

Muscle Quality, Muscle Mass, Muscle Strength, and Pulse Wave Velocity between
Healthy Young and Elderly Adults

by

Erin Dierickx

A Thesis Presented in Partial Fulfillment
of the Requirements for the Degree
Master of Science

Approved April 2017 by the
Graduate Supervisory Committee:

Chong Lee, Chair
Pamela Swan
Joseph Marsit
Jack Chisum

ARIZONA STATE UNIVERSITY

May 2017

ABSTRACT

Although maintaining an optimal level of muscle quality in older persons is necessary to prevent falls and disability, there has been limited research on muscle quality across age and gender groups. The associations of muscle quality, muscle strength, and muscle mass also remain less explored. Purpose: This study examined the muscle quality differences (arm and leg) between healthy young and elderly adults across gender groups. This study also examined the associations of muscle quality, muscle strength, and muscle mass in young and elderly adults, respectively. Methods: Seventy-one total subjects were recruited for this study within age groups 20-29 years old (20 females and 20 males) and 60-80 years old (18 females and 13 males). All participants completed anthropometric measures, dual-energy x-ray absorptiometry, pulse wave velocity, handgrip strength and leg strength tests, gait speed, and sit to stand test. Results: Young male adults had a greater leg muscle quality index (leg MQI) than did elderly male adults (21.8 Nm/kg vs. 16.3 Nm/kg, $p = 0.001$). Similarly, young female adults had a greater leg MQI than did old female adults (21.3 Nm/kg and 15.6 Nm/kg, $p < 0.001$). For arm muscle quality index (arm MQI), there was a gender difference in young adults ($p = 0.001$), but not for the elderly adults. Among elderly adults, there was a positive association between leg MQI and isometric leg strength ($r = 0.79$, $p < 0.001$). Notably, there was a negative association between leg MQI and leg lean mass ($r = -0.70$, $p < 0.001$) and between arm MQI and arm lean mass ($r = -0.58$, $p = 0.001$). In young adults, there was also a positive association between arm MQI and handgrip strength ($r = 0.53$, $p < 0.001$) and between leg MQI and isometric leg strength ($r = 0.81$, $p < 0.001$). There was no association between muscle quality and muscle mass in young adults. Conclusion:

Young adults had a greater leg muscle quality than did elderly adults in both men and women. Leg muscle quality is positively associated with leg muscle strength in both young and elderly adults but is inversely associated with leg muscle mass in the elderly adults.

TABLE OF CONTENTS

	Page
LIST OF TABLES.....	vi
LIST OF FIGURES.....	vii
CHAPTER	
1 INTRODUCTION.....	1
2 REVIEW OF LITERATURE.....	4
Sarcopenia.....	4
Group Definitions.....	5
Causes and Potential Components of Sarcopenia.....	6
Cachexia.....	7
Frailty.....	7
Sarcopenic Obesity.....	8
Osteoporosis.....	10
Osteosarcopenic Obesity.....	11
Environmental Influences.....	12
Prevalence of Sarcopenia.....	12
Methods of Measure.....	13
Sarcopenia as is Relates to Mortality.....	15
Sarcopenia and Disease.....	16
Heart disease.....	16
Cancer.....	17
Diabetes.....	18

CHAPTER	page
Sarcopenia and Muscle Quality.....	19
Sarcopenia and Muscle Mass and Strength.....	21
Muscle Quality, Muscle Mass, and Muscle Strength.....	22
Sarcopenia and Arterial Health.....	23
Summary.....	26
3 METHODS.....	27
Subjects.....	27
Research Design.....	27
Pulse Wave Velocity Measurement.....	28
Dynamometer Test.....	29
Handgrip Test.....	30
Gait Speed Measurement.....	30
Sit-to-Stand Test.....	30
Statistical Analysis.....	31
4 RESULTS.....	32
Subject Characteristics.....	32
Muscle Quality Index.....	33
Lean and Fat Mass.....	35
Muscle Strength.....	39
Arterial Health.....	41
Physical Functioning Tests.....	43
Muscle Quality, Muscle Strength, and Muscle Mass.....	43

CHAPTER	page
5 DISCUSSION.....	45
Muscle Quality Index	45
Muscle Quality, Muscle Mass, and Muscle Strength.....	46
Muscle Mass.....	46
Muscle Strength.....	47
Pulse Wave Velocity.....	48
Visceral Fat.....	49
Strengths of the Study.....	49
Limitations of the Study.....	50
Conclusion.....	50
REFERENCES.....	52
APPENDIX	
A CONSENT FORM.....	63
B IRB APPROVAL.....	68
C RECRUITMENT FLIER.....	70
D MUSCLE QUALITY STUDY RECRUITMENT SURVEY.....	72
E LIFESTYLE QUESTIONNAIRE.....	75

LISTS OF TABLES

Table	Page
1 Measurement Methods of Sarcopenia.....	14
2 Characteristics of the Study Participants Across Gender and Age Categories.....	32
3 Person Partial Correlations Among Muscle Quality, Muscle Mass, and Muscle Strength.....	44

LISTS OF FIGURES

Figure	Page
1 Average Leg MQI Difference by Gender.....	33
2 Average Leg MQI Difference by Age Group.....	34
3 Average Arm MQI Difference by Gender	34
4 Average Arm MQI Difference by Age Group.....	35
5 Average Leg Lean Mass (Right, kg) Difference by Gender.....	36
6 Average Leg Lean Mass (Right, kg) Difference by Age Group.....	37
7 Average Arm Lean Mass (Right, kg) Difference by Gender.....	37
8 Average Arm Lean Mass (Right, kg) Difference by Age Group.....	38
9 Average Visceral Fat Difference by Gender.....	38
10 Average Visceral Fat Difference by Age Group.....	39
11 Average Leg Muscle Strength Difference by Gender.....	40
12 Average Handgrip Strength Difference by Gender.....	40
13 Average Leg Muscle Strength Difference by Age Group.....	41
14 Average Handgrip Strength Difference by Age Group.....	41
15 Average Pulse Wave Velocity Difference by Gender.....	42
16 Average Pulse Wave Velocity Difference by Age Group.....	43

CHAPTER 1

INTRODUCTION

Age-related reduction in muscle mass (sarcopenia) and strength (dynapenia) is associated with muscle weakness and physical disability (Clark & Manini, 2010). Maintaining an optimal level of muscle mass and muscle strength is necessary to prevent falls and disability throughout a lifetime. Approximately 5-13% of adults (aged 70 or more) and 11-50% of adults (aged 80 or more) suffer from sarcopenia (Haehling et al., 2010, Morley, 2012). The prevalence of sarcopenia has been shown to vary greatly from 3.3% when using a muscle mass index in a combination of handgrip strength to 24.8% when including measures of gait speed, fat mass, and falls (Clynes et al., 2015).

Sarcopenia is associated with heart disease (Kim et al., 2015), various types of cancer (Villaseor et al., 2012), diabetes (Kim et al., 2014), and all-cause mortality (Chang & Lin, 2016). Risk factors for sarcopenia may include environmental factors, chronic diseases, and changes in hormone levels (Fielding, 2011; Ilich, 2016). Furthermore, components of sarcopenia may include cachexia, frailty, obesity (Cruz-Jentoft et al., 2010), and osteoporosis (Binkley et al., 2013) individually or in combinations.

The definition of sarcopenia remains in dispute worldwide. Recently, sarcopenia was defined as the combination of low muscle mass, low muscle strength, and/or low physical performance. The European Working Group on Sarcopenia in Older People (EWGSOP) and the Foundation for the National Institutes of Health (FNIH) have defined sarcopenia using the combination of low muscle mass and low muscle strength (Cruz-Jentoft, et al., 2010; Studenski et al., 2014). The International Working Group on Sarcopenia (IWGS) and the Society of Sarcopenia, Cachexia and Wasting Disorders

(SCWD) have defined sarcopenia using the combination of low muscle mass and low physical performance (Fielding et al., 2011; Morley et al., 2011). However, the validity and cross-validity of these cut points to define sarcopenia remain less clear. Other studies used pulse wave analysis and demonstrated that this noninvasive method is appropriate for evaluating sarcopenia (Fahs et al., 2010). Recently, several investigators have begun to focus more on measures of muscle quality and muscle function (Yamada et al., 2016; McGregor et al., 2014; Akin et al., 2015) rather than muscle mass alone. These measures, however, may require more expensive equipment and timely procedures.

Sarcopenia has most commonly been defined as a loss of muscle mass with aging. Whether muscle mass is the most appropriate measurement to reflect adverse health outcomes of muscle decline and aging remains less clear. Baumgartner et al. (1998) and Janssen et al. (2004) had defined sarcopenia using low lean mass in relation to disability. However, several studies have shown no association between skeletal muscle mass and physical functioning (Visser et al., 2000). According to the Health, Aging, and Body Composition Study, low lean mass is not associated with mortality, whereas muscle strength is positively associated with mortality in the elderly persons (Newman et al., 2006). Thus, defining sarcopenia using lean muscle mass alone remains controversial. Some investigators have also shown a significant association between muscle strength (i.e., handgrip or leg extension strength) and mortality (Lauretani et al., 1985), but elderly persons have a greater amount of adipose tissues in the muscles compared with young adults (Addison et al., 2014). Therefore, the combination of low lean mass and muscle strength is also not appropriate to define sarcopenia. Muscle quality, an indicator of muscle strength, is a better measure for sarcopenia (Barbat-Artigas et al., 2012).

However, there has been limited research on muscle quality across age and gender groups. The associations of muscle quality, muscle strength, and muscle mass also remain less explored. Therefore, the primary aim of this study was to examine mean difference for muscle quality across gender and age categories. The associations of muscle quality, muscle mass, and muscle strength were also assessed in young and elderly adults, respectively. The secondary aim of this study was to investigate gender and age differences in PWV, muscle mass, muscle strength, and body composition.

I hypothesize that males will have a greater muscle quality as compared with females across young and elderly persons; young healthy adults will have a higher muscle quality compared with elderly adults in both males and females. I hypothesize that there will be a significant and positive association between measures of muscle quality, muscle mass, and muscle strength in young and elderly adults. Lastly, I hypothesize that young adults will have greater muscle mass and muscle strength and a slower PWV compared with elderly adults in both men and women.

CHAPTER 2

REVIEW OF LITERATURE

Sarcopenia

Sarcopenia has been clinically defined in multiple ways. However, before developing a definition, the following questions must be answered. What is sarcopenia? What parameters define sarcopenia? What variables reflect these parameters? What are the best methods for measuring these variables? What are the cutoff points? And how might sarcopenia relate to other health outcomes? (Cruz-Jentoft, 2010).

Sarcopenia has typically been defined as the age-associated loss of skeletal muscle mass. However, evidence has shown that low muscle mass is poorly associated with function and disability. Therefore, some investigators have added a low muscle function or a muscle strength measure in addition to low muscle mass to define sarcopenia (Fielding et al., 2011; Cruz-Jentoft, 2010). If skeletal muscle mass is to be used to define sarcopenia, it is important to determine the cut points for low muscle mass associated with disability (Studenski et al., 2014).

It may also be important to determine the stages of sarcopenia and how it should be termed. Common terms to describe sarcopenia have included disease, disorder, and condition. ‘Disease’ is a definite morbid process with characteristic symptoms, ‘disorder’ describes an abnormality of function, and ‘condition’ is a state or mode of being (Koenigsberg, 1989). Bijlsma et al. (2013) consider using the severity, development and pathophysiological process to determine which term to use and therefore define sarcopenia as a disease due to the detrimental outcomes associated with it. Baumgartner et al. (1998) first proposed sarcopenia using relative skeletal muscle mass (appendicular

skeletal muscle mass adjusted for height squared, kg/m^2) more than 2 SDs below the sex-specific means of a reference population (men $<7.26 \text{ kg/m}^2$, women $<5.45 \text{ kg/m}^2$).

Group Definitions.

The European Working Group on Sarcopenia in Older People (EWGSOP) defined sarcopenia as a skeletal muscle mass index less than 7.26 kg/m^2 for males and less than 5.5 kg/m^2 for females. In addition, handgrip strength less than 30 kg for males and less than 20 kg for females and/or a gait speed less than 0.8m/s would categorize an individual as sarcopenic (Cruz-Jentoft, 2010). International Working Group on Sarcopenia (IWGS) diagnoses sarcopenia using measures of appendicular fat-free mass and physical performance. The IWGS defined sarcopenia as a gait speed less than 1.0 m/s and an appendicular skeletal muscle mass adjusted for height (aLM/Ht^2) $\leq 7.23 \text{ kg/m}^2$ for males and $\leq 5.67 \text{ kg/m}^2$ for females (Fielding, 2011). Foundation for the National Institutes of Health and Sarcopenia Project (FNIH) classified sarcopenia as a handgrip strength $<26 \text{ kg}$ for men and $<16 \text{ kg}$ for women as well as an appendicular lean body mass adjusted for BMI (aLM/BMI) <0.789 for males and <0.512 for females (Studenski, 2014). Furthermore, Binkley and colleagues (2013) clarified sarcopenia as a dysmobility syndrome. Individuals were diagnosed with the syndrome if they fell within three or more of the following categories: (1) skeletal mass index of $\leq 7.26 \text{ kg/m}^2$ in men and $\leq 5.45 \text{ kg/m}^2$ in women; (2) handgrip strength of $<30 \text{ kg}$ in men and $<20 \text{ kg}$ in women; (3) gait speed less than 1.0m/s; (4) leg lean mass to fat mass ratio of >0.39 in men and >0.67 in women; (5) T-score of <-2.5 and a fall in the last year (Clynes et al., 2015).

A study used various definitions of sarcopenia to determine its prevalence within the sample of 298 individuals aged 70-82 years old. The prevalence of sarcopenia was

3.3% using the cut points defined by EWGSOP, 8.3% according to IWGS standards, and 2.0% with the FNIH cut points. Using cut points established by Binkley and colleagues (2013), about 24.8% of individuals had dysmobility syndrome. When determining the association between falls and fractures within the last year with a diagnosis of sarcopenia, only the IWGS cut points for sarcopenia are adequate for determining whether individuals are at risk for adverse musculoskeletal events (Clynes et al., 2015). Therefore, if sarcopenia is defined as an individual's increasing frailty and a decrease in physical performance, then future definitions of sarcopenia should reflect risks for such events as falls and fracture. In the same study by Clynes et al. (2015), the prevalence of sarcopenia increased with age only when defined by EWGSOP, IWGS, and dysmobility syndrome. Therefore, future definitions of sarcopenia should consider factors that reflect the increase in an age given that sarcopenia is known as an age-related condition.

Causes and Potential Components of Sarcopenia

While sarcopenia is related to aging, the causes of sarcopenia, in part and apart from aging, may include sedentary, altered endocrine function, chronic disease, inflammation, insulin resistance and nutritional deficiencies (Fielding, 2011). Further underlying these causes, mechanisms such as protein synthesis, proteolysis, neuromuscular integrity and muscle fat content may contribute to the onset and progression of sarcopenia. In the process of aging, a decline in anabolic hormones such as growth hormone and insulin-like growth factor, as well as declines of estrogen and testosterone are noted in both males and females. These declines may contribute significantly towards the onset of various diseases and ultimately in the decline of function (Ilich, 2016). In addition, components of sarcopenia may include cachexia,

frailty, sarcopenic obesity (Cruz-Jentoft et al., 2010), and osteoporosis (Binkley et al., 2013).

Cachexia.

Loss of skeletal muscle occurs in various ways. When due to aging it is typically referred to as sarcopenia, when due to inactivity it is referred to as atrophy, and when due to the disease it is referred to as cachexia (Evans, 2010). Cachexia does not have a universally established definition but is commonly described as severe wasting accompanying disease states. These may include but are not limited to cancer, immunodeficiency disease, infections, rheumatoid arthritis, congestive cardiomyopathy, and Crohn's disease. Individuals with cachexia may lose equal amounts of fat and fat-free mass with the fat-free mass mainly coming from skeletal muscle (Thomas, 2007). However, cachexia may also still be present without the loss of fat mass (Evans et al., 2008). While cachexia and sarcopenia both lead to a decrease in muscle mass, sarcopenia alone does not lead to decreased appetite or greater decrease of fat mass as seen commonly in Cachexia. Also, differing from sarcopenia, cachexia is highly associated with increased cytokines and inflammatory disease (Thomas, 2007).

Frailty.

Frailty largely influences various age-associated diseases. However, its definition and relationship to sarcopenia lack consensus. Development of frailty may be due to inflammatory processes, hormonal changes, and body composition, which are also seen in cachexia and sarcopenia. Furthermore, frailty may be defined as "a geriatric syndrome of decreased reserve and resistance to stressors, resulting from cumulative declines across multiple physiologic systems, causing vulnerability to adverse health outcomes including

falls, hospitalization, institutionalization and mortality” (Bauer, 2008). Frailty may be regarded as comprising of psychological and sociological components rather than a physical component alone (Bauer, 2008). Both sarcopenia and frailty have various clinical definitions causing prevalence rates to vary greatly depending on which methods and cutoff points are used. In a study by Reijnierse et al. (2016), the aim was to determine the presence of sarcopenia and frailty within a clinically relevant geriatric outpatient population. The prevalence of frailty was greater than the prevalence of sarcopenia even when using different definitions and cutoff points. When frailty was defined using physical criteria (weight loss, exhaustion, physical inactivity, absolute walk times, and handgrip strength) (Fried et al., 2001), there was more concordance with sarcopenia than when defined using measures of mobility, activities of daily living and incontinence, and cognitive impairment (Rockwood et al., 1999). In conclusion, while sarcopenia and frailty both have physical components, they are two separate conditions and therefore should be assessed separately.

Sarcopenic Obesity.

Sarcopenic obesity occurs when lean body mass is lost, but fat mass is preserved or increased (Cruz-Jentoft, 2010). The combination of both conditions has been thought to increase the risk for poor health outcomes compared to either condition alone (Scott et al., 2016). However, a lack of consensus on both definitions limits future research and ability to determine concordance. Newman et al. (2003) found that when classifications of sarcopenia contained measures of height and fat mass, there was a stronger association with lower extremity function limitations. Specifically, in women and overweight or obese individuals, this study confirms that fat mass should be considered when

determining the prevalence of sarcopenia. According to Chang et al. (2015), persons with sarcopenia or obesity had poor lower extremity physical performance than those without either condition. In the existence of both sarcopenia and obesity, they found a synergistic impact on performance and therefore higher risk for functional impairment. On the other hand, Dufour et al. (2013) found that the combination of low lean mass with high-fat mass may not result in additional risk from either alone. It has been shown that BMI is not correlated with knee extension strength suggesting that BMI is not an appropriate measurement of mass when determining functional ability (Yamada et al., 2016). Within older subjects, the fat mass may be a stronger predictor of health outcomes than skeletal muscle mass suggesting cutoff points for muscle indices should include measures of adiposity (Heymsfield et al., 2015). In addition, obesity and strength measures better estimate risk for adverse health outcomes than joint obesity and muscle mass. It is controversial that fat mass may have a protective effect against mortality in older individuals; however, when combined with low muscle strength, the risk of mortality may increase (Stenholm et al., 2008)

Research, while using different methods to define them, has consistently found mobility limitations in sarcopenic individuals as well as in individuals with increased fat mass. This suggests that both conditions should be considered when defining each individually and it may be important to determine a sarcopenic scale for increased risk when other conditions are included.

Osteoporosis.

Osteoporosis is an age-related decline in the quantity and quality of bone, which is similar adverse health outcomes as sarcopenia (Binkley et al., 2013). The origination of the term of osteoporosis began in the 1940's until the mid-1990 for the medical community to determine a medical definition of osteoporosis (Bijlsma et al., 2012). In 1994, after the use of dual-energy x-ray absorptiometry (DXA) became more popular in use, the World Health Organization (WHO) defined osteoporosis as a bone density by a T-score of <-2.5 . A T-score of -1 or more was defined as normal bone density (World Health Organization, 1994). These cutoff points were established based on sensitivity and specificity to determine the occurrence of fractures. However, a distinct clinical outcome parameter to define sarcopenia lacks consensus and therefore causes a delay in establishing diagnostic criteria (Bijlsma et al., 2012). In a sample of 70-80-year-old home-dwelling women, Patil et al. (2013) found that osteopenia (as defined by WHO) was more prevalent (36 %) than sarcopenia (0.9 % defined by EWGSOP and 2.7 % defined by IWGS). The low prevalence rates of sarcopenia are due to the inaccurate definition of sarcopenia.

Verschueren et al. (2013) found that in a sample of men with a mean age of 59.6, the prevalence of sarcopenia was 11.6% using the relative appendicular skeletal muscle mass (RASM) cut points ($<7.26 \text{ kg/m}^2$) plus low muscle function. Appendicular lean mass, RASM, and fat mass were all positively associated with bone mineral density (BMD). Men with sarcopenia were more likely to have osteoporosis than those with an RASM of $>7.26 \text{ kg/m}^2$. This is consistent with a study using the same criteria (with the addition of females with an RASM of $>5.45 \text{ kg/m}^2$) by He et al. (2016) where subjects

with sarcopenia were twice as likely to have osteoporosis compared to those considered non-sarcopenic. Within a four-year longitudinal study on 538 non-sarcopenic women over the age of 75 years, Kim et al. (2015) showed that a greater BMD had a protective effect against handgrip strength decline and reduced walking speed. These studies may suggest a causal relationship between muscle mass and BMD which leads to potential interventions to determine if maintenance of muscle mass may prevent osteoporosis. However, in the attempt to define sarcopenia, it should be determined whether the relationship is reflected in measures of functionality.

In consensus with Vershueren et al. (2013), He et al. (2016) found a positive association between BMD and lean mass and a negative association between BMD and fat mass. Furthermore, muscle function assessed by handgrip strength was also significantly associated with BMD at all skeletal sites. This study included subjects of both genders, aged 18 to 97 and of three diverse races (He et al., 2016). Another issue arises with the awareness and attention of sarcopenia within the medical community. As shown through the number of hits in MEDLINE databases, sarcopenia only has a fraction of the attention in literature as compared to the term osteoporosis (Bijlsma et al., 2012).

Osteosarcopenic Obesity.

Ilich et al. (2016) outlined a new syndrome, osteosarcopenic obesity, as a triad of bone, muscle, and adipose tissue impairment. Ilich et al. (2014) compared functionalities (handgrip strength, normal/brisk walking speed, and single leg stance) in 250 postmenopausal women after categorizing them within various combinations of sarcopenia, osteoporosis, and obesity. Persons diagnosed in the osteosarcopenic obese group indicated poorer functionality than any other group (osteopenic obesity and

sarcopenic obesity). Definitions of sarcopenia are beginning to factor in measures of functionality to reflect the various components associated with sarcopenia as well as real life scenarios. Both fat mass and bone density have been shown to contribute to functional capabilities (Chang et al., 2015; Newman et al., 2003; He et al., 2016) and therefore measures of such should be considered within the spectrum of sarcopenia.

Environmental Influences

While sarcopenia has been regarded as a condition that occurs with aging, it is also understood that its pathology may include various mechanisms. Within the multifactorial underlies of sarcopenia, there may exist preventable outcomes. However, it is necessary to determine the pathway of which these factors influence sarcopenia. Zeng et al. (2016) found that factors such as nutrition, physical activity (PA), exercise, alcohol, and tobacco may influence muscle strength and performance. Within a group of 1008 men and women in Taiwan, sarcopenia was significantly related to poor nutrition status using the Mini-Nutrition Assessment. In the same population, the females who were sarcopenia had higher cigarette smoking rates, but no significant difference in habitual alcohol consumption (Liu et al., 2014). In summary, the role and potentially synergistic effects of lifestyle factors must be considered when defining sarcopenia.

Prevalence of Sarcopenia

According to EWGSOP, sarcopenia affects more the 50 million people worldwide (Cruz-Jentoft et al., 2016). For those aged 60-70 years old, it is estimated that 5-13% are sarcopenic which then increases to 11-50% for individuals aged 80 and older (Haehling et al., 2010). However, the prevalence is dependent upon the definition and cutoff points used and given that various definitions are in current use, which is difficult to compare

data and determine exact prevalence of sarcopenia. Therefore, it important to come to a consensual definition that will allow unity diagnoses and lead to further abilities to determine interventions.

Rates of sarcopenia may also differ depending on the inclusion of other components. In subjects who are overweight or obese (using BMI measurements), the prevalence of sarcopenia varies between definitions and gender. When using the lowest 20th percentile of residuals for LM and adjusting for height and fat mass, the prevalence of sarcopenia within the overweight (15.4% in males and 21.7% in women) and obese (11.5% for in men and 21% in women) groups were greater than when using aLM/ht^2 to define sarcopenia. Both criteria resulted in significantly different prevalence rates between genders (Newman et al., 2003).

Methods of Measure

With the definition of sarcopenia still in disagreement, studies up to date have used various measurements, combinations of measures, and methods to create cut off points for sarcopenia. The measurement methods to define sarcopenia are summarized in Table 1.

Table 1: Measurement Methods of Sarcopenia.

<u>Measurement</u>	<u>Sub-Measurements</u>	<u>Methods</u>
Anthropometry	Circumference, height (HT), weight (WT)	Scale, tape measure
Arterial stiffness	Pulse wave velocity (PWV), pulse wave analysis (PWA), blood pressure (BP), central blood pressure (CBP), augmentation index (AI)	SphygmoCor XCEL System
Body Composition	Fat mass (FM), fat-free mass (FFM), bone mineral density (BMD)	Bioelectrical impedance analysis (BIA), computerized tomography (CT), dual-energy X-ray absorptiometry (DEXA), magnetic resonance imaging (MRI)
Incidents	Fall frequency, fall likelihood	Survey
Muscular Strength/Power	Single-multiple repetition max, hand strength, isokinetic torque	Isokinetic, isotonic or isometric performances; hand dynamometer
Muscle Quality	Muscle size, fiber type, contractile characteristics, muscular aerobic capacity, intramuscular adipose tissue, muscle fibrosis, motor units, neuromuscular adaptation,	Muscle biopsy
Performance	Time	Gait speed (GS), stand up and go tests (TUG), chair sit-to-stand test (SST)

Sarcopenia as it Relates to Mortality

In a meta-analysis by Chang and Lin (2016), ten studies were evaluated for the association between sarcopenia and mortality rates. After following an average of 4.2 years (N = 3,797), the sarcopenic group had 1.9 times the risk for mortality than did the non-sarcopenic group. According to Landi et al. (2013), about 21.8% of subjects (aged 80-85 years) were sarcopenia using the EWGSOP criteria. After following an average of 7 years, about 67.4% of the sarcopenic subjects had died compared to only 41.4% of those who were not considered sarcopenic. According to the British Regional Heart Study (Atkins et al., 2014), both sarcopenia and obesity were associated with all-cause mortality and CVD mortality while subjects who had both conditions were at greatest risk for all-cause mortality. Increased CVD mortality may be explained by increased inflammation. However, when FM and FFM (using BIA) measurements adjusted for height were used to define sarcopenia, the difference between risk outcomes between the sarcopenic, obese, and sarcopenic obesity groups was no longer significant (Atkins et al., 2014). While previous studies confirm the effectiveness of using anthropometric measures of muscle over BIA measures (Stephen et al., 2009; Wannamethee et al., 2007), there is less research examining the relationship of mortality rates and sarcopenia when defined by muscle quality. Also, measures of FM and FFM can be more accurately measures through methods such as a DXA rather than BIA which can be influenced greatly by hydration levels.

Independent of disease and body weight, the mortality rate is associated with muscle strength in healthy men aged 45-68 (Rantanen et al., 2000). After a follow-up of 30 years, handgrip strength had a linear and inverse relationship with mortality rates with

minimal effect by BMI. On the other hand, when BMI was split into tertiles, increased handgrip strength was still found to have an effect on decreasing mortality risk (Rantanen et al., 2000). In another study with participants aged 70-79 years old (Newman et al., 2006), knee extension strength and handgrip strength were independent predictors of mortality, but not for lower lean mass as assessed via DXA (Newman et al., 2006). Frailty has also been shown to be a predictor of mortality; as frailty index increases, the mortality rates also increase (Tang et al., 2013).

Sarcopenia and Disease

Studies up to date have frequently focused on the association between diseases and frailty. Frailty has already been addressed as a component of sarcopenia allowing researchers to begin to understand the relationship between various disease states and sarcopenia. The presence of a cardiometabolic disorder increases an individual's frailty index and continues to increase with the addition of more cardiometabolic disorders. This suggests that the combination of cardiometabolic disorders as well as other health deficits have a synergistic effect upon frailty (Tang et al., 2013). In this section, various diseases that are related to aging will be examined as well as their correlation to sarcopenia and frailty.

Heart Disease.

Heart disease is the number one cause of death in the United States (AHA, 2017). In 2014, about 10.9% of adults were predicted to have a type of heart disease. For adults aged 65-74, the percentage increased to 24.6 and then to 35% for those older than 75 years. In the same survey with adults aged 65-74 years, the prevalence of hypertension, CHD, and stroke were 54.6%, 15.4%, and 5.4% (CDC, 2014). In a sample of Japanese,

non-sarcopenic women aged 75 and older, persons with a history of heart disease and hyperlipidemia resulted in a significantly greater risk of skeletal muscle index (mass/height²) decline, making them appropriate predictors of sarcopenia when defined by EWGSOP (Kim et al., 2015). In a study of men aged 60-79 years, Atkins et al. (2014) found that sarcopenia and sarcopenic obesity were not significantly associated with greater risk of CHD events or CVD events after adjustment for lifestyle factors. However, this study only used measures of mid-arm muscle circumference and, alternatively, BIA to determine FM and FFM to define sarcopenia. It may be possible that measures of mass are not suitable for determining risk for heart disease.

Cancer.

In 2014 it was estimated that about 19.8% of adults aged 65-74 years had cancer of any type. For adults aged 75 or greater, the prevalence increased to 28% (CDC, 2014). Sarcopenia may serve as a useful independent prognostic predictor of surgical outcomes (Jogleker, 2014). However, research on cancer surgery should focus on measures of sarcopenia that reflect muscle function rather than muscle mass alone (Vildan, 2015). Sarcopenia is common in Non-Small Cell Lung Cancer (NSCLC). Using skeletal muscle mass measures, the prevalence of sarcopenia is present in all BMI categories (Baracos et al., 2010). However cross-sectional measurements of the psoas muscle measured by CT did not correlate significantly with poorer survival rates from NSCLC. The median survival rate of non-sarcopenic patients was 14 months, and sarcopenic patients were 12 months ($p = 0.22$) (Phillips et al., 2016). In a study by Srdic et al. (2016) subjects included 100 Caucasian patients with NSCLC stage IIIB or IV. Sarcopenia was determined using CT to measure lumbar skeletal muscle index (total muscle cross-

sectional area at L3 divided by height squared). Time to tumor progression was not significantly different between patients with and without sarcopenia. In a study of 471 breast cancer patients, 75 were classified as sarcopenia (two SD below young healthy adult mean of aLM/ht²). After a mean follow-up of 9.2 years, sarcopenia was independently associated with all-cause mortality and women with sarcopenia had a greater risk of breast cancer-specific mortality. However this association was not significant (Villasenor et al., 2012). Muscle mass seems to be a common method in current research examining the association of cancer and sarcopenia. The association of cancer with sarcopenia using measurements of muscle quality, strength, and function are less known and should be further investigated. Associations with various types of cancer should also be examined.

Diabetes.

As of 2012, it was estimated that about 9.3% of the population had diabetes and the prevalence increases to 25.9% in old people ages 65 or more (CDC.gov, 2012). In a study of Korean patients, those with diabetes mellitus had a threefold increase in risk for sarcopenia (Kim et al., 2010). Kim et al. (2014) found that the muscle quality in adults (aged 65 years or older), calculated as the total skeletal mass divided by weight, was significantly lower in both male and female subjects with diabetes. Type II diabetic patients had about a two to fourfold greater risk of low muscle mass compared with non-diabetic patients adjusted for age, BMI, and current smokers. Older males with Type II diabetes showed an accelerated decline in leg lean mass compared to their normoglycemic counterparts (Leenders et al., 2013). Within the same study, the diabetic group also had decreased appendicular skeletal mass, leg extension strength and

decreased performance as measured in slower sit-to-stand test times). Various studies have observed decreases in handgrip strength (Sayer et al., 2007), gait speed (Volpato et al., 2012), and quadriceps power (Kalyani et al., 2013) in elder individuals with diabetes. However, Ohara et al. (2014) found that antidyslipidemic drug and antidiabetic drug were both significantly associated with lower handgrip strength in a sample of middle- age to older participants, which indicates an importance of controlling for medications for confounding factors. Sarcopenia has been shown to be an independent risk factor for diabetes but only in participants older than 74 years (Koo et al., 2016). In summary, diabetes may have a strong correlation with muscle mass, strength, function, power, and quality; all of which have been shown to be components of sarcopenia.

Sarcopenia and Muscle Quality

Rather than muscle strength or muscle mass, muscle quality is representative of the muscle's ability to function. This can be measured through force production, muscle composition, and most specifically the contractile element: the sarcomere. In research, muscle quality is defined as muscle strength (determined through performance test) normalized by muscle mass (determined most accurately through DXA) (Fragala, Kenny, & Kuchel, 2015).

Within a sample of 1880 adults (aged 70 to 79), consisting of men and women of both white and African American races, muscle strength, mass, and quality were assessed over three years. A significant decline in muscle quality, strength (Nm)/ muscle mass (kg), was observed, and a significant loss of strength was noted in subjects even when lean mass was maintained or gained (Goodpaster et al., 2006). This study confirms that

muscle quality should be considered when determining loss of function due to aging and therefore when defining sarcopenia.

Kennis et al. (2014) assessed changes in the muscles of middle-aged men aged 45-49 years at baseline and at a 9.45-year follow-up. After follow-up, there was an increase in muscle mass but a significant decrease in strength and power assessments. During aging, the decline of muscle quality can be attributed to various factors. A contributor may include increased extracellular water in skeletal muscle. In a study of elderly adults (60-95 years olds), extracellular water/intracellular water was significantly and negatively correlated with knee extension strength and GS. Extracellular water in skeletal muscle increased with age (Yamada et al., 2016). Other dimensions of muscle quality may include muscle composition, architecture, ultrastructure, and sarcomeres (Fragala, Kenny & Kuchel, 2015).

The prevalence of sarcopenia increases with aging. Sarcopenia is also associated with multiple adverse outcomes. Therefore, developing ideal prevention programs for sarcopenia is important to promote public health in the geriatric societies. However, it is first necessary to develop an acceptable definition of sarcopenia as a tool to screen sarcopenia across individual, community, and state levels. While most definitions to date have used measures of muscle mass, muscle quality is beginning to be recognized as a more appropriate measure to reflect functional decline with age. Current research investigating muscle quality decline have used longitudinal study designs including only middle-aged to elderly subjects. No research to date has investigated the difference between healthy young adults and elderly adults. While it is expected that elderly adults will have a significantly lower muscle quality, it is important to investigate this

relationship to set norms and establish a new sarcopenic index that includes measures of muscle quality.

Sarcopenia and Muscle Mass and Strength

In adulthood, skeletal muscle mass makes up about 45% of the body weight. This number then declines to about 27% during the elderly stage (Robert et al., 2001). Initial definitions of sarcopenia have focused on this loss of muscle mass as it was considered to be a determinate of strength loss in aging. Within older adults decreases in muscle mass are associated with decreases in strength. However, the decline in strength and performance occurs at a more rapid rate than muscle mass (Goodpaster et al., 2006; Zeng et al., 2016). This occurrence may be due to a decrease in type II muscle fibers during aging (Nilwik et al., 2013), approximately 43% reduction in the type II fiber size, and a decline in muscle fibers as well as fiber atrophy (Anderson, 2002). While decreases in strength and CSA due to aging are noted in various studies, Walter et al. (2008) examined how individual skeletal muscle fibers that are preserved throughout aging maintain force capacity to accommodate for decreases in strength and CSA.

In a sample of home-dwelling women (aged 70-80 years), Patil et al. (2013) assessed the associations of sarcopenia diagnostic criteria and osteopenia relevance with functional ability. In this study, osteopenia (as defined by WHO) was more prevalent (36%) than sarcopenia (0.9% defined by EWGSOP and 2.7% defined by IWGS). Individuals with a low skeletal muscle index had a higher lean mass percentage, lower fat mass percentage but showed no significant differences in age or outcome measures of gait speed and handgrip strength from those with a high skeletal muscle index. Also, women with a faster gait speed had lower body weight, lower fat mass percentage, higher

total body lean mass, and performed better on the get up and go (TUG) test, chair stand test and leg extension force (Patil et al., 2013). Akin et al. (2015) found that when GS and handgrip strength were used to define sarcopenia, it resulted in a greater prevalence rate than when using measures of muscle mass. Visser et al. (2000) examined the associations of the muscle mass, performance, and muscle strength in the lower body. In conclusion, leg muscle mass was not an independent determinant of lower-extremity performance after adjustment for body fat and leg muscle strength, suggesting that leg muscle strength may act as a mediator between muscle mass and performance.

Muscle Quality, Muscle Mass, and Muscle Strength

Zeng et al. (2016) evaluated factors associated with sarcopenia and their correlation with strength and physical performance within a young group (aged 20-59 years) and older group (aged >59 years). There was a significant difference in GS, handgrip strength and repeated chair sit-to-stand times between both groups. Interestingly, GS significantly correlated with handgrip strength and chair sit-to-stand times only within the older group. These studies conclude that greater focus should be allocated to declining functional ability rather than solely on decreases in muscle mass when assessing sarcopenia.

Lean mass has consistently been shown to significantly correlate with strength (Newman et al., 2013). Specifically, Chen et al. (2013) found this correlation in individuals aged 50 and older using measures of appendicular skeletal muscle mass and isokinetic quadriceps strength. This relationship, however, was significantly modified by obesity. Reed et al. (1991) also found a significant correlation between muscle mass and muscle strength in older adults (mean age = 71.7 years). They also examined a significant

age and lean body mass effect to muscle quality noting a decline with increasing age and increasing lean body mass. The relationship between muscle mass and strength differs according to gender and age (Hayashida et al., 2014). When looking at the association between quality, mass, and strength of muscle, quality has been shown to have a stronger association with strength measures than measures of muscle mass (Ismail et al., 2015). Strength has also been shown to have stronger correlations with measures of physical function (Hayashida et al., 2014) than did muscle mass, showing a possible synergistic effect of fat mass and leg strength (Bouchard et al., 2011). These studies conclude that mass alone does not have a strong correlation towards declining functional ability and therefore may not be predictive of muscle quality decline with age.

Sarcopenia and Arterial Health

Atherosclerosis is another leading cause of morbidity and mortality in elderly people and is associated with various other diseases. As arteries become stiff, the PWV increases causing the reflecting wave from the heart to return sooner. It also increases central systolic pressure and central pulse pressure (AtCore Medical, 2013). Higher baseline arterial stiffness can be predictive of later development of incident hypertension (Kaess et al., 2012).

In the study by Ohara et al. (2014), 1593 middle-aged to older patients were classified as sarcopenic if their handgrip strength or skeletal muscle mass (as measured via BIA) was more than 1 standard deviation from the mean of the reference group (age less than 50 years) or the lowest 20% of the measured population. Measures of central pulse pressure (PP), radial augmentation index (AI), and arterial stiffness (as measured by brachial to ankle pulse wave velocity (baPWV)) were all significantly and independently

associated with sarcopenia when defined by either criterion. Ohara et al. (2014) found that thigh muscle CSA was significantly and negatively associated with radial AI and radial PP in both genders. Also, thigh CSA correlated significantly and independently with central BP in both genders and with baPWV in only males. In a group of 496 healthy middle-aged to elderly subjects, thigh muscle CSA corrected for body weight (CSA/BW) was an independent determinant of baPWV, BP, age, and antihypertensive drug use. In men, baPWV was an independent risk for the presence of sarcopenia (Ochi et al., 2010). In other studies, a significant relationship between artery stiffness and muscular strength has also been measured; however, the relationship only occurred with central measures and not peripheral measures (Fahs et al., 2010). Central BP may be a better predictor of CVD than brachial pressure because it better reflects arterial stiffness and wave reflections (Roman, et al., 2009).

In a sample of 427 Korean individuals aged 52-95 years, men had a significantly greater arm and leg skeletal muscle mass (measured using BIA), and thigh circumference than the females in the study. On the other hand, females had significantly greater radial AI, central SBP, and TUG test time. There was a significant and inverse relationship between limb muscle mass and AI with a greater association found in males.

Interestingly, the association only remained in males when adjusted for body mass index, systolic blood pressure, total cholesterol, high-density-lipoprotein-cholesterol, fasting glucose, insulin, smoking, and alcohol intake. There was no significant relationship between arm muscle mass and AI or limb muscle mass and brachial BP (Lee et al., 2014).

Studies have also evaluated other measures of muscle and their associations with measures of arterial stiffness. Muscle mass volume calculated as thigh mass area divided

by the femoral shaft area (TMA/FSA) has been shown to be inversely related with baPWV in diabetic, hemodynamic patients (Kato et al., 2011). Relative upper body strength measured by 1RM bench press divided by weight was also found to be inversely associated with PWV and AI. Interestingly, in this study, VO_{2peak} was found not to alter the association of muscle strength and arterial stiffness suggesting that they are related independent of fitness (Fahs et al., 2010). In addition, visceral obesity (defined as a visceral fat area of greater than 100cm^2) was significantly associated with higher baPWV while the combination of both sarcopenia and obesity was associated with a significantly greater increase in baPWV and radial AI than either condition alone (Ohara et al., 2014).

Abbatelcola et al. (2012) found that baseline PWV is associated with the sarcopenic index (aLM/ht^2) over time in adults aged 70-79 years. Alternatively, measures of physical activity (questionnaire), physical performance (walking, chair-stand, and balance tests), and handgrip strength measured at baseline were not associated with arterial stiffness measurements taken two years later (Van Dijk et al., 2015). These studies show that PWV may be a determinate of sarcopenia (using measures of mass), but there may not be a long-term effect of physical fitness activity and muscle strength on arterial health.

Studies have consistently shown the association between arterial stiffness and skeletal muscle when using measures of mass and strength. Therefore, PWV may be an appropriate option for assessing sarcopenia. However, muscle quality may be a more relevant and appropriate measure for sarcopenia than muscle mass or strength alone (Barbat-Artigas et al., 2012). Therefore, when evaluating associations between arterial stiffness and sarcopenia, measures of muscle quality should be considered.

Summary

Increasing life expectancy and the decline of physical function with age make it important for current research to explore the mechanisms contributing to this decline. The role of skeletal muscle has been shown to correlate with adverse health outcomes including physical disability, various components of frailty, and mortality. Research up to date has been limited to studies examining the role of muscle mass and strength. It has been established that strength is a better correlate to function than muscle mass yet research lacks in whether the quality of muscle may be an even better measure to represent function decline with age. Furthermore, research has yet to examine the difference in muscle quality, mass, and strength among young healthy adults and elderly adults. This study aims to add this data to the current research and serve as a preliminary study for establishing indices of muscle quality to define sarcopenia.

CHAPTER 3

METHODS

Subjects

Participants for this study were recruited via fliers, online posts, and University announcements within the Downtown Phoenix area. Seventy-one total subjects were recruited for this study within age groups 20-29 years old (20 females and 20 males) and 60-80 years old (18 females and 13 males). Eligibility was determined using an online questionnaire and PAR-Q. Eligibility criteria included the ability to perform physical activity without chest pain or feelings of dizziness, or any other reasons given by a medical professional and no joint or bone problem that could be made worse through physical activity. For young participants (aged 20-29), we recruited healthy subjects who had no personal history of chronic diseases and not taking any hypoglycemic and hypertensive medications. For old participants (aged 60-80), we included those subjects with chronic diseases to increase recruitment and to examine possible associations between different disease states and sarcopenia. All procedures were approved by the Arizona State University Institutional Review Board and written informed consent was obtained from subjects prior to participation. All participants were given a detailed description of the protocol prior to their participation.

Research Design

All eligible participants were required to schedule a single visit to the ASU Arizona Biomedical Collaborative building that lasted approximately two hours. All participants signed an informed consent and completed demographic characteristics, medical histories, and personal health habit questionnaire. Body height and weight were

measured using a standardized physician's scale. Waist girth was measured using a plastic tape measure with a metal spring on end to maintain consistent tension. The measurement was taken at the midpoint between the anterior superior iliac crest and the lowest lateral portion of the ribs. Dual-energy X-ray absorptiometry (DXA) was used to measure body composition, bone mineral density (BMD), and arm and leg appendicular skeletal muscle mass by a licensed technician (Lunar iDXA, GE Healthcare, Madison, WI). Participants were required not to wear any metal during the scan. The scan took the duration of approximately seven minutes with the subject lying face up on the table. Results were not shared with the participant until the individual's data collection was complete.

Pulse Wave Velocity Measurement.

All participants completed PWV assessment. The participant was then instructed to lie supine on a padded table in a quiet dimly lit room. A standardized physician's sphygmomanometer was used to measure left arm brachial BP and HR at 0 minutes and 10 minutes after lying down. Once the second measure was taken, the researcher then applied a different brachial arm cuff (appropriately sized to the individual subject without clothing between cuff and arm) as part of the SphygmoCor XCEL System, which was used to run a Pulse Wave Analysis (PWA) and measure Pulse Wave Velocity (PWV). At the fifteen-minute mark, the PWA was initialized, and the subject was instructed to remain still without talking for the duration of the cuff inflation, deflation, and partial inflation. The AtCore Medical program measured BP, calculated Augmentation Pressure (AP) as the incident pressure waveform during systole subtracted from the reflected wave and calculated Augmentation Index (AIx) by dividing the Pulse Pressure (PP) from the

AP (AtCore Medical, 2013). This was repeated three times with two minutes between each measure. The brachial cuff was then removed, and an appropriate sized femoral cuff was placed on the upper left thigh. The researcher palpated for the strongest carotid pulse and made a small mark on the skin and then palpated for the strongest femoral pulse. Measurements were taken from the suprasternal notch to the mark at the carotid site, suprasternal notch to the top of the femoral cuff, and from the femoral pulse to the top of the femoral cuff. Applanation tonometry is used by the researcher, placed in the carotid artery, to record pressure waveforms. The subject was instructed to remain still without talking for the duration of the test. When regular carotid pulse was detected, the femoral cuff inflated and remained inflated until quality waveforms were simultaneously acquired for 10 seconds at both sites. Carotid and femoral artery waveforms and pulse wave time between the carotid and femoral arteries were measured. PWV was computed as the distance (D) between the carotid and femoral arteries divided by the time difference (Δt) between the two sites ($PWV=D/\Delta t$) (AtCore Medical, 2013). Once again, results were not shared with the participant until the individual's data collection was complete.

Dynamometer Test.

The CSMI HUMAC NORM Isokinetic Dynamometer was used to measure knee flexion and extension torque. The chair and dynamometer settings were adjusted specifically for the test and for each individual participant. The seat belt and straps across the dominate thigh and lower leg were all tightened to allow minimal movement without discomfort to the subject. Knee ROM was then set by moving the leg to full extension and flexion specific to each individual. The protocol consisted of 4 sets: a practice set of two repetitions, one set of three repetitions at 120 degrees per second, one set of three

repetitions at 90 degrees per second, and one set of three isometric (0 degrees per second) knee extensions at an angle of 60 degrees. There was an allotted 30 seconds of rest between each set and between the isometric extension repetitions. Prior to beginning the test, subjects were given a detailed explanation to move through full ROM (excluding the isometric contractions) with the maximal effort for each repetition. Subjects were cheered on and motivated to try their best. *Leg MQI* was calculated as the mass of the right leg in kg (as measured by DXA) divided by the average of the two highest knee isometric extension force productions in Nm (kg/Nm) (Fragala et al., 2015).

Handgrip Test.

Handgrip strength was measured using Takei Physical Fitness Test dynamometer. The dominant hand was measured with the subject standing and their arm at a position parallel to the floor. *Arm MQI* was calculated as the mass of the right arm in kg divided by the average of the two measured handgrip strengths in kg (kg) (Fragala et al., 2015).

Gait Speed Measurement.

Gait speed was measured over a 5-meter distance that was taped out on the floor. The subject began on the first line and once given a pre-discussed cue they were instructed to begin walking as fast as they can pass the second line. The researcher began the time on the stopwatch at the queue and stopped once the participant reached the second line (Hardy et al., 2007). The times were converted into meters per second (m/s), and the fastest of the two trials was used for data analysis.

Sit-to-Stand Test.

The five times sit-to-stand-test (SST) was used to assess functionality and lower muscular power. The subjects were instructed to sit in the standard armless chair (not

secured to the wall or the ground) as far back as possible with maintaining feet contact on the floor and arms across their chest. The participant was instructed to stand up fully and sit back down five times as quickly as possible. The same test procedure as the walk test was given to initiate the test and the timer. The researcher stopped the time when the buttocks touched the chair after the fifth repetition. A practice trial was allowed (Lambert et al., 2013). Times for the walk test and SST were given to the participant after each trial to help increase motivation and the fastest time of the two trials was used for data analysis. The researcher also provided verbal encouragement during all strength and performance tests.

Statistical Analysis

Descriptive statistics were computed as means and standard deviations. The normality assumptions for all outcome measures were justified by Shapiro-Wilk tests. General linear models were used to test mean differences for MQIs, muscle mass, muscle strength, and pulse wave velocity across gender and young and elderly adults. Age-, sex-, and race-adjusted partial Pearson correlations were used to examine the associations of muscle quality, muscle strength, and muscle mass in young and elderly adults, respectively. All statistical procedures were performed by Statistical Analysis Systems software (SAS Institute). All statistical significance will be determined by $p < 0.005$.

CHAPTER 4

RESULTS

Subject Characteristics

Seventy-one volunteers who responded and completed the online survey were determined eligible for the study. Each person came into the laboratory for a one time visit. The healthy young adults consisted of 20 males and 20 females (ages 20-29 years). The elderly group consisted of 13 males and 18 females (ages 60-80 years). Descriptive statistics for the study participants across gender and age categories are presented in Table 2.

*Table 2. Characteristics of the study participants across gender and age categories**

	Young Males		Elderly Males		p-value	Young Females		Elderly Females		p-value
n	20		13			20		18		
Age	23.6 ± 2.2		70.8 ± 4.4		<.0001	22.7 ± 2.2		67.8 ± 4.8		<.0001
Ht (cm)	180 ± 6.5		172.9 ± 5.7		0.0032	165.7 ± 6.3		161.7 ± 5.2		0.0433
Wt (kg)	82.8 ± 9.4		86.5 ± 17.1		0.4265	61.2 ± 8.3		74.8 ± 22.2		0.0150
BMI	25.5 ± 2.1		28.9 ± 5.5		0.0168	22.2 ± 2.5		28.5 ± 8.1		0.0022
gait speed (m/s)	2.2 ± 0.3		1.9 ± 0.2		0.0008	2.0 ± 0.3		1.7 ± 0.3		0.0007
Sit to Stand (sec)	6.7 ± 1.4		9.2 ± 1.6		<.0001	7.4 ± 1.6		10.2 ± 3.8		0.0045
SBP (mmHg)	123.4 ± 8.0		132.0 ± 17.2		0.0618	110.6 ± 8.8		127.5 ± 12.6		<.0001
DBP (mmHg)	70.2 ± 5.9		76.2 ± 7.2		0.0132	66.0 ± 6.2		75.9 ± 7.5		<.0001
AP	0.8 ± 3.0		12.0 ± 7.5		<.0001	1.5 ± 3.9		13.0 ± 5.1		<.0001
AIX	-3.7 ± 9.8		22.0 ± 13.1		<.0001	-1.4 ± 12.0		28.7 ± 9.9		<.0001
PWV (m/s)	5.7 ± 0.6		9.0 ± 2.2		<.0001	5.1 ± 0.7		8.1 ± 1.1		<.0001
VIS (cm ³)	357.9 ± 261.9		2263.3 ± 1416.0		<.0001	118.9 ± 178.9		1485.8 ± 1127.8		<.0001
grip (kg)	54.5 ± 8.9		41.9 ± 7.1		0.0002	32.4 ± 6.7		25.0 ± 4.2		0.0003
RA lean (kg)	4.7 ± 0.7		3.5 ± 0.6		<.0001	2.4 ± 0.4		2.1 ± 0.5		0.0311
MQI Arm (kg)	11.6 ± 1.6		12.2 ± 2.5		0.398	13.4 ± 1.8		12.2 ± 2.7		0.1064
leg strength (Nm)	234.3 ± 38.4		141.5 ± 31.3		<.0001	150.2 ± 39.9		99.8 ± 25.6		<.0001
RL lean (kg)	10.87 ± 1.4		8.9 ± 1.5		0.0004	7.0 ± 1.1		6.7 ± 1.5		0.3819
MQI Leg (Nm/kg)	21.8 ± 4.3		16.3 ± 4.2		0.0012	21.3 ± 4.9		15.6 ± 4.8		0.0009

Note. *Values are expressed as M±SD; BMI is calculated as weight in kg divided by height in meters squared; SBP = systolic blood pressure (mmHg); DBP=diastolic blood pressure (mmHg); AP = augmentation pressure calculated as incident pressure waveform during systole subtracted from the reflected wave; AIX = augmentation index is calculated as AP/ pulse pressure); PWV = pulse wave velocity computed as the distance (D) between the carotid and femoral arteries divided by the time difference (Δt) between the two sites; VIS = visceral fat area (cm³); RA lean = right arm lean mass as computed by DXA (kg); MQI Arm = muscle quality of the arm calculated as the handgrip strength divided by RA lean; leg strength is determined by isometric knee extensor performance on the dynamometer (Nm); RL lean = right leg lean mass as computed by DXA (kg); MQI Leg = muscle quality index of the leg calculated as the leg isometric strength divided by RL lean.

Muscle Quality Index

There was no statistical gender difference in *leg MQI* across young (21.8 Nm/kg vs. 21.3 Nm/kg, $p = 0.51$) and elderly (16.3 Nm/kg vs. 15.6 Nm/kg, $p = 0.50$) adults (Figure 1). However, there was a significant statistical difference in *leg MQI* between young and elderly adults. As shown in Figure 2, young male adults had a greater *leg MQI* as compared with elderly male adults (21.8 Nm/kg vs. 16.3 Nm/kg, $p = 0.001$). Young female adults also had a greater *leg MQI* when compared with elderly female adults (21.3 Nm/kg and 15.6 Nm/kg, $p < 0.001$) (Figure 2). For *arm MQI*, as shown in Figure 3, there was significant gender difference in young adults (11.6 kg/kg and 13.4 kg/kg, $p = 0.001$), but not for the elderly adults (12.2 kg/kg and 12.2 kg/kg, $p = 0.53$). There were no statistical differences in *arm MQI* between young and elderly men and women, respectively ($p > 0.10$) (Figure 4).

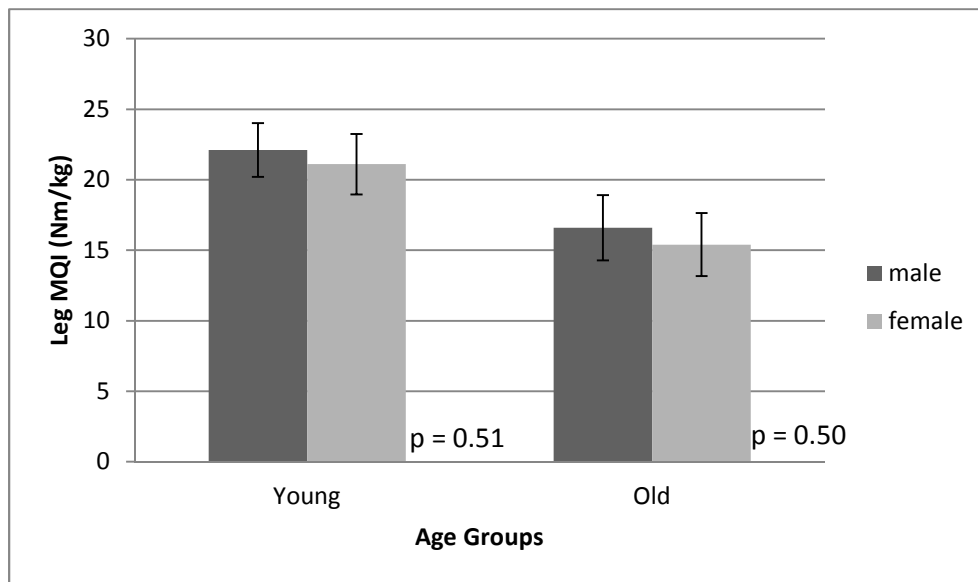


Figure 1: Average leg MQI difference by gender. Bars, 95% confidence interval.

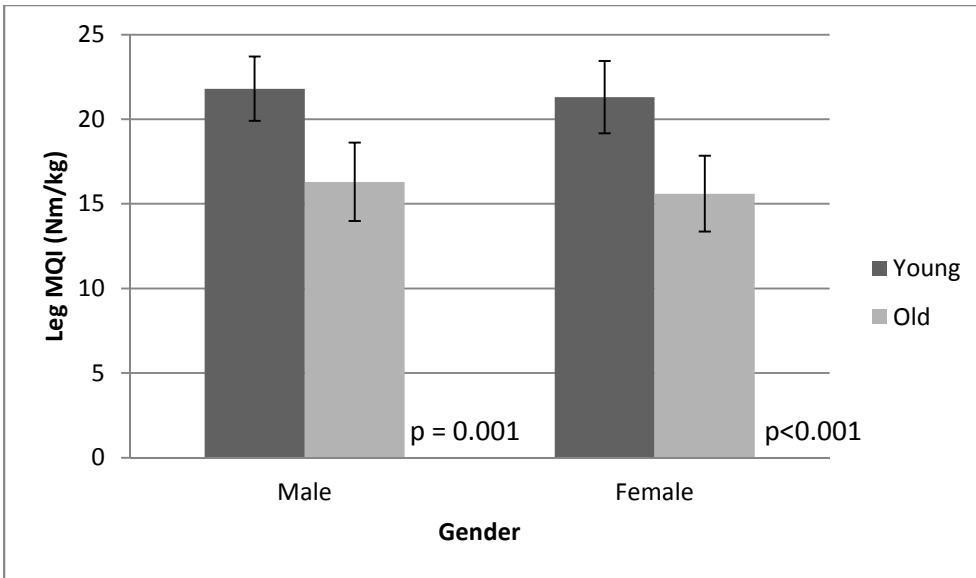


Figure 2: Average leg MQI difference by age groups. Bars, 95% confidence interval.

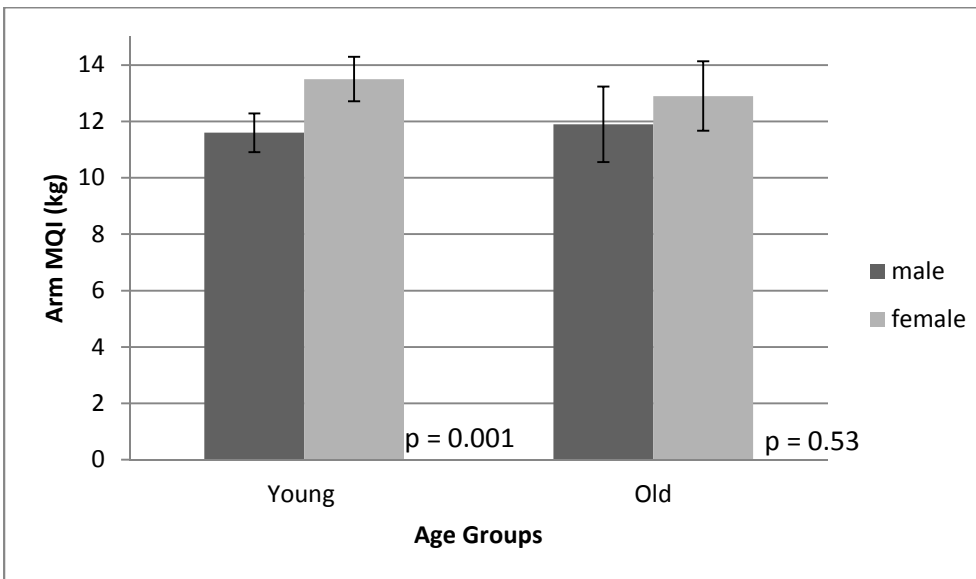


Figure 3: Average arm MQI difference by gender. Bars, 95% confidence interval.

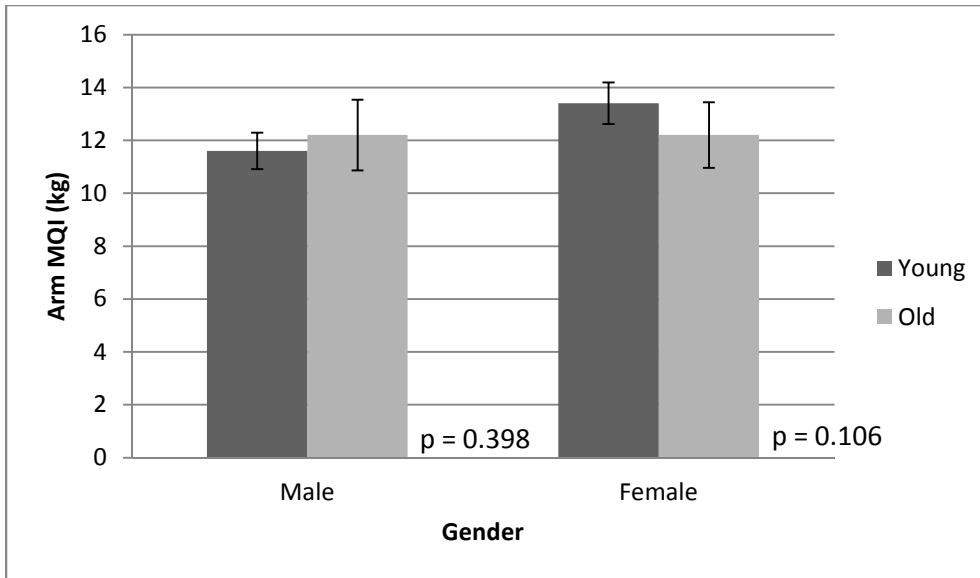


Figure 4: Average arm MQI difference by age groups. Bars, 95% confidence interval.

Lean and Fat Mass

As shown in Figure 5, there was a significant gender difference in leg lean mass (right) in young and elderly adults. Young males had greater leg lean mass as compared with young female counterparts (10.7 kg vs. 7.2 kg, $p < 0.001$) (Figure 5). Elderly males also had greater leg lean mass than did elderly females (9 kg vs. 6.6 kg, $p < 0.001$). Younger males had greater leg lean mass than did elderly males (10.9 kg vs. 8.9 kg, $p < 0.001$), but there was no statistical difference in leg lean mass in young and elderly females (7.0 vs. 6.7 kg, $p = 0.38$) (Figure 6). Figure 7 shows average arm lean mass by gender groups. Young males had greater arm lean mass (right, kg) when compared with young female adults (4.7 kg vs. 2.5 kg, $p < 0.001$). As shown in Figure 7, elderly males also had greater arm lean mass than did elderly females (3.6 kg vs. 2.1 kg, $p < 0.001$). Both young males and females had greater arm lean mass than did elderly male and female adults (all $p < 0.04$) (Figure 8) (males: 4.7 kg vs. 3.5 kg, $p < 0.001$; females: 2.4 kg vs. 2.1

kg, $p = 0.03$).

There was a significant gender difference in total fat in both young and elderly adults, respectively. Young females had a greater fat mass than did young males (27.9kg vs. 18.4kg, $p < 0.001$); Elderly females also had a greater fat mass than did elderly male adults (44.4kg vs. 34.7kg, $p < 0.001$). However, young males had a greater visceral fat compared with young females (357.3 cm^3 vs. 119.4 cm^3 , $p = 0.003$) (Figure 9). Although elderly males had a greater visceral fat when compared with elderly females, there was no statistical difference (2331.7 cm^3 vs. 1436.4 cm^3 , $p = 0.075$). Both elderly male and female adults had greater visceral fat than did young male and female counterparts, respectively (all $p < 0.001$) (Figure 10). Males had greater BMD than did females across young and elderly age categories (all $p < 0.001$).

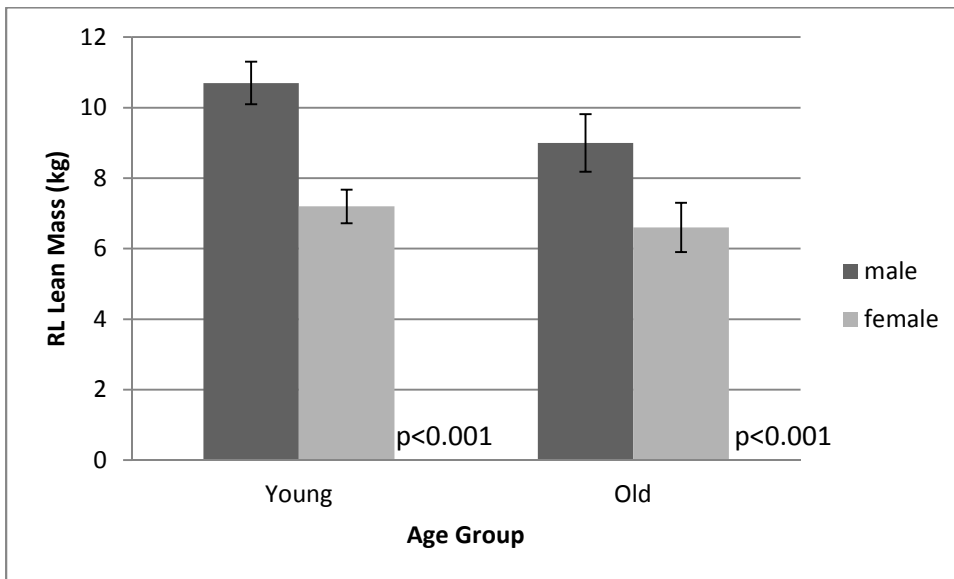


Figure 5: Average leg lean mass (right, kg) by gender. Bars, 95% confidence interval.

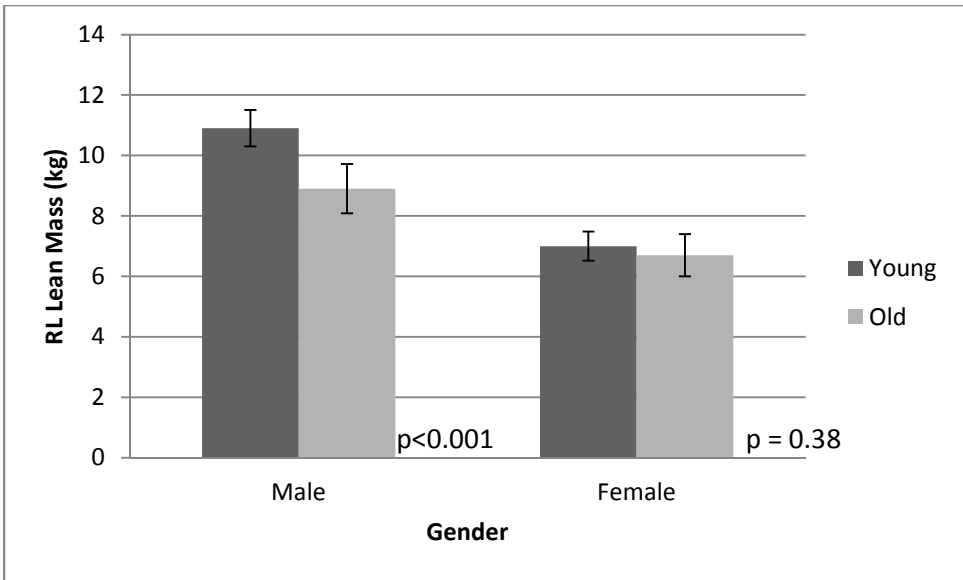


Figure 6: Average leg lean mass (right, kg) by age group. Bars, 95% confidence interval

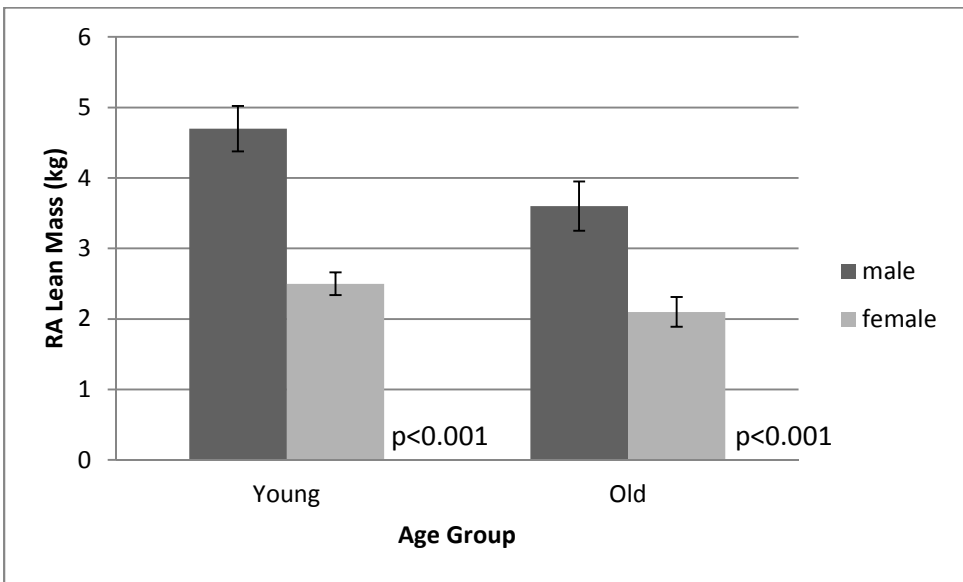


Figure 7: Average arm lean mass (right, kg) by gender. Bars, 95% confidence interval.

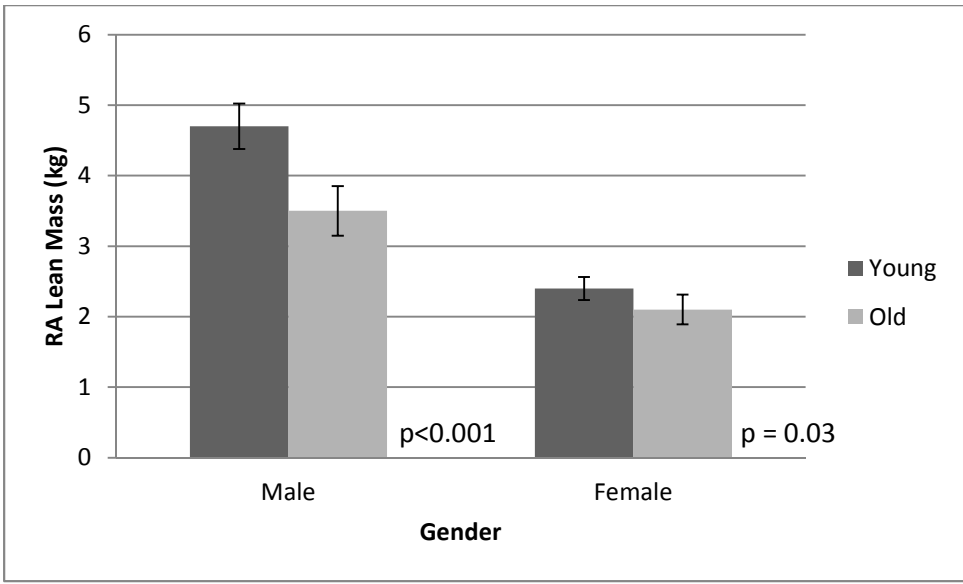


Figure 8: Average arm lean mass (right, kg) by age group. Bars, 95% confidence interval.

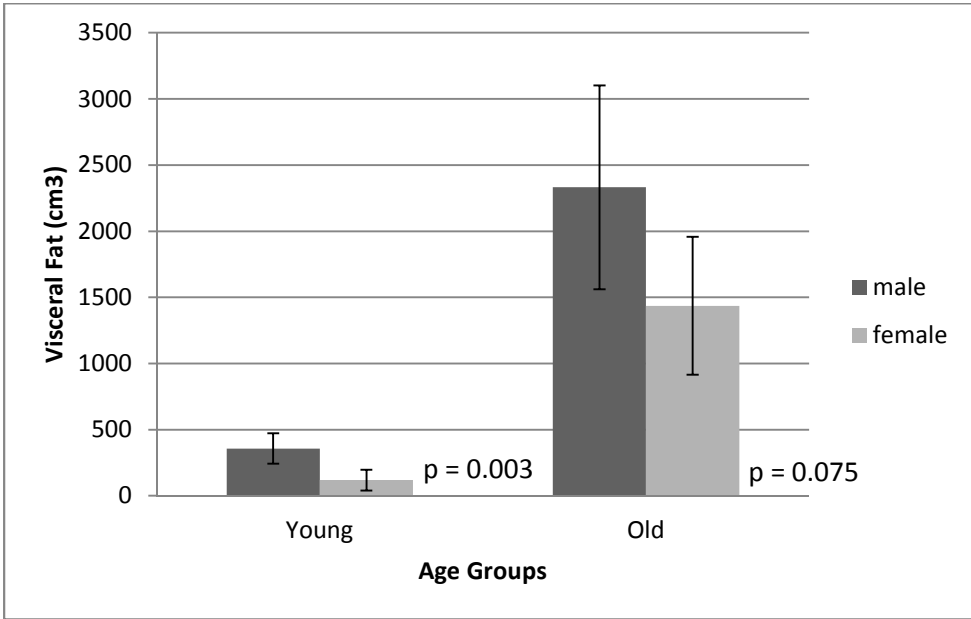


Figure 9: Average visceral fat difference by gender. Bars, 95% confidence interval.

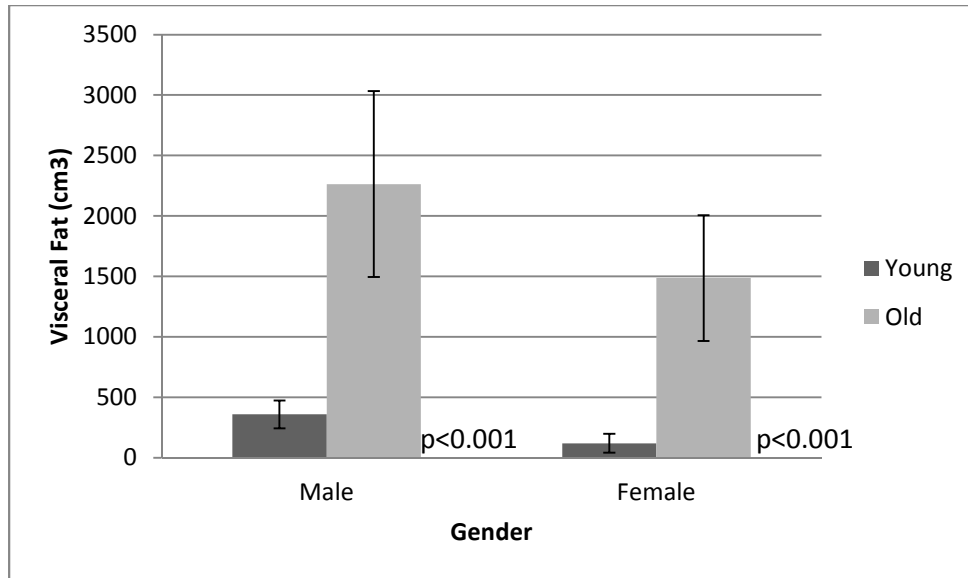


Figure 10: Average visceral fat difference by age group. Bars, 95% confidence interval.

Muscular Strength

There was a significant gender difference in leg isokinetic strength, leg isometric strength, and handgrip strength. Young males had greater isometric leg strength (233.7 N m vs. 150.8 N m, $p < 0.001$) and handgrip strength (54 kg vs. 33 kg, $p < 0.001$) than did young females, respectively (Figures 11 & 12). Elderly males also had a greater isometric leg strength (145.7 N m vs. 96.8 N m, $p < 0.001$) and handgrip strength (41.8 kg vs. 25.1 kg, $p < 0.001$) than did elderly females, respectively (Figures 11 & 12). Young male and female adults had greater isometric leg strength as compared with elderly male and female adults, respectively (all $p < 0.001$) (Figure 13) (males: 234.3 N m vs. 141.5 N m, $p < 0.001$; females: 150.2 N m vs. 99.8 N m, $p < 0.001$). Young male and female adults also had greater handgrip strength as compared with elderly male and female adults, respectively (all $p < 0.001$) (Figure 14) (males: 54.5 kg vs. 41.9 kg, $p < 0.001$; females: 32.4 kg vs. 25 kg, $p < 0.001$). Similarly, young and elderly males had significantly greater

isokinetic leg strength at 90 deg/sec and 120 deg/sec than did young and elderly females, in the respective group (all $p < 0.001$).

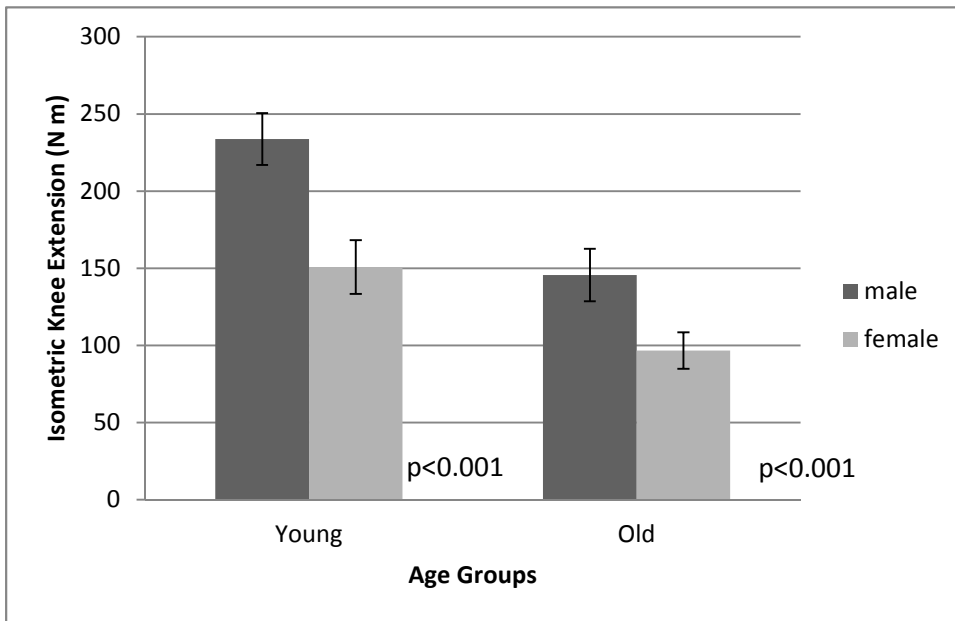


Figure 11: Average leg muscle strength difference by gender. Bars, 95% confidence interval.

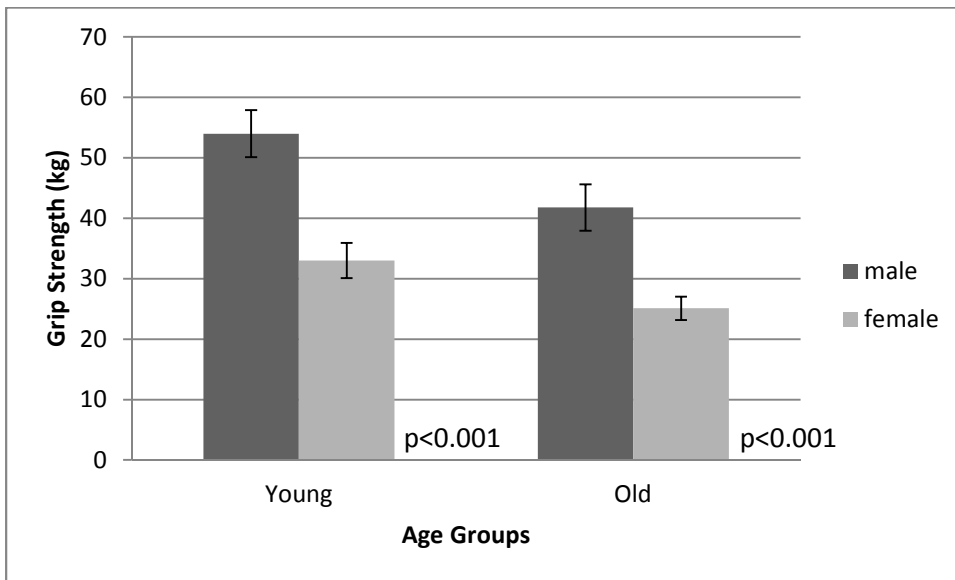


Figure 12: Average handgrip strength difference by gender. Bars, 95% confidence interval.

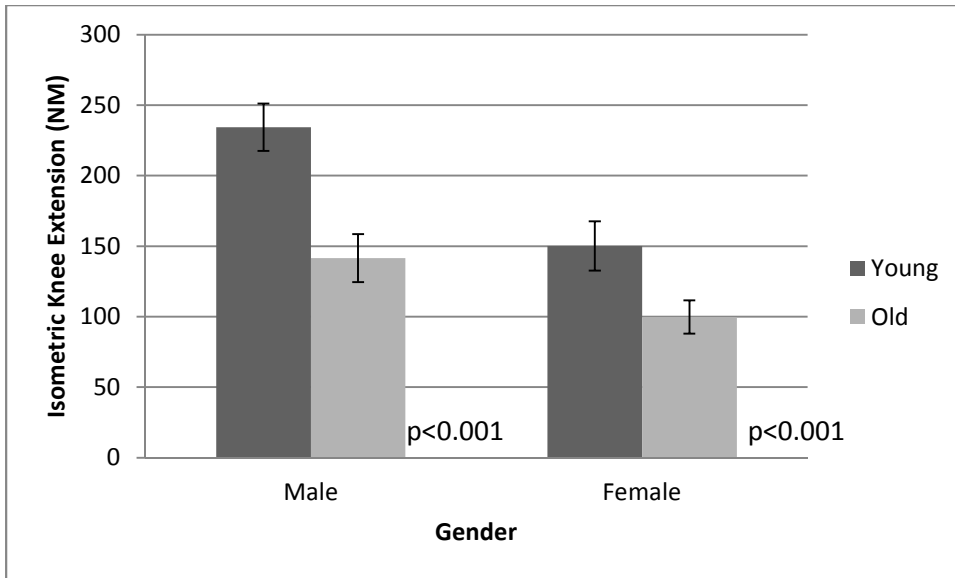


Figure 13: Average leg muscle strength difference by age group. Bars, 95% confidence interval.

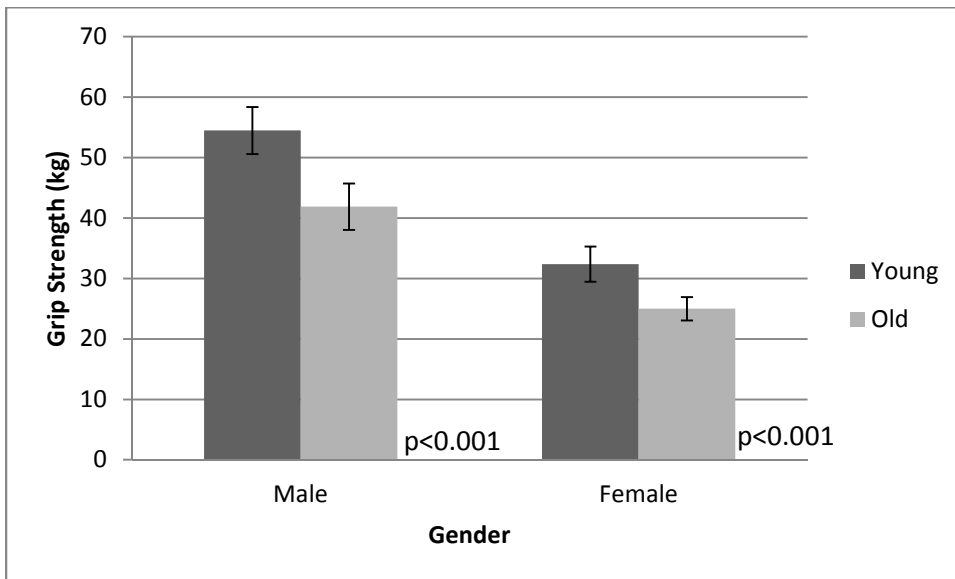


Figure 14: Average handgrip strength difference by age group. Bars, 95% confidence interval.

Arterial Health

As shown in Figure 15, young males had faster PWV than did young females (5.7 m/s vs. 5.1 m/s, $p = 0.01$), but there was no statistical gender difference of PWV in the

elderly (9.0 m/s vs. 8.1 m/s, $p = 0.2$). However, elderly males and females had faster PWV when compared with young male and female adults, respectively (males: 9.0 vs. 5.7 m/s, $p < 0.001$; females 8.1 vs. 5.1 m/s, $p < 0.001$) (Figure 16).

There was no statistical difference in AP and AIX between young males and females ($p > 0.38$) and between elderly males and females ($p > 0.18$). However, elderly males and females had greater AP and AIX than did young males and female counterparts (all $p < 0.001$). Means of AP and AIX were 0.8 and -3.7 in young males and 12.0 and 22.0 in the elderly males. Means of AP and AIX were 1.5 and -1.4 in young females and 13.0 and 28.7 in the elderly females.

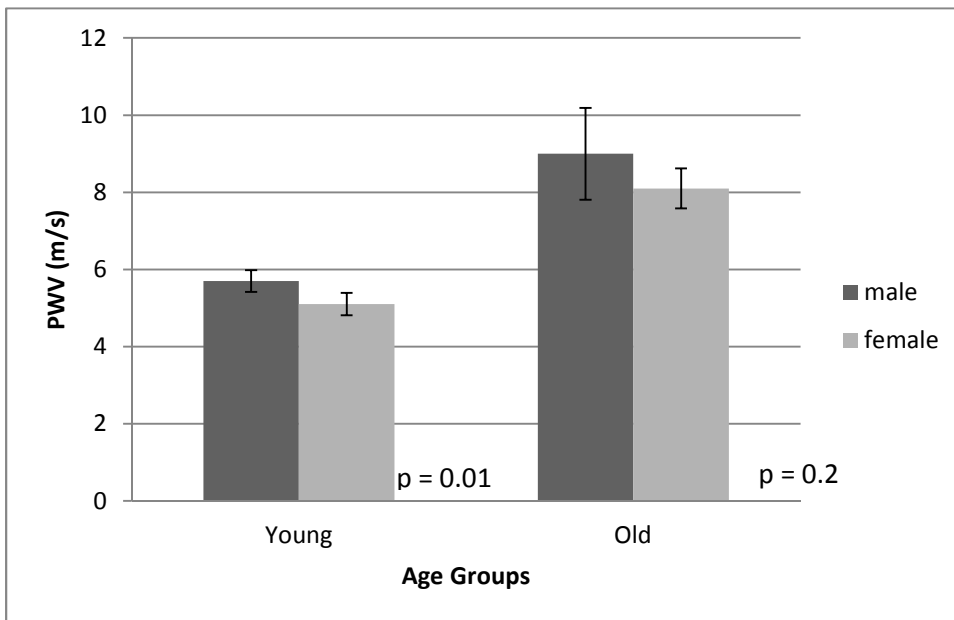


Figure 15: Average pulse wave velocity difference by gender. Bars, 95% confidence interval.

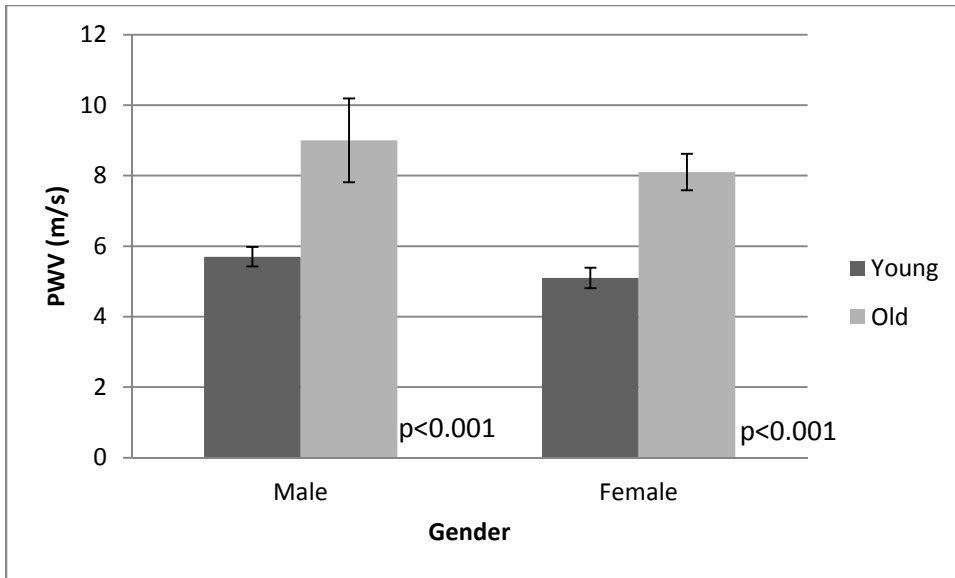


Figure 16: Average pulse wave velocity difference by age group. Bars, 95% confidence interval.

Physical Functioning Tests

Males had greater gait speed than females in both young (2.2 vs. 2.0 m/s, $p = 0.03$) and elderly adults (1.9 vs. 1.7, m/s, $p = 0.04$). Younger males and females had better gait speed than did elderly males and females, respectively (males: 2.2 vs. 1.9 m/s, $p < 0.001$; females: 2.0 vs. 1.7 m/s, $p < 0.001$). This suggests that males are faster gait speed than did females within both age groups. Young males and females had faster sit-to-stand time than did elderly males and females (all $p < 0.006$), but there was no gender difference in sit-to-stand time in young and elderly adults, respectively (all $p > 0.11$).

Muscle Quality, Muscle Strength, & Muscle Mass

Among elderly adults, there was a positive association between *arm MQI* and handgrip strength ($r = 0.42$, $p = 0.25$) and between *leg MQI* and isometric leg strength ($r = 0.79$, $p < 0.001$) (Table 3). However, there was a negative association between *arm MQI* and arm lean mass ($r = -0.58$, $p = 0.001$) and between *leg MQI* and leg lean mass ($r = -$

0.70, $p < 0.001$). In young adults, there was also a positive association between *arm MQI* and handgrip strength ($r = 0.53$, $p < 0.001$) and between *leg MQI* and isometric leg strength ($r = 0.81$, $p < 0.001$). The association between *arm MQI* and arm lean mass was -0.30 ($p = 0.07$), and between *leg MQI* and leg, lean mass was -0.18 ($p = 0.30$).

*Table 3: Person Partial Correlation Coefficients Among Muscle Quality, Muscle Mass, and Muscle Strength In Young and Elderly Men and Women**

Arm	MQI	Muscle Mass	Muscle Strength	Leg	MQI	Muscle Mass	Muscle Strength
Elderly Adults							
MQI	1	.	.	MQI	1	.	.
Muscle Mass	-0.58	1	.	Muscle Mass	-0.70	1	.
Muscle Strength	0.42	0.41	1	Muscle Strength	0.79	-0.17	1
Young Adults							
MQI	1	.	.	MQI	1	.	.
Muscle Mass	-0.30	1	.	Muscle Mass	-0.18	1	.
Muscle Strength	0.53	0.61	1	Muscle Strength	0.81	0.39	1

Note. *Adjust for age, sex, and race; *Arm MQI* = muscle quality of the arm calculated as the grip strength divided by RA lean; Arm muscle mass = right arm lean mass as computed by DXA (kg); Arm strength = dominate arm grip strength (kg); *Leg MQI* = muscle quality index of the leg calculated as the leg isometric strength divided by RL lean; Leg muscle mass = right leg lean mass as computed by DXA (kg); Leg strength = dominate leg isometric knee extensor performance on the dynamometer (Nm).

CHAPTER 5

DISCUSSION

Although muscle quality is a significant risk factor for muscle weakness, physical mobility, disability, and mortality, there has been little research on muscle quality across age and gender groups. The associations of muscle quality, muscle strength, and muscle mass also remain less explored. The primary objective of this study was to determine whether MQI differs across gender and age categories and whether MQI relates to muscle strength and muscle mass in young and elderly adults. The secondary objective was to test mean differences in muscle mass, muscle strength, and PWV, and visceral fat between young healthy adults and elderly adults.

The main finding of this study was that young male adults had a greater *leg MQI* than did elderly male adults. Similarly, young female adults also had a greater *leg MQI* than did elderly female adults. Interestingly, *leg MQI* is positively associated with isometric leg strength in both young and elderly adults. However, *leg MQI* is negatively associated with leg muscle mass in both young and elderly adults.

Muscle Quality Index

The present study assessed *arm MQI* and *leg MQI* difference between a healthy young reference group (aged 20-29 years) and an elderly group (aged 60-80 years). To our knowledge, this is the first cross-sectional study to evaluate muscle quality in these age groups. Previous studies have focused on whole body MQI or *leg MQI*, where the present study is the first to evaluate both dominate *arm MQI* and *leg MQI* separately. A particular novel finding was a significant mean difference in *leg MQI* between young and elderly adults in men and women. Prior findings of muscle quality decline with age

(Kennis et al., 2014) have shown that this outcome is to be expected. However, our results show that *arm MQI* was not significantly different between young and elderly groups in either gender. These results imply that *leg MQI* may be a better measure than *arm MQI* to define sarcopenia

Muscle Quality, Muscle Mass, and Muscle Strength

A novel finding in the present study is that there is a positive association between *arm MQI* and handgrip strength and between *leg MQI* and isometric leg strength, and a negative association between *arm MQI* and arm lean mass and between *leg MQI* and leg lean mass in both young and old adults. To the best of our knowledge, this is the first study to examine these associations in a cross-sectional study design. However, in a study of older adults (aged 55 years or more), muscle quality also had a positive association with leg strength and a negative association with muscle mass (Bouchard et al., 2011). Ismail et al. (2011) also found an inverse relationship between muscle quality of the rectus femoris (measured by ultrasound) and grip strength (corrected for body weight) yet no association between muscle quality and lean body mass. The results of the present study confirm that muscle quality may be a more significant indicator of muscle changes due to aging than muscle mass. Additionally, these changes are present in both the upper and lower appendicular regions. These findings suggest that mass alone does not protect against muscle quality declines with age.

Muscle Mass

Our findings indicate a greater mean RL lean mass and RA lean mass in males compared to females in both age groups. There was also a greater mean RL lean mass and RA lean mass in young adults compared to the elderly adults. This difference was

significant except for in females for the RL lean mass. This is not the only study to identify a difference in muscle mass between gender and between young healthy adults and elderly adults. However, methods of measures vary amongst studies. In this study, DXA was used to determine RA lean mass and RL lean mass. Similarly, Visser (2000) used DXA to measure leg muscle mass in 3075 participants aged 70-79 years old, showing greater muscle mass in males than females. Goodpaster et al. (2006) found, after a three-year time span, a significant decline in leg lean mass as measured by DXA in both white and Black men and women. When using BIA to measure body composition, Zeng et al. (2016) still found a significant difference in lean mass and appendicular skeletal mass between gender and age groups (young, aged 20-59 years; old, aged ≥ 60 years).

Only one study examined muscle mass difference between young and elderly adults across type 2 diabetic and non-diabetic persons using a cross-sectional study (Koo et al., 2016). Using DXA to estimate ASM in a Korean sample of 12,792 subjects, Koo et al. (2016) showed a significant reduction in ASM and ASM/BW across age groups (25-39, 45-64, and ≥ 75 years) in persons with or without diabetes.

Muscle Strength

The present study found that males had greater muscle strength than did females. Young adults had a greater dominate arm handgrip strength and dominated leg isometric knee extensor strength compared to the elderly adults. Our findings are consistent with other studies, showing that muscular strength declines with age. The present study evaluated muscle strength difference between young (aged 20-29 years) and elderly adults (aged 60-80 years), whereas other studies have evaluated declines in muscle and strength within a longitudinal study design. According to the Health, Aging, and Body

Composition (Health ABC) Study, the rates of annual leg strength loss for white and black men and women (aged 70-79 years) were: 3.4% in white men, 4.1% in black men, 2.6% in white women, and 3.0% in black women (Goodpaster et al., 2006). Von Haehling et al. (2010) reported that muscle strength declines by 1.5% annually after about age 50 years.

Zeng et al. (2006) found a significant difference in GS, handgrip strength and repeated chair sit-to-stand times between a younger and older group, which is consistent with our finding. Several studies have also shown that low muscle mass is associated with physical disability (Jassen et al., 2004; Baumgartner et al., 1998). However, Newman et al. (2006) reported that lower lean mass was not a predictor of mortality in the elderly adults aged 70-79 years. Several investigators have shown (Newman et al., 2006; Stenholm et al., 2008) that muscle strength is a better risk factor for mortality over muscle mass.

An interesting finding from our data is that *arm MQI* was not significantly different between age groups even though arm lean mass was significantly different between age groups. Prior research has demonstrated that MQ is a more relevant measure to assess functional decline with age (Barbat-Artigas et al., 2012). Therefore, the results of the present study confirm that lean muscle mass changes may not reflect changes in muscle efficiency throughout aging (particularly in the arm).

Pulse Wave Velocity

Consistent with AlGhartif et al. (2013), the current study found a mean difference in PWV between males and females. Young males had a greater PWV than young females; AlGhartif et al. (2013) found a steeper longitudinal increase in PWV in males.

Elderly persons had greater PWV than did young persons, which is consistent with findings from Lee et al. (2012) who found a significant difference in BMI-matched young and old groups (mean age 27.3 and 75.6 respectively).

Visceral Fat

The present study found a significant mean difference in visceral fat between age groups. This is consistent with a cross-sectional study that measured a significant mean difference in visceral fat, measured by computed tomography, between BMI-matched young and old groups (mean age 27.3 and 75.6 respectively) (Lee et al., 2012). In the present study, males had a greater visceral fat area than females; however, the difference was only significant in the younger group. This may be explained by a small sample size for the older male group.

Most studies have used CT, or MRI scans to measure visceral fat area (Linder et al., 2016). Kaul et al. (2012) estimated visceral fat across gender and BMI categories using DXA and CT and found a strong agreement between the two methods (2012).

Strengths of the Study

This is the first cross-sectional study to evaluate differences in MQ, muscle mass, muscle strength, PWV, and visceral fat between young healthy and elderly adults. Our findings are consistent with prior research on muscle mass, muscle strength, PWV, and visceral fat. Another strength of our study was the use of DXA to measure arm and leg lean mass as well as visceral fat which has been determined the gold standard for measurements of body composition and has demonstrated reliability and validity (von Hurst et al., 2016; Kaul et al., 2012).

Limitations of the Study

The following limitations of the study should be considered. First, we had a small representation of non-whites subjects. This may limit our results because it has been shown that mass and strength decline may occur at different rates between races (Goodpaster et al., 2006). Second, due to lack of recruitment, our sample size for the older male group was small compared to the other groups. This may explain the lack of a significant difference between males and females in the older group for arm and *leg MQI* and visceral fat area. Another limitation was that dominant leg and hand were used for strength measures in each individual. However, only right arm and right leg lean mass measures were used in the calculation of arm and *leg MQI*. This was determined because only a small fraction of subjects was dominated in their left arm or leg. Finally, measures were not adjusted for lifestyle factors. Research has shown that various environmental or health factors may influence the muscle strength and performance (Zeng et al., 2016). However, the objective of this study was to evaluate differences between genders and age groups and serve as a preliminary study for developing a muscle quality index.

Conclusion

Our results indicate that young male adults had a greater *leg MQI* than did elderly male adults. Similarly, young female adults had a greater *leg MQI* than did elderly female adults. Notably, *leg MQI* is positively associated with isometric leg strength in both young and elderly adults. However, *leg MQI* is negatively associated with leg muscle mass in both young and elderly adults.

The findings in this research serve a preliminary basis to establishing a new MQI that defines sarcopenia. Given that muscle quality is an important measure of the

functionality of muscle, this study is the first step towards future research in developing interventions that prevent and possibly treat sarcopenia.

REFERENCES

- Abbatecola, A. M., Chiodini, P., Gallo, C., Lakatta E., Sutton-Tyrrell, K., Tyllavsky, F.A.,...Harris, T. (2012). Pulse wave velocity is associated with muscle mass decline: *Health ABC study*. *Age*, 34, 469-478.
- Addison O., Marcus, R. L., Lastayo, P. C., & Ryan, A. S. (2014). Intermuscular fat: a review of the consequences and causes. *Int J Endocrinol*, 2014.
- Akin, S., Mucuk, S., Ozturk, A., Mazicioglu, M., Gocer, S., Arguvanli, S., & Safak, E. (2015). Muscle function-dependent sarcopenia and cut-off values of possible predictors in community-dwelling Turkish elderly: calf-circumference, midarm muscle circumference and walking speed. *European Journal of Clinical Nutrition*, 69, 1087-1090.
- Alfonso, J., Cruz-Jentoft, Baeyens, J.P., Bauer, J. M., Boirie, Y., Cederholm, T.,... Zamboni, M. (2010). Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. *Age Ageing*, 39 (4), 412-423.
- AlGhatrif, M., Strait, J. B., Morrell, C. H., Canepa, M., Wright, J., Elango, P.,... Lakkatta, E. G. (2013). Longitudinal trajectories of arterial stiffness and the role of blood pressure. *Hypertension*, 62, 934-941.
- American Heart Association. Heart Disease and Stroke Statistics 2017 at a Glance. Available at: http://www.heart.org/idc/groups/ahamah-public/@wcm/@sop/@smd/documents/downloadable/ucm_491265.pdf. Accessed February 1, 2017.
- Anderson, J. L. (2002). Muscle fiber type adaptation in the elderly human muscle. *Scandinavian Journal of Medicine & Science in Sports*, 13, 40-47.
- AtCore Medical, (2013). SphygmoCor XCEL System Training.
- Atkins J., Whincup, P., Morris, R., Lennon, L., Papacosta, O., & Wannamethee, G. (2014). Sarcopenic obesity and risk of cardiovascular disease and mortality: A population-based cohort study on older men. *JAGS*, 62, 253-260.

- Baracos, V. E., Reiman, T., Mourtzakis, M., Gioulbasanis, I., & Antoun, S. (2010) Body composition in patients with non-small cell lung cancer: a contemporary view of cancer cachexia with the use of computed tomography image analysis. *Am J Clin Nutr*, 91, 1133S–1137S.
- Barbat-Artigas, S., Rolland, Y., Zamboni, M., & ubertin-Leheudre, M. (2012). How to assess functional status: a new muscle quality index. *J Nutr Health Aging*, 16, 67–77.
- Baumgartner, R. N., Koehler, K. M., Gallagher, D., Romero, L., Heymsfield, S. B., Ross, R. R.,...Lindeman, R. D. (1998). Epidemiology of sarcopenia among the elderly in New Mexico. *Am J Epidemiol*, 147(8), 755-763.
- Bauer, J. M., & Sieber, C. C. (2008). Sarcopenia and frailty: a clinician's controversial point of view. *Exp Gerontol*, 43, 674–8.
- Bijlsma, A. Y., Meskers, C. G., Westendorp, R. G., & Maier, A. B. (2012). Chronology of age-related disease definitions: osteoporosis and sarcopenia. *Ageing Research Review*, doi:10.1016/j.arr.2012.01.001.
- Binkley N, Krueger D, & Buehring B (2013) What's in a name revisited: should osteoporosis and sarcopenia be considered components of “dysmobility syndrome?”. *Osteoporos Int* 24:2955–2959
- Bouchard, D. R., Heroux, M., & Janssen, I. (2011). Association between muscle mass, leg strength, and fat mass with physical function in older adults: influence of age and sex. *Journal of Aging and Health*, 23(2), 313-328.
- Centers for Disease Control and Prevention. 2012 National Diabetes Fact Sheet. Available at: <https://www.cdc.gov/diabetes/pubs/statsreport14/national-diabetes-report-web.pdf>. Accessed February 1, 2017.
- Centers for Disease Control and Prevention. Summary Health Statistics National Health Interview Survey 2014. Available at: https://ftp.cdc.gov/pub/Health_Statistics/NCHS/NHIS/SHS/2014_SHS_Table_A-3.pdf. Accessed February 2, 2017.
- Centers for Disease Control and Prevention. Summary Health Statistics National Health Interview Survey. Available at: https://ftp.cdc.gov/pub/Health_Statistics/NCHS/NHIS/SHS/2014_SHS_Table_A-1.pdf. Accessed February 1, 2017.

- Chang, S. F., & Lin, P. L. (2016). Systematic literature review and meta-analysis of the association of sarcopenia with mortality. *World Views on Evidence Based Nursing*, 13(2), 153–162.
- Chen, L., Nelson, D. R., Zhao, Y., Cui, Z., & Johnston, J. A. (2013). Relationship between muscle mass and muscle strength, and the impact of comorbidities: a population-based, cross-sectional study of older adults in the United States. *BMC Geriatrics*, 13(74).
- Ching, I. C., Kuo, C. H., Ding, C. C., Chih, H. W., Cheng, C. L., Chao A. H.,...Ching, Y. C. (2015). The impacts of sarcopenia and obesity on physical performance in the elderly. *Obesity Research & Clinical Practice*, 9(3), 256–265.
- Clark, B. C. & Manini, T. M. (2010). Functional consequences of sarcopenia and dynapenia in the elderly. *Curr Opin Clin Nutr Metab Care*, 13(3), 271-276.
- Clynes, M. A., Edwards, M. H., Buehring, B., Dennison, E. M., Binkley, N., & Cooper, C., (2015). Definitions of sarcopenia: associations with previous falls and fracture in a population sample. *Calcif Tissue Int*, 97, 445-452.
- Cruz-Jentoft, A. J., Baeyens, J. P., Bauer, J. M., Boirie, Y., Cederholm, T., Landi, F.,...Zamboni, M. (2010). Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. *Age Ageing*, 39(4), 412-423.
- Dufour, A. B., Hannan, M. T., Murabito, J. M., Kiel, D. P., McLean, R. R. (2013). Sarcopenia definitions considering body size and fat mass are associated with mobility limitations: the Framingham Study. *J Gerontol A Biol Sci Med Sci*, 68, 168–74.
- Esmee, M., Reijnierse, M., Marijke, C., Trappenburg, Blauw, G. J., Verlaan, S.,...Maier, A. B. (2016). Common Ground? The Concordance of Sarcopenia and Frailty Definitions. *Journal of the American Medical Directors Association*, 17(4), 371.e7-371.e12.
- Evans, W. J. (2010). Skeletal muscle loss: cachexia, sarcopenia, and inactivity. *Am J Clin Nutr*, 91(4), 1123-1127.
- Evans, W. J., Morley, J. E., Argiles, J., Bales, C., Baracos, V., Guttridge, D.,...Anker, S. D. (2008) Cachexia: a new definition. *Clin Nutr*, 27, 793–9.

- Fahs, C. A., Herrernan, K.S., Ranadive, S., Jae, S.Y., & Fernhall, B. (2010). Muscular strength is inversely associated with aortic stiffness in young men. *Medicine & Science in Sports & Exercise*, 42(9), 1619-1624.
- Fielding, R. A., Vellas, B., Evans, W. J., Bhasin, S., Morley, J. E., Newman, A. B.,...Zamboni, M. (2011). Sarcopenia: an undiagnosed condition in older adults. Current consensus definition: prevalence, etiology, and consequences. International working group on sarcopenia. *J Am Med Dir Association*, 12(4), 249-56.
- Fragala, M. S., Kenny, A. M., & Kuchel, G. A., (2015). Muscle quality in aging: a multi-dimensional approach to muscle functioning with applications for treatment. *Sports Med*, 45, 641-658.
- Fried, L. P., Tangen, C. M., Walston, J., Newman, A. B., Hirsch, C., Gottdiener, J.,...McBurnie, M. A.(2001). Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci*, 56(3), M146.
- Goodpaster, B. H., Park, S. W., Harris, T. B., Kritchevsky, S. B., Nevitt M., Schwartz, A. V.,...Newman, A. V. (2006). The Loss of Skeletal Muscle Strength, Mass, and Quality in Older Adults: The Health, Aging and Body Composition Study. *J Gerontol A Biol Sci Med Sci*, 61(10), 1059-1064.
- Hardy, S. E. (2007). Improvement in usual gait speed predicts better survival in older adults. *J Am Geriatr Soc*, 55(11), 1727-1734.
- Hayshida, I., Tanimoto, Y., Takahashi, Y., Kusabiraki, T., & Tamaki, J. (2014). Correlation between muscle strength and muscle mass, and their association with walking speed, in community-dwelling elderly Japanese individuals. *Plos One*, 9(11), e111810.
- He, H., Liu, Y., Tian, Q., Papasian, C. J., HU, T., & Deng, H. W. (2016). Relationship of sarcopenia and body composition with osteoporosis. *Osteoporosis Int*, 27(2), 473-482.
- Heymsfield, S. B., Gonzales, M. C., Lu, J., Jia, G., & Zheng, J. (2015). Skeletal muscle mass and quality: evolution of modern measurement concepts in the context of sarcopenia. *Proceedings of the Nutrition Society*, 74, 355-366.

- Ilich, J. Z., Inglis, J. E., Kelly, O. J., & McGee, D. L. (2015). Osteosarcopenic obesity is associated with reduced handgrip strength, walking abilities, and balance in postmenopausal women. *Osteoporosis International*, 26(11), 2587–2595.
- Ilich, J. Z., Kelly, O. J., & Inglis, J. E., (2016). Osteosarcopenic obesity syndrome: what is it and how can it be identified and diagnosed? *Current Gerontology and Geriatrics Research*, 1-7.
- Ismail, C., Zabal, J., Hernandez, H. J., Woletz, P., Manning, H., Teixeira, C.,...Harris-Love, M. O. (2015). Diagnostic ultrasound estimates of muscle mass and muscle quality discriminate between women with and without sarcopenia. *Frontiers in Physiology*, 6(302).
- Janssen, I., Baumgartner, R. N., Ross, R., Rosenberg, I. H., & Roubenoff, R. (2004). Skeletal muscle cutpoints associated with elevated physical disability risk in older men and women. *Am J Epidemiol*, 159(4), 413-421.
- Joglekar, S., Asghar, A., Mott, S. L., Johnson, B. E., Button, A. M., Clark, E., & Mezhir, J. J. (2014). Sarcopenia is an independent predictor of complications following pancreatectomy for adenocarcinoma. *J Surg Oncol*, 111(6), 771-775.
- Kaess, et al. (2012). Arterial stiffness predicts hypertension. *JAMA*, 308(9), 875-881.
- Kalyani, R. R., Tra, Y., Hsin-Chieh, Y., Egan, J. M., Ferrucci, L., & Brancati, F. L. (2013). Quadriceps strength, quadriceps power, and gait speed in older US adults with diabetes mellitus: Results from the National Health and Nutrition Examination Survey, 1999–2002. *J Am Geriatr Soc*, 61, 769–775.
- Kato, A., Ishida, J., Endo, Y., Takita, T., Furuhashi, M., Maruyama, Y., & Odamaki, M. (2011). Association of abdominal visceral adiposity and thigh sarcopenia with changes of arteriosclerosis in haemodialysis patients. *Nephrology, dialysis, transplantation*, 26(6), 1967-1976.
- Kaul, S., Rothney, M. P., Peters, D. M., Wacker, W. K., David, C. E., Shapiro, M. D., & Ergun, D. L. (2012). Dual-energy x-ray absorptiometry for qualification of visceral fat. *Obesity*, 20(6), 1313-1318.
- Kennis, E., Verschueren, S., Van Roie, E., Thomis, M., Lefevre, J., & Delecluse. (2014). Longitudinal impact of aging on muscle quality in middle-aged men. *AGE*, 36, 9689.

- Kim, H., Suzuki, T., Kim, M., Kojima, N., Yoshida, Y., Hirano, H.,...Yoshida, H. (2015). Incidence and predictors of sarcopenia onset in community-dwelling elderly Japanese women: 4-Year follow-up study. *Journal of the American Medical Directors Association*, 16(1), 85.e1–85.e8.
- Kim, K. S., Park, K. S., Kim, M. J., Kim, S. K., Cho, Y. W., & Park, S. W. (2014). Type 2 diabetes is associated with low muscle mass in older adults. *Geriatr Gerontol Int*, 14, 115–121.
- Kim, T. N., Park, M. S., Yang, S. J., et al. (2010). *Diabetes Care*, 33, 1497–1499.
- Koenigsberg, R. (1989). *Churchill's Illustrated Medical Dictionary*. Churchill Livingstone, New York.
- Koo, B., Roh, E., Yang, Y., & Moon, M. (2016). Difference between old and young adults in contribution of β -cell function and sarcopenia in developing diabetes mellitus. *Journal of Diabetes Investigation*, 7(2), 233-240.
- Lambert, K., Horn, L., et al., (2013). Five Times Sit to Stand Test.
- Landi, F., Cruz-Jentoft, A. J., Liperoti, R., Russo, A., Giovannini, S., Tosato, M.,...Onder, G. (2013). Sarcopenia and mortality risk in frail older persons aged 80 years and older: results from the SIRENTE study. *Age and Ageing*, 42(2), 203 - 203.
- Lee, S., Youm, Y., Kim, C., Lee, W., Choi, W., Chu, S.,...Kim, H. (2014). Association between skeletal muscle mass and radial augmentation index in an elderly Korean population. *Archives of Gerontology and Geriatrics*, 59, 49-55.
- Lee, Y., Shin, H., Vassy, J. L., Kin, J. T., Cho, S. I., Kang, S. M.,...Lim, S. (2012). Comparison of regional body composition and its relation with cardiometabolic risk between BMI-matched young and old subjects. *Atherosclerosis*, 224, 258-265.
- Lauretani, F., Russo, C. R., Bandinelli, S., Bartali, B., Cavazzini, C., Di Iorio, A.,...Ferrucci, L. (2003). Age-associated changes in skeletal muscles and their effect on mobility: an operational diagnosis of sarcopenia. *J Appl Physiol*, 95(5), 1851-1860.

- Leenders, M., Verdijk, L. B., van der Hoeven, L., Adam, J. J., van Kranenburg, J., Nilwik, R., & van Loon, L. J. C. (2013). Patients with type 2 diabetes show a greater decline in muscle mass, muscle strength, and functional capacity with aging. *J Am Med Dir Assoc*, 14, 585–592.
- Linder, N., Schaudinn, A., Garnov, N., Bluher, M., Dietrich, A., Schutz, T.,...Busse, H. (2016). Age and gender specific estimation of visceral adipose tissue amounts form radiological images in morbidly obese patients. *Scientific Reports*, 22261
- McGregor, R. A., Cameron-Smith, D., & Poppitt, S.D. (2014). It is not just muscle mass: a review of muscle quality, composition and metabolism during aging as determinant of muscle function and mobility in later life. *Longevity & Healthspan*, 3-9.
- Morley, J. E. (2010). Sarcopenia in the elderly. *Family Practice*, 29, i44-i48.
- Morley, J. E., Abbatecola, A. M., Argiles, J. M., Baracos, V., Bauer, J., Bhasin, S.,...Cederholm, T. (2011). Sarcopenia with limited mobility: an international consensus. *J Am Med Dir Assoc*, 12(6), 403-409.
- Newman, A. B., Kupelian V., Marjolein, V., Simonsick E., Goodpaster, B., Nevitt, M.,...Harris, T.B., (2003). Sarcopenia: alternative definitions and associations with lower extremity function. *Journal of American Geriatrics Society*, 51, 1602-1609.
- Newman, A. B., Kupelian, V., Visser, M., Simonsick, E. M., Goodpaster, B. H., Kritchevsky,...Harris, T.B. (2006). Strength, but not muscle mass, is associated with mortality in the health, aging, and body composition study cohort. *Journal of Gerontology*, 61(1), 72-77.
- Newman, A. B., Kupelian, V., Visser, M., Simonsick, E., Goodpaster, B., Nevitt, M.,... Harris, T. B. (2003). Sarcopenia: Alternative Definitions and Associations with Lower Extremity Function. *Journal of The American Geriatrics Society*, 51(11), 1602.
- Nilwik, R., Snijders, T., Leenders, M., Grown, B. B. L., van Kranenburg, J., Verdijk, L. B., & van Loon, L. J. C. (2013). The decline in skeletal muscle mass with aging in mainly attributed to a reduction in type II muscle fiber size. *Experimental Gerontology*, 48(5), 492-498.

- Ochi, M., Kohara, K., Tabara, Y., Kido, T., Uetani, E., Ochi, N.,...Miki, T. (2010). Arterial stiffness is associated with low thigh muscle mass in middle-aged to elderly men. *Atherosclerosis*, 212, 327-332.
- Oharaa, M., Koharaa, K., Tabarab, Y., Igasea, M., & Mikia, T. (2015). Portable indices for sarcopenia are associated with pressure wave reflection and central pulse pressure:theJ-SHIP study. *International Journal of Cardiology*, (33)2.
- Oharaa, M., Koharaa, K., Tabarab, Y., Ochia, M., Nagaia, T., Igasea, M., & Mikia, T. (2014). Sarcopenic obesity and arterial stiffness, pressure wave reflection and central pulse pressure: *The J-SHIP study*. *International Journal of Cardiology*, 174(1), 214–217.
- Patil, R., Uusi-Rasi, K., Pasanen, M., Kannue, P., Karinkanta, S., & Sievanen, H. (2013). Sarcopenia and osteopenia among 70-80-year-old home-dwelling Finnish women: prevalence and association with functional performance. *Osteoporosis Int*, 24(3), 787-796.
- Phillips, I., Tenny, J., Gunn, L., Nimako, K., Hug, A., Allan, L., & Ezhil, V. (2016). Sarcopenia in lung cancer. *European Journal of Surgical Oncology (EJSO)*, 42(11), S238.
- Rantanen, T., Harris, T., Leveille, S. G., Visser, M., Foley, D., Masaki, K., & Guralnik, J. M. (2000). Muscle strength and body mass index as long-term predictors of mortality in initially healthy men. *J Gerontol A Biol Sci Med Sci*, 55(3), M168-M173.
- Reed, R. L., Pearlmutter, L., Yochem, K., Meredith, K. E., & Mooradian, A. D. (1991). The relationship between muscle mass and muscle strength in the elderly. *Journal of the American Geriatrics Society*, 39, 555-561.
- Robert, C. L., Wang, Z., & Heymsfield, S. B. (2001). Skeletal muscle mass and aging: regional and whole-body measurement methods. *Canadian Journal Applied Physiology*, 26(1), 102-122.
- Rockwood, K., Stadnyk, K., MacKnight, C., McDowell, I., Hebert, R., & Hogan, D. B. (1999). A brief clinical instrument to classify frailty in elderly people. *Lancet*, 353, 205-206.

- Roman, M. J., Devereux, R. B., Kizer, J. R., Okin, P. M., Lee, E. T., Wang, W.,...Calhoun, D. (2009). High central pulse pressure is independently associated with adverse cardiovascular outcome: The strong heart study. *JACC*, 54(18), 1730-1734.
- Sayer, A. A., Robinson, S. M., Patel, H. P., Shavlakadze, T., Cooper, C., & Grounds, M. D. (2013). New horizons in the pathogenesis, diagnosis and management of sarcopenia. *Age Ageing*, 42(2), 145-50.
- Sayer, A. A., Syddall, H. E., Dennison, E. M., Martin, H. J., Phillips, D. I. W., Cooper, C., & Byrne, C. D. (2007). Gripstrength and the metabolic syndrome: Findings from the Hertfordshire Cohort Study. *QJM*, 100(11), 707–713.
- Scott, D., & Hirani, V. (2016). Sarcopenic obesity. The impacts of sarcopenia and obesity on physical performance in the elderly. *European Geriatric Medicine*, 7, 214-219.
- Srdic, D., Plestina, S., Sverko-Peternac, A., Nikolac, N., Simundic, A. M., & Samarzija, M. (2016). Cancer cachexia, sarcopenia and biochemical markers in patients with advanced non-small cell lung cancer-chemotherapy toxicity and prognostic value. *Support Care Cancer*, 24(11), 4495-4502.
- Stenholm, S., Harris, T. B., Rantanen, T., Visser, M., Kritchevsky, S. B., & Ferrucci, L. (2008). Sarcopenic obesity: definition, cause and consequences. *Current Opinion in Clinical Nutrition and Metabolic Care*, 11, 693-700.
- Stephen, W. C., & Janssen, I. (2009). Sarcopenic-obesity and cardiovascular disease risk in the elderly. *J Nutr Health Aging*, 13, 460–466.
- Studenski, S. A., Peters, K. W., Alley, D. E., Cawthon, P. M., McLean, R. R., Harris, T. B., ... Vassileva, M. T. (2014). The FNIH Sarcopenia Project: Rationale, Study Description, Conference Recommendations, and Final Estimates. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*, 69(5), 547–558.
- Tang, Z., Wang, C., Song, X., Shi, J., Mitnitski, A., Fang, X.,...Rockwood, K. (2013). Co-occurrence of cardiometabolic diseases and frailty in older Chinese adults in the Beijing Longitudinal Study of Ageing. *Age and Ageing*, 42(3), 346 - 346.
- Thomas, D. R. (2007). Loss of skeletal muscle mass in aging: examining the relationship of starvation, sarcopenia and cachexia. *Clin Nutr*, 26, 389–99.

- Van Dijk, S. C., Swart, K. M. A., Ham, A. C., Enneman, A. W., Van Wijngaarden, J. P., Feskens, E. J., & Van der Velde, N. (2015). Physical fitness, activity and hand-grip strength are not associated with arterial stiffness in older individuals. *Journal of Nutrition Health and Aging*, 19(7).
- Verschueren, S., Gielen, E., O'Neill, T. W., Pye, S. R., Adams, J. E., Ward, K. A.,...Boonen, S. (2013). Sarcopenia and its relationship with bone mineral density in middle-ages and elderly European men. *Osteoporosis Int*, 24(1), 87–98.
- Vildan, B. S. (2015). Limitations of the definition of sarcopenia in cancer surgery. *Journal of Surgical Oncology*, 112(1), 116-116.
- Villaseñor, A., Ballard-Barbash, R., Baumgartner, K., Baumgartner, R., Bernstein, L., McTiernan, A., & Neuhaus, M. L. (2012). Prevalence and prognostic effect of sarcopenia in breast cancer survivors: the HEAL Study. *J Cancer Surviv*, 6(4), 398-406.
- Visser, M., Newman, A. B., Nevitt, M. C., Kritchevsky, S. B., Stamm, E. B., Goodpaster, B. H., & Harris, T. B. (2000). Reexamining the sarcopenia hypothesis. Muscle mass versus muscle strength. *Annals of the New York Academy of Sciences*, 904, 456-461.
- Volpato, S., Bianchi, L., Lauretani, F., Lauretani, F., Bandinelli, S., Guralnik, S.,...Ferrucci, L. (2012). Role of muscle mass and muscle quality in the association between diabetes and gait speed. *Diabetes Care*, 35(8), 1672–1679.
- Von Haehling, S., Morley, J. E., & Anker, S. D. (2010) An overview of sarcopenia: facts and numbers on prevalence and clinical impact. *J Cachex Sarcopenia Muscle*, 1(2), 129–133.
- von Hurst, P. R., Walsh, D. C. I., Conlon, C. A., Ingram, M., Kruger, R., & Stonehouse, W. (2016). Validity and reliability of bioelectrical impedance analysis to estimate body fat percentage against air displacement plethysmography and dual-energy x-ray absorptiometry. *Nutrition and Dietetics*, 73(2), 197-204.
- Walter, R. F., Reid, K. F., Philips, E. M., Krivickas, L. S., Hughes, R. R., & Fielding, R. A. (2008). Muscle fiber size and function in elderly humans: a longitudinal study. *Journal of Applied Physiology*, 105(2), 637-642.

- Wannamethee, S. G., Shaper, A. G., Lennon, L., & Whincup, P. H. (2007). Decreased muscle mass and increased central adiposity are independently related to mortality in older men. *Am J Clin Nutr*, 86, 1339–1346.
- World Health Organization, (1994). Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. report of a WHO study group. WHO Technical Report Series, *Geneva: World Health Organization*, 843.
- Yamada, Y., Yoshida, T., Yokoyama, K., Watanabe, Y., Miyake, M., Yamagata, E.,...Study, K. (2016). The extracellular to intracellular water ratio in upper legs is negatively associated with skeletal muscle strength and gait speed in older people. *J Gerontol A Biol Sci Med Sci*, 00(00), 1-6
- Zeng, P., Han, Y., Pang, J., Wu, S., Gong, H., Zhu, J.,...Zhang, T. (2016). Sarcopenia-related features and factors associated with lower muscle strength and physical performance in older Chinese: a cross-sectional study. *BMC Geriatrics*, 16(45).

APPENDIX A
CONSENT FORM

CONSENT FORM

Title: Establishing New Definition of Sarcopenia using Muscle Quality Index

Introduction

The purposes of this form are (1) to provide you with information that may affect your decision as to whether or not to participate in this research study, and (2) to record your consent if you choose to be involved in this study.

Researchers

Dr. Chong Lee, Associate Professor of School of Nutrition and Health Promotion (SNHP), invite your voluntary participation in a research study being performed at Arizona State University (ASU).

Purpose

The purpose of this study is to establish a new definition of sarcopenia using “muscle quality index” in men and women.

Description of Research Study

To be eligible to participate in this study, you must be 20 to 29 years of age or 60 to 80 years of age. Any individuals who had a personal history of heart disease, stroke, cancer, respiratory disease, or type 2 diabetes will be excluded. All participants should meet minimum qualification to participate in physical activity (e.g., muscle strength and normal walk tests) assessed by physical activity readiness questionnaire (PAR-Q) or received exercise-clearance form from their physician. As a research participant, you will need to have one visit to ASU Downtown Campus. You may need to bring comfortable clothes and walking shoes during your visit. The entire testing procedures are as follows.

Testing Procedures

You will be scheduled to meet with researchers at ASU Downtown Campus. At the first meeting (SNHP research laboratory, ABC building, 1st floor, Room #166), researchers will reconfirm your current health condition (e.g., normal, fever, cold, etc.) to determine whether you are suitable to participate the study. If you are in good health condition, researchers will explain the study protocol in detail and will ask you to sign a consent form before the study starts, following the “Informed Consent Process for Research.” Then, you will be asked to complete a brief health history questionnaire including demographics (e.g., age, gender, race, etc.), medication use, lifestyle behaviors (e.g., smoking habits, alcohol intake, dietary habits, and physical activity level), and functional health status.

Second, you will undergo simple physical performance and clinical evaluation including anthropometric (e.g., body weight, height, and waist girth) and blood pressure measurements, hand-handgrip strength and isokinetic leg extension and elbow flexion

tests, gait speed and timed sit to stand tests, pulse-wave velocity measurement, and dual-energy X-ray absorptiometry (DEXA) assessment.

Body height and weight will be assessed using a standardized physician's scale. Waist girth will be measured laterally at the point midway between the iliac crest and the lowest lateral portion using a plastic tape measure. Seated blood pressure will be measured after 5 min of rest with the use of a random-zero sphygmomanometer. Hand-grip strength will be assessed by a handgrip strength dynamometer. Isokinetic leg extension and elbow flexion-extension tests will be used to measure muscle strength in both arm and leg. Gait speed will be evaluated by a five-meter normal walk test. Timed sit to stand test will be conducted using a standard armless chair with a stopwatch. Pulse wave velocity (PWV) will be measured using SphygmoCor System by a certified technician. You will be asked to lay down on a comfortable table. The technician will measure both carotid and femoral artery waveforms, and pulse wave time between the carotid and femoral arteries. Then, the PWV will be computed as the distance (D) between the carotid and femoral arteries divided by the time difference (Δt) between the two sites ($PWV = D/\Delta t$). Dual-energy X-ray absorptiometry (DEXA) will be used to measure body composition and appendicular skeletal muscle mass by a licensed technician (Lunar iDXA, GE Healthcare, Madison, WI). For DEXA scan, you will be asked to lie face up on an open, padded table for 7 minutes while the scanner arm of the DEXA machine passes over the entire body. You can wear regular clothing, removing any metals from your body. You will be exposed to a small amount of radiation (1-4 microSieverts) that is within an acceptable range per the FDA. For comparison, the radiation for a typical x-ray is 30 to 40 microSieverts.

Overall, an estimated time of testing all of these tests will last approximately 2 hours.

Risks

There are no known risks associated with this study. Although DEXA uses a minor amount of radiation, experts report that the health risk associated with this small amount of radiation is very minimum.

Benefits

There will be no benefits to participants. However, this study will provide some valuable information about your bone and muscle health and body composition status.

New Information

If the researcher finds new information during the study, we will provide this new information to you.

Confidentiality

All information obtained in this study is strictly confidential unless the law requires disclosure. The results of this research study will be used in reports, presentations, and publications, but your name or identity will not be revealed. To maintain the confidentiality of your research, the principal investigator, Dr. Lee will use subject codes

on all data collected, keep a master list separate and secure from all data collected, and limit access to all confidential information to the study investigators.

Withdrawal Privilege

You may withdraw the study at any time for any reason without penalty. Your decision will not affect you in any way or harm any relationship you have with Arizona State University.

Costs and Payments

The researcher wants your decision to be voluntary. The researcher recognizes that participation may pose some inconvenience. To compensate you, you will receive \$25 gift card after completion of the study.

Compensation for Illness and Injury

If you agree to participate in the study, then your consent does not waive any of your legal rights. However, in the event of harm, injury, or illness arising from this study, neither Arizona State University nor the researchers can give you any money, insurance coverage, free medical care, or any compensation for such injury. Major injury is not likely but if necessary, a call to 911 will be placed.

Voluntary Consent

Any questions you have concerning the research study or your participation in the study, before or after your consent, can be answered by Dr. Chong Lee (Chong.Lee@asu.edu or 602-827-2282). If you have any questions about your rights as a participant in this research, or if you feel that you will be placed at risk, you may contact the Chair of Human Subjects Institutional Review Board, through the Office of Research Integrity and Assurance, at (480) 965-6788.

This form explains nature, demands, benefits and any risk of the project. By signing this form, you agree knowingly to assume any risks involved. Remember, your participation is voluntary. You may choose not to participate or to withdraw your consent and discontinue participation at any time without penalty or loss of benefit. In signing this consent form, you are not waiving any legal claims, rights, or remedies. A copy of this consent form will be given to you.

Your signature below indicates that you consent to participate in the above study.

Subject's Signature	Printed Name	Date
Contact phone number	Email	

Investigator’s Affidavit

“I certify that I have explained to the above individual nature and purpose, the potential benefits, and possible risks associated with participation in this research study, have answered any questions that have been raised and have witnessed the above signature. These elements of Informed Consent conform to the Assurance given by Arizona State University to the Office for Human Research Protections to protect the rights of human subjects. I have provided the subject/participant a copy of this signed consent document.”

Signature of Investigator

Date

APPENDIX B
IRB APPROVAL

APPROVAL: EXPEDITED REVIEW

Chong Lee
SNHP: Exercise Science and Health Promotion
602/827-2282
Chong.Lee@asu.edu

Dear Chong Lee:

On 4/14/2016 the ASU IRB reviewed the following protocol:

Type of Review:	Initial Study
Title:	Establishing New Definition of Sarcopenia using Muscle Quality Index
Investigator:	Chong Lee
IRB ID:	STUDY00004240
Category of review:	(2)(a) Blood samples from healthy, non-pregnant adults, (4) Noninvasive procedures, (9) Convened IRB determined minimal risk
Funding:	Name: Piper Health Solutions Consortium
Grant Title:	
Grant ID:	
Documents Reviewed:	<ul style="list-style-type: none"> • HRP-503b.docx, Category: IRB Protocol; • Health Questionnaires.pdf, Category: Recruitment Materials; • Award letter_2015 Seed Funding-Lee.pdf, Category: Sponsor Attachment; • FollowUpSurvey.doc.pdf, Category: Recruitment Materials; • Adults Needed for Muscle Health Research-flyer.pdf, Category: Recruitment Materials; • Follow-Up Email Contents.pdf, Category: Recruitment Materials; • CONSENT FORM.pdf, Category: Consent Form;

APPENDIX C
RECRUITMENT FLIER

Adults Needed for Muscle Health Research

SNHP at ASU is looking for young and elderly men and women (21 to 29 or 60 to 80 years of age) for muscle health research. This study will provide you most updated information about your **bone and muscle health** and **body composition status** using dual-energy X-ray absorptiometry (DEXA) and Isokinetic dynamometers. Participants need only one visit to ASU Downtown Campus (**Compensation: \$30, 2 hours total**). Participation in this study is entirely voluntary.

To request more information or to apply for the study, please visit our recruitment site:

<https://www.surveymonkey.com/r/56TN9KN>

APPENDIX D

MUSCLE QUALITY RESEARCH RECRUTMENT SURVEY

Muscle Quality Research

Follow-Up Survey

This survey is a pre-screening questionnaire for our Muscle Health Study. Please complete the survey as accurate as possible. All information will be kept in confidential. The eligibility status of your study participation will be notified by email.

1. What is your email address?

2. What is your age? _____ (years of age)

3. Do you have a personal history of any of the following diseases? Please check the appropriate box(es).

- Type 2 diabetes
- Heart Disease
- Stroke
- Cancer
- Other Chronic Diseases
- No

4. Has your doctor ever said that you have a heart condition and that you should only do physical activity recommended by a doctor?

- Yes
- No

5. Do you feel pain in your chest when you do physical activity?

- Yes
- No

6. In the past month, have you had chest pain when you were not doing physical activity?

Yes

No

7. Do you lose your balance because of dizziness or do you ever lose consciousness?

Yes

No

8. Do you have a bone or joint problem (for example, back, knee or hip) that could be made worse by a change in your physical activity?

Yes

No

9. Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart condition?

Yes

No

10. Do you know of any other reason you should not do physical activity?

Yes

No

APPENDIX E
LIFESTYLE QUESTIONNAIRE

General Information

Numeric ID

This is a brief questionnaire for participant’s health, demographics, lifestyle information, and functional health status. Please complete this survey as accurate as possible. All information will be kept in confidential.

What is your age? _____(years)

Please check the appropriate box(es) or fill the blanks.

What is your gender? Male Female

Are you pregnant? Yes No

What is your race?

Non-Hispanic Whites African-American

Hispanic Asian Other

Please list any current medication uses?

What is your smoking status?

Never smoked Former smoker Current smoker

On average how many alcoholic drinks per week? (1 drink = 1 beer [12 oz.] or 1 wine [5 oz. glass] or 1 hard liquor [1.5 oz.])

None 7 per week 14 per week 14 or more per week

On average, how many days (frequency) do you exercise per week?
_____ days/wk.

What is the intensity of the workouts?

Low (e.g., slow walking, standing)

Moderate (e.g.: brisk walking, bicycling, dancing)

Vigorous (e.g.: jogging or running, fast cycling, fast swimming)

How long (minutes) do you exercise in each session?

_____minutes

How many servings of fruits and vegetables do you eat **per day**?

(1 serving= 1 Medium Fruit; 1 Cup Leafy Vegetables)

Less than 4.5 cups/servings

4.5 or more cups/servings

How many servings of fish do you eat per week? (1 serving= 3.5-oz)

Less than 2

2 or more

How many servings of fiber-rich whole grains do you eat per day?

(1 serving= 1 Slice Whole Grain Bread)

Less than 3

3 or more

What is your total sodium intake per day?

Less than 1500 mg

1500 mg or more

How many ounces of sugar-sweetened beverages do you consume per week?

(1 Serving of Soda = 12 oz)

Less than 36 oz.

36 oz. or more

How much difficulty do you have in lifting and carrying 10 pounds?

None Some A lot or Unable

How much difficulty do you have walking across a room?

None Some A lot or Unable

How much difficulty do you have transferring from a chair or bed?

None Some A lot or Unable

How much difficulty do you have climbing a flight of 10 stairs?

None Some A lot or Unable

How many times have you fallen in the past year?

None Some A lot or Unable