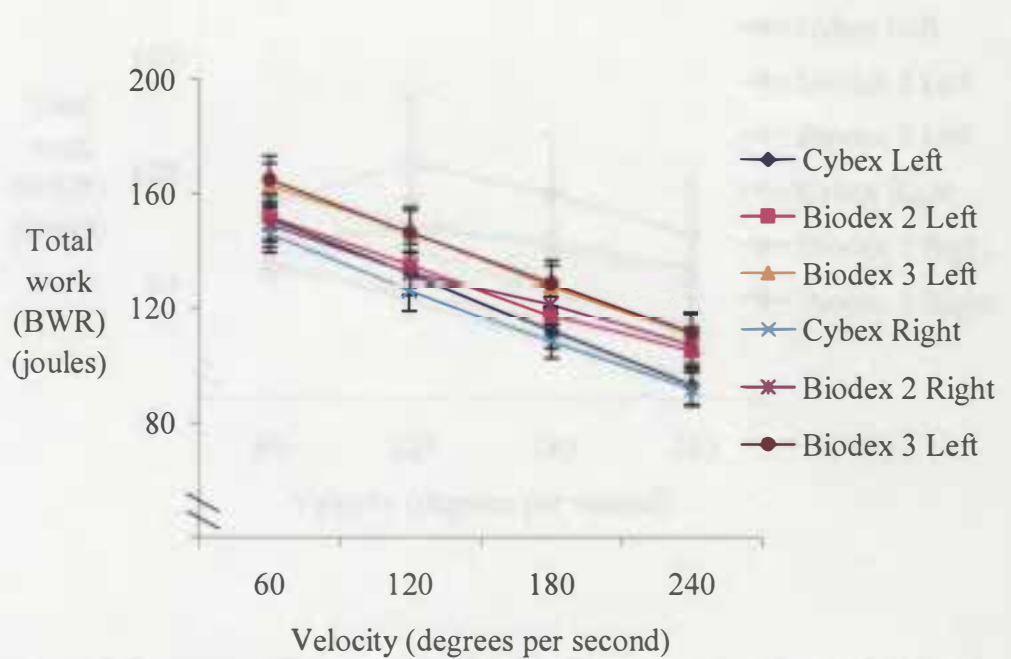


Figure 5. Isokinetic TW generated by the extensors on the Cybex, Biodex 2 and Biodex 3 Dynamometers at 60, 120, 180 and 240° s^{-1} .

Figure 6 represents the isokinetic TW values for the flexors (left and right) at 60, 120, 180 and 240° s^{-1} for each isokinetic dynamometer. The Cybex on average generated the lowest TW over 60, 120, 180 and 240° s^{-1} for the left ($60^\circ \text{ s}^{-1} = 88 \pm 6.4$ J; $120^\circ \text{ s}^{-1} = 74.4 \pm 6.2$ J; $180^\circ \text{ s}^{-1} = 59.6 \pm 5.5$ J; $240^\circ \text{ s}^{-1} = 48 \pm 5$ J) and right ($60^\circ \text{ s}^{-1} = 90.2 \pm 6.6$ J; $120^\circ \text{ s}^{-1} = 92.4 \pm 18$ J; $180^\circ \text{ s}^{-1} = 76.9 \pm 15.8$ J; $240^\circ \text{ s}^{-1} = 65.8 \pm 16$ J) legs. Followed by B2 for the left ($60^\circ \text{ s}^{-1} = 85.6 \pm 7.3$ J; $120^\circ \text{ s}^{-1} = 76.8 \pm 6.7$ J; $180^\circ \text{ s}^{-1} = 67.7 \pm 5.8$ J; $240^\circ \text{ s}^{-1} = 59.6 \pm 5.2$ J) and right ($60^\circ \text{ s}^{-1} = 94.6 \pm 6.9$ J; $120^\circ \text{ s}^{-1} = 100 \pm 17.7$ J; $180^\circ \text{ s}^{-1} = 94.5 \pm 18.6$ J; $240^\circ \text{ s}^{-1} = 85.3 \pm 18.2$ J) legs. The B3 produced the highest TW values at 60° s^{-1} (Left = 122.2 ± 7.1 J; Right = 108.2 ± 6.5 J), 120° s^{-1} (Left = 102.4 ± 6.8 J; Right = 122.5 ± 23.4 J), 180° s^{-1} (Left = 92.15 ± 6.8 J; Right = 111.5 ± 21.2 J) and 240° s^{-1} (Left = 81.4 ± 5.7 J; Right = 97.3 ± 17.5 J).

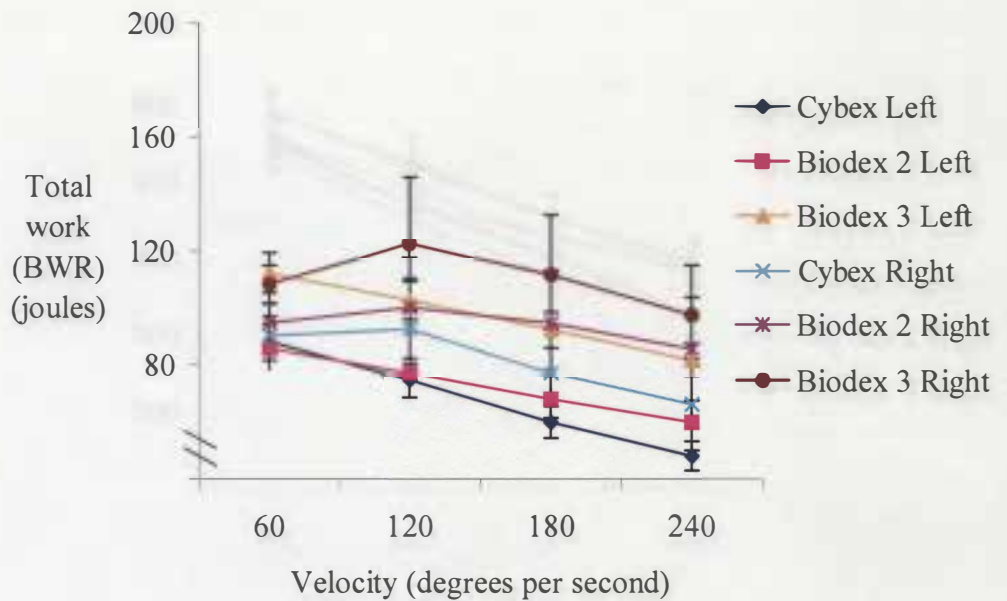


Figure 6. Isokinetic TW generated by the flexors on the Cybex, Biodex 2 and Biodex 3 Dynamometers at 60, 120, 180 and 240° s⁻¹.

Figure 7 represents the isokinetic STW values for the extensors (both left and right legs) at 60, 120, 180 and 240° s⁻¹ for each isokinetic dynamometer. The Cybex generated the lowest STW values compared with B2 and B3. At 60° s⁻¹ the left leg produced 554.5 ± 29.6 J, 556 ± 29.6 J and 586.6 ± 29 J, the right leg produced STW values of 534.4 ± 24.5 J, 545.8 ± 29.9 J and 585.6 ± 32 J for the Cybex, B2 and B3 respectively. At 120° s⁻¹ the left leg produced 466.3 ± 25.7 J, 487.9 ± 29.1 J and 514.7 ± 28.6 J compared with 446.2 ± 22.8 J, 468.1 ± 27.8 J and 521.8 ± 35.7 J for the right leg on the Cybex, B2 and B3 respectively. At 180° s⁻¹ the left leg generated 399.8 ± 23.3 J, 423.7 ± 26.4 J and 449.4 ± 29.4 J and for the right leg 376.1 ± 22.8 J, 427.5 ± 25.2 J and 451.8 ± 30.8 J for the Cybex, B2 and B3 respectively. By 240° s⁻¹ the STW decreased to 324 ± 23.6 J, 382.4 ± 22.9 J and 396.7 ± 28.9 J for the left leg and 321.6 ± 23 J, 383.7 ± 24.1 J and 391 ± 29 J for the right leg on the Cybex, B2 and B3 respectively.

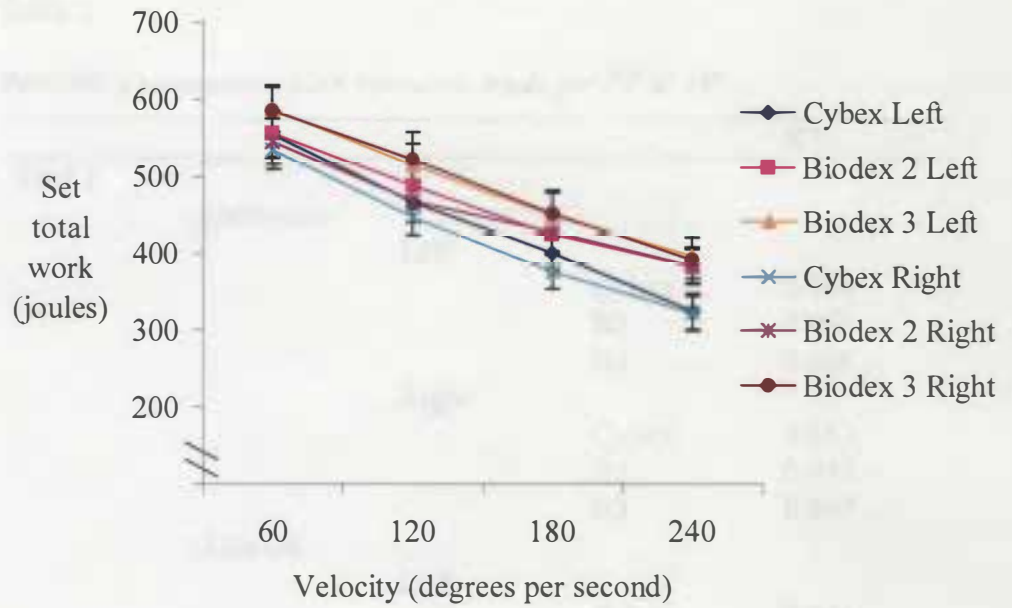


Figure 7. Isokinetic STW produced by the extensors on the Cybex, Biodex 2 and Biodex 3 Dynamometers at 60, 120, 180 and 240° s⁻¹.

Table 2 represents the within group measures for the two isometric trials at 45° on the Cybex, B2 and B3. The relationship between the two trials is highly reliable (Cybex = 0.932 – 0.974; B2 = 0.920 – 0.986; B3 = 0.866 – 0.966).

Table 2

Reliability measures within isometric trials for PT at 45°.

				ICC
Trial 1	Extension	Left	Cybex	0.974
			B2	0.968
			B3	0.866
		Right	Cybex	0.967
			B2	0.959
			B3	0.897
	Flexion	Left	Cybex	0.956
			B2	0.980
			B3	0.911
		Right	Cybex	0.932
			B2	0.986
			B3	0.900
Trial 2	Extension	Left	Cybex	0.950
			B2	0.963
			B3	0.933
		Right	Cybex	0.933
			B2	0.920
			B3	0.966
	Flexion	Left	Cybex	0.963
			B2	0.957
			B3	0.930
		Right	Cybex	0.962
			B2	0.946
			B3	0.945

Table 3 represents the within group measures for the two isokinetic trials at $60^{\circ} \text{ s}^{-1}$ on the Cybex, B2 and B3. PT and TW values are illustrated in the table for Cybex (PT = 0.730 – 0.955; TW = 0.860 – 0.979), B2 (PT = 0.901 – 0.963; TW = 0.876 – 0.989) and B3 (PT = 0.734 – 0.969; TW = 0.876 – 0.993).

Table 3

Reliability measures within isokinetic trials for PT and TW at 60° s⁻¹.

				ICC	
				PT 60°	TW 60°
Trial 1					
Extension					
Left					
	C		0.927	0.947	
	B2		0.926	0.876	
	B3		0.939	0.926	
Right					
	C		0.730	0.860	
	B2		0.932	0.935	
	B3		0.734	0.901	
Flexion					
Left					
	C		0.944	0.928	
	B2		0.954	0.921	
	B3		0.951	0.876	
Right					
	C		0.891	0.979	
	B2		0.963	0.989	
	B3		0.880	0.993	
Trial 2					
Extension					
Left					
	C		0.927	0.962	
	B2		0.901	0.878	
	B3		0.937	0.918	
Right					
	C		0.929	0.910	
	B2		0.918	0.938	
	B3		0.935	0.899	
Flexion					
Left					
	C		0.955	0.933	
	B2		0.954	0.948	
	B3		0.969	0.962	
Right					
	C		0.912	0.978	
	B2		0.952	0.962	
	B3		0.953	0.988	

Table 4 represents the within group measures for STW and ROM of the two isokinetic trials at 60° s⁻¹ on the Cybex, B2 and B3. The STW is fairly reliable (Cybex = 0.799 – 0.919; B2 = 0.843 – 0.936; B3 = 0.760 – 0.891). Both B2 and B3 are not as reliable for the ROM as the Cybex dynamometer (Cybex 0.787 – 0.885; B2 0.591 – 0.972; B3 0.598 – 0.841).

Table 4

Reliability measures within isokinetic extension trials for STW and range of movement at 60° s⁻¹.

			ICC	
			STW	ROM
Trial 1	Left	C	0.883	0.787
		B2	0.843	0.591
		B3	0.784	0.773
	Right	C	0.799	0.885
		B2	0.936	0.905
		B3	0.760	0.841
Trial 2	Left	C	0.919	0.797
		B2	0.913	0.972
		B3	0.891	0.788
	Right	C	0.841	0.805
		B2	0.867	0.951
		B3	0.825	0.598

Table 5 represents PT between group measures for flexion and extension of the isometric trials at 45° and 60° on the Cybex, B2 and B3. The best value of the two trials at 45° was used for analysis. Peak torque is fairly reliable (Flexion = 0.823 – 0.949; Extension = 0.664 – 0.922).

Table 5

Reliability measures between isometric trials for PT.

		ICC		
		Flexion	Extension	
45°	Left	C	0.894	0.781
		B2	0.884	0.815
		B3	0.919	0.922
	Right	C	0.865	0.886
		B2	0.949	0.801
		B3	0.909	0.871
60°	Left	C	0.862	0.784
		B2	0.836	0.895
		B3	0.890	0.835
	Right	C	0.823	0.664
		B2	0.922	0.896
		B3	0.938	0.846

Table 6 represents PT between group measures for flexion and extension of the isokinetic trials at 60, 120, 180 and 240° s⁻¹ on the Cybex, B2 and B3. PT is reliable (Flexion = 0.759 – 0.937; Extension = 0.765 – 0.971).

Table 6

Reliability measures between isokinetic extension and flexion trials for PT.

		ICC		
		Flexion	Extension	
$60^{\circ} s^{-1}$	Left	C	0.933	0.841
		B2	0.915	0.925
		B3	0.925	0.918
	Right	C	0.861	0.885
		B2	0.892	0.765
		B3	0.880	0.918
$120^{\circ} s^{-1}$	Left	C	0.759	0.811
		B2	0.870	0.787
		B3	0.928	0.946
	Right	C	0.925	0.916
		B2	0.907	0.928
		B3	0.918	0.922
$180^{\circ} s^{-1}$	Left	C	0.885	0.924
		B2	0.934	0.908
		B3	0.884	0.954
	Right	C	0.889	0.872
		B2	0.881	0.931
		B3	0.920	0.926
$240^{\circ} s^{-1}$	Left	C	0.921	0.873
		B2	0.923	0.906
		B3	0.937	0.971
	Right	C	0.825	0.880
		B2	0.852	0.918
		B3	0.891	0.924

Table 7 represents TW between group measures for flexion and extension of the isokinetic trials at $60^{\circ} s^{-1}$, $120^{\circ} s^{-1}$, $180^{\circ} s^{-1}$ and $240^{\circ} s^{-1}$ on the Cybex, B2 and B3. The TW is fairly reliable ($60^{\circ} s^{-1} = 0.645 - 0.930$; $120^{\circ} s^{-1} = 0.617 - 0.987$; $180^{\circ} s^{-1} = 0.696 - 0.971$; $240^{\circ} s^{-1} = 0.679 - 0.978$).

Table 7

Reliability measures between isokinetic extension and flexion trials for TW.

		ICC		
		Flexion	Extension	
60° s ⁻¹	Left	C	0.904	0.854
		B2	0.781	0.645
		B3	0.930	0.876
	Right	C	0.833	0.759
		B2	0.765	0.784
		B3	0.890	0.786
120° s ⁻¹	Left	C	0.861	0.819
		B2	0.764	0.617
		B3	0.914	0.876
	Right	C	0.987	0.875
		B2	0.961	0.666
		B3	0.961	0.895
180° s ⁻¹	Left	C	0.799	0.880
		B2	0.867	0.696
		B3	0.898	0.874
	Right	C	0.958	0.821
		B2	0.971	0.742
		B3	0.948	0.902
240° s ⁻¹	Left	C	0.886	0.881
		B2	0.815	0.679
		B3	0.872	0.915
	Right	C	0.978	0.880
		B2	0.973	0.717
		B3	0.888	0.886

Table 8 represents STW between group measures for flexion and extension of the isokinetic trials at 60, 120, 180 and 240° s⁻¹ on the Cybex, B2 and B3. The STW is not as reliable (range 0.519 – 0.892). Both B2 and B3 are not reliable for ROM (B2 = 0.258 – 0.465; B3 = 0.505 – 0.598) compared with the Cybex (range 0.599 – 0.858).

Table 8

Reliability measures between isokinetic extension trials for STW and ROM.

		ICC		
		STW	ROM	
$60^{\circ} s^{-1}$	Left	C	0.835	0.656
		B2	0.632	0.320
		B3	0.869	0.510
	Right	C	0.668	0.837
		B2	0.722	0.465
		B3	0.780	0.570
$120^{\circ} s^{-1}$	Left	C	0.785	0.623
		B2	0.597	0.307
		B3	0.814	0.543
	Right	C	0.779	0.765
		B2	0.700	0.359
		B3	0.871	0.582
$180^{\circ} s^{-1}$	Left	C	0.799	0.669
		B2	0.519	0.299
		B3	0.850	0.514
	Right	C	0.772	0.858
		B2	0.787	0.376
		B3	0.838	0.570
$240^{\circ} s^{-1}$	Left	C	0.861	0.599
		B2	0.614	0.258
		B3	0.877	0.505
	Right	C	0.829	0.852
		B2	0.728	0.395
		B3	0.892	0.598

H.1.7 Discussion

Our findings demonstrate that neither of the isokinetic dynamometers is comparable with each other for isometric torque, slow and high velocity torques, TW or ROM.

Isometric PT was measured at 45° and 60° on each dynamometer for both left and right limbs. The degree of discrepancy between isometric PT values suggests the isokinetic dynamometers are not capable of producing valid measures for comparison. The largest difference was recorded between the B2 and B3 (31.1% and 44.6%) for left and right limbs during extension and (52.3% and 32.3%) during flexion at 45°.

Discrepancies were also observed as the angle changed from 45° to 60° (Extension = 41.8% and 40.9%; Flexion = 32.7% and 17.8%). At 45° the Cybex and B3 produced the closest extension values for the left leg PT (difference = 1.2%). The right limb was less consistent with the Cybex and B3 being 7.3% apart. Flexion contractions were very similar at 45° (0.3% and 2.7%) for the left and right limbs. At 60° PT was 2.9% and 4.9% different between the Cybex and B3. However flexion showed greater differences (15.6% and 14%).

Assuming that each subject performed the exercises with the same amount of strength and motivation on each dynamometer the differences reported between machines should be accounted for when comparing results. The differences between left and right limbs could be due to the subjects being predominantly dominant on the right side. A larger variation is also seen in angles closer to 90° flexion therefore caution should also be taken with varying angles.

Measures of isokinetic PT revealed the greatest amount of variation. These discrepancies were as large as 6% at 60° s⁻¹, 4.7% at 120° s⁻¹, 3.7% at 180° s⁻¹ and 3.6% at 240° s⁻¹ for extension exercises. Flexion on the other hand produced higher differences (60° s⁻¹ = 13.5%; 120° s⁻¹ = 15.6%; 180° s⁻¹ = 19.4%; 240° s⁻¹ = 24.1%). As seen in Figures 3 and 4 the measures over each velocity varied suggesting the dynamometers are unreliable at slower velocities compared with higher velocities for extension and unreliable for all velocities in the flexion exercises performed.

The biggest differences in TW were seen between the B3 and Cybex followed closely by the B2 isokinetic dynamometer. Slight differences were seen in the right limb for extension ($60^{\circ} \text{ s}^{-1} = 13.1\%$; $120^{\circ} \text{ s}^{-1} = 16.1\%$; $180^{\circ} \text{ s}^{-1} = 18.9\%$; $240^{\circ} \text{ s}^{-1} = 21.4\%$). The greatest variation was seen in TW for flexion ($60^{\circ} \text{ s}^{-1} = 27.5\%$; $120^{\circ} \text{ s}^{-1} = 37.6\%$; $180^{\circ} \text{ s}^{-1} = 54.6\%$; $240^{\circ} \text{ s}^{-1} = 69.7\%$).

The main discrepancy in ROM was seen between the B3 and B2, followed by the Cybex. There seemed to be a constant difference between the B3 and B2 isokinetic dynamometers with a 25.1% difference at $60^{\circ} \text{ s}^{-1}$, 26% at $120^{\circ} \text{ s}^{-1}$, 26.5% at $180^{\circ} \text{ s}^{-1}$ and 26.7% difference at $240^{\circ} \text{ s}^{-1}$ for the left limb and a similar pattern arose in the right ($60^{\circ} \text{ s}^{-1} = 21.3\%$; $120^{\circ} \text{ s}^{-1} = 19.5\%$; $180^{\circ} \text{ s}^{-1} = 19.2\%$; $240^{\circ} \text{ s}^{-1} = 19.5\%$).

Over the years changes have been seen in the control of acceleration and velocity from earlier versions of the Biodex isokinetic dynamometer (Feiring et al., 1990; Brown et al., 1993). Drouin, Valovich-McLeod, Shultz, Gansneder and Perrin (2003) was the first study to test the reliability of the B3. There is an abundance of literature on the reliability of the B2 isokinetic dynamometer (Feiring et al., 1990; Gross et al., 1991; Brown et al., 1993; Iossifidou & Baltzopoulos, 1998; Drouin et al., 2003). Since the Cybex is now out of production only a few studies report the reliability of the Cybex and its earlier versions (Gross et al., 1991; Kannus, 1992; Li et al., 1996; Dolny et al., 2001).

Feiring, Ellenbecker and Derscheid (1990) performed a reliability study on the B2 isokinetic dynamometer and found test re-test coefficients for PT at 60, 180, 240 and $300^{\circ} \text{ s}^{-1}$ (range 0.82 – 0.98) to be quite high. Gross, Huffman, Phillips and Wray (1991) found ICC's ranging from 0.67 to 0.97 for non-windowed PT and angular work at 60 and $180^{\circ} \text{ s}^{-1}$ on the B2 isokinetic dynamometer. Pincivero, Lephart and Karunakara (1997) also reported on the B2 and found results were reliable between PT, TW and average power at 60 and $180^{\circ} \text{ s}^{-1}$. The ICC's ranged from 0.88 – 0.97 and 0.82 – 0.96 for 60 and $180^{\circ} \text{ s}^{-1}$ respectively.

Brown, Whitehurst, Bryant and Buchalter (1993) investigated the reliability of the PT measures using the B2 isokinetic dynamometer. At $450^{\circ} \text{ s}^{-1}$ an average of 68.2 Nm and 72.1 Nm were observed on Day One and Two respectively. Between measures the correlation was $r = 0.95$. However the test did not state the measurement validity therefore it is not known if the velocity was actually obtained in the MVC's performed (Drouin et al., 2003).

Compared to a study by Drouin et al. (2003) using the B3 isokinetic dynamometer similar correlations between testing days were found. Drouin et al. (2003) stated that compared with their findings it seemed that the preselected velocity in Brown et al. (1993) study was not obtained. As the present study only assessed velocities as fast as $240^{\circ} \text{ s}^{-1}$ the measurements can not be compared however it can be concluded that even though day to day reliability may be high, torque measurements between different isokinetic dynamometers are not always valid.

Lund et al. (2005) also performed a reliability study on the B3 isokinetic dynamometer and found it to be highly reliable and no learning effect even when comparing a retrial 20 minutes post or a week later. Drouin et al. (2003) stated that the B3 provides mechanically reliable PT measurements as well as position and velocity with same day trials and trials on different days. Drouin et al. (2003) also states that velocity measures up to $300^{\circ} \text{ s}^{-1}$ are valid, however this decreases as the velocities increase. Li, Wu, Maffulli, Chan and Chan (1996) is the only study, to the author's knowledge, that tested the reliability of the Cybex 6000 model. The reliability of PT, TW and average power were measured. Peak torque was highly reliable (0.82 – 0.91), followed by TW (0.76 – 0.89) and average power (0.71 – 0.88). The knee extensors proved to be the most reliable as a result of test-retest variability and greater significance was seen at a velocity of $120^{\circ} \text{ s}^{-1}$ (Li et al., 1996).

Torque measurements and performance in muscular activity can be affected by fitness levels, motivation, anxiety and position set up on test day. Other factors such as acknowledging the instructions, time of the day, visual and verbal feedback can also affect results (Lenaerts, Verbruggen & Duquet, 2001). Due to scheduling problems with timetables, time of day could not be controlled. Fitness levels varied due to the mix of males and females and the investigator tried to keep the emotional levels of motivation high and any anxiety low however different lifestyles may have been a contributing factor and was not controlled.

Dynamometer set up was noted during every test day however minor changes were made for a few subjects mainly as a cause of subject discomfort. Studies have actually reported poor reliability when measuring lower extremity muscles because of the inability of testers to stabilise the dynamometer against explosive power (Fenter et al., 2003). This was quite evident on the B2. Position was controlled as much as possible. Visual and verbal feedback was present for every test day and protocol instructions were understood before participating. Protocol sequence was also strictly standardised and executed.

H.1.8 Conclusion

There are numerous isokinetic dynamometers on the market and the differences between these individual machines, even of the same model, can vary (Spencer, 2001). Results should only be compared with other isokinetic dynamometers with the same computer software (Drouin et al., 2003). The three isokinetic dynamometers used in this study continuously produced inconsistent values for PT and TW in isometric and isokinetic exercises. Comparing results from different models should always be avoided when testing any population.