The contributions of peripheral muscle strength, disease severity, and physical activities of daily living to arm and leg ergometry capacity in chronic pulmonary disease patients.

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Attestation of Authorship

I hereby declare that this submission is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person (except where explicitly defined in the acknowledgements), nor material which to a substantial extent has been submitted for the award of any other degree or diploma of a university or other institution of higher learning.

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List of Abbreviations

1RM	One Repetition Maximum
6MWT	Six Minute Walk Test
6MWD	Six Minute Walk Distance
6PBRT	Six Minute Peg Board and Ring Test
ACSM	American College of Sports Medicine
ADL-D	Activity of Daily Living-Dyspnoea (questionnaire)
ATS	American Thoracic Society
BF%	Body Fat Percentage
BMI	Body Mass Index
BODE	Body mass index, Obstruction, Dyspnoea, Exercise capacity
CET	Cycling Endurance Test
COPD	Chronic Obstructive Pulmonary Disease
CPD	Chronic Pulmonary Disease
FEV_1	Forced Expiratory Volume in one Second
FEV_1%	Forced Expiratory Volume in one Second percentage predicted
FFM	Fat-Free Mass
FM	Fat Mass
FVC	Forced Vital Capacity
FVC%	Forced Vital Capacity percentage predicted
GOLD	Global Initiative of Chronic Obstructive Lung Disease
IPAQ	International Physical Activity Questionnaire
MET	Metabolic Equivalent
MRC	Medical Research Council
NHC	National Health Committee
OSA	Obstructive Sleep Apnoea
PADL	Physical Activities of Daily Living
$Pain_{peak}$	peak pain (during ergometry testing
RPE	Rating of Perceived Exertion
UULEX	Unsupported Upper Limb Exercise Test
VO_{2max}	maximal oxygen uptake (during ergometry testing)
VO_{2peak}	peak oxygen uptake (during ergometry testing)
WHO	World Health Organisation
W_{peak}	peak wattage (during ergometry testing)

Abstract

Chronic Pulmonary Disease (CPD) often causes a reduction in physical activity and lower limb dysfunction. Exercise tolerance generally declines across the stages of CPD, which might be related to a reduction in physical activities of daily living, due to breathing discomfort or increased leg/arm fatigue. The contributions of specific aspects of disease severity and deconditioning to exercise tolerance remains unclear. In addition, it is uncertain whether patients with CPD have reduced upper limb function, or if upper body aerobic training capacity (arm ergometry) may be preserved. To provide insight into why patients adopt a more sedentary lifestyle, the aims of this study were to determine: (1) the combined and individual contributions of physical activities of daily living (type and volume) and FEV_1 to arm and leg ergometry capacity of patients with CPD; and (2) the predictability and odds ratio of high arm and leg ergometry capacity in CPD individuals with high and low arm and leg strength, while controlling for stage of disease, body composition and gender.

Forty-four CPD patients, 16 males and 28 females (mean age = 59.8 ± 11.9 years), with a FEV_1 of 22-89% predicted (mean FEV_1% predicted = 54.6 ± 18.3) participated. All participants completed spirometry, International Physical Activity Questionnaire and Activities of Daily Living-Dyspnoea questionnaire, Medical Research Council grade, anthropometric assessment, sub-maximal arm and leg ergometry testing, grip strength, and isokinetic quadriceps and hamstrings strength and endurance testing. To determine contributing and predictor variables of arm and leg ergometry capacity, a progressive statistical procedure was implemented leading to multiple linear and binary regression analyses.

No statistically significant relationships ($p>0.05$) were found between total activity, upper body activity and lower body activity, and peripheral muscle strength and aerobic capacity (controlling for age, gender and percentage body fat). Multiple regression analysis demonstrated that quadriceps strength (Nm), FEV_1% and grip strength (kg) predicted 64% of peak wattage during submaximal leg ergometry testing (adjusted R^2 = 64%, F = 26.387, p=0.00). Quadriceps strength showed the highest predictability of peak leg ergometry wattage (p=0.00, beta 0.844 and t=6.238), followed by grip strength and FEV_1% (p=0.038, β=-0.270, t=-2.143 and p=0.028, β=-0.230, t=2.279, respectively). A second regression analysis determined that quadriceps strength (Nm), FEV_1% and grip strength (kg) predicted 53% of peak wattage during submaximal arm ergometry testing (adjusted R^2=0.53, F=17.018, p=0.00). Quadriceps strength was the only independent variable that showed predictability of peak arm ergometry wattage (p=0.00, beta 0.793 and t=5.125). The odds ratio analysis indicated that CPD patients with high quadriceps strength have 13.76 times higher odds of having high peak arm ergometry wattage. This odds ratio equated to an 85% probability of having high arm ergometry peak wattage if quadriceps strength is high.

In summary, the main factors predicting leg ergometry capacity were quadriceps strength FEV_1 and grip strength. Quadriceps strength was the only statistically significant predictor of peak arm ergometry wattage, suggesting that a reduction in leg function is associated with a reduction in arm function. This study highlights the importance of assessing upper and lower limb strength in patients with CPD, and endorses the incorporation of specified lower limb strength training in pulmonary rehabilitation, especially for those with reduced strength and physical activity levels. Pulmonary rehabilitation programs should incorporate both aerobic exercise and lower limb strength training.

Chapter 1. Introduction

Chronic pulmonary disease (CPD) is a common medical term used to describe respiratory conditions causing progressive airflow limitation that is not fully reversible (World Health Organisation [WHO], 2013). Chronic pulmonary disease most commonly includes chronic bronchitis, emphysema, chronic obstructive pulmonary disease (COPD), bronchiectasis, asthma, interstitial lung disease, pulmonary hypertension and obstructive sleep apnoea syndrome. In New Zealand, respiratory disease is a significant cause of morbidity and mortality, which places a major burden on the healthcare system of New Zealand (National Health Committee [NHC], 2013). In the mid-central region of the North Island of New Zealand, 95% of avoidable respiratory deaths are caused by chronic obstructive pulmonary disease (COPD) and between 2-3% are due to asthma (Central Region's Technical Advisory Services Limited, 2008).

Effective management of CPD in New Zealand requires an integrated healthcare model. Specific guidelines for the management of COPD are outlined by Abramson et al. (2009), on behalf of the Thoracic Society of Australia and New Zealand and the Australian Lung Foundation in the 'COPDX' plan, which considers Confirming diagnosis (C), Optimising function (O), Preventing deterioration (P), Developing support (D) and managing eXacerbations (X). Pulmonary rehabilitation, with the main component being exercise training, is one goal of the 'optimising function' category. Exercise-based rehabilitation is an important component in the management of CPD, with the focus to improve physical function largely via an increase in exercise tolerance (Eisner et al., 2011). The ability to exercise is a major limiting factor when it comes to the physical rehabilitation of patients with CPD. Exercise capacity becomes limited as disease state progresses, which is largely due to increasing symptoms and systemic complications. This can prevent patients from exercising at an intensity or duration that provides sufficient overload which is needed to elicit physiological adaptations (Koutedakis, Metsios, & Stavropoulos-Kalinoglou, 2006). Exercise intensity is often restricted to low levels in CPD in order to maintain an adequate duration and vice versa, due to symptom limitations (Maltais et al., 1997). Accordingly, the predominant focus of exercise-based rehabilitation for pulmonary patients is to gradually increase cardiovascular function (aerobic capacity) by placing controlled but increasing demands on their cardiovascular system (Cooper, 2003).

The effectiveness of this exercise approach has been thoroughly researched and the consensus is that the potential impact of exercise training is limited by the severity of the disease (Cooper, 2001; Sietsema, 2001). Killian et al. (1992) redirected the focus of research on exercise-based rehabilitation away from pulmonary function and aerobic capacity, and focused on systemic limitations. Compared to the degree of dyspnoea, a more crucial exercise training limitation during maximal leg ergometry was the intensity of leg effort (Killian et al., 1992), confirming that disability and treatment of CPD extends well beyond lung function.

The mechanisms responsible for leg fatigue during aerobic exercise in CPD patients were discussed in a review study by Stendardi, Grazzini, Gigliotti, Lotti and Scano (2005). These authors concluded that leg fatigue in patients with CPD during aerobic exercise occurs as a result of blood flow redistribution and peripheral muscle alterations. When the body is hypoxic, as a result of inadequate ventilation/perfusion, blood flow is redistributed away from the periphery to the major organs (Kent et al., 2011). Blood flow to the working muscles during lower limb exercise is further reduced when the respiratory muscles become fatigued, due to increased work of breathing (Harms et al., 1997).

Over time, hypoxemia and the redistribution of blood flow results in structural changes to skeletal muscle fibres (Sietsema, 2001; Kent et al., 2011). As forced expiratory volume in one second (FEV_1) decreases, inspiratory muscles become chronically overloaded due to the increased work of breathing from hyperinflation and obstruction, causing an increase in type I muscle fibres in the diaphragm (Levine et al., 2003). In the lower limbs, there is a reduction of type I (slow twitch oxidative) fibres and augmentation of the proportion of type IIb (fast twitch glycolytic) fibres (Kim, Mofarrahi, & Hussain, 2008). In further support, meta-analysis data reveal that the proportion of type I fibres in the vastus lateralis correlates strongly with obstruction severity, as defined by FEV_1 (r=0.56; p<0.001), and moderately with BMI[1] (r=0.34; p<0.001) in patients with severe-very severe COPD (Gosker, Zeegers, Wouters, & Schols, 2007b).

Moreover, a relationship has been established between leg fatigue, exercise tolerance and lower limb muscle strength in cardiorespiratory patients (Hamilton, Killian, Summers, & Jones, 1995).

[1] BMI = body mass index

The authors made three important observations: 1) muscle strength contributed significantly to the intensity of leg effort and dyspnoea at a given power output; 2) peak exercise capacity was reduced in individuals with lower quadriceps strength; and 3) it was quantified that a doubling of strength is associated with a decrease in leg effort by 25% and dyspnoea by 30%. These findings are important as they identified the impact of quadriceps strength on maximal work capacity and severity of symptoms. This study concluded that cardiorespiratory patients have peripheral muscle weakness (quadriceps strength) and that quadriceps strength was a significant contributor to exercise capacity. The implication of this study was the emphasised need for assessment and therapeutic management of lower limb dysfunction. Furthermore, a review by Debigaré and Maltais (2008) concluded that exercise limitations of CPD patients is largely determined by lower limb dysfunction, specifically fatigability, muscle atrophy, and structural muscle fibre changes, which impacts lower body strength. Quadriceps strength in particular impacts dramatically on quality of life and physical independence (Donaldson, Maddocks, Martolini, Polkey, & Man, 2012), and strength has been reported as a significant predictor of healthcare utilisation in COPD patients (Decramer, Gosselink, Troosters, Verschueren, & Evers, 1997).

Additionally, there is scientific evidence indicating that frequency of muscle recruitment and activation in CPD patients largely determines the degree of dysfunction in a given muscle. In this regard, researchers have demonstrated that the degree of skeletal muscle dysfunction in COPD patients is not homogeneous between various muscle groups. For example, Franssen, Broekhuizen, Janssen, Wouters, and Schols (2005) identified that COPD patients with skeletal muscle dysfunction had a higher dysfunction in leg strength than in arm strength, when compared to healthy individuals. Lower extremity muscles are chronically under-loaded due to inactivity and disuse, while upper extremity muscles are less under-loaded (Kim et al., 2008). This under-loading of the lower extremity muscles contributes to lower extremity muscle dysfunction. Poor lower extremity functioning (as measured by the short performance physical battery) and poor exercise performance is related to a greater risk of COPD-related disability (Eisner et al., 2011). It was concluded that the management of COPD needs to be complimented with a comprehensive rehabilitation programme including exercise training to help prevent poor lower extremity function and COPD-related disability (Eisner et al., 2011).

To date, lower limb function in CPD has received a lot of attention in the literature, however, fewer studies have reported on upper limb function. There is still uncertainty regarding the comparative declining effect of CPD on arm and leg function. Owens et al. (1988) compared arm and leg ergometry in eight patients with moderate COPD and found that oxygen consumption during arm and leg ergometry were the same at similar heart rate responses, even though arm ergometry was at a significantly lower wattage. However, it is unclear from this study whether arm ergometry results in less limb fatigue and/or dyspnoea at similar heart rates, and therefore an improved ability to exercise. Franssen, Wouters, Baarends, Akkermans, and Schols (2002) investigated the mechanical efficiency (determined by peak load of the exercise and the difference between resting and exercise energy expenditure) of arm and leg exercise in patients with COPD compared to healthy controls. In contrast to the findings of Owens et al. (1988), those patients with COPD exhibited a preserved mechanical efficiency during sub-maximal arm exercise in contrast with a markedly decreased leg efficiency, concluding that exercise tolerance of the upper limbs appears to be relatively high in comparison to the lower limbs in COPD patients (Franssen et al., 2002). However, they did not explore this concept at different stages of the disease. It is unknown whether the progression of the disease affects the efficiency of arm exercise vs. leg exercise.

Lower limb muscle function in CPD patients can be improved with physical exercise (Rochester, 2003). Improving leg strength and endurance may result in less leg fatigue (better exercise tolerance) and improved functional exercise capacity during submaximal and maximal graded leg ergometry testing. Arm ergometry may serve as an alternative method of exercise testing and aerobic exercise training given the muscles of the upper limbs are less affected (less muscle fibre redistribution and atrophy) compared to the lower limbs (Owens et al., 1988). As a consequence, CPD patients may have the potential to perform upper limb exercise at higher heart rates for longer without experiencing extremity muscle fatigue.

The ability to exercise generally declines across the stages of CPD progression. This reduction might be related to individuals reducing their level of Physical Activities of Daily Living (PADL), due to dyspnoea and/or increased leg/arm fatigue. The reasons why persons with CPD adopt a more sedentary lifestyle are complex and could be dependent on the individual. Novel insights

into the specific limitations of exercise are needed to develop effective exercise training modalities, and ways to maintain physical activity levels in CPD patients.

There is a lack of scientific studies exploring whether CPD patients demonstrate better trainability potential (ability to exercise for longer durations with less dyspnoea and limb fatigue) during arm ergometry as compared to leg ergometry. Improvements in the trainability of CPD patients may allow them to better maintain (if not improve) current aerobic capacity. In addition, it is unclear from scientific studies whether a relationship exists between peripheral muscle strength and PADL (type and volume), and whether there is an association between peripheral muscle strength and the exercise trainability across stages of disease progression. Improvements in aerobic capacity, along with muscular strength and endurance, will likely improve the physical functioning of CPD patients in their everyday lives. This thesis therefore set out to explore these gaps in the literature.

1.1. Aim of the thesis

This thesis aimed to:

1. investigate the combined and individual contributions of physical activities of daily living (type and volume) and FEV_1 to arm and leg ergometry capacity of patients with CPD;
2. determine the predictability and odds ratio of high arm and leg ergometry capacity in CPD individuals with high and low arm and leg strength, while controlling for stage of disease, body composition and gender.

It was hypothesised that:

1. Individuals that do more physical activities of daily living involving the arms and legs will show better respective arm ergometry and leg ergometry capacity.
2. Independent of stage of disease, body composition and gender:
    - leg strength contributes significantly to leg ergometry capacity; and
    - arm strength contributes significantly to arm ergometry capacity.

Chapter 2. Literature Review

Chapter 2 reviews the latest research findings relating to the upper and lower body aerobic exercise capacity and strength of patients with CPD. The main focus of the literature discussed in this section will be directed towards COPD, as the vast majority of the literature available on the topic being discussed is specific to COPD. As there are marked similarities in pulmonary and systemic manifestations of COPD and other chronic respiratory diseases (Goldstein, 2005; Holland, Wadell, & Spruit, 2013), the information may be applied to other chronic respiratory conditions. Additionally, in a clinical setting they undertake the same pulmonary exercise rehabilitation programmes (Holland et al., 2013; Rochester, Fairburn, & Crouch, 2014).

2.1. Introduction to Chronic Pulmonary Disease

As previously stated in Chapter 1, the major determinant of CPD is chronic airflow limitation that is not fully reversible, which is primarily due to increased airflow resistance as a result of obstruction, inflammation, and/or damage to the airways and lung parenchyma (WHO, 2013). Chronic pulmonary diseases have a progressive nature, and symptoms, namely breathlessness, chronic cough, and increased phlegm production, can flare up during exacerbations (WHO, 2013). These diseases are often under diagnosed and can reach life threatening stages before they are detected by medical professionals (Doherty, 2006).

2.1.1. Obstructive vs. Restrictive Pulmonary Diseases

Diagnosis of CPDs are based on symptoms, thorough examination of patient history, lung function testing, and optimal treatment regimen trials (GOLD, 2014). Spirometry is used to assess lung function by measuring the volume and flow of air inhaled and exhaled. The key values used for diagnosis are forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), and the FEV_1/FVC ratio. On conclusion of the spirometry test, the values are displayed as absolute values, as well as percentage predicted value based on age, sex, height, weight and ethnicity. Essentially, the values can then classify individuals into obstructive and restrictive pulmonary disease categories as follows: obstruction is present when FEV_1 is reduced compared to the percentage and the FEV_1/FVC ratio is < 0.7; and restriction is present if the FEV_1/FVC ratio is > 0.7 and FVC is < 80% predicted (Mason et al., 2010). Additionally, some CPDs may present with

a combination of obstruction and restriction when their FEV_1/FVC ratio is > 0.7 but both their FEV_1 and FVC% predicted values are reduced. It must be noted that some CPDs can cause obstruction of the airways, but may not fit the diagnostic criteria of COPD. For example, the cause of the obstruction may be a secondary complication of another CPD, such as asthma or bronchiectasis, and not fit the diagnostic characteristics for COPD (Athanazio, 2012; Lange, 2013).

2.1.2. Chronic Obstructive Pulmonary Disease

Chronic obstructive pulmonary disease is a predominant and thoroughly researched pulmonary condition. It is an umbrella term that encompasses those lung conditions which become chronic, cause obstruction of the airways, have a history of exposure to noxious gases, and result in irreversible damage to the lungs. Chronic obstructive pulmonary disease is diagnosed, according to GOLD (2014), as a post-bronchodilator FEV_1/FVC ratio of <0.7, a history of exposure to noxious gases, and a reduced FEV_1. The World Health Organisation (WHO, 2008) stated that COPD affects 210 million people worldwide, and has caused 3 million deaths annually. Furthermore, the WHO (2008) predicted that by 2030 COPD will become the third leading cause of death worldwide. Likewise, COPD has a considerable impact on the health of the New Zealand population, affecting 15% of the adult population (200,000 people) older than 45 years of age (WHO, 2008).

2.1.3. Other Chronic Pulmonary Diseases

Asthma is a chronic disease of the airways characterised by inflammation and bronchial hypersensitivity resulting in intermittent episodes of semi-reversible/reversible airway obstruction (Cruz, Bousquet, & Khaltaev, 2007). The key distinction between asthma and other chronic airway diseases is that the airflow obstruction is reversible in the initial stages of the disorder, but as time goes on, some patients will develop permanent obstruction as a consequence of airway remodelling (NHC, 2013). It is estimated that there are currently 235 million people worldwide who have been diagnosed with asthma (WHO, 2013), and 250,000 people worldwide die from asthma annually. Asthma is generally known as a condition diagnosed in childhood, however more and more adults and elderly individuals are being diagnosed. In 2006/07, 109,900 children and 348,400 adults, or nearly 460,000 New Zealanders in total had been diagnosed with asthma

(NHC, 2013). In 2011/12, one in nine New Zealand adults (11.0%), and one in seven children aged 16 years and younger (14.0%) had asthma (NHC, 2013).

Bronchiectasis is an abnormal, chronic enlargement of the bronchi. Patients with bronchiectasis have a chronic cough, elevated phlegm production, and bacterial infections develop in the enlarged bronchi that result in inflammation that furthers the bronchial damage and the loss of lung function (O'Donnell, 2008). Diagnosis is made by high resolution computerise tomography. Bronchiectasis is characterised by airflow obstruction, phlegm production and hyperinflation and is associated with decreased health related quality of life and reduced functional exercise capacity (O'Donnell, 2008). While bronchiectasis is often a complication of a previous lung infection or injury, it could also be due to an underlying systemic illness (O'Donnell, 2008). According to NHC (2013), clinical estimates of bronchiectasis in New Zealand are between 272 and 341 per 100,000 people, and the total cost of hospitalisation of patients with bronchiectasis have been approximated to $5 million (1.9% of total costs).

Obstructive sleep apnoea (OSA) is characterised by recurring episodes of obstruction of the upper airway during sleep preventing normal breathing, which may result in hypoxemia (Cruz et al., 2007; Fauci et al., 2008). Causes of OSA include obesity, abnormal upper airway anatomy and/or other obstructions of the upper airway passages (Fauci et al., 2008). According to a New Zealand-based population survey, OSA affects approximately 4.4% and 4.1% of Māori and non-Māori men, and 2.0% and 0.7%, Māori and non-Māori women, respectively (Mihaere et al., 2009). Total annual healthcare burden of OSA for New Zealanders aged 30–60 years were estimated at a cost of $40 million (NHC, 2013).

2.2. Severity of Chronic Pulmonary Disease

Due to the progressing nature of these diseases, early detection is important as, unfortunately, death and disability eventuate (Doherty et al., 2006). In order for medical practitioners to diagnose and determine severity COPD, Doherty et al. (2006) promotes the use of the medical research council (MRC) dyspnoea scale, Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification and BODE index classification.

Based on FEV_1% predicted values, GOLD (2014) has developed diagnostic and disease classification guidelines (Table 2-1). These guidelines, along with the MRC scale, are commonly

used in research to classify individuals into categories of disease severity. The MRC scale classifies dyspnoea on a five point likert scale to determine severity of breathing impairment during exercise, walking or typical activities of daily living.

Table 2-1.
The GOLD classification for diagnosis and classification of chronic obstructive pulmonary disease.

Grade	Stage	Diagnostic Criteria*
I	Mild	$FEV_1 \geq 80\%$ predicted
II	Moderate	$50\% \geq FEV_1 \leq 80\%$ predicted
III	Severe	$30\% \geq FEV_1 \leq 50\%$ predicted
IV	Very Severe	$FEV_1 < 30\%$ predicted Or $FEV_1 < 50\%$ predicted plus chronic respiratory failure

Note. *ratio $FEV_1/FVC < 0.7$; chronic respiratory failure is defined as arterial partial pressure of oxygen (PaO_2) less than 8.0 kPa (60 mmHg) with or without arterial partial pressure of CO_2 ($PaCO_2$) greater than 6.7 kPa (50 mmHg) while breathing air at sea level.

The BODE index includes walking ability measured by the six minute walk test as part of its disease severity classification framework. The BODE index is a validated multidimensional grading system and is regarded as a better predictor of death from respiratory causes than FEV_1 alone (Doherty et al., 2006) and can predict the number of exacerbations in these individuals (Marin et al., 2009). The BODE-index has four dimensions including: body mass index (B), degree of airflow obstruction (O), dyspnoea (D), and exercise capacity (E).

Several organisations have developed guidelines for the classification and management of CPD, including: GOLD classification (Vestbo et al., 2013), The American Thoracic Society/European Respiratory Society (Celli et al., 2004), Canadian Thoracic Society (O'Donnell et al., 2008), and The Thoracic Society of Australia and New Zealand (Abramson et al., 2009). The general consensus is that disease severity range from mild to very severe, with a decreasing FEV_1 and/or FVC being classed as more severe.

Early detection is important as pulmonary rehabilitation is just as effective in the earlier stages of CPD, and hence may delay disease progression (Chee & Sin, 2008; Takigawa et al., 2007). Improving exercise capacity is important for the long term survival of COPD patients as exercise

training can slow disease progression (Garcia-Aymerich, Lange, Benet, Schnohr, & Anto, 2007). Measuring exercise capacity of patients with CPD is important, as they tend to have a reduced exercise capacity compared to non-COPD individuals (Gosselink, Troosters, & Decramer, 1996; Hamilton et al., 1995; Johnson-Warrington., 2014).

Few studies have reported on the physical activity patterns of people with CPD. In general, it seems these patients prefer to avoid exercise and the reasons for that are not entirely clear. From this perspective there has been increasing awareness and scientific interest in the response of individuals with CPD to exercise and the potential benefits of using planned/structured physical activity and PADL to delay physical decline in people with CPD (American Thoracic Society/European Respiratory Society, 2006).

2.3. Exercise Intolerance and Physical Inactivity in CPD patients.

Exercise tolerance and functional status are impaired in patients with CPD causing disability and a decrease in quality of life (Eisner et al., 2011). Although the causes of the reduction on exercise capacity in CPD are complex, some of this decline may be attributed to a reduction in physical activity levels. Reduced levels of physical activity, such as less involvement in PADL, have been reported in patients with CPD (Watz, Waschki, Meyer, & Magnussen, 2009b). Physical activity becomes increasingly harder to perform as patients with CPD experience the progressive decline in lung function (Celli, 1998). The decline in lung function is accompanied by an increase in symptoms, namely dyspnoea and/or leg fatigue, which leads to greater exercise limitation (Cooper, 2001). The volume, intensity and duration of the physical activity is limited by the CPD patient's perception and severity of their symptoms. As a result, a downward spiral can evolve, as a greater reduction in the amount of PADL performed leads to further deconditioning (Préfaut, Varray, & Vallet, 1995).

Exercise limitation in COPD patients results from a complex interaction of central (lungs) and peripheral (limbs) factors (Debigaré & Maltais, 2008). Chronic Pulmonary Disease patients have an increased metabolic demand due to abnormal gas exchange, hyperinflation, and increased dead space ventilation, which leads to an increased work of breathing (Ofir, Laveneziana, Webb, Lam, & O'Donnell, 2008). Respiratory muscles become overloaded to supply the body with adequate oxygen, causing an increased demand of oxygen utilisation of the respiratory muscles,

and resultant dyspnoea occurs (O'Donnell & Laveneziana, 2007). When oxygen demand is increased during activity a smaller proportion of the already limited oxygen supply is available for the working muscles (Laghi & Tobin, 2003). These respiratory complaints may contribute to the systemic complications associated with CPD which contribute to leg fatigue.

2.3.1. Symptoms during exercise

Research indicates that exercise in COPD patients is often more limited by leg effort than dyspnoea (Killian et al., 1992). Dyspnoea and leg effort were examined in COPD patients and normal subjects during leg ergometry (Killian et al, 1992). Leg effort limited exercise in 46% of COPD patients and 36% of normal subjects, whereas 26% of patients with COPD and 22% of normal subjects were limited by dyspnoea. However, this study did not compare dyspnoea and leg effort ratings in varying degrees of airway obstruction. Leg effort might, as a consequence, be more prevalent as a barrier to exercise as the disease progresses.

Hamilton et al. (1995) investigated the relationship of leg effort with peripheral muscle strength and maximal exercise capacity in healthy individuals and patients with cardiorespiratory disorders. A significant relationship was found between maximal exercise capacity and quadriceps strength in all groups. Likewise, a significant relationship was found between leg effort, cycling wattage and quadriceps strength in all groups ($p<0.001$). Poor quadriceps strength may cause low power output and higher leg effort during exercise, suggesting that improving quadriceps strength can decrease leg fatigue at a given exercise intensity. An important finding was that for a given quadriceps strength, leg effort was greater for the cardiorespiratory patients than normal subjects when cycling at the same intensity. This shows that cardiorespiratory patients experience more leg effort than healthy subjects and therefore have greater exercise limitations. Hamilton et al. (1995) concluded that in cardiorespiratory patients, leg fatigue is related to leg strength and exercise capacity, which may be worsened with deconditioning. Moreover, in CPD patients reduced PADL may lead to deconditioning (Préfaut et al., 1995), which may contribute to the alterations in peripheral muscle function often seen in CPD patients (Gosselink et al., 1996). Lower limb dysfunction in CPD patients is common and is caused by structural changes to the muscle, which leads to a reduction in skeletal muscle strength and endurance (Gosselink et al., 1996; Serres, Gautier, Préfaut, & Varray, 1998).

2.4. Lower Limb Impairments in Chronic Pulmonary Diseases

Debigaré and Maltais (2008) illustrated that lower limb muscle dysfunction is caused by a combination of anthropometrical and biochemical (physiological) impairments. These impairments include a reduced cross-sectional area and muscle wasting and a muscle fibre shift from type I to type IIb (Gosker et al., 2003), decreased muscle oxidative capacity and capillarisation, and decreased mitochondrial function (Gosker, Hesselink, Duimel, Ward, & Schols, 2007a). These non-respiratory, systemic impairments and functional limitations were shown to be critical determinants of disability in patients with COPD (Eisner et al., 2011), and are a major limitation to exercise in CPD (Debigaré & Maltais, 2008). Lower limb muscle dysfunction is not always related to lung function, as such limitations have been evident across all stages of CPD (Seymour et al., 2010; Donaldson et al., 2012). Seemingly, these physiological and anthropometric impairments present as a reduction in lower limb strength and endurance.

2.4.1. Reduced lower limb strength

Reduced quadriceps strength and thigh cross sectional area have been reported in patients with CPD, when compared to healthy individuals (Bernard et al., 1998). Impairment in lower limb strength of people with CPD has an impact on the health care system, as a reduction in quadriceps strength of CPD patients is associated with an increased utilization of health care services (Decramer et al., 1997), and can be used as a predictor of mortality (Swallow et al., 2007).

Peripheral muscle dysfunction, specifically quadriceps weakness, has been found across all stages of COPD (Seymour et al., 2010), even in those with mild/moderate disease. However, quadriceps weakness does not occur during moderate COPD with normal physical activity levels and fat-free mass (FFM) (Degens, Sanchez, Horneros, Heijdra, Dekhuijzen, & Hopman, 2005). Their findings suggest that lower limb dysfunction may be prevented by maintaining physical activity levels and lower limb muscle mass (Degens et al., 2005). Early physical rehabilitation interventions may be useful for avoiding the decline in physical activity associated with CPD and aid in preserving lower limb muscle dysfunction and in preventing the associated exercise limitations.

Hamilton et al. (1995) quantified that a 2-fold increase in quadriceps strength was associated with a 1.5-fold increase in maximal exercise capacity in cardiorespiratory patients. Their result suggests that quadriceps strength can determine the intensity of exercise that CPD patients can perform. Furthermore, they reported that a 2-fold increase in quadriceps strength was associated with a 30% decrease in the intensity of leg fatigue at a given power output, suggesting that strengthening the quadriceps can improve exercise tolerance and decrease symptoms associated with CPD during exercise tolerance testing (Hamilton et al., 1995).

2.4.2. Reduced lower limb endurance

Lower limb exercise endurance is significantly impaired in CPD patients when compared with healthy controls (Serres et al., 1998). Moreover, quadriceps endurance has been reported to be more affected in CPD patients than quadriceps strength (Coronell et al., 2004). Specifically, Coronell et al. (2004) reported that quadriceps endurance was reduced by 77% and quadriceps strength was reduced by 43% in CPD patients, compared to healthy controls. The impairment in quadriceps endurance was present even in those with mild to moderate COPD with normal physical activity levels. Their findings demonstrated the importance of muscle endurance testing and may explain the reduction in cycling endurance time seen in COPD (Coronell et al., 2004).

Contractile fatigue of the quadriceps occurs after cycling in a significant proportion of patients with COPD (Saey et al., 2003), which may limit cycling duration. After bronchodilation, no significant improvements in cycling endurance time (measured by cycling at a constant rate of 80% of the peak wattage obtained during a maximal incremental leg ergometer test) were shown in those who experience quadriceps fatigue, suggesting that peripheral muscle fatigue is involved in limiting exercise endurance in patients with COPD (Saey et al., 2003). Furthermore, a smaller increase in cycling endurance time of patients with COPD was seen after bronchodilation in those who report leg fatigue as the main limiting symptom, compared to dyspnoea (Deschênes, Pepin, Saey, LeBlanc, & Maltais, 2008).

Leg fatigue tolerance at the end of exercise and aerobic capacity were independently related to cycling endurance time (Vivodtzev et al., 2011). The authors speculated that non-respiratory impairments may be stronger determinants of endurance time than air flow limitation, as the differences in endurance time occurred independently of pulmonary function.

2.4.3. Relationship of lower limb dysfunction and severity of air flow obstruction

Changes in peripheral muscle dysfunction accelerate with ascending disease severity causing a decrease in physical function (Eliason, Abdel-Halim, Arvidsson, Kadi, & Piehl-Aulin, 2009). This finding indicates that those with increasing CPD severity have greater functional limitations. The relationship between aspects of lower limb muscle dysfunction and disease severity will now be discussed.

Associations between disease severity (FEV_1) and quadriceps structure and function have been reported. For example, quadriceps strength and muscle cross sectional area have displayed positive correlations with FEV_1% predicted (Bernard et al., 1998). Additionally, meta-analysis data revealed that the proportion of type I fibres in the vastus lateralis correlated with FEV_1 and BMI in patients with moderate to severe COPD (Gosker et al., 2007b).

While the above findings of Bernard et al. (1998) show that a reduction in quadriceps strength may increase with disease progression, quadriceps weakness is present across all stages of disease severity. For instance, Seymour et al. (2010) found significant differences in quadriceps strength between healthy individuals and CPD patients for all GOLD stages. Despite the fact that the highest percentage of patients with quadriceps weakness was in GOLD stage 4 (38%), quadriceps weakness was apparent at early stages (GOLD stage 1).

Moreover, maximum cycling wattage has been strongly associated with FEV_1 ($r=0.71$, $p>0.05$) (Haccoun, Smountas, Gibbons, Bourbeau, & Lands, 2002). In this study, a combination of FEV_1 and quadriceps endurance explained most of the variability in maximum cycling wattage (Haccoun et al., 2002). Similarly, Serres et al. (1998) demonstrated that disease severity, physical activity levels and lower limb endurance are inter-related and the authors speculated that the three variables are cofactors that progress together. Their findings demonstrated that FEV_1 correlated moderately with quadriceps endurance ($r=0.52$, $p<0.05$) and physical activity levels ($r=0.63$, $p<0.05$) (Serres et al., 1998). Physical inactivity is apparent across all stages of COPD, with a gradual decrease across the stages (Troosters et al., 2010). Exercise intolerance is apparent in CPD patients as of GOLD stage I, which begins to have an impact of PADL as of GOLD stage 2 (Díaz et al., 2013).

Likewise, Jehn et al. (2011) demonstrated that daily walking activity is indicative of disease severity in 107 patients with COPD (GOLD stage 2-4). Steps per day, time spent walking (at passive, active and fast paced intensities), and total walking time differed significantly between GOLD stages 2-4, and fast walking was negatively associated with GOLD stage, BODE index, and the MRC dyspnoea scale. Walking time (min/day) and intensity were significant and independent predictors of a BODE score ≥ 6. These findings indicate that walking time and intensity are significant and independent predictors of disease severity and can be used to predict the probability of poor prognosis of patients with COPD using the BODE index. Jehn et al. (2011) concluded that exercise training is needed in COPD patients to improve functional capacity and walking ability to potentially slow the progression of the disease. To date, the main body of literature has investigated exercise tolerance specific to the lower limbs. There has been little focus on the role of the upper limbs in the reduction of physical activity levels, exercise intolerance and increase in disease severity.

2.4.4. Upper limb vs. lower limb function

Ventilation and heart rate are higher for arm ergometry during both maximal and submaximal exercise at a given level of oxygen consumption (Owens et al., 1988). During maximal ergometry testing, the maximum ventilation and heart rates achieved were similar for arm ergometry and leg ergometry, however the maximum wattage and oxygen consumption obtained were lower for the arms. It is unclear from this study whether arm ergometry resulted in more or less dyspnoea and/or limb fatigue at similar heart rates or oxygen consumption. Castagna, Boussuges, Vallier, Prefaut, and Brisswalter (2007) reported no significant differences in dyspnoea severity between peak arm and leg exercise COPD patients. The authors observed differences between arm and leg aerobic capacity in COPD patients and only a slight reduction in arm exercise capacity was reported in COPD patients compared to healthy controls. Additionally, no statistically significant differences were seen in mechanical efficiency during arm exercise between COPD and controls, but mechanical efficiency was significantly decreased during leg cycling in COPD. These findings suggest that there is less upper limb dysfunction in COPD compared to lower limb.

Upper limb muscle strength (triceps and biceps) and handgrip strength have been shown to be significantly reduced in CPD patients compared to healthy controls (Clark, Cochrane, Mackay, &

Paton, 2000; Gosselink et al., 1996). In contrast, Heijdra et al. (2003) showed no differences in handgrip strength between patients with CPD and controls, however this was based on an average of 3 attempts rather than the maximum. Peripheral muscle weakness has been apparent in the upper body along with the lower body, however, upper limb strength appears to be better preserved compared to lower limb strength in patients with CPD (Bernard et al., 1998). Their findings demonstrated that lower body strength (quadriceps), upper body strength (pectoralis major and latissimus dorsi), and thigh cross sectional area were all significantly reduced in COPD when compared to healthy controls, however, the reduction in strength and type I fibres were proportionately greater for the quadriceps than the pectoralis major and latissimus dorsi (Bernard et al., 1998). In contrast, Franssen et al. (2005) reported that quadriceps and biceps strength were significantly reduced compared to healthy controls, and they were equally affected (65 $\pm$ 3% and 67 $\pm$ 3% respectively). When the participants were split into fat free mass depleted and non-FFM depleted COPD patients, quadriceps strength and endurance were significantly lower in the FFM depleted subgroup, however, biceps strength and endurance and handgrip strength were comparable between the two subgroups. This finding suggests that more of the muscle atrophy in the FFM depleted participants occurred in the lower limbs compared to the upper limbs.

These above findings suggest that upper limb function is somewhat preserved as lower limb endurance declines in COPD patients. Chronic Pulmonary Disease patients may reduce the use of their lower limbs (potentially through a decrease in walking), while the use of the upper limbs remain unchanged, however no studies were found which compared upper and lower limb activity levels. During rest, the shoulder girdle muscles are often used as accessory respiratory muscles to help facilitate the increase in breathing resistance, and are as a consequence quite active during quiet breathing in COPD patients (Bevegard, Freyschuss, & Strandell, 1966). Recruitment of accessory respiratory muscles could mean that the upper extremity muscles are less under loaded than the lower extremity, and could be the reason for the apparent preservation of upper limb function. However in patients with COPD, arm activity results in a significant increase in metabolic and ventilatory demand, which is emphasised during arm elevation, resulting in dyspnoea, dynamic hyperinflation, and a consequent decrease in performance during arm specific PADL (Celli, Rassulo, & Make, 1986; Martinez, Couser, & Celli, 1991; Velloso et al., 2003). During arm specific PADL the muscles of the shoulder girdle are used as accessory

muscles of respiration due to the increased work in breathing, causing an increase in oxygen demand (Laghi & Tobin, 2003). Ventilatory constraints and the resultant breathlessness causes limitation during arm specific PADL, which highlight the importance of upper limb exercise training (Velloso, Stella, Cendon, Silva, & Jardim, 2003). Upper limb exercise training may reduce the physical demands of PADL involving the upper limbs, as Couser, Martinez, and Celli (1993) reported that eight weeks of upper limb exercise training (including arm ergometry and unsupported arm exercise) resulted in significantly reduced ventilatory and metabolic demands during unsupported arm exercise testing.

2.5. Body Composition

Low BMI and FFM are common in CPD patients, and can be used to predict poor prognosis (Schols, Broekhuizen, Weling-Scheepers, & Wouters, 2005). A BMI of <21 as part of the BODE index decreases the likelihood of long term survival in CPD (Doherty et al, 2006). While a BMI of <18.5 $kg.m^2$ is considered underweight according to the WHO, a BMI of <21 $km.m^2$ is considered the underweight cut off in CPD (Celli et al, 2004; ATS, 2014). Low BMI in CPD (<21 $kg.m^2$) is more common in severe stages due to muscle atrophy (Eliason et al, 2009). Body mass index is a simple method of classifying individuals into body mass categories, however it does not measure the components of body composition. Assessing FFM in CPD needs consideration, as reduced FFM levels have been reported in male and female CPD patients with a normal BMI (Vestbo et al, 2006). Fat-free mass is an independent predictor of mortality in CPD (Schols et al., 2005), which supports the use of body composition assessment when considering severity of disease in CPD patients.

On the other hand, a higher BMI has been associated with higher FEV_1% predicted (Vibhuti et al, 2007), and a BMI >25 emerged as an independent predictor of better long term survival in CPD patients (Lainscak et al, 2011). A BMI greater than 25 is likely to improve patient prognosis if the higher BMI is associated with a higher amount of FFM. However, if the extra body mass is due to an increase in fat mass (FM), it may increase the risk of co-morbidities such as obesity, metabolic syndrome, diabetes, psychological disorders, and cardiovascular diseases (Chatila, Thomashow, Minai, Criner, & Make, 2008; Franssen & Rochester, 2014; Watz, Waschki, Kirsten, et al., 2009a).

In the early stages of COPD visceral FM is associated with a decrease in exercise tolerance and contributes to low grade systemic inflammation, which in turn is associated with mortality in CPD (Ramachandran, McCusker, Conners, Zuwallack, & Lahiri, 2008; Van den Borst et al, 2012). Obesity has become increasingly prevalent in CPD and its impact on exercise tolerance, exercise dyspnoea and prevalence of markers for metabolic syndrome during early stages of COPD also needs consideration, according to Sava, Maltais, and Poirier (2011). Obesity decreases lung function and is associated with increased dyspnoea independent of airflow obstruction (Sin, Jones, & Man, 2002), suggesting that obese patients with CPD may experience more dyspnoea. Even when obese and overweight patients have less severe airflow obstruction compared to normal BMI patients, they experience more symptoms (Sava et al., 2010; Vibhuti et al 2007). According to Monterio et al. (2012), increased FM contributes to muscle pain and fatigue during exercise, which contributes to decreased physical activity and lower exercise intolerance in CPD. The decline in PADL and exercise tolerance may cause patients to show symptoms like dyspnoea during physical exertion at FEV_1 levels that are normally considered equal to early stage disease development. Patients with COPD who were physically inactive were more predisposed to present with lower FFM percentages and higher FM percentages (Monterio et al., 2012).

Obese CPD patients entering pulmonary rehabilitation programmes commonly have reduced six minute walk distance but not constant work rate cycling endurance times (Sava et al., 2010), indicating that increased FM produces greater functional limitations during weight bearing activities in CPD patients. In this study, normal weight (BMI 21-25 $kg.m^2$), overweight (BMI 25-30 $kg.m^2$) and obese (BMI>30 $kg.m^2$) CPD patients displayed the same magnitude of improvements in cycling endurance time and six minute walk distance. The differences in six minute walk distance between high and low BMI were maintained even after exercise rehabilitation, validating the impact high BMI has on weight bearing activities (Sava et al., 2010).

Exercise training for CPD patients can increase FFM, or delay the decline of FFM due to hypoxia and deconditioning (Franssen et al., 2004). Fat-free mass is an independent predictor of mortality in CPD (Schols et al., 2005), which supports the use of body composition assessment when considering CPD severity, and supports exercise rehabilitation techniques that focus on

improvement and preservation of lean mass. In terms of body composition, pulmonary rehabilitation should aim to increase FFM and decrease FM, while attaining a normal BMI.

2.6. Exercise Testing

Exercise testing is crucial for measuring the physiological impact of CPD on the physical function of patients. Exercise testing is important for the construction of personalized exercise rehabilitation programmes for CPD patients to enable the best possible outcomes, and to measure the effectiveness of exercise rehabilitation programmes. Exercise testing can include exercise tolerance testing and peripheral muscle strength testing. Methods differ between researchers and organizations and are dependent on available equipment, accessibility, cost of administration, and degree of validity and reliability. Below is a summary of common exercise testing methods used in pulmonary rehabilitation, as reported in the scientific literature.

2.6.1. Aerobic capacity testing

Gas exchange measurement during treadmill exercise, leg ergometry or arm ergometry is still considered the most accurate way of determining cardiopulmonary ability of early and mid-stage pulmonary disease individuals. Progressive incremental exercise protocols are normally used which involves workload increases every 1-2 minutes until volitional exhaustion (American College of Sports Medicine [ACSM], 2014). Maximal incremental exercise tests are useful in the evaluation of CPD patients, but require expensive equipment that necessitates regular maintenance and qualified professionals to supervise testing. The most commonly reported cardiopulmonary exercise test in CPD is maximal incremental leg ergometry (Bernard et al., 1999; Franssen et al., 2005; Troosters, Gosselink, & Decramer, 2000; Spruit et al., 2002; Mador et al., 2011). Cardiopulmonary exercise testing to measure maximal oxygen uptake is a valid and reliable method of testing aerobic capacity in patients with CPD (American Thoracic Society [ATS], 2003). Clear guidelines for testing in clinical populations have been outlined by the American Thoracic Society and the American Heart Association (ATS, 2003; American Heart Association, 2010).

Constant work rate leg ergometry testing, or cycle endurance test (CET) is often used in conjunction with incremental leg ergometry testing (Simpson, Killian, McCartney, Stubbing, & Jones, 1992; Spruit et al., 2002; Mador et al., 2011). For the purpose of measuring cycling

endurance time, an intensity of 60-80% of peak workload achieved in the maximal incremental leg ergometer test is selected and patients are encouraged to cycle for as long as they can until fatigue. Constant load leg ergometry testing has been shown to be a reliable and valid method for measuring exercise endurance in patients with COPD (van't Hul, Gosselink, & Kwakkel, 2003).

Where maximal exercise is not appropriate, submaximal ergometry testing is an alternative exercise testing method which uses equations to predict VO_{2max}. Typically, it involves 2-4 stages or 3-4 minutes of continuous exercise with regular increases in workload with each stage. The YMCA submaximal leg ergometry test is commonly used in clinical populations when cardiopulmonary exercise testing is either unavailable or unsafe. Heart rates are recorded in the last minute of each stage, with the aim being to achieve a steady state heart rate (within 6bpm) (ACSM, 2014). This submaximal ergometry test has been found to be valid and reliable at predicting peak oxygen uptake, via an extrapolation method of submaximal exercise intensity and heart rates in a healthy population (Beekley et al., 2004).

The six minute walk test (6MWT) is a self-paced field walking test that has become a popular method to assess the functional ability of patients with CPD (American Thoracic Society, 2002). This test measures the distance a person can walk quickly on a flat, hard surface in 6 minutes. The test requires a 30m walkway but no exercise equipment. The self-paced 6MWT is generally used to assess patient's sub-maximal functional capacity. Most patients choose their own intensity during the test and are allowed to stop and rest when needed. Most PADL are performed at submaximal levels of exertion so the 6MWT may be a better reflector of the level of functioning of PADL than maximal incremental tests (Pitta et al., 2005). Although the test is quick and easy to administer, it does not measure peak oxygen uptake or evaluate the mechanisms of exercise limitation. For this reason, it has been recommended that the 6MWT be used in conjunction with maximal incremental exercise tolerance testing (American Thoracic Society, 2002).

Incremental maximal and sub-maximal exercise testing may be used for arm ergometry also. To determine maximal exercise tolerance in CPD patients using arms, researchers have adopted the maximal incremental exercise test protocols originally used for leg ergometry and treadmill testing and used it for arm ergometry. Arm ergometry may be used as an additional testing method to assess differences in upper and lower limb function in CPD (Owens et al., 1988; Carter, Holiday,

Stocks, & Tiep, 2003). A review by Janaudis-Ferreira et al. (2011) suggested that arm ergometry may be the best method for measuring peak supported arm exercise capacity and endurance in CPD patients as it is easy to standardise and has been demonstrated to be a valid and reliable test to measure the aerobic capacity.

Unsupported upper limb exercise tests (UULEX), the 6 minute pegboard and ring test (6PBRT) and the grocery shelving task, are alternative upper limb exercise testing methods (Janaudis-Ferreira et al., 2011). They require minimal equipment and are easy to administer in a clinical setting. These tests mimic upper body PADL more than arm ergometry and are useful for assessing upper body function during upper body PADL tasks. Unsupported upper limb tests involve self-paced exercise intensity and may not be useful for accurately assessing exercise capacity.

2.6.2. Peripheral muscle testing

Peripheral muscle strength and endurance testing is important for assessing systemic manifestations of CPD such as muscle dysfunction. Isokinetic dynamometers are considered the gold standard when measuring dynamic muscle strength and endurance. It consists of an adjustable chair constructed next to a swivel able dynamometer with changeable lever arms allowing testing of different muscles groups at various velocity and speed ranges. The machine measures muscle force at a set velocity, providing maximal torque values. Muscle strength is commonly expressed as maximal voluntary contraction. The most commonly tested muscle in COPD patients is the quadriceps at an angular velocity of $60^{o}.s^{-1}$ (Robles et al., 2011).

Handheld dynamometers, which tests the participant's ability to exert force in a pre-set joint angle against the assessor, has been used to test upper and lower body strength in CPD (Robles et al., 2011). Handheld dynamometers are small and portable and have been shown to have excellent reliability and to correlate with isokinetic dynamometry ($r=0.332-0.617$, $p<0.001$) (Whiteley et al., 2012). They can however, only measure isometric muscle force at various joint angles and cannot measure strength continuously through the full range of motion (Stark, Walker, Phillips, Fejer, & Beck, 2011), such as is the case with isokinetic dynamometer testing. They are also dependent on the strength of the assessor.

Handgrip force measured using a handgrip dynamometer has been used as an indicator of upper body strength in CPD (Shah, Nahar, Vaidya, & Salvi, 2013). Low grip strength is related to an increase risk of multiple chronic diseases and hence premature mortality (Cheung, Nguyen, Au, Tan, & Kung, 2013). In CPD, handgrip strength may be used as a quick functional measure of prognosis, as decreased handgrip strength is associated with an increased risk of mortality and exacerbations (Puhan, Siebeling, Zoller, Muggensturm, & ter Riet, 2012).

One repetition maximum (1RM) is a reliable method of evaluating maximal strength in untrained middle-aged individuals (Levinger et al., 2009); and has been used to test upper and lower body strength in CPD patients (Bernard et al., 1999). Repetition maximum is the maximal amount of weight that can be lifted with one contraction, and can be performed with any machine or free weights (ACSM, 2014). If it is unsafe to test true 1RM, it can be accurately predicted with an equation for up to 10 repetitions (Reynolds, Gordon, & Robergs, 2006).

2.7. Exercise Training

The Australian lung foundation (2014) recommends exercise training as an essential part of the rehabilitation process. Their current evidence-based recommendations are outlined in Table 2-2 below, which incorporates upper and lower body aerobic and strength exercise training. The ultimate goals of pulmonary rehabilitation are to improve CPD patients' physical function and quality of life, increase participation in daily activities, and reduce health care utilization (Troosters, Casaburi, Gosselink, & Decramer, 2005). A review of the practical recommendations for exercise training in patients with CPD by Gloeckl, Marinov, and Pitta (2013) summarises the benefits of exercise training. These benefits can include improvements in quality of life, increased peripheral muscle strength and endurance, increased aerobic capacity, improved psychological health profiles, improved balance, reductions in dyspnoea and fatigue perception at rest and during exercise, decreased hospitalisations, and increased survival rates. The benefits of exercise training are dependent on the individual goals and training components used in rehabilitation interventions. New research into the contributions of factors limiting exercise tolerance of CPD patients may enhance the research focus on examining and establishing specific exercise rehabilitation guidelines for optimal exercise mode, intensity, frequency and/or volume of training.

Table 2-2.
Australian Lung Foundation (2014) exercise training guidelines for patients with chronic pulmonary disease.

	Mode	**Intensity**	**Protocol**	**Duration**	**Frequency**
Lower limb	Endurance Training				
	Walking training (Ground-based)	80% average speed on 6MWT 75% peak speed on incremental shuttle walk Dyspnoea rating of 3 (moderate)	Continuous or interval	30 minutes	4 or 5 times a week that includes 2 or 3 supervised sessions and home exercise training
	Walking training (Treadmill)	As for ground-based walking training but reduce speed by 0.5 to 1 kmph until familiar with treadmill	Continuous or interval	30 minutes	4 or 5 days a week that includes 2 or 3 supervised sessions and home exercise training
	Stationary cycle training (if possible)	Dyspnoea rating of 3 (moderate)	Continuous or interval	30 minutes	4 or 5 days a week that includes 2 or 3 supervised sessions and home exercise training
	2) Strength training	10 RM (repetition maximum)		10 reps (1 set)	2 or 3 times a week with at least 1 day rest between sessions
Upper limb	Endurance training				
	Unsupported arm exercise	Determine the weight that the patient can only lift 15 times		15 reps (1 set)	4 or 5 times a week that includes 2 or 3 supervised sessions and home exercise training
	Arm ergometry	Dyspnoea rating of 2 or 3 (slight or moderate)			
	2) Strength training	10 RM (repetition maximum)		10 repetitions (1 set)	2 or 3 times a week with at least 1 day rest between sessions

Notes. 6MWT = 6 minute walk test, kmph = kilometres per hour, reps = repetitions, RM = repetition maximum.

2.7.1. Lower limb benefits of exercise training

Lower limb exercise training in CPD patients has been well-established in pulmonary rehabilitation due to the impact of lower limb muscle dysfunction on the physical functioning of these patients (Casabur et al., 1999). Traditionally, exercise rehabilitation for CPD patients was focused mostly on lower limb aerobic exercises such as cycling and walking (Chester et al., 1977; Cockcroft, Saunders, & Berry, 1981). Consistent research findings indicating the relative pronounced lower limb dysfunction apparent in CPD patients gave reason for lower limb strength training to be introduced as part of the physical rehabilitation of CPD patients. Improvements in exercise tolerance, such as improved maximum cycling wattage, submaximal cycling endurance and walking distance, as a result of lower limb strength training have been well documented (Rochester, 2003). Table 2-3 provides a summary of exercise training interventions studies that targeted lower limb strength training and exercise capacity conditioning of CPD patients.

The duration of the exercise training protocols ranged from 2-6 months, with a training frequency of 2-3 days per week. The pre and post exercise training aerobic capacity measures included maximal incremental leg ergometry testing, CET at 60-80% of peak work rate determined by incremental leg ergometry, 6MWT, and treadmill endurance walking. Five of the seven studies used at least two of these lower limb aerobic capacity tests. Leg ergometry testing results are expressed as peak wattage, VO_{2max}, and VO_{2peak}. Lower limb strength measures utilized in the studies listed in Table 2-3 includes isokinetic strength and endurance testing of the quadriceps and hamstrings, 1RM seated leg extension and leg press testing, and quadriceps fatigability (endurance) measured by twitch force.

Four studies incorporated aerobic training and strength training as part of their exercise protocols. Two studies included only strength training, while two studies compared aerobic and strength training protocols. There were marked similarities between the aerobic and strength training protocols. Aerobic training included leg ergometry and walking (treadmill or ground) or a combination of the two. All five studies that included leg ergometry determined intensity by percentage of peak wattage, with the initial wattage ranging from 30-60%. Treadmill walking speed was determined by 6MWT speed and ground walking speed was at a self-selected intensity. The majority of strength training protocols included machine weighted exercised, namely, seated leg press, knee flexion and knee extension. Intensity ranged from 1-3 sets of 8-

12 repetitions and training resistance was set at 50-70% of maximal strength. Progression of exercise intensity was dependent on symptoms (Borg score) and individual improvements, which were assessed on a weekly basis, with the aim of reaching 70-85% of their maximal strength.

The major findings of the eight studies outlined in table 2-3 were that leg ergometry capacity (peak wattage, VO_{2max}, and VO_{2peak}) of CPD patients improve statistically significantly with lower limb aerobic and strength training protocols lasting 8 weeks to 6 months. A longer training programme duration and the utilization of combined aerobic and strength training exercises generally produced better effect on walking ability and measures of VO_{2peak}. One study (Simpson et al., 1992), for example, did not include an aerobic exercise training component (apart from 5 minutes of warm-up cycling) and reported no significant post-training differences in maximal incremental leg ergometry wattage. This finding occurred despite the improvements in leg extension 1RM (44%) and leg press 1RM (16%).

The type of aerobic ability test utilized to measure effect also appeared to impact on the outcome. Cycle endurance test time and 6MWD for instance improved significantly independent of whether aerobic training and strength training are used in isolation or in combination. Incremental cycle ergometer testing requires respondents to manipulate increasingly higher cycle wattage as the test proceeds while maintaining a pre-determined cycle speed. It is quite possible therefore that outcome measures such as CET time or 6MWD, which do not require the participant to manipulate increasingly higher amounts of training loads at a pre-determined speed, are more prone to show improvements in studies that did not combine aerobic and strength training protocols.

Table 2-3.
Summary of the effects of exercise training interventions on lower limb strength and exercise capacity in CPD.

Study	Dur/Freq	Outcome measures	Exercise protocol	Training load	Progressions	Lower limb findings
Simpson et al., 1992 n=34 FEV_1=18-96%	3 x pw 8 weeks	Isometric strength: quadriceps, hamstrings 1RM: single knee extension and leg press CET, 6MWT, & Incremental leg ergometry	Warm up: 5 min low resistance leg ergometry RT: single leg extension, single leg press	RT: 3 x 10 reps at 50% 1RM	Increased to 85% 1RM	44% increase in leg extension 1RM and 16% increase in leg press 1RM (p<0.01) 23% increase max isometric force for quadriceps (240 ± 23.6 to 301 ± 25.3 N, p<0.01) CET significantly improved by 53% (518 ± 69 to 898 ± 95 seconds, p<0.01) No sig. increases max incremental leg ergometry capacity
Bernard et al., 1999 n=45 GOLD 2-3	12 weeks 3 x pw	Quad strength Incremental leg ergometry 6MWD	AE: Leg ergometry RT: leg press & knee extension	30min 2 x 8-10 reps 60% 1RM	Increased to 3 x 8-10 at 80% 1RM	AE + RT: 8% increase in thigh CSA (160 ± 36 to 171 ± 38 cm^2, p<0.0001); 20% increase in quad strength (57 ± 20 to 67 ± 21kg, p<0.0001); 12% increase in W_{peak} (p<0.05) 21% 6MWD increase (411±81 to 499±68m, p<0.001) AE: 9% increase in quad strength (51±12 to 56±11kg, 0.05); and a 17% increase in 6MWD (388±78 to 454 ±50m, p<0.0005) 19% increase in W_{peak} (non-significant)
Clark et al., 2000 n=26, GOLD I	12 weeks 2 days pw	Isotonic strength Isokinetic strength Treadmill endurance walk Incremental leg ergometry	RT: body squat, calf leg, press knee flexion, knee extension	3 x 10 reps 70% Max	70% Max recalculated at 6 weeks	Quadriceps strength increased by 7.6±7.2kg (p<0.01) in training group (controls = 0.4±4.8kg) 4205J increase in walking endurance (p<0.001) Increase in isometric quadriceps work (320J, p<0.05)
Troosters et al., 2000 n=34 FEV=41± 16%	6 months 2-3 x pw	6MWT Isometric quad strength Incremental leg ergometry	Leg ergometry treadmill walking stair climbing RT: quadriceps	60% W_{peak} 6MWTspeed 2min, 1-3 reps 3 x 10 reps 60% 1RM	Increase to 80%	Sig. differences in change between training and control groups in 6MWD (p=0.01), W_{peak} (p=0.003), VO_{2max} (p=0.02), quadriceps strength (p=0.004) Correlation between improvements in 6MWD and quad strength (r=0.38, p<0.05)

Notes. pw = per week, RM = repetition maximum, CET = cycling endurance time, 6MWT = six minute walk test, 6MWD = six minute walk distance, N = newtons, RT = resistance training, AE = aerobic exercise, sig. = statistical significance, reps = repetitions, W_{peak} = peak wattage, J = joules.

Table 2-3. Continued.

Study	Dur/Freq	Outcome measures	Exercise protocol	Training load	Progressions	Lower limb findings
Spruit et al., 2002 AE n = 16 RT n = 14 FEV1=38 ±13%	12 weeks 3 x pw	Quadriceps peak torque Quad, Hamstring force CET at 70% W_{peak} incremental leg ergometry 6MWT	Walking, Leg ergometry, RT: quadriceps, hamstrings	60% 6MWT speed 30% W_{peak}- 3x8 reps at 70% 1RM	Up to 25 min at 75% W_{peak} Weekly increases of 5% 1RM	Sig. increases in 6MWD for RT (38 ± 50 m, p<0.01) and AE (41 ± 43, p<0.002) Sig. increase W_{peak} for RT (15 ± 16W, p<0.01) and AE (14 ± 13W, p<0.001) Sig. increase VO_{2peak} of 89 ± 166 $mL.L^{-1}$ (p<0.05) for AE, but not RT (106 ± 253 $mL.min^{-1}$, p=0.21)
Franssen et al, 2005 n = 87 GOLD 3	8 weeks 3 days pw	FFM (Bioelectrical impedance) Isokinetic quadriceps strength & endurance Incremental leg ergometry	Submaximal leg ergometry Treadmill walking Gymnastics Strength training	50-60% W_{peak} 20min 20min 30min NS	Based on subject improvement	Quadriceps strength and endurance increase of 20% (p<0.01) FFM increase of 1.5 ± 0.3kg (p<0.001) W_{peak} increase of 15 ± 2W (p<0.001) VO_{2max} increase of 137 ± 26mL/min (p<0.01)
Alexander et al., 2008 AE+RT n=10 FEV1= 29.8±13%	8 weeks 2 x pw	1RM seated leg press lower body strength (chair stand), 8-foot up and go 6MWT	Treadmill Leg ergometry RT: seated leg press	Combined aerobic = 20min 1-2 x 12 reps	Increase to 40 min Based on RPE 11-13	14% increase in 6MWD (321 ± 32 to 365 ± 105m) Non sig. increase in leg press 1RM of 2% (106 ± 32kg to 107 ± 36kg) Note: p-values not reported.
Mador et al 2011 n=20 FEV_1= 42±13% pred.	8 weeks 3 x pw	6MWT Incremental leg ergometry CET 60-70% W_{peak} Quad strength & twitch force	Leg ergometry Treadmill walking Calisthenics with and without small weights	50% W_{peak} 80% 6MWT speed NS	5-10% increase when borg scores <5	Sig. increases (p<0.05) in 6MWD of 10 ± 15.8% (414 ± 134 to 446 ± 128m), W_{peak} of 23.1 ± 33.3% (52.9 ± 22.1 to 64.4 ± 26.8W, and CET of 384 ± 352% (6 ± 3 to 24.7 ± 12.5min). All sig. difference compared to controls. Improvements in quad strength NS (baseline = 42.8 ± 9.8kg) Quad fatigability sig. (p<0.05) reduced after training. No differences between training and control groups.

Notes. pw = per week, RT = resistance training, AE = aerobic exercise, CET = cycling endurance time, W_{peak} = peak wattage, 6MWT = six minute walk test, RM = repetition maximum, 6MWD = six minute walk distance, reps = repetitions, RPE = rating of perceived exertion, sig = statistical significance, FFM = fat-free mass, NS = not stated.

The representative outcome measure to monitor improvements in lower limb strength in the eight studies reported in Table 2-3 was quadriceps strength. Quadriceps strength improved across the seven studies by 16-44%. Three studies reported on quadriceps endurance but used three different outcome measures, making it difficult to compare. The one study which provided pre- and post-quadriceps endurance isokinetic data reported a 20% increase in quadriceps endurance (Franssen et al., 2005). The information summarized in Table 2-3 provides strong evidence of a direct relationship between measures of leg strength and the ability to perform cardiovascular tests that involve the lower limb. This relationship appears to exist independent from stage of disease development, as the GOLD stage of the participants in all of the studies ranged from mild or moderate to severe or very severe airflow obstruction.

2.7.2. Upper limb training

To optimize the ability of CPD patients to perform PADLs researchers have also investigated the impact of upper limb exercise training on upper limb strength and aerobic capacity. Table 2-4 reviews seven upper limb exercise training intervention studies. The duration of the exercise training protocols ranged from 6-12 weeks with a training frequency of 2-3 days per week, with the exception of one study that exploited daily exercise training (Ries et al., 1988). Upper limb aerobic training consists of arm ergometry, unsupported arm exercise, and resistance exercises targeting the pectorals, deltoids, rhomboids, latissimus dorsi, biceps and triceps muscle groups.

The exercise training protocols are dissimilar across the seven studies making them difficult to compare. Six of the seven studies included upper limb strength training and five reported on the strength training outcomes. The strength training protocols across these studies ranged from 1-3 sets of 8-15 repetitions, which is similar to the leg strength training protocols (Table 2-3). Four studies reported significant improvements in upper body strength using various measures of strength, namely 1RM testing for arm curl, chest press, lateral pull down and incline bench press, isometric force for elbow flexion and extension and shoulder flexion and abduction, and handgrip dynamometry. The one study that reported non-statistically significant improvements in upper body strength (grip strength) had a small sample size and high standard deviations which would have impacted on the statistical significance.

Four studies included arm ergometry training, however only two reported post assessment data (Ries et al., 1988; Gigliotti et al., 2005). Both of these studies reported significant increases in

arm ergometry endurance time. One study compared arm ergometry and unsupported arm exercise training, with both training protocols impacting positively on arm ergometry endurance and measures of perceived dyspnoea and arm fatigue at a given work rate (Gigliotti et al., 2005). Overall, three of the upper limb exercise training studies reported improvements in dyspnoea at a given exercise intensity (Ries et al., 1988; Gigliotti et al., 2005; Janaudis-Ferreira et al., 2011).

Improvements after arm exercise training can include increases in arm exercise endurance, upper body muscle strength, reduced dyspnoea and arm fatigue and improve health-related quality of life (Janaudis-Ferreira et al., 2011). However, it is unclear how upper body training compares to lower body training, and which modalities produce the largest improvements in exercise symptoms, quality of life and performance during PADL. The potential to use arm ergometry to lengthen or improve the effectiveness of training sessions in an attempt to increase gains in aerobic capacity remains unclear.

Table 2-4.
Summary of the effects of exercise training interventions on upper limb strength and exercise capacity in CPD.

Study	Dur/Freq	Outcome measures	Exercise protocol	Training load	Upper limb findings
Ries et al, 1988 n=45 moderate-severe COPD	6 weeks 1-2 x daily	Arm ergometry UULEX	Arm ergometry Walking RT or PNF	RT = 1-2 x 10 reps, 10RM PNF = 3 x 4-10 reps, 6RM	Number of lifts on unsupported arm exercise test and endurance time on the arm ergometer increased in both upper training groups
Simpson et al., 1992 n=34 FEV_1=38%	8 weeks 3 x pw	Isometric handgrip strength 1RM: arm curl	Warm up: 2 min arm ergometry RT: arm curl	3 x 10 reps at 50-85% 1RM	33% increase in arm curl 1RM ($p<0.01$) Sig. increase max isometric force for biceps (28 ± 2.6 to 33 ± 3.2 N, $p<0.01$)
Bernard et al., 1999 n=45, Gold 2-3	12 weeks 3 x pw	1RM Pectoralis major, Latissimus dorsi	RT: chest press, lat pull down	30min 2-3 x 8-10 reps 60-80% 1RM	15% increase in pectoralis major strength (64 ± 16 to 73 ± 17kg, $p<0.0001$); 8% increase in latissimus dorsi strength (53 ± 12 to 56 ± 11kg, $p<0.05$)
Spruit et al., 2002 AE n=16 RT n=14	12 weeks 3 x pw	shoulder abduction, & elbow flexion force Handgrip force	Arm ergometry RT: pectorals, biceps, triceps, deltoids,	4-9 min 3x8 reps, 70% 1RM	non-sig. increase in handgrip strength for RT (8 ± 15%, $p=0.09$) and AE (30 ± 62%, $p=0.07$)
Gigliotti et al, 2005 n=12 GOLD 2-3	6 weeks NS	Arm ergometry VO_2 Dysnoea/Arm effort Ventilation	UAE: repeated shoulder abduction and extension, and ring and peg board SAE: Arm ergometry	UAE: as tolerated SAE: 80% of peak work rate	A significant increase in arm exercise endurance ($p < 0.001$) at a standardized work rate, ventilation, exercise dyspnea, and arm effort significantly decreased, while the decrease in IC was significantly less ($p < 0.01$) post training.
Alexander et al., 2008 AE n=10 AE+RT n=10	8 weeks 2 x pw	1RM incline bench press upper body strength (arm curl)	Arm ergometry RT: incline bench press, lateral pulldown, lateral arm raise, triceps pushdown, upright row, bicep curl	Combined aerobic = 20-40min 1-2 x 8-15 reps	Non sig. increase in incline bench press 1RM of 5.4% (34 ± 13 to 35 ± 13kg) Note: p-values not reported.
Janaudis-Ferreira et al, 2011 n=36 patients with COPD	6 weeks 3 x pw	Dyspnea during PADL 6PBRT & UULEX Dyspnoea & Arm fatigue Isometric hand-held dynamometer (EF, EE, SF, SE, SAb, SAd)	RT biceps, triceps, pectoralis major and minor, latissimus dorsi, deltoids, and rhomboids	2 x 10-12 reps 10-12 RM	The arm resistance training programme improved arm function (19.7%) and arm exercise capacity (15.30%) and arm strength (EF 11.4%, EE 14.8%, SF 10.5%, SAb 13.4%). Significant improvements in dyspnea during ADL, however no increase in dyspnea seen with an increase in arm exercise capacity.

Notes. UULEX = unsupported upper limb exercise test, RT = resistance training, PNF = proprioceptive neuromuscular fascilitation, N = newtons, AE = aerobic exercise, UAE = unsupported arm exercise, SAE = supported arm exercise, RM = repetition maximum, 6PBRT = 6min peg board and ring test, PADL = acticities of daily living, EE = elbow flexion, EE = elbow extension, SF = shoulder flexion, SE = shoulder extension, Sab = shoulder abduction, SAd = shoulder adduction.

2.8. Conclusion

Research evidence is clear and consistent that disease progression and lower limb dysfunction impact negatively on aerobic capacity. As the disease increases in severity, the amount of activity CPD patients are able to do not only decreases, but they also report more symptoms of dyspnoea during exercise. Upper limb muscle function appears to be less affected than the lower limb and hence there may be a potential to use arm ergometry to lengthen or improve the effectiveness of exercise training sessions to speed up or maximise the improvements in aerobic capacity.

Chronic pulmonary disease severity increases with a decline in pulmonary function. Disease severity can be classified from mild-very severe based on FVC and FEV_1 % predicted acquired through spirometry testing. Research evidence is clear and consistent that disease progression, reduced levels of physical activity, and lower limb dysfunction impact negatively on aerobic capacity. There appears to be a downward spiral that exists: as the disease severity increases, the physical profile of the patient decreases, which in turn results in an increase in symptoms.

A relatively new area of research focuses on the impact of CPD on upper body aerobic capacity, strength and fibre type changes. The relative importance of this relates to the possibility of enhanced ability to perform upper body conditioning given upper body muscle function seems to be less affected than lower limb function, and hence there may be potential to use arm ergometry to lengthen or improve the effectiveness of training sessions in an attempt to increase gains in aerobic capacity.

In attempt to enhance the training ability of CPD patients it is important to identify specific exercise limitations in this population and to assess how much impact each limitation has on the overall functioning of these individuals. This knowledge will enhance the understanding of the behavioural and physiologic mechanisms behind the reduction in physical activity, and contribute to the construction of effective exercise rehabilitation programmes to improve the outcomes of CPD patients.

Chapter 3. Method

3.1. Study Design

A cross-sectional research design was used to investigate the within group relationships of pulmonary, strength, and physiological measures of patients with mild to very severe airflow obstruction. All participants completed three one hour assessments, with 24 hours minimum between. Appointment 1 consisted of informed consent, health screening, pulmonary function testing and IPAQ (International physical activity questionnaire), MRC (Medical Research Council), and ADL-D (Activity of daily living–Dyspnoea) questionnaires. Appointment 2 included resting haemodynamics, anthropometric assessment, sub-maximal leg ergometry testing, and grip strength testing. Appointment 3 included resting haemodynamics, sub-maximal arm ergometry testing, and isokinetic quadriceps/hamstrings strength and endurance testing. The study protocol had prior approval of research-ethics from the central lower-north island ethic committee of New Zealand.

3.2. Participants

Forty-four patients referred by the Palmerston North Hospital Pulmonary clinic to the U-kinetics exercise and wellness clinic for 12-weeks of exercise-based rehabilitation participated. Written informed consent was obtained from all participants of the study. The participants had not been involved in structured exercise training for at least one year prior to participation in the study.

All of the participants had been diagnosed with a chronic pulmonary condition (or a combination) by a General Practitioner or Respiratory Physician including: chronic bronchitis, emphysema, COPD, bronchiectasis, asthma, and obstructive sleep apnoea syndrome.

The descriptive and disease severity characteristics of the participants are displayed in Table 3-1. The study participants included 44 CPD patients, 16 males and 28 females, with a mean age of 59.8 ± 11.9 years. The mean FEV_1% predicted was 54.6 ± 18.3, indicating GOLD stage 2 (moderate CPD). Participant's FEV_1% predicted ranged from 89-22% (mild to very severe airflow obstruction).

Table 3-1.
Participant descriptive and disease severity characteristics.

	Mean ± SD	Range
Age	59.8 ± 11.9	26-72
Weight (kg)	87.3 ± 20.6	41.9-142.1
BMI (kg.m^2)	33.2 ± 11.0	18.8-51.9
BF%	30.6 ± 13.1	12.9-60.0
FVC%	70.6 ± 13.2	39-95
FEV1%	54.6 ± 18.3	22-89
GOLD stage	2	1-4

Notes. BMI=body mass index; BF%=body fat percentage, FVC% = forced vital capacity percentage predicted, FEV_1% = forced expiratory flow in one second percentage predicted, GOLD = GOLD = Global Initiative of Chronic Obstructive Lung Disease**.**

The number of respondents in each disease severity category, based on the GOLD classification, is displayed in Figure 4-1. For the purpose of this thesis, disease severity categories were merged to form two groups, due to the low number of respondents in the mild (n=4) and very severe categories (n=5). Mild and Moderate CPD stages (GOLD 1-2) were combined to form the "Mild-Mod" group (n=28) and severe and very severe CPD stages (GOLD 3-4) were combined to form the "Severe+" group (n=16). The Mild-Mod group included 10 males (35.7%) and 18 females (64.3%); and the Severe+ group included 6 males (37.5%) and 10 females (62.5%).

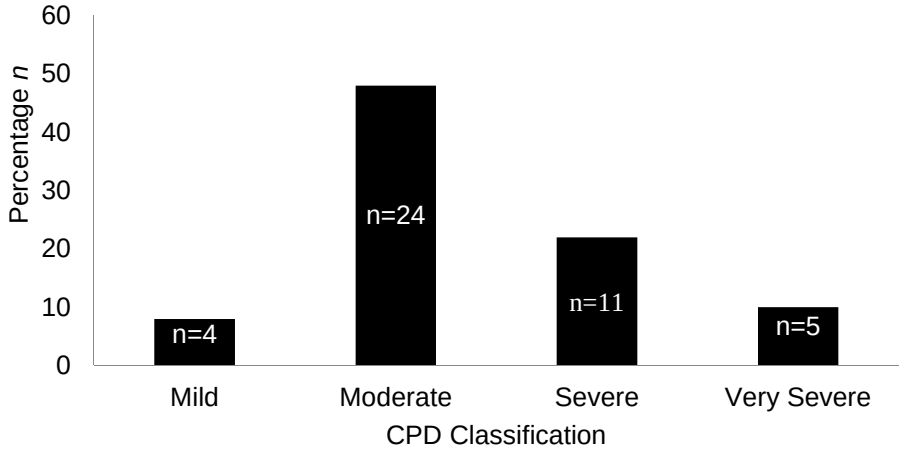

Figure 3-1. Number and percentage of participants in disease severity categories based on GOLD classification.

3.3. Data Collection

3.3.1. Resting haemodynamics

Resting heart rate and blood pressure were measured after the participant had been in a supine position for 5 minutes in a quiet room. Resting heart rate was obtained with the values shown on an electrocardiogram system (custo cardio 100, Custo-Med, Germany). Resting blood pressure was measured three times manually using a stethoscope and sphygmomometer (Diagnostix™ 720, American Diagnostics Corporation, Hauppauge, NY), and the lowest blood pressure reading was recorded.

3.3.2. Anthropometric measures

Stature was assessed with shoes removed with a wall mounted stadiometer (model 222, Seca, Hamburg, Germany). Body mass was measured on a calibrated electronic scale (Tanita, Cloverdale, Western Australia 6985) with the shoes and as much clothing removed as possible. Body mass index (BMI) was calculated by dividing body mass (kg) by stature (m) squared. Skin-fold thickness of six sites (triceps, subscapular, supra-iliac, abdominal, thigh and medial calf) were measured with Harpenden callipers (CE 0120, BATY International, RH15 9LB, England) according to the guidelines of the International Society for the Advancement of Kinanthropometry (Marfell-Jones, Stewart, & Marfell-Jones, 2006). Body fat percentage was calculated using Yuhasz's (1974) six-site formula for males [sum of 6 skinfolds x 0.1051 + 2.588], and for females [(sum of 6 skinfolds x 0.1548 + 3.58].

3.3.3. Sub-maximal exercise tests

Leg ergometry

All participants completed a modified version of the YMCA sub-maximal leg ergometer testing protocol (ACSM, 2014) for estimation of $VO_{2max.}$ Testing was performed on a leg ergometer (ec3000e, Custo-med, Germany). The test comprised an unloaded one minute warm-up, followed by three 4 minute stages. Participants started on 20-30 Watts for the first stage and then power output was gradually increased with each stage depending on rating of perceived exertion (RPE), pain and dyspnoea scores, and heart rate and blood pressure responses. Power output was increased at the end of the 4th minute of each stage if the 3rd and 4th minute heart rates were within a steady state (± 6 bpm) and no symptom limitations were present. The aim was to reach

either 70% of the age adjusted maximum heart rate using Karvonen's Formula [(220 - age - resting heart rate) x 0.7 + resting heart rate], or any symptom limitation according to the ACSM absolute and relative contra-indications for terminating exercise testing (ACSM, 2014).

Electrocardiography (ECG) was used to monitor heart waveform and rhythm during exercise testing using the Mason and Likar (1966) modified electrode placement provided by McArdle, Katch, & Katch (2010). Arm electrodes were positioned medial to the anterior deltoid 1-2cm below the right and left clavicle and foot electrodes were positioned over the lower ribs.

Power increments were decided by experienced Clinical Exercise Physiologists, based on heart rate response, Borg scores, physical signs, blood pressure response, and the ECG. Heart rate was recorded every minute of each stage using the heart rate reading on the ECG. Exercise blood pressure was manually recorded during the last minute of each stage.

The following equation was used to calculate VO_{2max} [VO2 = ((10.8 x work rate in watts) / body mass) + 7] (ACSM, 2014).

Arm ergometry

All participants performed an incremental multi-stage sub-maximal arm ergometry test (ACSM, 2014). Testing was performed on a Technogym Arm Ergometer (Top Excite 700, Technogym, Casena, Italy). Participants sat upright with both feet on the ground and at a distance that their arms were slightly flexed while undertaking the arm ergometry test. Participants performed one minute warm-up of unloaded arm cycling, before completing three stages of 3 minutes.

Participants started at 20-30 Watts and power increments were decided by professional judgment of experienced Clinical Exercise Physiologists, based on heart rate response, Borg scores, physical signs, and blood pressure response. The aim was to either reach 70% of age-adjusted maximal heart rates (using Karvonen's formula as above), a RPE score of higher than 14 or a wattage equal to or greater than 42% as obtained during the last stage on the leg ergometry assessment, according to Carter et al. (2003). Test termination points included the presence of symptom limitation based on the ACSM's (2014) guidelines for early termination.

The following equation was used to calculate VO_{2max} [VO2 = ((18 x work rate in watts) / body mass) + 3.5] (ACSM, 2007). If peak wattage beyond 42% of leg ergometry wattage were required for subjects to reach the same maximum heart rates as obtained during leg ergometry, the test

continued beyond 3 stages until they reached the required heart rate, or the clients requested to stop.

Dyspnoea, fatigue and RPE scores

Dyspnoea was measured during each stage of arm and leg ergometry using the Borg dyspnoea scale (Borg, 1998). Perceived exertion was measured using the Borg RPE scale. Perceived arm and leg fatigue was recorded using the Borg CR-10 scale (Borg, 1998). Subjects were instructed to report a number describing their perception of limb fatigue during each stage of respectively arm and leg ergometry. The Borg CR-10 scale is a general intensity scale with ratings from 0-12 that has previously been used to measure extremity pain/fatigue during exercise (Carter et al., 2003).

3.3.4. Pulmonary function testing

Spirometry was performed in order to verify the degree of airway obstruction, with consideration to the ratio FEV_1/FVC, so that participants could be classified into mild ($FEV_1 \geq 80\%$ predicted), moderate (predicted $50\% \leq FEV1 < 80\%$), severe (predicted $30\% \leq FEV1 < 50\%$) and very severe (predicted $FEV1 < 30\%$) obstruction categories (GOLD, 2014). Spirometry was performed using a hand-held spirometer (EasyOne, nnd Medizintech AG, 8005 Zurich, Switzerland), which was calibrated prior to each test with a 3L syringe. Participants performed the FEV_1 and FVC manoeuvre according to the American Thoracic Society guidelines (ATS, 2005). The participants sat in an upright position with both feet on the floor wearing a nose peg when performing the test, and were instructed to breathe in as deeply as they could, seal their lips around the mouthpiece, and blow out as hard, fast and as long as possible. Subjects performed three attempts and the best attempt was recorded.

3.3.5. Peripheral muscle strength testing

Upper body

Upper limb strength was measured by grip strength using a Baseline Hydraulic Hand Dynamometer (Irvington New York, 10533 U.S.A). Two attempts were performed on each side for familiarization and highest reading was recorded. The grip strength test started with the arm in shoulder abduction of 90 degrees, with the elbow in full extension (0^0 of flexion). The subject was instructed to grip the hand dynamometer as hard as they could, lower the arm down to the

side of the body squeezing the tool with a maximum effort. The dynamometer was reset to zero prior to each reading.

Lower body

Lower limb strength and endurance was measured by knee flexion and extension using an Isokinetic muscle dynamometer (HUMAC norm, model 502140, Computer Sports Medicine, Inc., Stoughton, MA 02072, USA). The dynamometer was calibrated according to standard settings outlined by the user manual with the axis of rotation in line with subject's femoral epicondyles. The dynamometer was corrected for gravity. Range of motion (ROM) was set to at least 90°. Subjects completed one trial set of 5 repetitions at 60 and 180°.s^{-1} for familiarization and then one set of 5 repetitions at 60°.s^{-1} and one set of 15 repetitions as fast as possible at 180°.s^{-1}. Each set was separated by a 60 second rest interval, which has been found to be an adequate rest period during isokinetic testing to avoid fatigue (Parcell, Sawyer, Tricoli, & Chinevere, 2002). Subjects were instructed to flex and extend their knee as hard and as fast as they could for the full duration of the test. This quadriceps/hamstring strength and endurance testing protocol has been used on healthy, inactive, elderly individuals (Malliou et al., 2003).

3.3.6. Dyspnoea

All subjects completed the MRC scale (Fletcher, Elmes, Fairbairn, & Wood, 1959) for the purpose of determining severity of dyspnoea and stage of disease. All subjects completed the Activity of Daily Living Dyspnoea (ADL-D) scale (Yoza, Ariyoshi, Honda, Taniguchi, & Senjyu, 2009), which contains 15 items for assessing activity of daily living in patients with CPD. Subjects provide a dyspnoea score of 4 (not at all) to 0 (maximal) for each item, with a lower score indicating more severe dyspnoea.

3.3.7. International Physical Activity Questionnaire (IPAQ)

Current Physical Activities of daily living (PADL) were assessed using the International Physical Activity Questionnaire (IPAQ) – Long Form. The IPAQ has 4 distinct PADL groupings, distinguishing between job-related, transport, domestic and recreational (sport and leisure) PADL. The IPAQ captures participation according to days and minutes of activity and segregates between walking, moderate and vigorous activity by multiplying the various activity minutes with a MET factor (8 METs for vigorous activity; 4 METs for moderate activity and 3.3 METs for

walking). The questionnaire provides a total activity METs per minute score as well as individual METs per minute scores for each of the four PADL groups. The IPAQ is currently considered the gold standard of physical activity questionnaires, which has acceptable validity when assessing levels and patterns of physical activity in adults (Hagströmer, Oja, & Sjöström, 2006).

A comprehensive and detailed interview was used in conjunction with the IPAQ to determine the amount of upper and lower body PADL participants performed on a daily basis. This was done in order to compare the impact of daily upper and lower body physical activities on aerobic capacity (arm and leg ergometry) and measures of arm and leg strength.

3.4. Data Analysis

Statistical analyses were performed using STATISTICA (Version 7.0) and SPSS (Version 22). Descriptive statistics are presented as means ± standard deviation. The data set presented with normal distribution. Accordingly, a total of 8 statistical procedures were conducted including t-tests, partial correlations, ANOVA, multiple linear regressions and a binary logistical regression as follows:

Between group differences regarding anthropometric, PADL, aerobic and strength values were analysed using unpaired t-tests for disease severity groups and gender.

A factorial ANOVA was conducted to explore the independent relationships of PADL and GOLD stage with measures of arm and leg aerobic capacity and strength. The Tukey's post-hoc test was used to determine sub-group significance. Wilks Lambda and ETA^2 analysis was used to determine the combined and individual contributions of measures of PADL (type and volume) and FEV_1 to arm and leg ergometry capacity of patients with CPD.

Partial correlations were performed - controlling for age, gender, and BF% - to assess relationships between measures of aerobic capacity (upper and lower body arm ergometry capacity), measures of strength (grip and isokinetic quadriceps and hamstrings), pulmonary function and physical activity (total activity and upper and lower body activity). The aim of the partial correlations were to determine whether the ANOVA finding, that physical activity negates the detrimental effect of disease development on certain measures of strength and arm aerobic capacity, will sustain after statistical control for the influence of external variables such as BF%, gender, and age.

Two multiple linear regressions were conducted to determine if peak arm and leg ergometry wattage could be predicted with quadriceps strength, grip strength and FEV_1. A check for multi-collinearity was completed and variables with r < 30 and > 90 were excluded. This analysis provided more specific information about individual contributions. A binary logistic regression analysis was used to examine the predictability of upper body function (arm ergometry) by quadriceps strength.

For the purpose of the ANOVA and the binary logistical regression statistical analyses the respondents were placed in groups. For the ANOVA respondents were grouped according to "high" and "low" regarding participation in total PADLs and FEV_1%. For total PADL level was split at the 50th percentile and FEV_1% was split according to GOLD groups at 50% predicted (Mild-moderate = low, and severe-very severe = high). The physical activity levels of the participants was generally low and there were only 16 respondents with severe and very severe COPD (FEV_1 <50%). The 50th percentile of the group distribution was henceforth selected for PADLS and FEV_1 to ensure enough participants in the groups. For the multiple linear and binary logistical regressions participants were grouped for each of the variables used into relative "high" and "low" categories. Peak arm and leg ergometry wattage, quadriceps strength, and grip strength were split at the 60th percentile, while upper and lower body PADLs, and FEV1% were again split at the 50th percentile of the group distribution. Grouping at the 60th percentile are generally recommended for binary and regression analysis because the aim is to distinguish predictability of either poor or good performers (Thomas, Nelson, & Silverman, 2012).

3.4.1. Participant groups for further analysis:

For the statistical analyses, the participants were not grouped according to sex for three reasons. Firstly, the numbers of male and female participants were similar in the two disease severity groups. Secondly, the thesis aimed to investigate the influence of disease severity, rather than gender, on arm and leg ergometry capacity. Finally, although one could argue that males and females may respond differently during exercise and have different relationships between the variables measured, the sample size was too small to split the groups further.

Chapter 4. Results

The results reported below have been organised into themes relating to the outcome measures. Firstly, comparisons of male and female participants are reported. The results then split into sections regarding participant descriptive/anthropometric characteristics, disease severity, aerobic, strength and physical activity measures. Each section reports the t-test, and ANOVA statistics of the specified variable groups. These sections are then followed by a partial correlation of strength, aerobic and physical activity variables. The chapter concludes with the reporting of the prediction statistical procedures (multiple linear regression and binary regression analyses) that were conducted.

4.1. Comparison of Male and Female Participants

4.1.1. Descriptive/anthropometric measures

A comparison of descriptive data for male and female CPD patients is displayed in Table 4-1. Body fat percentage was 15.9% higher in females compared to males ($p<0.001$), while body mass was comparable between males and females. There were no significant differences between males and females for age or BMI.

Table 4-1.
Comparison of males and female participants for descriptive and anthropometric data.

	Total (n=44) $\bar{X}$ ± SD	Male (n=16) $\bar{X}$ ± SD	Female (n=28) $\bar{X}$ ± SD	t-value	p-value
Age	59.8 ± 11.9	63.50 ± 9.2	57.68 ± 12.9	1.59	0.12
Body mass (kg)	87.3 ± 20.6	89.45 ± 13.9	86.04 ± 23.7	0.53	0.60
BMI	33.15 ± 11.0	29.69 ± 4.1	35.13 ± 13.1	-1.61	0.11
BF%	30.56 ± 13.1	20.41 ± 7.7	36.36 ± 12.0	-4.77	<0.001

Note. BMI=body mass index, BF%=body fat percentage.

4.1.2. Disease severity

There were no significant differences between males and females for any of the disease severity measures (Table 4-2).

Table 4-2.
Comparison of males and female participants for disease severity measures.

	Total (n=44) $\bar{X}$ ± SD	Male (n=16) $\bar{X}$ ± SD	Female (n=28) $\bar{X}$ ± SD	t-value	p-value
FVC%	70.6 ± 13.2	71.1 ± 13.0	70.4 ± 13.6	0.18	0.86
FEV_1%	54.6 ± 18.3	50.6 ± 19.7	55.2 ± 17.8F	-0.27	0.78
MRC Grade	2.0 ± 0.9	2.1 ± 0.9	2.3 ± 0.9	-0.72	0.48

Note. FVC% = forced vital capacity percentage predicted, FEV_1% = forced expiratory flow in one second percentage predicted, MRC = Medical Research Council.

4.1.3. Peripheral muscle strength

Males displayed significantly higher grip strength, quadriceps strength and hamstring strength ($p<0.001$) compared to female participants (Table 4-3). Quadriceps and hamstrings endurance were comparable for males and females.

Table 4-3.
Comparison of males and female participants for peripheral strength measures.

	Total (n=44) $\bar{X}$ ± SD	Male (n=16) $\bar{X}$ ± SD	Female (n=28) $\bar{X}$ ± SD	t-value	p-value
Grip strength (kg)	30.9 ± 10.4	41.1 ± 8.6	25.1 ± 5.8	7.37	<0.001
Quad strength (Nm)	103.7 ± 35.0	129.4 ± 24.6	89.0 ± 31.6	4.40	<0.001
Ham strength (Nm)	53.1 ± 19.5	66.94 ± 16.0	45.2 ± 16.9	4.12	<0.001
Quad endur. (Nm)	88.4 ± 14.1	88.9 ± 12.3	88.2 ± 15.3	0.16	0.87
Hamstring endur. (Nm)	98.7 ±30.9	90.1 ± 16.8	103.6 ± 36.0	-1.41	0.17

Note. Quad endur. = quadriceps endurance, Hamstring endur. = hamstring endurance.

4.1.4. Arm and leg ergometry

The total group mean for arm ergometry VO_{2peak} was comparable to the group mean VO_{2peak} for leg ergometry (Table 4-4). There were significant differences between males and females for peak arm ergometry wattage ($p=0.01$), peak leg ergometry wattage ($p=0.02$), and leg ergometry VO_{2peak} ($p=0.03$). Male leg ergometry VO_{2peak} was significantly higher than females ($p=0.03$), however no difference was seen between males and females for arm ergometry VO_{2peak}. No statistically significant differences were seen between sexes for either arm or leg ergometry pain scores.

Table 4-4.
Comparison of males and female participants for arm and leg ergometry measures.

	Total (n=44) $\bar{X}$ ± SD	Male (n=16) $\bar{X}$ ± SD	Female (n=28) $\bar{X}$ ± SD	t-value	p-value
Leg VO_{2peak}	21.8 ± 5.9	24.3 ± 6.7	20.4 ± 4.9	2.23	0.03
Leg $Watt_{peak}$	49.3 ± 19.1	57.8 ± 20.2	44.5 ± 17.0	2.24	0.02
Leg $Pain_{peak}$	3.3 ± 1.8	2.8 ± 1.6	3.6 ± 1.9	-1.41	0.17
Arm VO_{2peak}	21.6 ± 6.3	21.67 ± 6.6	21.5 ± 6.2	0.06	0.95
Arm $Watt_{peak}$	38.9 ± 11.7	45.0 ± 12.8	35.4 ± 9.6	2.84	0.01
Arm $Pain_{peak}$	3.3 ± 1.5	3.34 ± 1.6	3.3 ± 1.5	0.17	0.86

Note. VO_{2peak} = peak oxygen consumption (mL/kg.min), $Watt_{peak}$ = peak ergometry wattage, $Pain_{peak}$ = peak pain score during ergometry.

4.1.5. Physical activities of daily living

Male's total physical activity level was 12.6% higher than females. Males reported a significantly (p=0.02) higher level of vigorous physical activity and walking activity (p=0.05) than females (Table 4-5).

Table 4-5.
Comparison of males and female participants for physical activity of daily living measures.

	Total (n=44) $\bar{X}$ ± SD	Male (n=16) $\bar{X}$ ± SD	Female (n=28) $\bar{X}$ ± SD	t-value	p-value
Total activity*	3074 ± 3320	3342 ± 4586	2921 ± 2408	0.40	0.69
Vigorous activity*	313 ± 1042	798 ± 1643	36 ± 103	2.47	0.02
Moderate activity*	2242 ± 2283	1743 ± 2269	25278 ± 2281	-1.10	0.28
Walking activity*	524 ± 762	815 ± 1149	358 ± 334	1.98	0.05

Note. *Activity measured in MET (metabolic equivalents) minutes/week.

4.2. Participant's Descriptive/Anthropometric Characteristics

4.2.1. GOLD group comparison

Table 4-6 provides data of the comparisons between the two CPD groups (mild-moderate vs. severe+) for the descriptive/anthropometric data. Although the two groups mean age differed by 7 years and body mass and the mild-mod group was on average 12.3kg heavier, these differences were not significant (p=0.06 and p=0.05, respectively). There were no statistically significant differences (p>0.05) between the two groups in terms of any of the anthropometric variables.

Table 4-6.
Comparison of GOLD groups for descriptive and anthropometric data.

	Total (n=44) $\bar{X}$ ± SD	Mild-Moderate (n=28) $\bar{X}$ ± SD	Severe+ (n=16) $\bar{X}$ ± SD	t-value	p-value
Age	59.8 ± 11.9	57.3 ± 13.5	64.3 ± 6.7	1.93	0.06
Body mass (kg)	87.3 ± 20.6	91.8 ± 22.0	79.4 ± 15.5	-1.98	0.05
BMI	33.2 ± 11.0	35.2 ± 12.8	29.7 ± 5.4	-1.63	0.11
BF%	30.6 ± 13.1	32.3 ± 14.0	27.5 ± 11.0	-1.18	0.24

Note. BMI = body mass index, BF% = body fat percentage.

4.2.2. Relationship of CPD stage and physical activities of daily living with descriptive and anthropometric data

Results of a factorial ANOVA, where the dependent and independent relationships of disease severity and physical activity volume were compared with participant characteristics, are reported in Table 4-7. No statistically significant differences were found between any of the physical activity and disease severity groups for participant characteristic data. It is important to note the comparative large standard deviation of group a (age = 16.22) and group b (body mass = 29.02) due to two outliers which ended up in those groups. These high standard deviations, as well as the small sample sizes had an impact on statistical significance.

Table 4-7.
Combined and individual relationships of CPD stage and total PADL with descriptive and anthropometric data, as determined with a factorial ANOVA.

		CPD Stage					
	PADL (min/week)	Mild-Moderate				Severe +	
			X	SD		*X*	SD
Age	Low	a	55.7	16.2	c	64.5	5.6
	High	b	59.3	9.6	d	64.0	8.1
Body Mass	Low	a	95.7	14.6	c	77.4	16.3
	High	b	86.5	29.0	d	81.5	15.6
BMI	Low	a	37.7	14.4	c	28.0	4.8
	High	b	31.8	10.0	d	31.3	5.6
Body fat %	Low	a	35.2	14.4	c	24.4	8.5
	High	b	28.5	13.1	d	30.6	12.9

Note. Group a = mild-moderate CPD and low PADL level (n= 16), group b = mild-moderate CPD and high PADL level (n= 12), group c = severe+ CPD and low PADL level (n= 8), and group d = severe+ CPD and high PADL level (n= 8).

The F-ratio, p-values, ETA^2, and Wilks Lambda scores of the factorial ANOVA for the descriptive and anthropometric data are reported in Table 4-8. The Eta^2 calculations indicated that CPD

disease stage shows larger (non-significant) independent contributions than total PADL minutes to the variances of age, body mass, BMI, body fat percentage.

The Wilks Lambda scores (Table 4-8) indicated that the two independent variables in combination (CPD stage and total PADL minutes) explained small portions of the variances in age (100-90.3=9.7%), body mass (100-87.9=12.1%), BMI (100-88.7=11.3%), and body fat percentage (100-90.4=9.6%).

Table 4-8.
The f-ratio, p-values, ETA^2 and Wilks Lambda scores of the factorial ANOVA investigating the relationships of CPD stage and total PADL with descriptive and anthropometric data.

Dependent variables	ANOVA groups	F-ratio	p-values	Eta^2	Wilks Lambda
Age	CPD stage	3.326	0.076	27.4	90.3
	Total PADL	0.181	0.673	6.39	
	Combined	1.428	0.249	9.67	
Body Mass	CPD stage	3.438	0.071	27.5	87.9
	Total PADL	0.173	0.679	6.17	
	Combined	1.836	0.156	12.1	
BMI	CPD stage	2.267	0.140	22.4	88.7
	Total PADL	0.137	0.713	5.51	
	Combined	1.701	0.182	11.3	
Body fat %	CPD stage	1.143	0.292	16.1	90.4
	Total PADL	0.004	0.951	0.94	
	Combined	1.411	0.254	9.57	

4.3. Disease Severity

4.3.1. GOLD group comparison

The mean FEV_1% was 54.64±18.27, indicating GOLD stage 2 (moderate COPD), ranging from 22-89% (very severe to mild CPD). The groups showed statistically significant differences with regard to FVC% (p<0.002) and FEV_1% (p<0.0001), and MRC grade (p<0.003) (Table 4-9).

Table 4-9.
Comparison of GOLD groups and disease severity measures.

	Total (n=44) X ± SD	Mild-Moderate (n=28) X ± SD	Severe+ (n=16) X ± SD	t-value	p-value
FVC%	70.6 ± 13.2	75.18 ± 11.4	62.7 ± 12.6	-3.36	0.002
FEV_1%	54.6 ± 18.3	65.93 ± 10.7	34.9 ± 9.8	-9.54	0.0001
MRC Grade	2.4 ± 0.8	1.9 ± 0.7*	2.8 ± 0.9	3.19	0.003

Note. FVC% = forced vital capacity percentage predicted, FEV_1% = forced expiratory flow in one second percentage predicted, MRC = Medical Research Council.

4.3.2. Relationship of CPD stage and physical activities of daily living with other measures of disease severity

Statistically significant differences were evident with the MRC grade and FVC% predicted (Table 4-10). The ANOVA split participants into four groups according to physical activity volume and GOLD stages. Group a, refers to participants with mild-moderate CPD and low physical activity levels. Group b refers to participants with mild-moderate CPD and high physical activity levels. Group c includes participants with severe CPD and low physical activity levels. Group d refers to participants with severe CPD and high physical activity levels.

The Tukey post hoc test (Table 4-10) demonstrated that groups a (low PA and mild-moderate stage) and b (high PA but mild-moderate CPD stage) displayed better MRC grade scores than groups c (low PA and severe to very severe CPD stage), with a set p-value of <0.05. Group a also presented with a statistically significantly higher mean FVC% when compared to groups c and d (p<0.05).

Table 4-10.
Combined and individual relationships of CPD stage and total PADL with other makers of disease severity, as determined with a factorial ANOVA.

			CPD Stage			
	Total PADL (min/week)		Mild-Moderate		Severe +	
			X	SD	*X*	SD
MRC Grade	Low	a	1.9[c]	0.6	c 3.1 [a b]	0.83
	High	b	2.9[c]	0.9	d 2.4	0.74
ADL-D	Low	a	52.0	7.2	c 49.9	4.91
	High	b	49.9	7.4	d 50.4	4.67
FVC%	Low	a	77.4 [c d]	13.6	c 62.1[a]	12.3
	High	b	72.3	13.2	d 63.1[a]	13.8

Note. MRC = Medical Research Council, ADL-D = dyspnoea during activities of daily living, FVC% = forced vital capacity percentage predicted.
Group a = mild-moderate CPD and low PADL level (n= 16), group b = mild-moderate CPD and high PADL level (n= 12), group c = severe+ CPD and low PADL level (n= 8), and group d = severe+ CPD and high PADL level (n= 8).
[a] indicates statistical significant (p<0.05) difference from group a, [b] indicates statistical significant (p<0.05) difference from group b, [c] indicates statistical significant (p<0.05) difference from group c, and [d] indicates statistical significant (p<0.05) difference from group, *as found with the Tukey post-hoc test.*

The data in Table 4-11 indicated that CPD stage contributed independently and significantly to the variances of FVC% predicted (44.5%; p=0.003), MRC grade (43.3%; p=0.003) and peak leg ergometry wattage (31.4%; p=0.035). Total activity did not contribute significantly to the variances of any of the dependent variables. As a combination, CPD stage and Total Activity contributes

statistically significantly to the variances of FVC% (23.6%; *p* = 0.012) and MRC grade (27.4%; p=0.005).

Table 4-11.
The f-ratio, p-values, ETA^2 and Wilks Lambda scores of the factorial ANOVA investigating the relationship of CPD stage and total PADL with other markers of disease severity in CPD patients.

Dependent variables	ANOVA groups	F-ratio	p-values	Eta^2	Wilks Lambda
FVC%	CPD stage	10.356	0.003	44.5	76.4
	Total PADL	0.282	0.598	7.33	
	Combined	4.121	0.012	23.6	
MRC Grade	CPD stage	10.257	0.003	43.1	72.6
	Total PADL	1.266	0.267	15.2	
	Combined	5.030	0.005	27.4	
ADL-D	CPD stage	0.159	0.693	6.23	97.6
	Total PADL	0.143	0.708	5.90	
	Combined	0.306	0.821	2.24	

Notes. MRC = Medical Research Council, ADL-D = dyspnoea during activities of daily living, FVC% = forced vital capacity percentage predicted.

4.4. Peripheral Muscle Strength

4.4.1. GOLD group comparison

The mean quadriceps strength, as measured by peak torque, for the total group was 103.67 ± 34.99 Nm, and mean hamstring strength was 53.10 ± 19.47 Nm for the total group. Statistically significant differences were found between the two GOLD groups for quadriceps strength and hamstrings strength ($p<0.05$). No differences existed between GOLD groups for grip strength, quadriceps endurance or hamstrings endurance.

Table 4-12.
Comparison of GOLD groups for peripheral strength measures.

	Total (n=44) $\bar{X}$ ± SD	Mild-Moderate (n=28) $\bar{X}$ ± SD	Severe+ (n=16) $\bar{X}$ ± SD	t-value	p-value
Grip strength (kg)	30.9 ± 10.4	31.8 ± 10.6	29.4 ± 10.3	-0.73	0.47
Quad strength (Nm)	103.7 ± 35.0	111.3 ± 37.7	90.3 ± 25.6	-1.97	0.05
Ham strength (Nm)	53.1 ± 19.5	57.5 ± 21.0	45.4 ± 13.8	-2.06	0.04
Quad endur. (Nm)	88.4 ± 14.1	87.2 ± 14.1	90.5 ± 14.4	0.73	0.47
Hamstring endur. (Nm)	98.7 ± 30.9	96.3 ± 25.2	102.8 ± 39.7	0.67	0.50

Note. Quad endur. = quadriceps endurance, Hamstring endur. = hamstring endurance.

4.4.2. Relationship of CPD stage and physical activities of daily living with peripheral muscle strength

Results of a factorial ANOVA, where the dependent and independent relationships of disease severity and total PADL participation were compared with peripheral muscle strength measures, are reported in Table 4-13. No statistically significant differences were found between any of the physical activity and disease severity groups for the peripheral muscle strength data.

Table 4-13.
Combined and individual relationships of CPD stage and total PADL living with peripheral muscle strength, as determined with a factorial ANOVA.

		CPD Stage					
	PADL (min/week)	Mild-Moderate			Severe +		
			X	SD		*X*	SD
Grip strength	Low	a	33.0	9.7	c	32.6	13.1
	High	b	30.2	11.9	d	26.2	5.5
Quad strength	Low	a	116.9	38.0	c	98.1	33.8
	High	b	103.8	37.6	d	82.6	11.2
Hamstring strength	Low	a	61.5	21.2	c	44.5	18.1
	High	b	52.2	20.4	d	46.3	9.0
Quad endurance	Low	a	89.4	10.7	c	93.9	17.9
	High	b	84.3	17.7	d	87.1	10.0
Hamstring endurance	Low	a	94.6	12.7	c	119.3	48.7
	High	b	98.7	36.4	d	86.4	19.5

Note. Group a = mild-moderate CPD and low PADL level (n= 16), group b = mild-moderate CPD and high PADL level (n= 12), group c = severe+ CPD and low PADL level (n= 8), and group d = severe+ CPD and high PADL level (n= 8).

The F-ratio, p-values, ETA^2, and Wilks Lambda scores of the factorial ANOVA for the peripheral muscle strength data are reported in Table 4-14. The Eta^2 calculations indicated that CPD disease stage showed larger (non-significant) independent contributions than total PADL minutes to the variances of quadriceps strength and hamstrings strength. Total activity showed larger (non-significant) independent contributions than CPD stage to the variances of grip strength and quadriceps and hamstring endurance.

The Wilks Lambda scores (reported in Table 4-14) indicated that the two independent variables in combination (CPD stage and total activity minutes) explains small portions of the variances in grip strength (100-94.1=3.9%), quadriceps strength (100-87.5=12.5%), hamstrings strength (100-87.1=12.9%), quadriceps endurance (100-94.5=5.5%) and hamstrings endurance (100-88.1=11.9%).

Table 4-14.
The f-ratio, p-values, ETA^2 and Wilks Lambda scores of the factorial ANOVA investigating the relationships of CPD stage and total PADL with peripheral muscle strength measures.

Dependent variables	ANOVA groups	F-ratio	p-values	Eta^2	Wilks Lambda
Grip strength	CPD stage	0.441	0.511	10.2	94.1
	Total PADL	1.957	0.170	21.5	
	Combined	0.841	0.479	5.94	
Quad strength	CPD stage	3.514	0.068	27.7	87.5
	Total PADL	1.779	0.190	19.7	
	Combined	1.906	0.144	12.5	
Hamstring strength	CPD stage	3.753	0.059	28.6	87.1
	Total PADL	0.405	0.528	9.39	
	Combined	1.978	0.133	12.9	
Quad endurance	CPD stage	0.658	0.422	12.5	94.5
	Total PADL	1.745	0.194	20.3	
	Combined	0.770	0.518	5.46	
Hamstring endurance	CPD stage	0.430	0.516	9.74	88.1
	Total PADL	2.321	0.135	22.6	
	Combined	1.795	0.164	11.9	

4.5. Arm and Leg Ergometry

4.5.1. GOLD group comparisons

Participants with mild-moderate CPD demonstrated significantly higher (28%) peak leg ergometry wattage compared to the severe CPD group (p=0.03). The mild-moderate CPD group demonstrated a 17% higher peak arm ergometry wattage, which was close to meeting statistical significance (p=0.07). In addition, the leg pain scores reported during the ergometry testing were

20% greater for those with mild-moderate disease compared to severe disease, however the difference was not statistically significant (p<0.08). Arm pain scores were 23% higher in the mild-moderate CPD group, compared to the severe group (p=0.13).

Table 4-15.
Comparison of GOLD groups for arm and leg ergometery outcomes.

	Total (n=44) $\bar{X}$ ± SD	Mild-Moderate (n=28) $\bar{X}$ ± SD	Severe (n=16) $\bar{X}$ ± SD	t-value	p-value
Leg VO_{2peak}	21.8 ± 5.9	22.8 ± 6.4	20.1 ± 4.5	-1.50	0.14
Leg $Watt_{peak}$	49.3 ± 19.1	54.1 ± 21.0	40.9 ± 11.9	-2.30	0.03
Leg $Pain_{peak}$	3.3 ± 1.8	3.3 ± 1.7	2.7 ± 1.8	-1.78	0.03
Arm VO_{2peak}	21.6 ± 6.3	22.4 ± 6.5	20.1 ± 5.9	-1.16	0.07
Arm $Watt_{peak}$	38.9 ± 11.7	41.3 ± 11.8	34.7 ± 8.3	-1.84	0.08
Arm $Pain_{peak}$	3.3 ± 1.5	3.6 ± 1.6	2.8 ± 1.4	-1.54	0.13

Note. VO_{2peak} = estimated peak VO_2 (ml/kg/min), $Watt_{peak}$ = peak ergometry wattage, $Pain_{peak}$ = peak pain during ergometry.

4.5.2. Relationship of CPD stage and physical activities of daily living and arm and leg ergometry

Results of a factorial ANOVA, where the dependent and independent relationships of disease severity and physical activity volume were compared with arm and leg ergometry outcome measures, are reported in Table 4-15. No statistically significant differences were found between the physical activity and disease severity groups for any of the arm and leg ergometry outcome measures.

Table 4-16.
Combined and individual relationships of CPD stage and total PADL with arm and leg ergometry capacity, as determined with a factorial ANOVA.

		CPD Stage					
	Total PADL (min/week)	Mild-Moderate			Severe +		
			X	SD		*X*	SD
Leg $Watt_{peak}$	Low	a	58.8	20.0	c	41.9	14.6
	High	b	47.9	21.4	d	40.0	9.3
Leg VO_{2peak}	Low	a	22.4	4.7	c	19.4	5.2
	High	b	23.4	8.3	d	20.8	4.0
Leg RPE_{peak}	Low	a	12.8	1.6	c	12.9	1.7
	High	b	12.7	2.2	d	12.3	0.9
Leg $Dysp_{peak}$	Low	a	2.9	1.2	c	3.7	1.3
	High	b	2.7	0.8	d	2.9	1.2
Leg $Pain_{peak}$	Low	a	3.7	1.3	c	2.6	2.2
	High	b	3.6	2.3	d	2.8	1.6
Arm $Watt_{peak}$	Low	a	42.8	10.2	c	33.1	9.6
	High	b	39.8	15.9	d	36.3	6.9
Arm VO_{2peak}	Low	a	21.7	5.6	c	17.7	5.9
	High	b	23.4	7.6	d	22.6	5.0
Arm RPE_{peak}	Low	a	12.7	1.7	c	13.1	1.0
	High	b	12.6	1.6	d	11.5	1.2
Arm $Dysp_{peak}$	Low	a	2.4	0.7	c	2.5	1.5
	High	b	2.4	1.2	d	2.2	1.3
Arm $Pain_{peak}$	Low	a	3.7	1.6	c	3.2	1.5
	High	b	3.4	1.6	d	2.5	1.2

Notes. $Watt_{peak}$ = peak ergometry wattage, VO_{2peak} = estimated peak VO_2 (ml/kg/min), RPE_{peak} = peak rating of perceived exertion, $Dysp_{peak}$ = peak dyspnoea, $Pain_{peak}$ = peak pain during ergometry. Group a = mild-moderate CPD and low PADL level (n= 16), group b = mild-moderate CPD and high PADL level (n= 12), group c = severe+ CPD and low PADL level (n= 8), and group d = severe+ CPD and high PADL level (n= 8).

The F-ratio, p-values, ETA^2, and Wilks Lambda scores of the factorial ANOVA for the arm and leg ergometry data are reported in Table 4-16. The Eta^2 calculations indicated that CPD disease stage displayed larger (non-significant) contributions than overall physical activity minutes to the variances of peak leg ergometry wattage, peak leg ergometry VO_2, peak leg pain, peak arm ergometry wattage, and peak arm pain. Total activity displayed larger (non-significant) independent contributions than CPD stage to the variances of peak leg ergometry RPE score, peak arm ergometry VO_2, and peak arm ergometry RPE and dyspnoea scores.

The Wilks Lambda scores (reported in table 4-16) indicated that the two independent variables in combination (CPD stage and total activity minutes) explain small portions of the variances of peak leg ergometry wattage (100-83.6=16.7%) and peak arm ergometry RPE (100-87.9=12.3%), and less than 10% of the variances of the other arm and leg ergometry variables.

Table 4-17.
The f-ratio, p-values, ETA^2 and Wilks Lambda scores of the factorial ANOVA investigating the relationships of CPD stage and total PADL with arm and leg ergometry capacity in CPD patients.

Dependent variables	ANOVA groups	F-ratio	p-values	Eta^2	Wilks Lambda
Leg $Watt_{peak}$	CPD stage	4.725	0.035	31.4	83.6
	Overall Act	1.242	0.272	16.1	
	Combined	2.622	0.064	16.4	
Leg VO_{2peak}	CPD stage	2.247	0.142	22.9	94.0
	Total PADL	0.395	0.533	9.63	
	Combined	0.852	0.474	6.01	
Leg RPE_{peak}	CPD stage	0.131	0.719	5.57	98.3
	Total PADL	0.444	0.509	10.4	
	Combined	0.228	0.877	1.68	
Leg $Dysp_{peak}$	CPD stage	1.888	0.177	20.7	90.9
	Total PADL	1.888	0.177	20.7	
	Combined	1.339	0.275	9.13	
Leg $Pain_{peak}$	CPD stage	2.973	0.092	26.3	92.7
	Total PADL	0.019	0.891	2.08	
	Combined	1.044	0.384	7.26	
Arm $Watt_{peak}$	CPD stage	3.015	0.090	26.1	90.7
	Total PADL	0.005	0.943	1.08	
	Combined	1.424	0.250	9.65	
Arm VO_{2peak}	CPD stage	1.524	0.224	18.5	90.0
	Total PADL	2.882	0.097	25.5	
	Combined	1.485	0.233	10.0	
Arm RPE_{peak}	CPD stage	0.495	0.486	10.4	87.9
	Total PADL	3.543	0.067	27.9	
	Combined	1.838	0.156	12.1	
Arm $Dysp_{peak}$	CPD stage	0.022	0.896	0.62	99.2
	Total PADL	0.299	0.632	7.61	
	Combined	0.110	0.954	0.82	
Arm $Pain_{peak}$	CPD stage	2.195	0.146	22.5	92.2
	Total PADL	1.000	0.323	15.2	
	Combined	1.126	0.350	7.79	

Notes. $Watt_{peak}$ = peak ergometry wattage, VO_{2peak} = estimated peak VO_2 (ml/kg/min), RPE_{peak} = peak rating of perceived exertion, $Dysp_{peak}$ = peak dyspnoea, $Pain_{peak}$ = peak pain during ergometry.

4.6. Physical Activity

4.6.1. GOLD group comparisons:

Table 4-17 reports the comparison of GOLD groups for physical activity measures. No significant differences were found between the mild-moderate and severe-very severe groups for total, vigorous, moderate and walking activity. The severe CPD group displayed lower (64%) scores for vigorous activity compared to the mild-moderate CPD stage, although this was not statistically significant (p=0.58) due to the high standard deviations.

Table 4-18.
Comparison of GOLD groups for physical activity measures.

	Total (n=44) *X* ± SD	Mild-Moderate (n=28) *X* ± SD	Severe+ (n=16) *X* ± SD	t-value	p-value
Total activity*	3074 ± 3320	2838 ± 947	3209 ± 860	0.75	0.73
Vigorous activity*	313 ± 1042	380 ± 647	195 ± 1218	-0.56	0.89
Moderate activity*	2242 ± 2282	2178 ± 2194	2279 ± 2371	-0.14	0.57
Walking activity*	524 ± 762	558 ± 864	465 ± 559	-0.14	0.70

Note. *Activity measured in MET-minutes per week.

4.7. Partial Correlation

Partial correlations were consequently conducted to examine the relationships between measures of pulmonary function, leg ergometry capacity (arm and leg), strength (leg and grip) and physical activity levels (overall, lower body and upper body) while controlling for age, gender, and BF% (Table 4-18). Total activity and the amount of upper and lower body activity showed no statistically significant relationship ($p>0.05$) with measures of strength and aerobic capacity.

Predicted FEV_1% displayed a weak non-significant ($p>0.05$) correlation with quadriceps strength ($r=0.30$), and significant ($p<0.05$) moderate correlations with peak leg watt ($r=0.42$), peak arm watt ($r=0.33$), and hamstring strength ($r=0.41$).

Peak arm ergometry watt presented a strong positive association with peak leg ergometry watt ($r=0.81$, $P<0.05$). Peak leg watt demonstrated a moderate positive correlation with quadriceps strength ($r=0.51$, $p<0.05$) and hamstring strength ($r=0.47$, $p<0.05$). Peak arm watt correlated moderately with quadriceps strength ($r=0.58$, $p<0.05$) and hamstrings strength ($r=0.51$, $p<0.05$). No correlation was found between peak arm watt and grip strength ($r=-0.02$).

Grip strength demonstrated a significant negative correlation with peak pain during leg ergometry ($r=-0.34$, $p<0.05$). Arm pain and leg pain during ergometry had a moderate association ($r=0.62$, $p<0.05$), while quadriceps and hamstrings strength demonstrated a high association ($r=0.75$, $p<0.05$).

Perceived pain (arm and leg) during ergometry did not correlate with maximum wattage during the 3rd stage of both the arm ergometry (arm pain $r=0.04$; leg pain $r=-0.08$) and leg ergometry (arm pain $r=0.23$; leg pain $r=-0.02$) tests. In contrast, leg strength measures correlated moderately with arm and leg ergometry wattage (arm watt $r=0.58$; leg watt $r=0.51$, $p<0.05$).

Table 4-19.
Partial Correlations of the total group (n=44) between lung function, arm and leg ergometry capacity, peripheral muscle strength, and PADL type and volume, controlling for age, gender, and body fat percentage.

	Leg $Watt_{Peak}$	Leg $Pain_{peak}$	Arm $Watt_{Peak}$	Arm $Pain_{peak}$	Grip Strength	Quad Strength	Ham Strength
FVC%	0.29	-0.03	0.22	0.08	0.28	0.16	0.19
FEV_1%	0.42*	0.12	0.33*	0.22	0.17	0.30	0.41*
Leg $Watt_{Peak}$	-	-0.02	0.81*	0.23	-0.13	0.51*	0.47*
Leg $Pain_{peak}$	-0.02	-	-0.08	0.62*	-0.34*	0.13	0.13
Arm $Watt_{Peak}$	0.81*	-0.08	-	0.04	-0.02	0.58*	0.51*
Arm $Pain_{Peak}$	0.23	0.62*	0.04	-	-0.28	0.16	0.10
Grip Strength	-0.13	-0.34*	-0.02	-0.28	-	0.28	0.13
Quad Strength	0.51*	0.13	0.58*	0.16	0.28	-	0.75*
Ham Strength	0.47*	0.13	0.51*	0.10	0.13	0.75*	-
Quad Endur.	0.10	-0.29	0.05	-0.19	-0.13	-0.13	-0.17
Ham Endur.	0.01	-0.09	-0.03	-0.01	-0.08	0.11	0.02
Total activity	0.02	-0.09	0.15	-0.14	0.02	-0.11	-0.06
UB activity	0.14	-0.01	0.29	-0.02	-0.12	0.11	0.18
LB activity	0.30	0.01	0.16	0.24	-0.14	0.08	0.13

Note. VO_{2peak} = estimated peak VO_2 (ml/kg/min), $Watt_{peak}$ = peak ergometry wattage, $Pain_{peak}$ = peak pain during ergometry, Ham = hamstrings, Quad = quadriceps, Endur. = endurance, UB = upper body, LB = lower body.
*Indicates statistical significance at $p<0.05$.

4.8. Prediction of Arm and Leg Ergometry Wattage

A regression analysis was conducted to determine whether quadriceps strength (Nm), grip strength (kg) and FEV_1% were predictive of peak wattage during submaximal leg ergometry testing (Table 4-19). The adjusted R^2 indicated that 64% of the variability in peak leg ergometry wattage was explained by the independent variables. The F statistic was 26.387 with a significance level of p=0.00, indicating that we can reject the null hypothesis.

Quadriceps strength showed the highest predictability of peak leg ergometry wattage (p=0.00, beta 0.844 and t=6.238). The model predicts that for a one Nm increase in quadriceps strength (peak torque), peak leg ergometry wattage would increase by 0.5W, holding grip strength and FEV_1% fixed. Furthermore, grip strength and FEV_1% were significant predictors of peak leg ergometry wattage (p=0.038, β=-0.270, t=-2.143 and p=0.028, β=-0.230, t=2.279, respectively). The model predicts that a 1kg increase in grip strength would proliferate with a 0.5W increase in peak leg ergometry wattage; and a 1% higher in FEV_1 predicted value would increase peak leg ergometry wattage by 0.2W.

Table 4-20.
Regression analysis to determine whether quadriceps strength (Nm), grip strength (kg) and FEV_1% could predict peak wattage during submaximal leg ergometry testing.

	Adjusted R^2	F	p-value		
Model 1	0.693	26.387	0.000		
	B	Std. Error	Beta	t	p-value
Constant	3.678	7.110		0.517	0.608
Quad strength	0.461	0.074	0.844	6.238	0.000
Grip strength	0.496	0.232	0.270	2.143	0.038
FEV_1%	0.241	0.106	0.230	2.279	0.028

A second regression analysis was conducted to determine whether quadriceps strength (Nm), grip strength (kg) and FEV_1% were predictive of peak wattage during submaximal arm ergometry testing (Table 4-19). The adjusted R^2 indicated that 53% of the variability in peak leg ergometry wattage was explained by the independent variables. The F statistic was 17.018 with a significance level of p=0.00, indicating that we can reject the null hypothesis.

Quadriceps strength was the only independent variable that showed predictability of peak arm ergometry wattage (p=0.00, beta 0.793 and t=5.125). The model predicts that if you hold grip strength and FEV_1% fixed, a one Nm increase in quadriceps strength (peak torque), would equate to a 0.3W higher peak arm ergometry wattage.

Table 4-21.
Regression analysis to determine whether peak wattage during submaximal arm ergometry testing could be predicted by quadriceps strength (Nm), grip strength (kg) and FEV_1%.

	Adjusted R^2	F	p-value		
Model 1	0.53	17.018	0.000		
	B	Std. Error	Beta	t	p-value
Constant	12.991	4.978		2.610	0.013
Quad strength	0.265	0.052	0.793	5.125	0.000
Grip strength	0.184	0.126	0.163	1.132	0.264
FEV_1%	0.074	0.074	0.115	0.998	0.324

Quadriceps strength, as measured with an isokinetic dynamometer, was a statistically significant contributor to leg wattage and arm wattage in the two regression analyses (Tables 4-19 and 4-20). The results of the two standard regression analyses raised the question of how important leg strength is, and whether it could be used as a predictor of arm ergometer capacity. Is arm wattage dependent on the maintenance of leg strength?

4.9. Prediction of Arm Ergometry Wattage from Quadriceps Strength

A binary logistic regression analysis was therefore conducted to predict peak arm ergometry wattage with quadriceps strength (Table 4-21, Model 1). A test of the full model against the constant only model was statistically significant, indicating that quadriceps strength distinguishes with statistical significance between low and high arm ergometry wattage (chi square = 14.75, p=0.001). The Nagelkerke R^2 value indicated that quadriceps strength contributed 38.1% to the variance of peak arm ergometry wattage (obtained during the 3rd stage of the graded arm ergometry test).

The odds ratio was 13.76, indicating that if a CPD patient has high quadriceps strength they have a 13.76 times higher odds of having high peak arm ergometry wattage. This odds ratio equates to an 85.0% probability of having high arm ergometry peak wattage if quadriceps strength is high. The probability of having low peak arm ergometry wattage in presence of high quadriceps strength ability is 29.2%.

In Model 2, FEV_1% and grip strength were added to the prediction model, which had a negative impact on the prediction model, as the odd ratio decreased from 13.76 to 10.49. The chi square value was non-significant (*p*=0.915), which indicated that adding FEV_1% and grip strength does not improve the model's ability to predict arm ergometry wattage during the 3rd stage of the arm ergometry test.

Table 4-22.
Binary logistic regression analysis to predict arm ergometry wattage with quadriceps strength while controlling for stage of pulmonary disease, dyspnoea during physical activity and grip strength.

			Arm Ergometry Wattage					
Quad Strength	-2 Log likelihood	Nagelkerke R^2	B	S.E	Wald	OR	(95% CI)	*p*-value
Model 1	45.883	0.381	2.62	0.77	11.58	13.76	3.04-62.32	0.00
Model 2	45.705	0.385	2.35	1.00	5.56	10.50	1.49-74.17	0.02

Chapter 5. Discussion

5.1. Introduction

The primary aim of this thesis was to investigate the combined and individual contributions of physical activities of daily living (type and volume) and FEV_1 to arm and leg ergometry capacity of patients with CPD. The secondary aim was to examine the predictability and odds ratio of high arm and leg ergometry capacity in CPD individuals with high and low arm and leg strength, while controlling for stage of disease, body composition and gender.

The main findings of the present thesis were that the volume of PADL performed with the upper and lower body did not correlate with the respective upper and lower body strength or ergometry capacity measures. Hence the first hypothesis that individuals engaging in more PADL involving the arms and the legs will show better respective arm ergometry capacity and leg ergometry capacity, can be rejected. The regression analyses revealed that stage of disease, handgrip strength and leg strength contributed ($p<0.05$), independently from body composition and gender, to leg ergometry capacity (peak wattage). Arm strength did not contribute statistically significantly to arm ergometry capacity (peak wattage). Finally, the odds-ratio of the binary logistic regression, to predict peak arm ergometry wattage with quadriceps strength, demonstrated that CPD patients were 13.76 times more likely to have high peak arm ergometry wattage if their quadriceps strength was high. The second hypothesis that arm and leg strength measures would predict arm and leg ergometry capacity independently from body composition and gender, can consequently be accepted. Leg strength measures had better predictability (with regard to both arm and leg ergometry capacity) than handgrip strength.

5.2. Interpretation of main findings

5.2.1. Comparison of males and females

A comparison of sexes revealed that males and females were comparable in terms of age, weight, FVC% and FEV_1%. Females displayed a higher body fat percentage than males; and males displayed higher grip, quadriceps and hamstring strength, arm and leg ergometry peak wattage and VO_{2peak}, and levels of vigorous activity and walking. These results were expected and have been seen previously in CPD patients and healthy subjects (Carter et al., 2003; de Torres et al., 2005). The differences found in anthropometric and physiological measurements between male

and female participants revealed the importance of controlling for sex in the statistical analyses, and acknowledging the differences when interpreting the findings of this thesis. However, due to the small sample size there were not enough participants to further split the disease severity groups in terms of sex.

5.2.2. Participant descriptive/anthropometric characteristics

In this thesis, disease severity was not statistically significantly associated with age or anthropometric variables. A comparison of GOLD groups revealed that there were no significant differences between mild-moderate and severe+ groups with regard to age, body mass, BMI or BF% (Table 4-6). Furthermore, the factorial ANOVA revealed that there were no significant differences for age, body mass, BMI or BF% between participants with low or high PADL levels with mild-moderate or severe CPD (Table 4-7). These findings indicated that volume of physical activity and severity of CPD as a combination show poor relationships with body composition, age and gender. Similarly, it has been reported that FM and FFM were not important correlates of physical activities of daily living (Monteiro et al., 2012), suggesting that body composition is unrelated to the volume of PADLs performed in this population. In contrast to the findings of the t-test and ANOVA, it has been reported that low BMI is more prevalent with increased disease severity (Kim et al., 2014; Schols et al., 2005). However, Kim et al. (2014) concluded that the prevalence in low FFM was higher than that of low BMI and emphasised the importance of investigating specific aspects of body composition in addition to BMI.

Further investigation of the data (Table 4-7) revealed there was a noticeable (non-significant) difference between the mild-moderate CPD (groups a and b) and the severe CPD (groups c and d) groups with regard to age and the anthropometric variables. These differences might not statistically significant due to large standard deviations and small samples sizes. Two participants in particular had a causal influence on the standard deviations namely a woman that weighed 57kg (group b) and an elderly woman aged 71 years (group a). The individuals with severe + CPD (groups c and d) are on average 6.6 years older than the individuals with Mild-moderate CPD (groups a and b). Using the mean SD of groups a and b (because it's the largest) this age difference (between the mild-moderate and severe+ groups) equates to a moderate effect size difference (6.6/12.9 = 0.51). The mean body mass differences of the mild-moderate (groups a and b) and severe+ (groups c and d) also equate to a moderate effect size difference (11.7/21.7

= 0.54). This finding is captured by the ETA^2 values presented in Table 4-8, which shows that stage of disease contributed more to the variances of body mass, age, BMI and BF% than overall participation in physical activity.

In summary, GOLD stage appeared to contribute more to the variances in age, body mass, BMI and BF% than volume of physical activity, supporting the findings from previous studies that body composition may be associated with disease severity (Harik-Khan, Fleg, & Wise, 2002; Kim et al., 2014). Further investigation is needed to examine the complex interaction between body composition, physical activity levels and disease severity in the CPD population.

5.2.3. Other measures of disease severity

A comparison of GOLD groups revealed that participants with mild-moderate airflow obstruction presented with significantly higher FVC% predicted and a significantly lower MRC grade (Table 4-9). The significant differences between the GOLD groups for MRC grade and FVC%, and the high correlation between FEV1% and FVC% (r=0.79) justified the use of airflow obstruction (FEV_1%) as a single measure when splitting the groups according to disease severity.

5.2.4. Upper and lower body strength and ergometry capacity

Disease severity (GOLD stage) was associated with measures of upper and lower body physical functioning. The comparison of GOLD groups revealed that participants with mild-moderate airflow obstruction displayed significantly stronger hamstrings and quadriceps, suggesting that disease severity is associated with measures of lower body strength (Table 4-12). Additionally, patients with mild-moderate airflow obstruction demonstrated a significantly higher leg ergometry peak wattage and reduced leg fatigue scores than the severe group, indicating that those individuals with severe CPD had greater lower body exercise limitations (Table 4-15). Disease severity (FEV_1% predicted) was moderately associated with peak arm and leg ergometry wattage, suggesting that as CPD severity increases, both arm and leg functional capacity decreases. Similar findings have been reported for patients with chronic airflow obstruction by Carter et al., (2003), who found moderate associations between FEV_1 and peak arm ergometry wattage ($r=0.59$, $p<0.0001$), and peak leg ergometry wattage ($r=0.53$, $p<0.0001$). Previous studies have demonstrated moderate to high associations between FEV_1 and max/peak leg ergometry wattage (Haccoun et al., 2002), and VO_{2max} (Gosselink et al., 1996).

The findings of the present study and the above mentioned previously published literature verify that disease severity (FEV_1) is associated with measures of upper and lower body exercise capacity and lower body strength. Due to the cross-sectional construction of this study no causal conclusions can be made but the data does show moderate relationships between FEV_1 (stage of disease) and arm and leg ergometry capacity.

In the partial correlations (Table 4-19), peak leg ergometry wattage was associated with higher quadriceps strength (r=0.51) and hamstring strength (r=0.47), which is in line with previous studies who found associations between leg ergometry capacity and quadriceps strength (Gosselink et al., 1996; Hamilton et al., 1995; Hillman et al., 2012). Interestingly, an association was found between peak arm wattage and lower limb strength. None of the studies reviewed in chapter 2 reported this association. This finding in the present thesis was unexpected and will be discussed later in the chapter.

In the present study peak arm ergometry wattage was strongly associated with peak leg ergometry (r=0.81, p<0.05). In terms of peripheral muscle strength, however, comparison of CPD groups revealed that leg strength is more reduced in the severe CPD group than arm strength. There was less of a difference between the two GOLD groups for grip strength (7%, p=0.47) than quadriceps (19%, p=0.05) and hamstring strength (21%, p=0.04). A similar pattern was observed by Franssen et al. (2002), who observed a preserved upper limb exercise capacity compared to the lower limbs. The authors found that arm and leg peak wattage obtained during ergometry testing were similar (50 ± 3 vs 61 ± 4W, respectively), but the upper limbs were deemed less affected than the lower limb, as the maximum wattage of healthy controls for leg ergometry was approximately double that of the arms (205 ± 13 vs 108 ± 7W). Overall the upper limbs had less of a reduction than the controls, but similar functional values were found when the researchers compared arms and legs in COPD patients (Franssen et al., 2002).

In contrast, Carter et al. (2003) found a reduction in arm ergometry ability of 38% in comparison with leg ergometry, and indicated a greater metabolic demand for arm ergometry than leg ergometry. Differences in findings between Carter et al. (2003) and this thesis may be attributed to the study population, since only 38% of their study population were female, whereas, 64% of the subjects in the present study were female. In addition, the mean FEV_1% predicted values were higher for both males and females in the present thesis compared to Carter et al. (2003)

(55.21 ± 17.75% vs. 46.5 ± 10.9% for females, and 50.63 ± 19.71% vs. 40.2 ± 9.3% for males, respectively).

Total PADL (minutes/week) and GOLD stage, as a combination, did not explain major parts of the variability within any of the strength or ergometry capacity measures (Tables 4-14 and 4-17). However, it is important to note that overall physical activity contributed more to the variances of peak RPE during leg ergometry (10.4 versus 5.57), arm ergometry VO_{2peak} (25.5 versus 18.5), peak RPE during arm ergometry (27.9 versus 10.4) and peak arm ergometry dyspnoea (7.61 versus 0.62) than CPD stage (Table 4-17). Total PADL also evidenced larger contributions to the variances of grip strength (21.5 versus 10.2), quadriceps endurance (20.3 versus 12.5) and hamstring endurance (22.6 versus 9.74) in Table 4-14. This is in line with Andersson et al. (2013), who found lung function, walking speed, and muscle strength to be important correlates of physical activity in COPD patients. The strength of the relationships between overall participation in physical activity and the mentioned measures of strength and aerobic capacity in the current study is probably influenced by the fact that the participants in this study generally exhibited quite low levels of participation in physical activity. Only 11 participants met the recommended requirements for adequate/sufficient physical activity according to the IPAQ guidelines (IPAQ research committee, 2005), while none of the participants met the ASCM recommendations. This will be discussed in more detail in the Physical Activities of Daily Living section below.

5.2.5. Physical activities of daily living

In this thesis PADL was measured with the IPAQ, which was used in the t-tests, ANOVA and partial correlations. The comparison of GOLD groups revealed that no statistically significant differences between the mild-moderate and severe+ groups in terms of the total volume of PADL performed (Table 4-18). The partial correlations analysis supported this finding, showing no association ($p>0.05$) between disease severity (FEV_1 and FVC) and the total volume and ratio of upper and lower body PADL performed by CPD patients. However, while the total activity and the moderate activity levels of the two GOLD groups (mild-moderate versus Severe+) were similar, the mild-moderate group reported a 48.6% higher mean vigorous physical activity score than the severe+ CPD group (Table 4-18). The non-significant, reduced levels of vigorous activity in the severe+ group suggested that disease development impacted on the amount of high intensity physical activity performed on a daily basis.

In contrast to the findings of this thesis, previous studies have shown moderate associations between physical inactivity and disease severity progression (Pitta, Troosters, Probst, Lucas et al. (2006a); Watz et al., 2009b; Jehn et al., 2011; Katajisto et al., 2012; Andersson et al., 2013; Hartman, Boezen, de Greef, & ten Hacken 2013), which may contribute to the loss of strength and exercise capacity. Specifically, Andersson et al. (2013) reported that FEV_1 explained approximately 20% of the variability in physical activity levels in their study participants. Changes in both total activity and lower limb activity have been related to FEV_1, and higher levels of leg activity have been reported among subjects with better FEV_1 (Walker et al., 2008).

The Wilks Lambda scores reported for the ANOVA's (Tables 4-14 and 4-17) suggested that total PADL does not contribute (individually or in combination with CPD stage) much to the variances of muscle strength and ergometry capacity. Additionally, the volume of total PADL performed with the upper and lower body correlates poorly ($p>0.05$) with the respective measures of upper and lower body strength or ergometry determined aerobic capacity (Table 4-19). Hence the first hypothesis that individuals engaging in more PADL involving the arms and the legs will show better respective arm ergometry capacity and leg ergometry capacity, can be rejected. The hypothesis is rejected with acknowledgement that the data may be influenced by the low levels of physical activity in the group.

Four participants (9%) displayed low activity levels (0-599 MET minutes/week); 29 participants (66%) were moderately active (600-2999 MET minutes/week); and 11 participants (25%) were highly active (>3000 MET minutes/week), according to the IPAQ classification guidelines (IPAQ Research Committee, 2005). According to the ACSM guidelines for participation in physical activity for older adults, all the participants in the current study can be classed as physically inactive (Chodzko-Zajko et al., 2009). Differences between the IPAQ and the ACSM guidelines are that ACSM refers to physical activity outside of PADLs and the IPAQ includes PADLs. Regardless, of this difference only 25% of the participants, which were in the "highly active" group, exhibited levels sufficient enough to achieve health benefits according to the IPAQ guidelines. The type and volume of PADL performed may, therefore, not have been specific enough to maintain upper and lower body strength and aerobic capacity.

The findings of Katajisto et al. (2012) may explain the small contribution of physical activity to strength and aerobic capacity in the present study. The authors reported that sensation of

dyspnoea, pain, and discomfort felt during strenuous exercise contributed to the physical inactivity of patients with COPD. Discomfort or fear might have prevented the participants in the present study from performing PADLs at intensity high enough to maintain or improve their peripheral muscle strength and/or exercise capacity, which emphasises the importance of specified exercise training in this population. To provide more insight into the low levels of physical activity in this population investigation into the facilitators and barriers to physical activity in the CPD population of New Zealand is needed. New Zealand weather, for example, may restrict individuals with CPD to indoor activities, as varying weather conditions may exacerbate symptoms. No studies could be found on New Zealand weather and its role as an exercise barrier in CPD patients, however, detailed interviewing of the participants involved in the current study, prior to exercise testing (data not reported), suggested that the weather in the Manawatu region of New Zealand might indeed have been a factor that restricted involvement in outdoor PADL in this cohort.

The differences in the findings of this thesis and previously published literature, with regard to participation in physical activity and its relationships with measures of aerobic capacity, may be attributed to the self-report nature of the IPAQ. It is important to note that some participants may have overestimated their actual physical activity levels, especially those who take longer to perform activities due to a lower level of fitness, giving them an advantage as they look like they are physically active for longer but in reality they are actually doing less activity overall. It is likely that this is why the severe+ group displayed higher total PADL minutes than the mild-moderate group (3209 ± 860 vs 2838 ± 947 min/week) in Table 4-18. It has been reported that for self-report physical activity questionnaires participants are likely to underestimate sedentary activities and overestimate aerobic activities (Klesges et al., 1990).

5.2.6. Prediction of arm and leg ergometry wattage

The standard regression analysis to predict peak leg ergometry wattage revealed that quadriceps strength, FEV_1% predicted and grip strength explained 64% of the variability in peak leg ergometry wattage (Table 4-20). Quadriceps strength and FEV_1 showed the highest predictability of peak leg ergometry wattage ($p=0.00$, beta 0.844 and $t=6.238$, and $p=0.028$, $\beta=-0.230$, $t=2.279$, respectively). These findings support previous studies in which leg strength has emerged as a contributing factor to lower body exercise capacity and disease severity (Gosselink & Decramer, 1998; Steiner, Singh, & Morgan, 2005; Hillman et al., 2012). Peripheral muscle strength and

FEV_1% have an impact on lower limb aerobic capacity. Indeed, multivariate modelling has shown that 76% of the variance in 6MWD could be explained by lung function, quadriceps strength and lean leg mass (Hillman et al., 2012). Furthermore, in the present study grip strength was the third significant predictor of peak leg ergometry wattage (Table 4-20, p=0.038, β=-0.270, t=-2.143), indicating that upper body strength and lower body exercise capacity are interrelated. In support, strong associations have been reported between handgrip strength and leg ergometry capacity in COPD, namely VO_{2peak} (*r*=0.73), VO_{2max} (*r*=0.53) (Gosselink et al., 1996), and maximum wattage (*r*=0.76) (Müller, Viegas, & Patusco, 2012). In addition, grip strength has been associated with the 6MWT (*r* = 0.58) (Marino et al., 2010); and lat pull down 1RM (as a measure of upper body strength) was found to be a predictive factor of 6MWD (R^2=0.589) (Dourando et al., 2006). Even though Marino et al. (2010) and Dourando et al. (2006) use different aerobic capacity and/or strength measures compared to the present study, their findings still support that upper body strength and lower body exercise capacity are related in CPD patients.

The second standard regression analysis to predict peak arm ergometry wattage revealed that quadriceps strength, FEV_1% predicted and grip strength explained 53% of the variability in peak leg ergometry wattage (Table 4-21). Quadriceps strength was the only significant predictor of peak arm ergometry wattage. In support, the partial correlation demonstrated a moderate association between peak arm ergometry wattage and lower body strength (quadriceps r=0.58 and hamstring strength r=0.51, p<0.05). As mentioned previously in the chapter, no supporting evidence could be found in the literature on the relationship between leg strength and arm exercise capacity. However, previous studies have compared upper body strength with lower body strength, and upper body aerobic capacity with lower body aerobic capacity in CPD. Recently, Miranda, Malaguti, Marchetti, and Dal Corso (2014) compared middle deltoid and quadriceps femoris strength and endurance of 21 CPD patients with a mean FEV_1 of 46.1 ± 10.3% predicted. The researchers found deltoid and quadriceps similar with regard to absolute strength, but higher fatigability in the quadriceps indicating better upper body muscle (deltoid) fatigue resistance. Likewise, Franssen et al. (2005) reported that quadriceps and biceps muscle function are equally affected in severe COPD.

The binary logistical regression analysis revealed that respondents with high quadriceps strength scores were 13.8 times more likely to have a higher wattage during sub-maximal arm ergometry

testing. This equates to an 85.0% probability of having higher peak arm ergometry wattage if participants have stronger quadriceps. In support, stepwise regression analysis revealed leg strength to be the only significant contributor to performance during PADLs (Beta=0.547, $t(22) = 2.92$, $p = 0.008$) (Kato, Rodgers, Stickland, & Haennel, 2012). In the present study, quadriceps strength contributed to arm and leg exercise capacity in patients with CPD. For the purpose of the binary regression "high" and "low" peak wattage and quadriceps strength were split at the 60th percentile (114Nm). Clinically, this indicated that individuals with quadriceps strength testing scores below 114Nm have an 85% probability of not reaching 35W during the 3rd stage of arm ergometry testing.

The present thesis contributed to current knowledge by conducting a binary regression analysis to provide odds ratios and probabilities to predict arm and leg exercise capacity. The findings complemented those of both Miranda et al. (2014) and Franssen et al. (2005) which indicated that there is an association between upper and lower body function in terms of strength in CPD patients. In addition to the association between upper and lower body strength in CPD, the findings of the regression analyses demonstrated that quadriceps strength is not only associated with upper body strength, but also predicts upper body aerobic capacity. Leg strength measures had better predictability (with regard to both arm and leg ergometry capacity) than handgrip strength.

Based on the above findings of the regression analyses the second hypothesis that leg and arm strength measures would predict arm and leg ergometery capacity independently from body composition and gender, can be accepted. The results of the standard and binary logistical regression procedures conducted in this study indicated that upper body functional decline is highly related to lower body decline. Quadriceps strength was predictive of both leg and arm ergometry capacity. A potential explanation for this may be that commonly performed upper body PADLs also include leg involvement. Therefore, if there is a reduction in lower limb function this could cross over to upper body activities that require leg involvement.

5.3. Limitations

While the findings of this thesis provide novel insights into the contributions of upper and lower body strength to upper and lower body exercise capacity, it is acknowledged that there are some limitations to the present study that may impact on the reliability of the results and their

interpretations. These primarily include limitations to physiological measurements, physical activity measurement, and the sample size/study population.

5.3.1. Exercise capacity measurement

In the present study, only an indirect sub-maximal arm ergometry and leg ergometry method was used to estimate VO_{2max}. Direct gas exchange measures were not used in this study due to inaccessibility and safety of the participants, but it is acknowledged that cardiopulmonary exercise testing would have improved the accuracy of peak oxygen uptake measurement. However, medical supervision would have been required to perform maximal exercise testing for several high risk CPD patients and this was not feasible for this study. In addition, wearing a mask during exercise testing may pose additional anxiety and create more dyspnoea for the CPD patients. In defence, the extrapolation method used to predict VO_{2peak} from the YMCA submaximal leg ergometer test has been shown to provide accurate predictions values (Beekley et al., 2004). However, Garatachea, Cavalcanti, García-López, González-Gallego, and de Paz (2007) reported that predicted VO_{2max} was overestimated in healthy adults by 5.4% for men, and 11.8% for women for the YMCA protocol. Taking this overestimation into consideration, and acknowledging the fact that the participants in the present thesis were not healthy adults, peak intensity used in this study was based on symptom limits (i.e. the actual intensity where exercise needed to be terminated due to symptom limitation).

5.3.2. Physical activity measures

Daily physical activity was measured subjectively using the IPAQ. In a comparison of physical activity questionnaires/diaries and motion sensors, Pitta, Troosters, Probst, Spruit et al. (2006b) stated that care must be taken when using subjective methods of measuring PA, as they rely on patient memory and report. Accelerometers and motion sensors are more reliable methods to accurately quantify physical activity levels; however they can only accurately measure lower body activity. Measurement of hand/arm movements involving the carrying or lifting of objects cannot be tracked accurately. Questionnaires are inexpensive and easy to apply and provide subjective insights of the patient's views of their own physical activity levels; however, patients may underestimate sedentary activities or overestimate their true level of physical activity by 300% (Klesges et al., 1990). However, to enhance the reliability of our physical activity findings, the IPAQ questionnaire was completed under supervision of the researchers, and careful interviewing

of the participants was applied when recalling their physical activity of their last typical week in an attempt to avoid any under or overestimation of weekly physical activity.

5.3.3. Sample size and study population

A convenience sample (n=44) of CPD patients was used for the study, which was limited by the number of referrals to U-kinetics. It was not possible to control the number of participants, or the number of participants in the various GOLD stages. Accordingly, participants with severe and very severe CPD were grouped together, as were participants with mild and moderate CPD. The limitation with this approach was that the impact of disease severity could not be tracked as effectively as was intended. It may be useful to complete a study with a larger sample size and enough participants in the separate GOLD stage groups to compare outcomes.

Diagnostic/classification guidelines for COPD are that airway obstruction is evident with a post-bronchodilator FEV_1/FVC of <0.7; and disease severity can be classed from mild to very severe, which increases with a decrease in FEV_1 (GOLD, 2014). This thesis included participants with a COPD, chronic asthma, bronchiectasis, and obstructive sleep apnoea. Twelve subjects (27%) had a reduced FEV_1 but did not meet the < 0.7 ratio criteria, and were categorised as having restrictive lung disease. However, since there were no differences seen between any outcome measures when FVC and FEV_1% predicted were compared, and the fact that all of the study population showed some reduction in FEV_1% predicted, the GOLD classification system based on FEV_1% predicted was used to determine severity of disease. Diffusion capacity of the lung for carbon monoxide (DLCO) (the extent to which oxygen passes from the air sacs of the lungs into the blood) could have been another option of an indicator of disease severity, however this was not available for all participants.

5.4. Future Research

The present thesis aimed to determine whether FEV_1, peripheral muscle strength, symptoms during exercise and PADLs contributed to arm and leg ergometry capacity in participants with CPD. While all of the participants had been diagnosed with a CPD they had several different specific diagnoses. It would be useful to conduct a larger study with participants split into groups according to their specific diagnosis, to determine whether each condition demonstrated the same exercise limitations.

Although this study provided new insights into the relationships between leg strength and arm and leg ergometry, the impact of these variables on the participants quality of life was not considered. To expand on the present study, it would be useful to investigate whether leg strength and arm and leg ergometry capacity are associated with quality of life and/or self-efficacy measures of patients with CPD. This would provide insight into how reductions in physical functioning impact their everyday lives from the perception of the individual.

In the present study lower limb dysfunction (low quadriceps strength) was associated with a reduced upper and lower body exercise capacity. Further investigation into the mechanisms behind the reduction in lower limb strength in patients with CPD is needed. Lower limb muscle dysfunction can be amendable through exercise rehabilitation strategies (Debigaré & Maltais, 2008), however investigation into the specific components of strength training in CPD needs more attention. Would it be more beneficial to focus on lower limb strength training rather than continuous aerobic exercise training? What are the most effective method and dosage of strength training for improving primary outcomes?

Optimal exercise rehabilitation strategies need to be investigated to enhance the effectiveness of exercise training in this population. It is apparent that physiological characteristics differ in patients with CPD, and this is not necessarily related to stage of disease based on pulmonary function alone. Given that, it is evident that research is required to address the magnitude of individual responses from exercise training based on disease severity. Disease severity classification may need to take into account the impact of the disease on strength, aerobic capacity, and ability to perform PADLs. Exercise training programmes may need to be individualised to match the level of physical disability each individual has as a result of their condition. This in turn might enhance the understanding of how to gain maximum benefits from pulmonary rehabilitation to improve the quality of life of patients with CPD.

Additionally, further investigation into the relationship between arm and leg exercise capacity, peripheral muscle strength, and the ability to perform PADLs is needed. Investigation into how the benefits of supervised exercise training may be translated into an increase in PADLs is needed. The physical strain on patients with CPD during PADLs was not assessed in this study, which may be a useful tool for determining the specific physical limitations in the everyday lives of patients with CPD. Further investigation into the impact of CPD on overall functioning in the

everyday lives of patients with CPD may identify specific limitations that could be amended with exercise training, which may increase the volume and intensity of PADLs performed, and in turn slow the progressing of the physical decline seen in these individuals.

Alternative testing methods to determine severity of CPD are needed, especially for patients who are unable to perform spirometry due to contra-indications caused by co-morbidities. It would be interesting to investigate whether measures of grip strength, quadriceps strength or aerobic capacity may be used to identify disease severity in individuals where pulmonary function measures are unavailable. Grip strength and leg strength may pose an alternative method of assessing severity of disease if it is unsafe to perform spirometry, and to assess a patient's need for a funded pulmonary rehabilitation intervention. Leg strength can be easily assessed by hand-held dynamometry or a 1RM test if an isokinetic device in unavailable. Grip strength is inexpensive, quick to administer, requires minimal equipment, and can be easily performed. Grip strength may also be able to identify those who will not perform well in leg ergometry testing and may be helpful in estimating starting wattage and the level of the watt increments between the stages.

5.5. Clinical Implications

The findings of this thesis demonstrate the importance of maintaining and/or improving upper and lower body strength, in order to maintain arm and leg functional capacity. Upper and lower body strength measures were more important contributors to the participant's physical functioning than their weekly volume of PADLs. This indicated that the intensity of physical activity was more important than the amount of physical activity performed, as a higher intensity would place a greater demand on the peripheral muscles and aerobic system.

The importance of leg strength in CPD is well known and current exercise training guidelines include leg strength training as a part of rehabilitation of CPD patients. This thesis shows that there is a high association of leg strength to both arm and leg aerobic capacity, emphasising the need for improving and maintaining leg strength. Attention needs to be given to gaining maximum improvements in leg strength during exercise training interventions.

In addition, the inclusion of leg strength testing before an exercise training intervention is justified in this study, to identify those who have reduced leg strength. A goal of amending this will be a

key objective of the individual's specific exercise programme. It also justifies the need to test leg strength after rehabilitation interventions to monitor the effectiveness of exercise programmes on improving leg strength.

5.6. Conclusion

In attempt to enhance the exercise training of CPD patients it is important to identify specific exercise limitations in this population, and how much impact each limitation has on the overall functioning of these individuals. Effective exercise rehabilitation programmes are important to maximise the physical improvements gained by individuals with CPD so that they can maintain an improved quality of life for longer. As a result, this will reduce the healthcare burden, and the morbidity and mortality rates of patients with CPD.

It was well-established that lower limb muscle function is an important predictor of exercise capacity and mortality in CPD. This study adds to the current literature by proposing that lower limb muscle strength is an important contributor to arm exercise capacity in addition to leg exercise capacity, as measured by arm and leg ergometry.

Leg strength and leg ergometry capacity were directly related to arm ergometry capacity. These findings suggest that a reduction in leg function is associated with a reduction in arm function. It is important to note that the findings of this thesis demonstrated merely an association between upper and lower limb function, and does not indicate causation. However, a possible explanation could be that commonly performed PADLs involve legs as well as arms. Therefore if lower limb function is reduced and individuals with CPD start to avoid activities involving the legs, as a consequence arm activities that also involve standing or walking might also be avoided.

The findings of this thesis highlight the importance of assessing upper and lower limb strength in patients with CPD. This thesis endorses the incorporation of specified lower limb strength training in pulmonary rehabilitation, especially for those with reduced strength and physical activity levels. Pulmonary rehabilitation programs should incorporate both aerobic exercise and lower limb strength training.

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Borg CR10 scale (1998)

0	Nothing at all	“No P”
0.3		
0.5	Extremely weak	Just noticeable
1	Very weak	
1.5		
2	Weak	
2.5		
3	Moderate Light	
4		
5	Strong Heavy	
6		
7	Very strong	
8		
9		
10	**Extremely strong “Max P”**	
11		
●	Absolute maximum	Highest possible

Borg Dyspnea Scale

0	None
0.5	Very, very slight
1	Very slight
2	Slight
3	Moderate
4	Somewhat severe
5	Severe
6	
7	Very severe
8	
9	Very, very severe
10	Maximal

Borg's Rating of Percieved Exertion Scale (RPE)

6

7 Very, very light

8

9 Very light

10

11 Fairly light

12

13 Somewhat hard

14

15 Hard

16

17 Very hard

18

19 Very, very hard

20

Appendix B – MRC Grade

Medical Research Council dyspnoea scale (Tick one)

Grade	Degree of breathlessness related to activities	
1	Not troubled by breathlessness except on strenuous exercise	
2	Short of breath when hurrying or walking up a slight hill	
3	Walks slower than contemporaries on level ground because of breathlessness, or has to stop for breath when walking at own pace	
4	Stops for breath after walking about 100m or after a few minutes on level ground	
5	Too breathless to leave the house, or breathless when dressing or undressing	

Adapted from Fletcher C.M., Elmes P.C., Fairbairn A.S. et al. (1959). The significance of respiratory symptoms and the diagnosis of chronic bronchitis in a working population. *British Medical Journal, 2*:257-66.

Appendix C – ADL-D Scale

The Activity of Daily Living Dyspnoea scale

Name

- For each activity listed below, please rate your breathlessness on a scale between 0 and 4, where 4 is not at all and 0 is maximally severe.
- If you find some activities are not performed by you, please give your best estimate of breathlessness if you were to perform the task.
- Your responses should be for an 'average' day during the past week.
- Please response to all items.

	Not at all	Slight	Severe	Very Severe	Maximally Severe
Walking on level ground	4	3	2	1	0
Walking upstairs	4	3	2	1	0
Waking uphill	4	3	2	1	0
Walking inside the home	4	3	2	1	0
Straining to pass a bowel motion	4	3	2	1	0
Putting on and taking off jacket	4	3	2	1	0
Putting on and taking off trousers	4	3	2	1	0
Putting on and taking off socks	4	3	2	1	0
Washing face	4	3	2	1	0
Brushing teeth	4	3	2	1	0
Washing hair	4	3	2	1	0
Washing one's back	4	3	2	1	0
Washing feet	4	3	2	1	0
Bending over	4	3	2	1	0
Shopping	4	3	2	1	0

Appendix D – IPAQ

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE (October 2002)

LONG LAST 7 DAYS SELF-ADMINISTERED FORMAT

FOR USE WITH YOUNG AND MIDDLE-AGED ADULTS (15-69 years)

The International Physical Activity Questionnaires (IPAQ) comprises a set of 4 questionnaires. Long (5 activity domains asked independently) and short (4 generic items) versions for use by either telephone or self-administered methods are available. The purpose of the questionnaires is to provide common instruments that can be used to obtain internationally comparable data on health–related physical activity.

Background on IPAQ
The development of an international measure for physical activity commenced in Geneva in 1998 and was followed by extensive reliability and validity testing undertaken across 12 countries (14 sites) during 2000. The final results suggest that these measures have acceptable measurement properties for use in many settings and in different languages, and are suitable for national population-based prevalence studies of participation in physical activity.

Using IPAQ
Use of the IPAQ instruments for monitoring and research purposes is encouraged. It is recommended that no changes be made to the order or wording of the questions as this will affect the psychometric properties of the instruments.

Translation from English and Cultural Adaptation
Translation from English is encouraged to facilitate worldwide use of IPAQ. Information on the availability of IPAQ in different languages can be obtained at www.ipaq.ki.se. If a new translation is undertaken we highly recommend using the prescribed back translation methods available on the IPAQ website. If possible please consider making your translated version of IPAQ available to others by contributing it to the IPAQ website. Further details on translation and cultural adaptation can be downloaded from the website.

Further Developments of IPAQ
International collaboration on IPAQ is on-going and an ***International Physical Activity Prevalence Study*** is in progress. For further information see the IPAQ website.

More Information
More detailed information on the IPAQ process and the research methods used in the development of IPAQ instruments is available at www.ipaq.ki.se and Booth, M.L. (2000). *Assessment of Physical Activity: An International Perspective.* Research Quarterly for Exercise and Sport, 71 (2): s114-20. Other scientific publications and presentations on the use of IPAQ are summarized on the website.

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** and **moderate** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal.

PART 1: JOB-RELATED PHYSICAL ACTIVITY

The first section is about your work. This includes paid jobs, farming, volunteer work, course work, and any other unpaid work that you did outside your home. Do not include unpaid work you might do around your home, like housework, yard work, general maintenance, and caring for your family. These are asked in Part 3.

1. Do you currently have a job or do any unpaid work outside your home?

   ☐ Yes

   ☐ No → ***Skip to PART 2: TRANSPORTATION***

The next questions are about all the physical activity you did in the **last 7 days** as part of your paid or unpaid work. This does not include traveling to and from work.

2. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, heavy construction, or climbing up stairs **as part of your work**? Think about only those physical activities that you did for at least 10 minutes at a time.

   _____ **days per week**

   ☐ No vigorous job-related physical activity → ***Skip to question 4***

3. How much time did you usually spend on one of those days doing **vigorous** physical activities as part of your work?

   _____ **hours per day**
   _____ **minutes per day**

4. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads **as part of your work**? Please do not include walking.

   _____ **days per week**

   ☐ No moderate job-related physical activity → ***Skip to question 6***

5. How much time did you usually spend on one of those days doing **moderate** physical activities as part of your work?

_____ **hours per day**
_____ **minutes per day**

6. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **as part of your work**? Please do not count any walking you did to travel to or from work.

_____ **days per week**

☐ No job-related walking → ***Skip to PART 2: TRANSPORTATION***

7. How much time did you usually spend on one of those days **walking** as part of your work?

_____ **hours per day**
_____ **minutes per day**

PART 2: TRANSPORTATION PHYSICAL ACTIVITY

These questions are about how you traveled from place to place, including to places like work, stores, movies, and so on.

8. During the **last 7 days**, on how many days did you **travel in a motor vehicle** like a train, bus, car, or tram?

_____ **days per week**

☐ No traveling in a motor vehicle → ***Skip to question 10***

9. How much time did you usually spend on one of those days **traveling** in a train, bus, car, tram, or other kind of motor vehicle?

_____ **hours per day**
_____ **minutes per day**

Now think only about the **bicycling** and **walking** you might have done to travel to and from work, to do errands, or to go from place to place.

10. During the **last 7 days**, on how many days did you **bicycle** for at least 10 minutes at a time to go **from place to place**?

_____ **days per week**

☐ No bicycling from place to place → ***Skip to question 12***

11. How much time did you usually spend on one of those days to **bicycle** from place to place?

_____ **hours per day**
_____ **minutes per day**

12. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time to go **from place to place**?

_____ **days per week**

☐ No walking from place to place → ***Skip to PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY***

13. How much time did you usually spend on one of those days **walking** from place to place?

_____ **hours per day**
_____ **minutes per day**

PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY

This section is about some of the physical activities you might have done in the **last 7 days** in and around your home, like housework, gardening, yard work, general maintenance work, and caring for your family.

14. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, chopping wood, shoveling snow, or digging **in the garden or yard**?

_____ **days per week**

☐ No vigorous activity in garden or yard → ***Skip to question 16***

15. How much time did you usually spend on one of those days doing **vigorous** physical activities in the garden or yard?

_____ **hours per day**
_____ **minutes per day**

16. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, sweeping, washing windows, and raking **in the garden or yard**?

_____ **days per week**

☐ No moderate activity in garden or yard → ***Skip to question 18***

17. How much time did you usually spend on one of those days doing **moderate** physical activities in the garden or yard?

_____ **hours per day**
_____ **minutes per day**

18. Once again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, washing windows, scrubbing floors and sweeping **inside your home**?

_____ **days per week**

☐ No moderate activity inside home → ***Skip to PART 4: RECREATION, SPORT AND LEISURE-TIME PHYSICAL ACTIVITY***

19. How much time did you usually spend on one of those days doing **moderate** physical activities inside your home?

_____ **hours per day**
_____ **minutes per day**

PART 4: RECREATION, SPORT, AND LEISURE-TIME PHYSICAL ACTIVITY

This section is about all the physical activities that you did in the **last 7 days** solely for recreation, sport, exercise or leisure. Please do not include any activities you have already mentioned.

20. Not counting any walking you have already mentioned, during the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **in your leisure time**?

_____ **days per week**

☐ No walking in leisure time → ***Skip to question 22***

21. How much time did you usually spend on one of those days **walking** in your leisure time?

_____ **hours per day**
_____ **minutes per day**

22. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous** physical activities like aerobics, running, fast bicycling, or fast swimming **in your leisure time**?

_____ **days per week**

☐ No vigorous activity in leisure time → ***Skip to question 24***

23. How much time did you usually spend on one of those days doing **vigorous** physical activities in your leisure time?

_____ **hours per day**
_____ **minutes per day**

24. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like bicycling at a regular pace, swimming at a regular pace, and doubles tennis **in your leisure time**?

_____ **days per week**

☐ No moderate activity in leisure time → ***Skip to PART 5: TIME SPENT SITTING***

25. How much time did you usually spend on one of those days doing **moderate** physical activities in your leisure time?
_____ **hours per day**
_____ **minutes per day**

PART 5: TIME SPENT SITTING

The last questions are about the time you spend sitting while at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading or sitting or lying down to watch television. Do not include any time spent sitting in a motor vehicle that you have already told me about.

26. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekday**?

_____ **hours per day**
_____ **minutes per day**

27. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekend day**?

_____ **hours per day**
_____ **minutes per day**

This is the end of the questionnaire, thank you for participating.

Appendix E – Full Results Tables

Table 1.
Descriptive data of all participants and gender differences.

	Total X ± SD (n=44)	Male X ± SD (n=16)	Female X ± SD (n=28)	p-value
Age	59.80 ± 11.92	63.50 ± 9.18	57.68 ± 12.91	0.12
Weight	87.28 ± 20.58	89.45 ± 13.89	86.04 ± 23.72	0.60
BMI	33.15 ± 10.98	29.69 ± 4.06	35.13 ± 13.10	0.11
BF%	30.56 ± 13.08	20.41 ± 7.71	36.36 ± 11.98	<0.001
FVC%	70.64 ± 13.22	71.13 ± 13.03	70.36 ± 13.55	0.86
FEV_1%	54.64 ± 18.27	50.63 ± 19.71	55.21 ± 17.75	0.78
Leg VO_{2peak}	21.84 ± 5.86	24.34 ± 6.73	20.42 ± 4.88	0.03
Leg $Watt_{peak}$	49.32 ± 19.13	57.81 ± 20.16	44.46 ± 17.02	0.02
Leg $Pain_{peak}$	3.31 ± 1.82	2.81 ± 1.61	3.61 ± 1.89	0.17
Arm VO_{2peak}	21.59 ± 6.29	21.67 ± 6.64	21.54 ± 6.20	0.95
Arm $Watt_{peak}$	38.86 ± 11.71	45.00 ± 12.78	35.36 ± 9.62	0.01
Arm $Pain_{peak}$	3.29 ± 1.52	3.34 ± 1.62	3.26 ± 1.49	0.86
Grip strength	30.92 ± 10.39	41.13 ± 8.64	25.09 ± 5.79	<0.001
Quad strength	103.67 ± 34.99	129.38 ± 24.62	88.98 ± 31.59	<0.001
Ham strength	53.10 ± 19.47	66.94 ± 15.96	45.20 ± 16.85	<0.001
Quad endur	88.42 ± 14.11	88.88 ± 12.31	88.16 ± 15.26	0.87
Ham endur	98.71 ±30.94	90.09 ± 16.83	103.63 ± 36.03	0.17
Total activity	3074 ± 3320	3342 ± 4586	2921 ± 2408	0.69
Vigorous activity	313 ± 1042	798.13 ± 1643	36 ± 103	0.02
Moderate activity	2242 ± 2282	1743 ± 2269	2528 ± 2281	0.28
Walking activity	524 ± 762	815 ± 1149	358 ± 333	0.05

Table 2.
Comparison of Mild-Moderate and Severe+ CPD groups.

	Mild-Moderate (n=28) Mean SD	Severe+ (n=16) Mean SD	t-value	p-value
Age	57.25 ± 13.52	64.25 ± 6.70	1.93	0.06
BMI	35.15 ± 12.83	29.65 ± 5.37	-1.63	0.11
BF%	32.31 ± 14.00	27.49 ± 11.04	-1.18	0.24
FVC%	75.18 ± 11.44	62.69 ± 12.62	-3.36	0.002
FEV_1%	65.93 ± 10.69	34.88 ± 9.81	-9.54	0.0001
MRC Grade	1.96 ± 0.74	2.75 ± 0.86	3.19	0.003
Peak VO_2 leg	22.83 ± 6.38	20.12 ± 4.50	-1.50	0.14
Peak VO_2 arm	22.42 ± 6.48	20.13 ± 5.85	-1.16	0.25
Peak W leg	54.11 ± 20.95	40.93 ± 11.86	-2.30	0.03
Peak W arm	41.25 ± 11.81	34.69 ± 8.26	-1.84	0.07
Peak pain leg	3.28 ± 1.74	2.69 ± 1.83	-1.78	0.08
Peak pain arm	3.55 ± 1.57	2.83 ± 1.36	-1.54	0.13
Grip strength	31.79 ± 10.55	29.41 ± 10.27	-0.73	0.47
Quad strength	111.29 ± 37.70	90.34 ± 25.58	-1.97	0.055
Ham Strength	57.52 ±21.02	45.38 ± 13.83	-2.06	0.045
Quad endurance	87.23 ± 14.05	90.50 ± 14.43	0.73	0.47
Ham endurance	96.34 ± 25.17	102.84 ± 39.68	0.67	0.50
Total activity	2837.91 ± 947.35	3208.96 ± 860.31	0.75	0.73
Moderate activity	2177.5 ± 2193.7	2279.3 ± 2370.5	-0.14	0.89
Vigorous activity	380.27 ± 647.17	195.31 ± 1218.31	-0.56	0.57

Table 3.
Combined and individual relationships of CPD stage and Physical Activity with morphological, cardiovascular and strength variables as determined with a factorial ANOVA.

		CPD Stage					
	Total PADL (min/week)	Mild-Moderate			Severe +		
			X	SD		X	SD
Age	Low	a	55.69	16.22	c	4.50	5.58
	High	b	59.33	9.61	d	64.00	8.05
Body Mass	Low	a	95.74	14.57	c	77.41	16.27
	High	b	86.46	29.02	d	81.45	15.58
BMI	Low	a	37.65	14.39	c	27.98	4.84
	High	b	31.81	10.00	d	31.33	5.61
Percentage body fat	Low	a	35.20	14.35	c	24.36	8.50
	High	b	28.46	13.11	d	30.61	12.90
MRC Grade	Low	a	1.88[c]	0.61	c	3.1 [a b]	0.83
	High	b	2.08[c]	0.90	d	2.38	0.74
ADL/Dyspnea	Low	a	51.97	7.23	c	49.86	4.91
	High	b	49.92	7.44	d	50.38	4.67
FVC%	Low	a	77.38 [c d]	13.56	c	62.12[a]	12.29
	High	b	72.25	13.22	d	63.13[a]	13.77
Peak watt (leg)	Low	a	58.75	20.04	c	41.88	14.62
	High	b	47.92	21.36	d	40.00	9.26
Peak VO_2 (leg)	Low	a	22.44	4.73	c	19.40	5.15
	High	b	23.35	8.30	d	20.83	3.95
Peak RPE bike	Low	a	12.81	1.64	c	12.86	1.73
	High	b	12.71	2.22	d	12.25	0.89
Peak Dyspnea (bike)	Low	a	2.86	1.20	c	3.69	1.33
	High	b	2.71	0.84	d	2.86	1.16
Peak Pain (bike)	Low	a	3.72	1.26	c	2.56	2.16
	High	b	3.63	2.30	d	2.81	1.56
Peak watt (arm)	Low	a	42.81	10.16	c	33.13	9.61
	High	b	39.17	15.93	d	36.25	6.94
Peak VO_2 (arm)	Low	a	21.72	5.63	c	17.65	5.85
	High	b	23.35	7.63	d	22.62	5.00
Peak RPE (arm)	Low	a	12.69	1.66	c	13.13	0.99
	High	b	12.58	1.56	d	11.50	1.20
Peak Dyspnea (arm)	Low	a	2.41	0.71	c	2.50	1.54
	High	b	2.38	1.15	d	2.19	1.33
Peak pain (arm)	Low	a	3.66	1.60	c	3.19	1.51
	High	b	3.42	1.58	d	2.48	1.19
Grip strength	Low	a	32.97	9.66	c	32.63	13.12
	High	b	30.21	11.87	d	26.19	5.50
Quad strength	Low	a	116.88	38.02	c	98.06	33.79
	High	b	103.83	37.55	d	82.63	11.16
Hamstring strength	Low	a	61.50	21.19	c	44.50	18.08
	High	b	52.21	20.44	d	46.25	9.02
Quad endurance	Low	a	89.41	10.68	c	93.88	17.87
	High	b	84.33	17.70	d	87.13	10.03
Hamstring endurance	Low	a	94.59	12.72	c	119.31	48.72
	High	b	98.67	36.36	d	86.38	19.51

Note. Group a = mild-moderate CPD and low PADL level (n= 16), group b = mild-moderate CPD and high PADL level (n= 12), group c = severe+ CPD and low PADL level (n= 8), and group d = severe+ CPD and high PADL level (n= 8).

Table 4.
The f-ratio, p-values, ETA2 and Wilks Lambda scores of the factorial ANOVA investigating the relationship of CPD stage and total PADL (min) with arm and leg ability (strength and peak watt during ergometry) in CPD patients.

Dependent variables	ANOVA groups	F-ratio	p-values	Eta^2	Wilks Lambda
Age	CPD stage	3.326	0.076	27.4	90.3
	Total PADL	0.181	0.673	6.39	
	Combined	1.428	0.249	9.67	
Body Mass	CPD stage	3.438	0.071	27.5	87.9
	Total PADL	0.173	0.679	6.17	
	Combined	1.836	0.156	12.1	
BMI	CPD stage	2.267	0.140	22.4	88.7
	Total PADL	0.137	0.713	5.51	
	Combined	1.701	0.182	11.3	
Percentage body fat	CPD stage	1.143	0.292	16.1	90.4
	Total PADL	0.004	0.951	0.94	
	Combined	1.411	0.254	9.57	
FVC%	CPD stage	10.356	0.003	44.5	76.4
	Total PADL	0.282	0.598	7.33	
	Combined	4.121	0.012	23.6	
MRC Grade	CPD stage	10.257	0.003	43.1	72.6
	Total PADL	1.266	0.267	15.2	
	Combined	5.030	0.005	27.4	
ADL/Dyspnea	CPD stage	0.159	0.693	6.23	97.6
	Total PADL	0.143	0.708	5.90	
	Combined	0.306	0.821	2.24	
Peak watt (leg)	CPD stage	4.725	0.035	31.4	83.6
	Total PADL	1.242	0.272	16.1	
	Combined	2.622	0.064	16.4	
Peak VO_2 (leg)	CPD stage	2.247	0.142	22.9	94.0
	Total PADL	0.395	0.533	9.63	
	Combined	0.852	0.474	6.01	
Peak RPE bike	CPD stage	0.131	0.719	5.57	98.3
	Total PADL	0.444	0.509	10.4	
	Combined	0.228	0.877	1.68	
Peak Dyspnea (bike)	CPD stage	1.888	0.177	20.7	90.9
	Total PADL	1.888	0.177	20.7	
	Combined	1.339	0.275	9.13	
Peak Pain (bike)	CPD stage	2.973	0.092	26.3	92.7
	Total PADL	0.019	0.891	2.08	
	Combined	1.044	0.384	7.26	
Peak watt (arm)	CPD stage	3.015	0.090	26.1	90.7
	Total PADL	0.005	0.943	1.08	
	Combined	1.424	0.250	9.65	
Peak VO_2 (arm)	CPD stage	1.524	0.224	18.5	90.0
	Total PADL	2.882	0.097	25.5	
	Combined	1.485	0.233	10.0	
Peak RPE (arm)	CPD stage	0.495	0.486	10.4	87.9
	Total PADL	3.543	0.067	27.9	
	Combined	1.838	0.156	12.1	
Peak Dyspnea (arm)	CPD stage	0.022	0.896	0.62	99.2
	Total PADL	0.299	0.632	7.61	
	Combined	0.110	0.954	0.82	
Peak pain (arm)	CPD stage	2.195	0.146	22.5	92.2
	Total PADL	1.000	0.323	15.2	
	Combined	1.126	0.350	7.79	
Grip strength	CPD stage	0.441	0.511	10.2	94.1

	Overall Act	1.957	0.170	21.5	
	Combined	0.841	0.479	5.94	
Quad strength	CPD stage	3.514	0.068	27.7	87.5
	Overall Act	1.779	0.190	19.7	
	Combined	1.906	0.144	12.5	
Hamstring strength	CPD stage	3.753	0.059	28.6	87.1
	Overall Act	0.405	0.528	9.39	
	Combined	1.978	0.133	12.9	
Quad endurance	CPD stage	0.658	0.422	12.5	94.5
	Overall Act	1.745	0.194	20.3	
	Combined	0.770	0.518	5.46	
Hamstring endurance	CPD stage	0.430	0.516	9.74	88.1
	Overall Act	2.321	0.135	22.6	
	Combined	1.795	0.164	11.9	