

CHARACTERIZING THE IMPACT OF MUSCLE QUALITY ON LOWER-
EXTREMITY PHYSICAL FUNCTION IN OVERWEIGHT AND OBESE OLDER
WOMEN FOLLOWING A WEIGHT LOSS AND EXERCISE INTERVENTION

by

CHAD RICHARD STRAIGHT

(Under the Direction of Ellen M. Evans)

ABSTRACT

The population of older women living in the United States continues to grow rapidly and aging is accompanied by an increased risk for physical limitations. Muscle quality, which is traditionally defined as muscle strength or power per unit of muscle size, is a salient determinant of physical function in older adults and thus a potential target for intervention. Therefore, in the context of a 6-month exercise and diet-induced weight loss intervention for overweight and obese ($\text{BMI} \geq 25.0 \text{ kg/m}^2$) older (65-80 y) women, the primary aims of this dissertation were three-fold: 1) to examine the relative contributions of changes in muscle quality and body composition to changes in lower-extremity physical function (LEPF), 2) to determine the specific functional improvements associated with changes in various indices of whole-muscle performance, and 3) to examine the effects on mid thigh composition, and the interrelationships among changes in intermuscular adipose tissue (IMAT), muscle quality and LEPF.

For primary aim 1 ($n=38$), our linear regression model indicated that change in muscle quality (standardized $\beta = 0.64$, $p < 0.01$) was the strongest independent predictor

of change in a composite LEPF Z-score; however, change in body weight ($\beta = -0.30$, $p < 0.05$) was also a significant contributor. For primary aim 2 ($n=38$), a 1 N-m increase in knee muscle strength consistently predicted improvements in 6-minute walk distance (unstandardized β range = 0.310 to 0.505, $p < 0.05$) and 8-foot up-and-go time (β range = -0.010 to -0.012, $p < 0.05$), although leg power was more important for tasks requiring the transfer of body weight (e.g., sitting-to-standing). With regard to primary aim 3 ($n=25$), a reduction in mid thigh IMAT area was the strongest independent predictor of a change in performance on the 30-s chair stand (standardized $\beta = -0.80$, $p < 0.01$) while change in muscle quality was a significant predictor of change in 6-minute walk distance ($\beta = 0.48$, $p < 0.05$).

Changes in muscle quality and whole-body and regional composition significantly predict improvements in LEPF tests among overweight and obese older women following exercise and diet-induced weight loss.

INDEX WORDS: muscle quality, aging, exercise, weight loss, obesity, women

CHARACTERIZING THE IMPACT OF MUSCLE QUALITY ON LOWER-
EXTREMITY PHYSICAL FUNCTION IN OVERWEIGHT AND OBESE OLDER
WOMEN FOLLOWING A WEIGHT LOSS AND EXERCISE INTERVENTION

by

CHAD RICHARD STRAIGHT

B.S., University of Rhode Island, 2009

M.S., University of Rhode Island, 2011

A Dissertation Submitted to the Graduate Faculty of The University of Georgia in Partial

Fulfillment of the Requirements for the Degree

DOCTOR OF PHILOSOPHY

ATHENS, GEORGIA

2015

© 2015

CHAD RICHARD STRAIGHT

All Rights Reserved

CHARACTERIZING THE IMPACT OF MUSCLE QUALITY ON LOWER-
EXTREMITY PHYSICAL FUNCTION IN OVERWEIGHT AND OBESE OLDER
WOMEN FOLLOWING A WEIGHT LOSS AND EXERCISE INTERVENTION

by

CHAD RICHARD STRAIGHT

Major Professor: Ellen M. Evans
Committee: Mary Ann Johnson
Kevin K. McCully

Electronic Version Approved:

Suzanne Barbour
Dean of the Graduate School
The University of Georgia
August 2015

DEDICATION

I dedicate this dissertation to my parents, Ken and Sterry, who have never wavered in their unconditional love and support. You continue to inspire me, and I would not have been able to complete this degree without knowing that you are always in my corner. To my brothers, Matty and Jared, who always remind me that I need to take a breath and enjoy life. And to Lauren, who has stood by my side even while I desperately tried to relocate us back to New England, I am so grateful to have you. It wasn't always easy, but remember, "When it feels like you're going through hell, keep going."

ACKNOWLEDGEMENTS

I would like to express my deepest appreciation and gratitude to my doctoral mentor, Dr. Ellen Evans. You have taught me more than you will ever realize, both professionally and personally, and I am leaving Athens as a better educator, scholar and person than when I came here four years earlier. I would also like to thank Dr. Mary Ann Johnson and Dr. Kevin McCully for their guidance and mentorship during my career at the University of Georgia. Finally, I would like to acknowledge Dr. Matthew Delmonico, for cultivating my interest in research during my time at the University of Rhode Island, and by providing me with consistent encouragement and support as I have progressed as an academic.

There are too many people who have contributed to this dissertation, both directly and indirectly, to individually acknowledge in this section. So, for every lab mate, colleague or friend that I have had the opportunity to know at UGA, all I can say is thank you – I have learned something from all of you.

TABLE OF CONTENTS

	Page
ACKNOWLEDGEMENTS	v
LIST OF TABLES	ix
LIST OF FIGURES	xi
CHAPTER	
1 INTRODUCTION.....	1
1.1 Significance	1
1.2 Primary Aims	3
1.3 References	5
2 LITERATURE REVIEW: MUSCLE QUALITY IN OLDER ADULTS: WHAT ARE THE HEALTH IMPLICATIONS?.....	8
2.1 Abstract	9
2.2 Introduction	10
2.3 Changes in Body Composition: Hallmarks of the Aging Process.....	11
2.4 Muscle Quality	12
2.5 Future Directions	17
2.6 References	20
3 CHANGES IN MUSCLE QUALITY AND BODY WEIGHT PREDICT IMPROVEMENTS IN PHYSICAL FUNCTION FOLLOWING EXERCISE AND WEIGHT LOSS IN OVERWEIGHT AND OBESE OLDER WOMEN29	

3.1	Abstract	30
3.2	Introduction	31
3.3	Methods.....	32
3.4	Results.....	37
3.5	Discussion	39
3.6	References	45
4	SPECIFIC FUNCTIONAL IMPROVEMENTS ASSOCIATED WITH INCREASES IN WHOLE-MUSCLE PERFORMANCE IN OVERWEIGHT AND OBESE OLDER WOMEN FOLLOWING 6 MONTHS OF EXERCISE AND WEIGHT LOSS	57
4.1	Abstract	58
4.2	Introduction	59
4.3	Methods.....	61
4.4	Results.....	66
4.5	Discussion	68
4.6	References	74
5	MIDTHIGH INTERMUSCULAR ADIPOSE TISSUE AND MUSCLE QUALITY DIFFERENTIALLY PREDICT IMPROVEMENTS IN PHYSICAL FUNCTION FOLLOWING EXERCISE AND WEIGHT LOSS IN OVERWEIGHT AND OBESE OLDER WOMEN	83
5.1	Abstract	84
5.2	Introduction	85
5.3	Methods.....	86

5.4 Results.....	90
5.5 Discussion.....	92
5.6 References.....	97
6 SUMMARY AND CONCLUSIONS.....	110

LIST OF TABLES

	Page
Table 2.1: Summary of studies that have examined the relationship between muscle quality and health outcomes in older adults	26
Table 3.1: Participant characteristics	49
Table 3.2: Characteristics of the multicomponent exercise training intervention	50
Table 3.3: Baseline and post-intervention values for body composition, muscle quality and lower-extremity physical function.....	51
Table 3.4: Relative contributions of percent changes in body composition and muscle quality to a change in lower-extremity physical function Z-score	52
Table 4.1: Participant characteristics	77
Table 4.2: Characteristics of the multicomponent exercise training intervention	78
Table 4.3: Baseline, post and change values for indices of whole-muscle contractile performance and lower-extremity physical function	79
Table 4.4: Association between changes in muscle capacity and lower-extremity physical function using linear regression analysis	80
Table 4.5: Association between changes in muscle quality and lower-extremity physical function using linear regression analysis	81
Table 5.1: Participant characteristics	101
Table 5.2: Characteristics of the multicomponent exercise training intervention	102

Table 5.3: Baseline and post-intervention values for midthigh composition, muscle quality and physical n..... 103

Table 5.4: Multivariate linear regression analysis of changes in whole-body fat mass, midthigh intermuscular adipose tissue and muscle quality for changes in physical function..... 104

LIST OF FIGURES

	Page
Figure 3.1: Percent change from baseline to 6 months for measures of body composition and muscle quality	53
Figure 3.2: Percent changes from baseline to 6 months in measures of lower-extremity physical function.....	54
Figure 3.3: Comparison of change from baseline to 6 months in lower-extremity physical function Z-score between participants who increased muscle quality by $\geq 10\%$ and those who did not	55
Figure 3.4: Comparison of change from baseline to 6 months in lower-extremity physical function Z-score between participants who achieved $\geq 10\%$ loss of initial body weight and those who did not	56
Figure 4.1: Percent changes in muscle strength, power and quality from baseline to post-intervention.....	82
Figure 5.1: Percent changes from baseline to 6 months in mid thigh composition	105
Figure 5.2: Change from baseline to 6 months in percent of total thigh area occupied by intermuscular adipose tissue, subcutaneous adipose tissue and muscle	106
Figure 5.3: Bivariate association between changes in overall body mass and mid thigh subcutaneous adipose tissue cross-sectional area	107
Figure 5.4: Bivariate association between changes in overall body mass and mid thigh intermuscular adipose tissue cross-sectional area.....	108

Figure 5.5: Bivariate association between baseline midhigh intermuscular adipose tissue
cross-sectional area and change at 6 months 109

CHAPTER 1

INTRODUCTION

1.1 Significance

The population of older adults in the United States continues to grow, and it is estimated that adults aged 65 years and older will constitute 20% of the entire population by 2030¹. This is a concern as the likelihood of physical limitations increases with age; adults ≥ 80 years are ~2.5 times more likely to experience one or more physical limitations relative to those adults aged 50-59 years². However, the likelihood of functional limitations is greater in women than men at ages 65-74 y (31 vs. 24%), 75-84 y (46 vs. 37%), and 85+ y (66 vs. 50%), which highlights an increasing sex disparity in disability with advancing age³. Relative to men, older women tend to have greater absolute and relative adiposity^{4,5}, lower lean mass^{4,5}, lower muscle quality⁶⁻⁸, and lower physical activity levels^{9,10}, all of which may heighten susceptibility to physical functional decline. Maintaining physical function is paramount as it is a significant predictor of adverse health outcomes such as physical disability, institutionalization and mortality in older adults¹¹. Thus, identifying the most salient contributors to physical function among older adults, and particularly women, represents a major public health priority and contemporary research interest.

There are a myriad of factors that potentially impact physical function in older adults, and these have recently been reviewed in detail¹². Notably, muscle quality, traditionally defined as the ratio of muscle force per unit of muscle cross-sectional area^{13,14} or mass⁶, has been the focus of recent reviews on physical function in older adults^{12,15}. Indeed, muscle quality has emerged as a critical variable for physical performance among community-dwelling older adults^{7,16-18}. It has

been identified as an independent predictor of lower-extremity physical function, and this relationship has been evident using leg muscle strength^{7,16} and power¹⁸ as the measure of muscle capacity. However, muscle quality is lower in overweight and obese adults relative to their normal weight counterparts, and this has been reported in studies that defined muscle quality using strength^{6,17} and power¹⁹. In addition, while there is general agreement that muscle quality is important for physical function, whether or not it has predictive value beyond a measure of muscle capacity (strength or power) remains incompletely characterized. Both muscle strength²⁰⁻²² and power²³⁻²⁶ have been associated with physical function in older adults, but no study has concurrently examined the associations of muscle strength, power and quality with physical function in a cohort of older adults, which is particularly important under conditions of overweight and obesity. Low muscle quality in the presence of normal weight and a healthy body composition may not result in substantial physical limitations. However, if muscle quality is disproportionately low relative to the load to be moved (body mass), such as with overweight/obesity, it's importance for physical function may be attenuated relative to adiposity.

As discussed above, an accumulating body of evidence has highlighted the importance of muscle quality for physical function. Thus, an age-related decrease in MQ, which may be exacerbated by disordered body composition, underscores the urgent need for behavioral strategies, specifically weight management and physical activity/exercise to improve the likelihood of healthy aging. It is possible that increasing muscle quality can translate to improved physical performance, but minimal research exists evaluating these relationships²⁷. Notably, interventions can impact both components of muscle quality by altering muscle capacity (strength or power) and muscle size (mass or volume), and by reducing intermuscular adipose tissue (IMAT), which is associated with poor muscle quality²⁸. Although any intervention that

impacts one of the above components of muscle quality may translate to improved physical function, different interventions may operate primarily via distinct mechanisms (e.g., exercise can enhance strength and power relative to size, while weight loss may reduce IMAT). Furthermore, muscle quality has not been examined in the larger context of changes in body composition (adiposity and lean mass), such as in response to a weight loss intervention for overweight older adults. Currently, no study to date has examined whether exercise-induced changes in muscle capacity or quality translate to improved physical function in the context of weight loss among overweight and obese older women. Furthermore, understanding the relative contributions of improved muscle quality and body composition to changes in physical function is critical for informing the development of interventions for preventing physical disability.

1.2 Primary Aims

The overarching goal of this study was to evaluate the following questions in response to a six-month exercise and weight loss intervention in overweight and obese older women: 1) What are the relative contributions of changes in muscle quality and adiposity to changes in LEPF?; 2) Which index of muscle capacity or muscle quality is the strongest predictor of a change in lower-extremity physical function (LEPF)?; and, 3) Does baseline thigh IMAT volume influence the magnitude of change in muscle quality? In this context, the primary aims of the present study were three-fold:

Primary Aim 1: To determine the independent contributions of changes in adiposity (e.g., the load to be moved) and changes in muscle quality (e.g., ability to move the load) to a change in LEPF in overweight and obese older women following the weight loss and exercise intervention. *Hypothesis:* Based on previous literature¹⁶, it was hypothesized that a) change in muscle quality would be the strongest independent predictor of LEPF, but that relative adiposity

would also be a significant independent contributor, and b) the interaction between changes in adiposity and changes in muscle quality would be related to change in LEPF with a similar strength of association.

Primary Aim 2: To determine which index of muscle capacity or muscle quality most strongly predicts a change in LEPF following a six-month exercise and weight loss intervention in overweight and obese older women. *Hypothesis:* Based on previous studies that have reported a higher relative importance of muscle power compared to muscle strength for physical function²⁴⁻²⁶, it was hypothesized that a change in muscle quality (defined using muscle power) would be the strongest independent predictor of a change in LEPF in response to the intervention.

Primary Aim 3: To investigate the influence of thigh composition, specifically IMAT, on change in muscle quality and LEPF following a six-month exercise and weight loss intervention in overweight and obese older women. *Hypothesis:* Based on a previously reported relationship between IMAT and muscle quality^{29,30}, it was hypothesized that the change in IMAT would be associated with the change in muscle quality following the intervention, such that women with lower IMAT would have greater improvements in muscle quality and LEPF relative to women with higher IMAT.

1.3 References

1. Statistics. NCfH. *Health, United States, 1999: With Health and Aging Chartbook*. Hyattsville, MD: National Center for Health Statistics; 1999.
2. Holmes J, Powell-Griner E, Lethbridge-Cejku M, Heyman K. Aging differently: Physical limitations among adults aged 50 years and over: United States, 2001-2007. *NCHS Data Brief*. 2009;1-8.
3. Newman AB, Brach JS. Gender gap in longevity and disability in older persons. *Epidemiol Rev*. 2001;23:343-350.
4. Valentine RJ, Misic MM, Rosengren KS, Woods JA, Evans EM. Sex impacts the relation between body composition and physical function in older adults. *Menopause*. 2009;16:518-523.
5. Jankowski CM, Gozansky WS, Van Pelt RE, et al. Relative contributions of adiposity and muscularity to physical function in community-dwelling older adults. *Obesity (Silver Spring)*. 2008;16:1039-1044.
6. Newman AB, Haggerty CL, Goodpaster B, et al. Strength and muscle quality in a well-functioning cohort of older adults: the Health, Aging and Body Composition Study. *J Am Geriatr Soc*. 2003;51:323-330.
7. Fragala MS, Clark MH, Walsh SJ, et al. Gender differences in anthropometric predictors of physical performance in older adults. *Gend Med*. 2012;9:445-456.
8. Skelton DA, Greig CA, Davies JM, Young A. Strength, power and related functional ability of healthy people aged 65-89 years. *Age Ageing*. 1994;23:371-377.
9. Centers for Disease Control and Prevention. Trends in strength training--United States, 1998-2004. *MMWR Morb Mortal Wkly Rep*. 2006;55:769-772.
10. Sun F, Norman IJ, While AE. Physical activity in older people: a systematic review. *BMC Public Health*. 2013;13:449.
11. Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *J Gerontol*. 1994;49:M85-94.
12. Brady AO, Straight CR, Evans EM. Body composition, muscle capacity, and physical function in older adults: an integrated conceptual model. *J Aging Phys Act*. 2014;22:441-452.
13. Delmonico MJ, Harris TB, Visser M, et al. Longitudinal study of muscle strength, quality, and adipose tissue infiltration. *Am J Clin Nutr*. 2009;90:1579-1585.

14. Metter EJ, Lynch N, Conwit R, Lindle R, Tobin J, Hurley B. Muscle quality and age: cross-sectional and longitudinal comparisons. *J Gerontol A Biol Sci Med Sci*. 1999;54:B207-218.
15. Barbat-Artigas S, Rolland Y, Zamboni M, Aubertin-Leheudre M. How to assess functional status: a new muscle quality index. *J Nutr Health Aging*. 2012;16:67-77.
16. Mistic MM, Rosengren KS, Woods JA, Evans EM. Muscle quality, aerobic fitness and fat mass predict lower-extremity physical function in community-dwelling older adults. *Gerontology*. 2007;53:260-266.
17. Villareal DT, Banks M, Siener C, Sinacore DR, Klein S. Physical frailty and body composition in obese elderly men and women. *Obes Res*. 2004;12:913-920.
18. Straight CR, Brady AO, Schmidt MD, Evans EM. Comparison of laboratory- and field-based estimates of muscle quality for predicting physical function in older women. *J Aging Res Clin Practice*. 2013;2:276-279.
19. Brady AO, Straight CR, Schmidt MD, Evans EM. Impact of body mass index on the relationship between muscle quality and physical function in older women. *J Nutr Health Aging*. 2014;18:378-382.
20. Rantanen T, Guralnik JM, Izmirlian G, et al. Association of muscle strength with maximum walking speed in disabled older women. *Am J Phys Med Rehabil*. 1998;77:299-305.
21. Barbat-Artigas S, Rolland Y, Cesari M, Abellan van Kan G, Vellas B, Aubertin-Leheudre M. Clinical relevance of different muscle strength indexes and functional impairment in women aged 75 years and older. *J Gerontol A Biol Sci Med Sci*. 2013;68:811-819.
22. Bouchard DR, Heroux M, Janssen I. Association between muscle mass, leg strength, and fat mass with physical function in older adults: influence of age and sex. *J Aging Health*. 2011;23:313-328.
23. Bean JF, Kiely DK, Herman S, et al. The relationship between leg power and physical performance in mobility-limited older people. *J Am Geriatr Soc*. 2002;50:461-467.
24. Bean JF, Leveille SG, Kiely DK, Bandinelli S, Guralnik JM, Ferrucci L. A comparison of leg power and leg strength within the InCHIANTI study: which influences mobility more? *J Gerontol A Biol Sci Med Sci*. 2003;58:728-733.
25. Foldvari M, Clark M, Laviolette LC, et al. Association of muscle power with functional status in community-dwelling elderly women. *J Gerontol A Biol Sci Med Sci*. 2000;55:M192-199.
26. Suzuki T, Bean JF, Fielding RA. Muscle power of the ankle flexors predicts functional performance in community-dwelling older women. *J Am Geriatr Soc*. 2001;49:1161-1167.

27. Pinto RS, Correa CS, Radaelli R, Cadore EL, Brown LE, Bottaro M. Short-term strength training improves muscle quality and functional capacity of elderly women. *Age (Dordr)*. 2014;36:365-372.
28. Goodpaster BH, Carlson CL, Visser M, et al. Attenuation of skeletal muscle and strength in the elderly: The Health ABC Study. *J Appl Physiol*. 2001;90:2157-2165.
29. Visser M, Goodpaster BH, Kritchevsky SB, et al. Muscle mass, muscle strength, and muscle fat infiltration as predictors of incident mobility limitations in well-functioning older persons. *J Gerontol A Biol Sci Med Sci*. 2005;60:324-333.
30. Visser M, Kritchevsky SB, Goodpaster BH, et al. Leg muscle mass and composition in relation to lower extremity performance in men and women aged 70 to 79: the health, aging and body composition study. *J Am Geriatr Soc*. 2002;50:897-904.

CHAPTER 2
LITERATURE REVIEW
MUSCLE QUALITY IN OLDER ADULTS: WHAT ARE THE HEALTH
IMPLICATIONS?¹

¹Straight, C.R., Brady, A.O., and Evans, E.M. 2015. *American Journal of Lifestyle Medicine*.
2015;9:130-6.

Reprinted here with permission of the publisher.

2.1 Abstract

The population of older adults in the United States is steadily growing and identifying factors that contribute to healthy aging is a public health priority. Changes in body composition are a hallmark of the aging process and have been implicated in the loss of physical function among older adults. In particular, age-related declines in muscle strength and power occur at a faster rate than the loss of muscle mass (sarcopenia), and this suggests a decrease in muscle quality of older adults. Muscle quality has traditionally been defined as muscle function (strength or power) per unit of muscle size (mass or cross-sectional area) and a growing body of literature suggests that lower-body muscle quality may be critical for maintaining functional independence with age. However, the literature regarding the definition of muscle quality and its relationship with health outcomes in older adults has not been adequately reviewed. Thus, the aim of this report is to highlight the contemporary literature regarding age-related changes in muscle quality and its relationship with health outcomes in community-dwelling older adults.

2.2 Introduction

The percentage of adults aged 65 years and older continues to grow and it is estimated that this group will constitute 20% of the adult population in the United States by 2030¹. This is important as there is a substantial increase in the prevalence of physical limitations with age; adults ≥ 80 years are ~ 2.5 times more likely to experience one or more physical limitations (e.g., walking $\frac{1}{4}$ of a mile, climbing 10 steps, reaching overhead) than adults aged 50-59 years (43% vs. 17%, respectively)². Therefore, establishing the role of modifiable factors that contribute to physical function during aging is a major public health priority.

Muscle quality, traditionally defined as muscle force per unit of muscle cross-sectional area^{3,4}, is emerging as a salient contributor to health and physical function in older adults⁵⁻⁸. The ability to complete functional activities (rising from a chair, stair ascent), as well as success with other domains of physical function including gait speed and balance, is strongly determined by the major lower-extremity muscle groups (quadriceps, hamstrings, and gluteals). Therefore, it is likely that the quality of these muscle groups is critical for maintaining functional independence with age. Despite this, there remains a relative paucity of research delineating the importance of leg muscle quality for health outcomes (e.g., functional and metabolic parameters) in older adults. Recently, Barbat-Artigas et al.⁹ published a review article regarding different measurement techniques for assessing muscle quality in older adults. However, the relationship between leg muscle quality and health outcomes in older adults remains inadequately characterized and may have important clinical implications. Thus, this report seeks to review studies that have examined muscle quality in relation to health outcomes in community-dwelling older men and women. Better characterizing the health implications of muscle quality (e.g., its

relationship with various functional and metabolic outcomes in older adults) is valuable as it may help inform the development of intervention strategies to facilitate healthy aging.

We identified studies that examined muscle quality and health outcomes in older adults via literature searches on relevant electronic databases through June 2013 using specific search terms including “muscle quality,” “specific tension,” “specific strength,” “specific torque,” “specific power,” “normalized force,” “physical function,” “health outcomes,” and “older adults.” Our search was not constrained by the type of measurement technique used to define muscle function and muscle size. However, because our review is focused on measurement of leg muscle quality, studies that examined the quality of other muscle groups (e.g., plantar flexors, upper-extremity) in older adults have been excluded¹⁰⁻¹³. Lastly, although muscle quality has been examined in cohorts of young adults, this review is focused on community-dwelling older adults and is therefore limited to studies that involved non-institutionalized men and women aged ≥ 50 years.

2.3 Changes in Body Composition: Hallmarks of the Aging Process

Several adverse changes in body composition occur during the aging process, and these include a progressive reduction in skeletal muscle mass known as sarcopenia¹⁴. Sarcopenia, originally proposed by Rosenberg in 1989¹⁵, has been associated with functional impairment¹⁶ and physical disability^{17,18}, and has also been identified as a predictor of incident physical limitations among older adults^{19,20}. However, sarcopenia is accompanied by concomitant declines in muscle function (strength and power), which both occur at a faster rate than the loss of muscle mass⁹.

Dynapenia, the age-related loss of muscle strength²¹, is only partially explained by the decline in skeletal muscle mass (sarcopenia). For instance, it was recently shown that cross-

sectional area of the quadriceps muscle only accounted for 6-8% of the variability in muscle strength among older adults⁴. While a comprehensive review of the physiologic mechanisms underlying dynapenia is beyond the scope of this review, a brief discussion is warranted. It is likely that the complex interplay of neurologic and muscular mechanisms contributes to dynapenia, and these factors have previously been reviewed in detail^{22,23}. The most prominent mechanisms hypothesized to play a role in dynapenia include a reduction in central activation, decreased motor unit size and number (e.g., denervation of type II muscle fibers), as well as alterations in intrinsic force-generating capacity of muscle, excitation-contraction coupling, myocellular lipid infiltration and inflammatory cytokine production. Although additional research is necessary to elucidate the mechanisms most responsible for dynapenia, the above factors are likely instrumental in the more rapid decline in muscle strength relative to muscle size.

It has previously been reported that skeletal muscle mass declines at a rate of 6% per decade after age 50²⁴. In contrast, muscle strength and power decline at rates of 1-2% and 3.5% per year, respectively, in older adults²⁵, although the reported rate of decline has varied among studies²⁶. Notably, both low muscle strength^{27,28} and power^{29,30} have been implicated in the development of adverse health outcomes among older adults. Thus, the disproportionate reduction in muscle strength and power relative to mass suggests a decrease in muscle quality and may increase susceptibility to functional limitation and physical disability.

2.4 Muscle Quality

Measurement

Several published studies have examined the relationship between leg muscle quality and various health outcomes in community-dwelling older adults (see Table 1). However, because a

standardized assessment procedure for muscle quality has not been established, numerous definitions have been suggested and a variety of measurement techniques have been used. To our knowledge, studies that have investigated muscle quality have been conducted in research laboratories and thus used relatively expensive and sophisticated equipment. The most common measurement techniques for assessing leg muscle function include determination of strength via isokinetic dynamometry^{3-5,31-39}, isometric dynamometry^{36,40-45}, strain gauge⁴⁶, and assessment of strength or power using the one-repetition maximum technique^{44,47-51} or the Nottingham power rig⁶. Lower-extremity muscle size has been predominantly measured by estimating skeletal muscle mass via DXA scanning^{3,5,6,31-33,39,40,43,46-48,50,52}, although anthropometry⁵², ultrasound scanning⁴², and urinary creatinine excretion^{37,52} have also been used. In addition, other studies have used computed tomography^{4,34,36,38,49} and magnetic resonance imaging^{35,41,43-45,51} for quantification of muscle cross-sectional area or volume.

Age-Related Changes

Both cross-sectional^{3,35,52} and longitudinal^{4,31} studies have investigated age-related changes in leg muscle quality among community-dwelling older adults. For instance, Metter et al.⁵² reported that muscle quality (isometric knee extensor strength/leg lean mass) was 39% and 31% lower in men and women, respectively, from age 20 to 80 years. Importantly, the difference between young and older adults was similar (31% for men and 39% for women) when muscle size was determined using anthropometry to estimate cross-sectional area of the thigh. Likewise, Jubrias and colleagues³⁵ reported that muscle quality was 21% lower (~1.5% each year) from age 65 to 80 years in a cross-sectional study of older men and women. In a more recent cross-sectional analysis, Newman et al.³ reported that lower-extremity muscle quality (isokinetic knee extensor strength/leg lean mass) was 10% lower in men and 11% lower in women across ages 70

to 79 years. Other studies have observed age-related differences in some, but not all, indices of leg muscle quality^{36,37}. Therefore, there appears to be general agreement among cross-sectional studies that muscle quality is lower in older adults relative to their younger counterparts.

However, only a few longitudinal studies have determined the rate of decline in muscle quality among community-dwelling older adults. Goodpaster et al.³¹ reported that leg muscle quality declined at a rate of 5.4-8.6% over three years among older men and women. Likewise, Delmonico et al.⁴ found that leg muscle quality declined 13.1% and 11.1% over five years in older men and women, respectively. Although muscle size was quantified using different measurement instruments (DXA scanning vs. computed tomography), both studies provide evidence that the rate of decline in muscle quality exceeds that of sarcopenia (~6% per decade after age 50). However, both studies were conducted using a sample of well-functioning older men and women from the Health, Aging, and Body Composition Study cohort. In addition, both studies defined muscle quality using the same index of muscle strength (isokinetic dynamometry). It is unknown whether a similar age-related decline in muscle quality would be observed using a different index of muscle function (isometric strength, leg power).

Health Outcomes

As the population of older adults in the U.S. continues to grow, delineating the most salient contributors to functional and metabolic health is of considerable interest. In the context of this review, the health implications of muscle quality can be understood as its relationship with functional (e.g., ability to complete functional tasks, physical disability) and metabolic outcomes (e.g., glycemic control, intramuscular lipid infiltration) in community-dwelling older adults.

Physical function, as measured by various performance-based assessments, can predict health outcomes in older adults including self-reported physical disability⁵³ and mobility-related disability^{54,55}, as well as nursing home admission and mortality⁵³. Recently, multiple studies have indicated a relationship between muscle quality and physical function in community-dwelling older men and women^{5-8,46,47}. For instance, Misisic et al.⁵ found that muscle quality was a stronger independent predictor of lower-extremity physical function than aerobic fitness and fat mass. In that study, muscle quality explained 29-42% of the variance in dynamic physical function whereas the explained variance from aerobic fitness and fat mass was much lower (5-6%). Furthermore, we recently demonstrated that muscle quality (leg extension power/lower-extremity mineral-free lean mass) was an independent predictor of performance on the 6-minute walk, 8-foot up-and-go and 30-second chair stand in community-dwelling older women⁶. In contrast, Fragala et al.⁴⁷ reported a significant association between muscle quality and physical function (chair rise time and gait speed) in men, however this relationship was not observed in women. Muscle quality has also been implicated in the development of physical disability and risk of hospitalization. For instance, a recent study by Hairi et al.⁷ found that loss of muscle quality significantly increased risk for self-reported and performance-based functional limitation, as well as physical disability (activities of daily living) in older men. Moreover, Cawthon et al.⁸ reported that older adults with the lowest muscle quality had a 65% greater risk of hospitalization compared to those with the highest muscle quality.

While the above studies support the contribution of muscle quality to physical function, fewer studies have investigated the relationship between muscle quality and metabolic outcomes in older adults. However, Park et al.³³ reported an accelerated loss of leg muscle quality (isokinetic knee extensor strength/leg muscle mass) in older men and women with type 2

diabetes relative to nondiabetic adults. Notably, muscle quality was lowest among older adults who had been diagnosed with type 2 diabetes for \geq six years and in those adults with elevated glycosylated hemoglobin ($\text{HbA}_{1c} > 8.0\%$). In a different analysis using the Health ABC cohort, Goodpaster et al.³⁴ reported that the skeletal muscle attenuation coefficient (indicator of intramuscular lipid infiltration) of the midthigh was significantly associated with muscle quality. Those adults with a greater muscle attenuation value (lower intramuscular lipid content) had higher muscle quality. Interestingly, Newman et al.³ observed a quadratic relationship between overall body fat and muscle quality, such that muscle quality was lowest at the high and low extremes of body fatness and optimal at percent body fat ranges of 16-22% in men and 26-34% in women. Other research has shown that muscle quality is significantly lower in obese older adults relative to nonobese men and women³⁹. However, additional research is necessary to better characterize the impact of adiposity and weight status (normal weight vs. overweight/obese) on muscle quality in older adults.

Exercise Interventions

Regular aerobic and muscle-strengthening activity is recommended by the American College of Sports Medicine for maintenance of health and functional independence of older adults⁵⁶. In addition to a myriad of well-known health benefits, participation in exercise and physical activity can positively impact both components of muscle quality in older adults by altering muscle function (increasing strength/power), muscle size (increasing muscle mass) and reducing intramuscular lipid infiltration.

However, despite mounting evidence that suggests a relationship between muscle quality and health outcomes in older adults, very few intervention studies have included muscle quality as a primary outcome of interest^{44,45,48,50,51,57}. For example, Tracy et al.⁴⁴ found that nine weeks

of unilateral leg strength training resulted in significant increases in muscle quality of the trained leg in both men (+14%) and women (+16%). Similarly, Brooks and colleagues⁴⁸ conducted a 16-week study in older men and women with type 2 diabetes and found a substantial improvement in muscle quality of the exercise group (+28%) whereas a reduction in muscle quality was observed in the control group (-4%). Conversely, Reid et al.⁵⁰ reported changes in muscle quality (specific power) following an exercise intervention in older adults with mobility limitations (Short Physical Performance Battery score = 7.7). Specifically, muscle quality significantly improved following 12 weeks of high-velocity power training or slow-velocity resistance training compared to a control group.

Muscle lipid infiltration is associated with poor muscle quality³⁴, however it may also attenuate the magnitude of a training response following exercise. Marcus et al.⁴⁵ reported that 12 weeks of exercise training significantly improved muscle quality in older adults with low intramuscular adipose tissue, but this was not evident in those with greater levels. Thus, while exercise training appears to be an efficacious intervention strategy for improving leg muscle quality in older adults, its value is based on limited empirical evidence and additional training studies are needed in both healthy and functionally-limited older adults to corroborate these findings. In addition, no studies have attempted to determine if a change in muscle quality following a training intervention is associated with a change in physical function. Research should continue to explore the effects of training-induced changes in muscle quality and whether these translate to improved functional abilities in older adults.

2.5 Future Directions

Collectively, these findings suggest that muscle quality is an important contributor to health outcomes, including physical function and potentially the risk of metabolic disease, in

community-dwelling older adults. Further research will be necessary to ascertain the impact of muscle quality on different metabolic outcomes, however a small number of published studies do suggest a relationship.

This review also highlights the efficacy of exercise interventions (particularly resistance training) for improving muscle quality. However, these training studies were all conducted in research laboratories. Community-based exercise programs that use a lighter training stimulus, but that have greater translational value, should also be evaluated. We have previously reported the health benefits of community-based resistance training programs for older adults⁵⁸, however the impact of such interventions for ameliorating muscle quality should be further explored.

In addition, the potential benefits of weight loss interventions for muscle quality warrant further investigation. Recent studies have shown that weight loss can positively impact the health of obese older adults, such as eliciting improvements in physical function⁵⁹⁻⁶¹. Presently, the effects of weight loss interventions on muscle quality have not been well-characterized. It is plausible that weight loss could positively impact muscle quality by reducing mid-thigh muscle lipid infiltration⁶², which is elevated in obesity⁶³ and associated with muscle quality in older adults³⁴. However, no study has attempted to determine if a change in muscle lipid infiltration following weight loss is associated with improved muscle quality. Furthermore, higher protein consumption (~30% of energy intake) during intentional weight loss can help maintain skeletal muscle mass relative to changes in adiposity⁴³, and this may also have a beneficial effect. However, dietary-induced weight loss is typically accompanied by involuntary reductions in lean mass and exercise may help attenuate these changes^{64,65}. It has recently been shown that resistance training during intentional weight loss can significantly improve muscle power in older women, despite a decline in appendicular lean body mass⁶⁶. While this suggests improved

muscle function despite a change in lean mass, additional studies are needed to ascertain the effects of combined exercise and diet interventions on muscle quality in older adults.

Lastly, muscle quality has been exclusively determined in laboratory settings, and little research has been devoted to development of a measurement technique feasible for use in clinical settings by practitioners. It is likely that assessment of muscle quality in clinical settings may be limited by a number of factors (access to equipment, assessment time, ease of administration). Determination of muscle function and muscle size using inexpensive field-based methods may provide an opportunity for assessment of muscle quality in community-based and clinical settings. Recently, we reported that a field-based estimate of muscle quality (handgrip strength normalized for body mass index) predicted lower-extremity physical function similarly to a more sophisticated laboratory-based approach in community-dwelling older women⁶. However, other field-based techniques exist to measure both muscle function (e.g., manual muscle testing) and muscle size (e.g., bioelectrical impedance analysis). Future research should attempt to develop a standardized assessment protocol for measurement of muscle quality in clinical settings by practitioners, as this could prove beneficial for predicting physical function in older adults. Finally, establishing sex-specific cut-points for muscle quality (similar to those proposed for the diagnosis of sarcopenia) may have particular clinical utility for demarcating older adults at the greatest risk for development of future physical disability.

2.6 References

1. National Center for Health Statistics. *Health, United States, 1999: With Health and Aging Chartbook*. Hyattsville, MD: National Center for Health Statistics; 1999.
2. Holmes J, Powell-Griner E, Lethbridge-Cejku M, Heyman K. Aging differently: Physical limitations among adults aged 50 years and over: United States, 2001-2007. *NCHS Data Brief*. 2009(20):1-8.
3. Newman AB, Haggerty CL, Goodpaster B, et al. Strength and muscle quality in a well-functioning cohort of older adults: the Health, Aging and Body Composition Study. *J Am Geriatr Soc*. 2003;51:323-330.
4. Delmonico MJ, Harris TB, Visser M, et al. Longitudinal study of muscle strength, quality, and adipose tissue infiltration. *Am J Clin Nutr*. 2009;90:1579-1585.
5. Misic MM, Rosengren KS, Woods JA, Evans EM. Muscle quality, aerobic fitness and fat mass predict lower-extremity physical function in community-dwelling older adults. *Gerontology*. 2007;53:260-266.
6. Straight CR, Brady AO, Schmidt MD, Evans EM. Comparison of laboratory- and field-based estimates of muscle quality for predicting physical function in older women. *J Aging Res Clin Practice*. 2013, In Press.
7. Hairi NN, Cumming RG, Naganathan V, et al. Loss of muscle strength, mass (sarcopenia), and quality (specific force) and its relationship with functional limitation and physical disability: the Concord Health and Ageing in Men Project. *J Am Geriatr Soc*. 2010;58:2055-2062.
8. Cawthon PM, Fox KM, Gandra SR, et al. Do muscle mass, muscle density, strength, and physical function similarly influence risk of hospitalization in older adults? *J Am Geriatr Soc*. 2009;57:1411-1419.
9. Barbat-Artigas S, Rolland Y, Zamboni M, Aubertin-Leheudre M. How to assess functional status: a new muscle quality index. *J Nutr Health Aging*. 2012;16:67-77.
10. Morse CI, Thom JM, Mian OS, Muirhead A, Birch KM, Narici MV. Muscle strength, volume and activation following 12-month resistance training in 70-year-old males. *Eur J Appl Physiol*. 2005;95:197-204.
11. Thom JM, Morse CI, Birch KM, Narici MV. Triceps surae muscle power, volume, and quality in older versus younger healthy men. *J Gerontol A Biol Sci Med Sci*. 2005;60:1111-1117.
12. Kent-Braun JA, Ng AV. Specific strength and voluntary muscle activation in young and elderly women and men. *J Appl Physiol*. 1999;87:22-29.

13. Volpato S, Bianchi L, Lauretani F, et al. Role of muscle mass and muscle quality in the association between diabetes and gait speed. *Diabetes Care*. 2012;35:1672-1679.
14. Fielding RA, Vellas B, Evans WJ, et al. Sarcopenia: an undiagnosed condition in older adults. Current consensus definition: prevalence, etiology, and consequences. International working group on sarcopenia. *J Am Med Dir Assoc*. 2011;12:249-256.
15. Rosenberg IH. Summary comments. *Am J Clin Nutr*. 1989;50:1231-1233.
16. Janssen I, Heymsfield SB, Ross R. Low relative skeletal muscle mass (sarcopenia) in older persons is associated with functional impairment and physical disability. *J Am Geriatr Soc*. 2002;50:889-896.
17. Baumgartner RN, Koehler KM, Gallagher D, et al. Epidemiology of sarcopenia among the elderly in New Mexico. *Am J Epidemiol*. 1998;147:755-763.
18. Janssen I, Baumgartner RN, Ross R, Rosenberg IH, Roubenoff R. Skeletal muscle cutpoints associated with elevated physical disability risk in older men and women. *Am J Epidemiol*. 2004;159:413-421.
19. Visser M, Goodpaster BH, Kritchevsky SB, et al. Muscle mass, muscle strength, and muscle fat infiltration as predictors of incident mobility limitations in well-functioning older persons. *J Gerontol A Biol Sci Med Sci*. 2005;60:324-333.
20. Delmonico MJ, Harris TB, Lee JS, et al. Alternative definitions of sarcopenia, lower extremity performance, and functional impairment with aging in older men and women. *J Am Geriatr Soc*. 2007;55:769-774.
21. Clark BC, Manini TM. Sarcopenia \neq dynapenia. *J Gerontol A Biol Sci Med Sci*. 2008;63:829-834.
22. Manini TM, Clark BC. Dynapenia and aging: an update. *J Gerontol A Biol Sci Med Sci*. 2012;67:28-40.
23. Clark BC, Manini TM. What is dynapenia? *Nutrition*. 2012;28:495-503.
24. Lynch NA, Metter EJ, Lindle RS, et al. Muscle quality. I. Age-associated differences between arm and leg muscle groups. *J Appl Physiol*. 1999;86:188-194.
25. Skelton DA, Greig CA, Davies JM, Young A. Strength, power and related functional ability of healthy people aged 65-89 years. *Age Ageing*. 1994;23:371-377.
26. Doherty TJ. Invited review: Aging and sarcopenia. *J Appl Physiol*. 2003;95:1717-1727.

27. Newman AB, Kupelian V, Visser M, et al. Strength, but not muscle mass, is associated with mortality in the health, aging and body composition study cohort. *J Gerontol A Biol Sci Med Sci*. 2006;61:72-77.
28. Visser M, Deeg DJ, Lips P, Harris TB, Bouter LM. Skeletal muscle mass and muscle strength in relation to lower-extremity performance in older men and women. *J Am Geriatr Soc*. 2000;48:381-386.
29. Foldvari M, Clark M, Laviolette LC, et al. Association of muscle power with functional status in community-dwelling elderly women. *J Gerontol A Biol Sci Med Sci*. 2000;55:M192-199.
30. Bean JF, Kiely DK, Herman S, et al. The relationship between leg power and physical performance in mobility-limited older people. *J Am Geriatr Soc*. 2002;50:461-467.
31. Goodpaster BH, Park SW, Harris TB, et al. 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*. 2006;61:1059-1064.
32. Bouchard DR, Heroux M, Janssen I. Association between muscle mass, leg strength, and fat mass with physical function in older adults: influence of age and sex. *J Aging Health*. 2011;23:313-328.
33. Park SW, Goodpaster BH, Strotmeyer ES, et al. Accelerated loss of skeletal muscle strength in older adults with type 2 diabetes: the health, aging, and body composition study. *Diabetes Care*. 2007;30:1507-1512.
34. Goodpaster BH, Carlson CL, Visser M, et al. Attenuation of skeletal muscle and strength in the elderly: The Health ABC Study. *J Appl Physiol*. 2001;90:2157-2165.
35. Jubrias SA, Odderson IR, Esselman PC, Conley KE. Decline in isokinetic force with age: muscle cross-sectional area and specific force. *Pflugers Arch*. 1997;434:246-253.
36. Overend TJ, Cunningham DA, Kramer JF, Lefcoe MS, Paterson DH. Knee extensor and knee flexor strength: cross-sectional area ratios in young and elderly men. *J Gerontol*. 1992;47:M204-210.
37. Frontera WR, Hughes VA, Lutz KJ, Evans WJ. A cross-sectional study of muscle strength and mass in 45- to 78-yr-old men and women. *J Appl Physiol*. 1991;71:644-650.
38. Katsiaras A, Newman AB, Kriska A, et al. Skeletal muscle fatigue, strength, and quality in the elderly: the Health ABC Study. *J Appl Physiol*. 2005;99:210-216.
39. Villareal DT, Banks M, Siener C, Sinacore DR, Klein S. Physical frailty and body composition in obese elderly men and women. *Obes Res*. 2004;12:913-920.

40. Shin S, Valentine RJ, Evans EM, Sosnoff JJ. Lower extremity muscle quality and gait variability in older adults. *Age Ageing*. 2012;41:595-599.
41. Macaluso A, Nimmo MA, Foster JE, Cockburn M, McMillan NC, De Vito G. Contractile muscle volume and agonist-antagonist coactivation account for differences in torque between young and older women. *Muscle Nerve*. 2002;25:858-863.
42. Young A, Stokes M, Crowe M. The size and strength of the quadriceps muscles of old and young men. *Clin Physiol*. 1985;5:145-154.
43. Mojtahedi MC, Thorpe MP, Karampinos DC, et al. The effects of a higher protein intake during energy restriction on changes in body composition and physical function in older women. *J Gerontol A Biol Sci Med Sci*. 2011;66:1218-1225.
44. Tracy BL, Ivey FM, Hurlbut D, et al. Muscle quality. II. Effects Of strength training in 65- to 75-yr-old men and women. *J Appl Physiol*. 1999;86:195-201.
45. Marcus RL, Addison O, LaStayo PC. Intramuscular adipose tissue attenuates gains in muscle quality in older adults at high risk for falling. A brief report. *J Nutr Health Aging*. 2013;17:215-218.
46. Barbat-Artigas S, Rolland Y, Cesari M, Abellan van Kan G, Vellas B, Aubertin-Leheudre M. Clinical relevance of different muscle strength indexes and functional impairment in women aged 75 years and older. *J Gerontol A Biol Sci Med Sci*. 2013;68:811-819.
47. Fragala MS, Clark MH, Walsh SJ, et al. Gender differences in anthropometric predictors of physical performance in older adults. *Gend Med*. 2012;9:445-456.
48. Brooks N, Layne JE, Gordon PL, Roubenoff R, Nelson ME, Castaneda-Sceppa C. Strength training improves muscle quality and insulin sensitivity in Hispanic older adults with type 2 diabetes. *Int J Med Sci*. 2007;4:19-27.
49. Reid KF, Doros G, Clark DJ, et al. Muscle power failure in mobility-limited older adults: preserved single fiber function despite lower whole muscle size, quality and rate of neuromuscular activation. *Eur J Appl Physiol*. 2012;112:2289-2301.
50. Reid KF, Callahan DM, Carabello RJ, Phillips EM, Frontera WR, Fielding RA. Lower extremity power training in elderly subjects with mobility limitations: a randomized controlled trial. *Aging Clin Exp Res*. 2008;20:337-343.
51. Ivey FM, Tracy BL, Lemmer JT, et al. Effects of strength training and detraining on muscle quality: age and gender comparisons. *J Gerontol A Biol Sci Med Sci*. 2000;55:B152-157; discussion B158-159.

52. Metter EJ, Lynch N, Conwit R, Lindle R, Tobin J, Hurley B. Muscle quality and age: cross-sectional and longitudinal comparisons. *J Gerontol A Biol Sci Med Sci*. 1999;54:B207-218.
53. Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *J Gerontol*. 1994;49:M85-94.
54. Guralnik JM, Ferrucci L, Pieper CF, et al. Lower extremity function and subsequent disability: consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. *J Gerontol A Biol Sci Med Sci*. 2000;55:M221-231.
55. Vasunilashorn S, Coppin AK, Patel KV, et al. Use of the Short Physical Performance Battery Score to predict loss of ability to walk 400 meters: analysis from the InCHIANTI study. *J Gerontol A Biol Sci Med Sci*. 2009;64:223-229.
56. Nelson ME, Rejeski WJ, Blair SN, et al. Physical activity and public health in older adults: recommendation from the American College of Sports Medicine and the American Heart Association. *Circulation*. 2007;116:1094-1105.
57. Radaelli R, Botton CE, Wilhelm EN, et al. Low- and high-volume strength training induces similar neuromuscular improvements in muscle quality in elderly women. *Exp Gerontol*. 2013;48:710-716.
58. Straight CR, Lofgren IE, Delmonico MJ. Resistance training in older adults: are community-based interventions effective for improving health outcomes? *Am J Lifestyle Med*. 2012;6:407-414.
59. Miller GD, Nicklas BJ, Davis C, Loeser RF, Lenchik L, Messier SP. Intensive weight loss program improves physical function in older obese adults with knee osteoarthritis. *Obesity (Silver Spring)*. 2006;14:1219-1230.
60. Jensen GL, Roy MA, Buchanan AE, Berg MB. Weight loss intervention for obese older women: improvements in performance and function. *Obes Res*. 2004;12:1814-1820.
61. Beavers KM, Miller ME, Rejeski WJ, Nicklas BJ, Krichevsky SB. Fat mass loss predicts gain in physical function with intentional weight loss in older adults. *J Gerontol A Biol Sci Med Sci*. 2013;68:80-86.
62. Mazzali G, Di Francesco V, Zoico E, et al. Interrelations between fat distribution, muscle lipid content, adipocytokines, and insulin resistance: effect of moderate weight loss in older women. *Am J Clin Nutr*. 2006;84:1193-1199.
63. Goodpaster BH, Theriault R, Watkins SC, Kelley DE. Intramuscular lipid content is increased in obesity and decreased by weight loss. *Metabolism*. 2000;49:467-472.

64. Frimel TN, Sinacore DR, Villareal DT. Exercise attenuates the weight-loss-induced reduction in muscle mass in frail obese older adults. *Med Sci Sports Exerc.* 2008;40:1213-1219.
65. Delmonico MJ, Lofgren IE. Resistance training during weight loss in overweight and obese older adults: what are the benefits? *Am J Lifestyle Med.* 2010;4:309-313.
66. Marsh AP, Kyla Shea M, Vance Locke RM, et al. Resistance training and pioglitazone lead to improvements in muscle power during voluntary weight loss in older adults. *J Gerontol A Biol Sci Med Sci.* 2013;68:828-836.

REF #	Age (yr)	N	Subjects	Study Design	Muscle Function	Muscle Size	Major Findings
5	61-83	55	Men and women	Cross-sectional	Isokinetic dynamometry	DXA	MQ was the strongest independent predictor (compared to fat mass and aerobic capacity) of lower-extremity physical function and explained 29-42% of the variance
6	65-89	97	Women	Cross-sectional	Nottingham power rig	DXA	MQ was an independent predictor of 6-minute walk, 8-foot up-and-go, and 30-s chair stand; increasing MQ by 10% predicted a 2.7-4.4% improvement in physical function
7	≥ 70	1,705	Men	Cross-sectional	Spring gauge	DXA	Loss of MQ significantly elevated risk for self-reported and performance-based functional limitations, and physical disability
8	70-80	3,011	Men and women	Longitudinal	Isokinetic dynamometry	DXA	Older adults in the lowest quartile of MQ had a 65% greater risk of hospitalization relative to those in the highest quartile
32	≥ 55	1,280	Men and women	Cross-sectional	Isokinetic dynamometry	DXA	Fat mass and leg strength explained a greater percentage of variance in physical function than MQ

33	70-79	2,618	Men and women with and without T2DM	Longitudinal	Isokinetic dynamometry	DXA	MQ was significantly lower in men and women with T2DM than those without T2DM; adults with T2DM \geq 6 years and poor glycemic control ($HbA_{1c} > 8.0\%$) had lowest MQ
34	70-79	2,627	Men and women	Cross-sectional	Isokinetic dynamometry	CT	Greater midthigh muscle attenuation (lower intramuscular lipid infiltration) values were significantly associated with higher MQ
38	70-79	1,512	Men and women	Cross-sectional	Isokinetic dynamometry	CT	MQ was an independent predictor of skeletal muscle fatigue during knee extension and flexion
40	60-83	72	Men and women	Cross-sectional	Isometric dynamometry	DXA	MQ was significantly associated with spatial and temporal gait variability
46	≥ 75	1,462	Women	Cross-sectional	Strain gauge	DXA	Women in the lowest quartile of MQ were significantly more likely to report impairments with self-reported mobility, chair stand test, and usual and fast gait speed compared to women in the highest quartile
47	≥ 57	470	Men and women	Cross-sectional	1-RM	DXA	Significant association between MQ and physical function (chair rise time and gait speed) in men but not women

49	70-85	62	Healthy and mobility-limited men and women	Cross-sectional	1-RM	CT	MQ was significantly lower in mobility-limited adults relative to healthy adults; difference in MQ was 37.8% between healthy men and women and 13.9% between mobility-limited men and women
----	-------	----	--------------------------------------------	-----------------	------	----	---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

DXA = dual-energy X-ray absorptiometry

CT = computed tomography

1-RM = one-repetition maximum

T2DM = type 2 diabetes mellitus

CHAPTER 3

CHANGES IN MUSCLE QUALITY AND BODY WEIGHT PREDICT IMPROVEMENTS IN PHYSICAL FUNCTION FOLLOWING EXERCISE AND WEIGHT LOSS IN OVERWEIGHT AND OBESE OLDER WOMEN¹

¹Straight, C.R., Johnson, M.A., and Evans, E.M. To be submitted to *Age*.

3.1 Abstract

Purpose: To examine the relative contributions of changes in body composition and muscle quality to changes in lower-extremity physical function (LEPF) following a 6-month exercise and weight loss intervention in overweight and obese older women.

Methods: Thirty-eight overweight/obese ($BMI = 30.0 \pm 4.4 \text{ kg/m}^2$) older women (age = $69.3 \pm 4.1 \text{ y}$) completed a 6-month exercise and weight loss intervention. Body composition was measured via dual-energy X-ray absorptiometry and muscle quality (N-m/kg) was defined as isokinetic knee torque divided by upper-leg lean mass. The standardized scores of four objective measures of physical function were summed to yield a composite LEPF Z-score.

Results: At 6 months, there were significant reductions in body weight ($-9.6 \pm 3.5\%$, $p < 0.01$), absolute fat mass ($-6.8 \pm 2.4 \text{ kg}$, $p < 0.01$) and relative adiposity ($-4.9 \pm 2.1\%$, $p < 0.01$). There were also significant improvements in muscle quality ($+1.6 \pm 1.8 \text{ N-m/kg}$, $p < 0.01$) and individual measures of LEPF (12-57%, $p < 0.01$). Multivariate linear regression indicated that percent change in muscle quality was the strongest independent predictor of a change in LEPF Z-score (standardized $\beta = 0.64$, $p < 0.01$) and explained 34% of the variance. Percent change in overall body weight was also a significant predictor of change in LEPF Z-score ($\beta = -0.30$, $p < 0.05$) and independently accounted for 13% of the variance.

Conclusion: Changes in muscle quality and body weight are both independent predictors of a change in LEPF following exercise and weight loss in overweight and obese older women.

3.2 Introduction

Overweight and obesity among older adults have become major public health issues in the United States¹. According to data from the National Health and Nutrition Examination Survey, 69% of women aged ≥ 60 years were classified as overweight or obese (body mass index ≥ 25.0 kg/m²) in 2011-2012². Among a myriad of adverse health consequences, overweight and obesity have consistently been linked to reductions in physical function among older adults³⁻⁵, especially older women⁶⁻⁸. Likewise, exercise and weight loss interventions have been shown to be effective at improving physical function in overweight and obese older adults⁹⁻¹², but the most important independent predictors of the change in physical function in these studies were not examined. Characterizing the factors that account for the greatest percentage of variance in improvements in physical function is critical for the development of targeted interventions among overweight and obese older women toward the end of preventing physical disability.

A number of observational studies have identified both adiposity and muscle quality (strength/power per unit of muscle size) as salient determinants of physical function in the older adult cohort¹³⁻¹⁶. However, there is a paucity of literature regarding the relation between changes in adiposity and muscle quality and changes in physical function following interventions in older adults. A few studies have examined the relationship between changes in body composition and changes in physical function following weight loss interventions in overweight older adults, and found that decreases in body mass predicted improvements in physical function^{11,17,18}. However, only one of these studies examined whether a change in muscle strength or quality, during exercise and diet-induced weight loss, was related to an improvement in these functional outcomes¹¹. Conversely, a small number of studies have demonstrated a positive association between changes in muscle strength or quality and changes in specific functional tasks following

relatively short exercise interventions (e.g., 6-12 weeks) in older adults^{19,20}. However, those studies did not examine these relationships in the context of body composition changes for overweight and obese older adults undergoing intentional dietary-induced weight loss. Thus, the relationship between changes in body composition, muscle quality and physical function following interventions that integrate exercise training and diet-induced weight loss for older adults remains inadequately characterized. Improving physical function in older women, who have lower physical activity levels²¹, greater adiposity²² and lower muscle quality²³ relative to their male counterparts, is particularly important. Indeed, the prevalence of physical limitations among non-Hispanic white women increases from 28.2% at age 60-69 years to 55.4% in those aged ≥ 80 years, compared to 20.3 and 46.3%, respectively, for men²⁴.

In this context, the aim of the present study was to examine the relative contributions of changes in body weight and adiposity (e.g., the load to be moved) and changes in muscle quality (e.g., ability to move the load) to a change in lower-extremity physical function (LEPF) in overweight and obese older women following a 6-month exercise and weight loss intervention. Based on previous literature¹⁵⁻¹⁷, it was hypothesized that a) muscle quality would be the strongest independent predictor of a change in LEPF, and b) changes in body mass and adiposity (expressed in absolute and relative terms) would also be significant contributors with a similar strength of association.

3.3 Methods

Study Design

This study is a secondary analysis of a larger project that was designed to determine the effects of a 6-month exercise and weight loss intervention on body composition and LEPF in overweight and obese older women. For this analysis, only participants who 1) were enrolled in

the exercise and weight loss arms of the trial and, 2) achieved $\geq 3\%$ loss of baseline body weight, were included. All participants obtained medical clearance from their physician and provided written informed consent prior to enrollment. All procedures of this study were approved by the university's Institutional Review Board.

Participants

Community-dwelling, overweight and obese older women (n=38) completed the 6-month intervention and baseline and posttest measures. Women aged 65-80 y were eligible to participate in the study if they met the following inclusion criteria: body mass index ≥ 25.0 kg/m², stable body weight during the previous six months (within 2 kg), sedentary (defined as < 1 hr/wk of physical activity or < 2 exercise sessions per week in the past six months), non-smoking or tobacco using, and free of any chronic disease/condition that would preclude safe participation in exercise training or dietary restriction. Self-reported use of prescription medications was ascertained via a questionnaire and cognitive state was measured using the Mini-Mental State Examination²⁵.

Body Composition

Standing height and weight were measured with participants wearing light-weight clothing and no shoes. Height was obtained using a stadiometer (Seca, Model 242) with measures obtained to the nearest 0.1 cm. Weight was measured on a calibrated digital scale (Tanita, Model WB-110A). Whole-body and regional soft tissue composition (relative adiposity and mineral-free lean mass) was assessed via dual-energy X-ray absorptiometry (iDXA, GE Healthcare-Luna, Madison, WI). Regional analyses were performed per manufacturer's guidelines and involved bisecting the femoral neck and patella to measure mineral-free lean mass of the upper leg.

Muscle Strength and Quality

Maximal concentric isokinetic knee extension and flexion torque was measured at 60°/s via isokinetic dynamometry to provide a measurement of lower-body muscle strength (System 4 Pro, Biodex Medical Systems Inc, Shirley, NY). Participants performed 2 sets of 4 extension and flexion repetitions for the left and right legs. The greatest extension and flexion peak torque values for each leg were summed to calculate maximal concentric isokinetic knee torque at 60°/s. Muscle quality (N-m/kg) was calculated by dividing maximal isokinetic knee torque (N-m) by mineral-free lean mass of the upper leg (kg).

Lower-Extremity Physical Function

Performance-based physical function was measured using the 6-minute walk, 8-foot up-and-go, 30-s chair stand and transfer task. The 6-minute walk measures the greatest distance that an individual can walk in 6 minutes, and is a valid and reliable test of physical endurance in community-dwelling older adults²⁶. The 8-foot up-and-go test requires a person to stand up from a chair, walk around a cone located 8 feet away, and return to the chair as quickly as possible²⁷. This assessment is valid and reliable, and provides a measurement of dynamic balance, agility and speed in older adults²⁸. Each participant completed two trials of the 8-foot up-and-go test and the shortest time was used for analysis. The 30-second chair stand measured the number of times that an individual could rise to a full stand from a seated position without using their arms in 30 seconds²⁷, and has been identified as a valid and reliable instrument in older adults²⁹. Lastly, participants completed a transfer task, which requires them to sit down on the floor and then return to a standing position¹⁸. Similar to previous publications from our laboratory^{8,16}, we calculated a composite LEPF Z-score by summing the standardized values of each individual assessment to provide a global index of LEPF.

Exercise Intervention

All participants were expected to complete three 75-minute sessions of supervised exercise on nonconsecutive days during each week of the intervention for six months. All exercise sessions were conducted by trained graduate students in the Department of Kinesiology. The exercise intervention was a multicomponent program that integrated cardiorespiratory training, resistance training, balance, flexibility and functional activities in accordance with physical activity recommendations set forth in position stands by the American College of Sports Medicine^{30,31}. Cardiorespiratory training included 30 minutes of continuous exercise (walking on a treadmill, cycling or using an elliptical) at 70-80% of age-predicted maximal heart rate. Exercise intensity during the cardiorespiratory training was monitored throughout each session by recording heart rate and rating of perceived exertion at 10, 20, and 30 minutes of exercise. Participants performed three upper-body (chest press, shoulder press, and back row), three lower-body (leg press, knee extension, and knee curl), and one core (abdominal crunch) resistance training exercise during every session. Participants performed 2 sets of 8-10 repetitions at 65% of one-repetition maximum (1-RM) for each exercise until volitional fatigue. In addition, 4-RM testing for each resistance training exercise was conducted every 6 weeks during the intervention to reassess muscle strength and adjust training load accordingly. In addition to cardiorespiratory and resistance training, two 30-s sets of four different functional activities (chair rises, wall push-ups, lift-and-carry, and transfer task) were performed during every training session. Finally, ~5-10 minutes of balance and flexibility exercises were performed at the end of every training session.

Diet Intervention

All participants were prescribed a diet that was designed to facilitate ~10% loss of initial body weight at the end of the 6-month intervention via reduction of estimated energy needs by ~500 kcal/d. To ensure participants were meeting micronutrient needs during the intervention, all participants were provided with a multivitamin mineral supplement formulated for older women (Centrum® Silver® Women, Pfizer, Inc. Madison, NJ) that provided 800 IU of vitamin D and 500 mg of calcium.

During the initial phase of the intervention, all participants attended at least two individual sessions with a registered dietitian nutritionist or supervised nutrition graduate student for instruction regarding topics such as energy restriction and self-monitoring methods. For the remainder of the 6-month intervention, participants attended weekly educational/motivational group sessions (45-60 min) with the registered dietitian nutritionist or graduate student, as well as individual sessions in order to meet weight loss goals. Dietary records for all participants were monitored weekly and individual written feedback from the registered dietitian nutritionist or supervised graduate student was provided at each group session. The curriculum for the group sessions was designed according to Social Cognitive Theory³² and included topics such as general nutrition education and behavioral strategies for weight management. In addition, all participants were instructed to use a free online dietary intake monitoring application (MyFitnessPal.com). Trained staff monitored entries weekly and participants were provided individualized feedback throughout the intervention to help meet weight loss and nutrient goals.

Statistical Analysis

All statistical analyses were conducted using SPSS for Windows version 22.0 (SPSS Inc., Chicago, IL). Data were examined for normality via distribution statistics and visual inspection

of histograms. Several of the dependent variables (e.g., LEPF measures) at baseline and post-intervention were not normally distributed according to skewness and kurtosis values $> |2.0|$; thus, natural logarithmic transformations were performed. Pearson correlations were conducted to examine the bivariate associations between body composition, muscle quality and measures of LEPF at baseline. Paired samples t-tests were used to determine within-group changes in all measures of body composition, muscle quality and LEPF. Multivariate linear regression models were created to examine the relative contributions of changes in body weight, adiposity and muscle quality to a change in the composite LEPF Z-score following the 6-month intervention. All regression analyses were controlled for baseline values of body weight, adiposity and muscle quality. To further explore our primary aim, a categorical analysis in which participants were dichotomized into groups according to magnitude of change in muscle quality and body weight (e.g., $< 10\%$ vs. $\geq 10\%$) was performed. Separate one-way analysis of covariance (ANCOVA) models were created to examine the effects of a $\geq 10\%$ change in muscle quality (controlled for percent change in body weight) and $\geq 10\%$ in body weight (controlled for percent change in muscle quality) on change in LEPF Z-score. A power calculation was conducted based on the ability to detect a correlation between a change in muscle quality and a change in physical function following the intervention. In order to detect a relationship between change in muscle quality and change in LEPF Z-score ($r = 0.45$) with a strength of association similar to previous studies^{11,19}, and assuming $\alpha = 0.05$ and power of 0.80, a sample size of 36 was necessary. Statistical significance was set at $p < 0.05$ for all tests.

3.4 Results

Descriptive characteristics for the sample are presented in Table 1. The mean age for the participants was 69.3 ± 4.1 y and the mean BMI was 30.0 ± 4.4 kg/m². Adherence to the exercise

intervention (defined as the mean percentage of total exercise sessions attended) was $75.6 \pm 5.7\%$ (60.8 ± 5.1 total sessions). Mean data from the exercise intervention for each component of training (e.g., cardiorespiratory, resistance) at different time points of the study are presented in Table 2.

Changes in body composition and muscle quality following the intervention are presented in Table 3. There was a significant reduction in overall body mass (-7.6 ± 2.9 kg or $-9.6 \pm 3.5\%$), with 17 of the 38 participants (44.7% of the sample) achieving $\geq 10\%$ loss of initial body weight. Accordingly, there were significant decreases in BMI (2.9 ± 1.2 kg/m², $p < 0.01$) and waist circumference (8.0 ± 6.1 cm). Likewise, absolute fat mass decreased by 6.8 ± 2.4 kg ($p < 0.01$) and relative adiposity was reduced by $4.9 \pm 2.1\%$ ($p < 0.01$). Additionally, there was a minor, but significant, decrease in upper-leg mineral-free lean mass (-0.3 ± 0.5 kg, $p < 0.01$). In contrast, there was a significant increase in isokinetic knee torque at $60^\circ/\text{s}$ ($+16.5 \pm 25.5$ N-m, $p < 0.01$), which resulted in a corresponding increase in muscle quality ($+1.6 \pm 1.8$ N-m/kg, $p < 0.01$). A comparison of percentage changes in measures of adiposity and muscle quality is presented in Figure 1. With regard to LEPF, there were significant improvements in the 6-minute walk ($+58.9 \pm 33.7$ m, $p < 0.01$), 8-foot up-and-go (-0.84 ± 0.74 s, $p < 0.01$), 30-s chair stand ($+7.8 \pm 5.0$ stands, $p < 0.01$) and the transfer task (-4.26 ± 5.67 s, $p < 0.01$). Relative to baseline values, the magnitude of improvement in individual LEPF assessments ranged from 12-57% (Figure 2).

Multivariate linear regression models were created to examine the relative contributions of changes in body weight, adiposity and muscle quality to a change in the composite LEPF Z-score following the intervention (Table 4). Percent change in muscle quality was the strongest independent predictor of a change in LEPF Z-score (standardized $\beta = 0.64$, $p < 0.01$) and accounted for $\sim 34\%$ of the variance. The percent change in body mass was also a significant

predictor of the change in LEPF Z-score (standardized $\beta = -0.30$, $p < 0.05$) and independently explained ~13% of the variance. However, when an interaction term was added to the model, percent changes in muscle quality and body weight did not significantly interact to predict change in composite LEPF Z-score ($p > 0.05$). In addition, the independent association between changes in absolute and relative adiposity and changes in LEPF Z-score were examined in separate regression models. However, change in absolute fat mass and relative adiposity were not related to the change in LEPF Z-score, whereas muscle quality was a significant predictor and explained ~30% of the variance among the change in LEPF Z-score in these models.

To further explore our primary aim, a categorical analysis in which participants were dichotomized into groups according to magnitude of change in muscle quality and body weight (e.g., $< 10\%$ vs. $\geq 10\%$). Figure 3 shows that participants who increased muscle quality by 10% or more ($n = 12$) had a significantly greater change in composite LEPF Z-score compared to those who did not ($n = 26$), even when controlling for percent change in body weight (1.03 vs. -0.48, $p < 0.05$, Cohen's $d = 0.87$). In contrast, in Figure 4, there was no significant difference in change in LEPF Z-score between those who lost $\geq 10\%$ ($n = 17$) of initial body weight and those who lost $< 10\%$ ($n = 21$), when adjusting for percent change in muscle quality (0.34 vs. -0.27, $p = 0.30$, Cohen's $d = 0.35$).

3.5 Discussion

The purpose of this study was to examine the relative contributions of changes in body mass, adiposity and muscle quality to changes in physical function following a 6-month exercise and weight loss intervention in overweight and obese older women. We provide novel evidence that an increase in muscle quality is the strongest independent contributor of an improvement in a composite LEPF Z-score; however, a reduction in body mass also predicted an improvement in

the composite Z-score. Our findings suggest that muscle quality (+8.8%) can be significantly improved in the presence of clinically meaningful diet-induced weight loss (-9.6%) among overweight and obese older women, and that while both of these changes positively contribute to improved LEPF, change in muscle quality is the strongest determinant of improved physical function.

A novel element of this study is the examination of changes in both muscle quality (e.g., the ability to transfer body weight) and body weight/adiposity (e.g., the load to be transferred) to changes in a composite Z-score of objective LEPF tests following exercise and intentional diet-induced weight loss in overweight and obese older women. Using multivariate linear regression, we found that change in muscle quality was the strongest predictor of a change in LEPF Z-score (standardized $\beta = 0.64$) and explained ~34% of the variance, even when adjusting for the effects of weight loss. In addition, our ANCOVA model revealed a large effect for change in LEPF Z-score between older women who increased muscle quality by $\geq 10\%$ and those who experienced a smaller magnitude of change, independent of percent changes in overall body mass. Thus, the major findings from our study suggest that an increase in muscle quality is a more important determinant of an improvement in global LEPF than change in body mass following exercise and weight loss in overweight and obese older women. These findings are congruent with previous cross-sectional research from our laboratory that reported muscle quality has the strongest association with LEPF in older adults, explaining 24-42% of the variance in performance on different functional tasks^{15,16}. Taken together, our findings suggest that interventions designed to increase muscle quality may confer substantial improvements in LEPF. The Centers for Disease Control and Prevention²⁴ indicate that over 31% of adults aged 70-79 y report having one or

more physical limitations (e.g., walking a ¼ mile, climbing 10 steps, etc.), thus interventions that can improve the trajectory of functional health during aging are a public health priority.

Our findings regarding the importance of muscle quality for physical function are in accordance with the results of previous clinical intervention trials involving older adults. For example, Villareal et al.¹¹ found a relationship between change in knee strength and change in Physical Performance Test score (partial $r = 0.42$), when adjusting for change in body weight, in a sample of 17 obese older men and women with a similar magnitude of weight loss (-8.4%). However, the independent contributions of changes in knee strength and body weight were not examined in a single regression analysis in that study, thereby precluding inferences regarding the relative importance of each for improvements in physical function. Likewise, Marsh et al.¹⁹ observed an association between changes in knee extension strength and a chair stand test ($r = -0.41$), but not the 4-m walk or total short physical performance battery score, following 12 weeks of resistance training, but not weight loss, in 45 older adults with self-reported difficulties in activities of daily living. However, caution should be used when comparing the results of our study to those of previous research due to differences in methodological characteristics, such as the sex of the sample (women vs. men + women), health of participants (ostensibly healthy vs. self-reported difficulties with function), intervention type (multicomponent exercise + weight loss vs. resistance training) and intervention duration (6 months vs. 12 weeks).

In addition to the association between muscle quality and LEPF Z-score, our regression analysis revealed that a reduction in overall body weight was a significant predictor of improved physical function following the intervention, which is in accordance with previous research^{11,17,18}. For example, Mojtahedi et al.¹⁸ found that a reduction in body mass predicted improvements in the 8-foot up-and-go ($r^2 = 0.15$) and a transfer task ($r^2 = 0.18$) following 6

months of weight loss in older women. Likewise, in an analysis of pooled data from three randomized controlled trials of intentional weight loss in older adults, Beavers et al.¹⁷ found that overall weight loss (-7.8 kg or 8.4%) was significantly associated with improvements in self-reported mobility disability and gait speed, but not with change in objective measures such as the chair stand or short physical performance battery score. However, while we found that weight loss predicted an improvement in physical function, we found no relation between changes in adiposity (expressed via absolute or relative terms) and change in LEPF Z-score. In contrast, Beavers et al.¹⁷ found that a decrease in absolute fat mass significantly predicted improvements in mobility disability and gait speed. Similarly, Mojtahedi et al.¹⁸ found that a reduction in relative mid-thigh subcutaneous adipose tissue (derived via magnetic resonance imaging) predicted improvements in physical function. However, the study by Mojtahedi et al.¹⁸ employed a very light training stimulus (flexibility exercises and low- to moderate-intensity walking), and neither of these studies examined the relationship between changes in body composition and physical function while statistically adjusting for changes in muscle strength/quality. Our study contributes to this literature by indicating that a reduction in overall body weight predicts an improvement in physical function, even in the presence of a significant increase in leg muscle quality. The mechanism through which weight loss contributes to improved physical function is not entirely clear, however a number of putative mechanisms have been discussed³³. For instance, findings from the Baltimore Longitudinal Study of Aging suggest that altered gait patterns in obese older adults result in compromised physical function³⁴. Thus, it is possible that weight loss improves physical function by reducing the biomechanical burden on lower extremity joints during ambulation. However, additional research is needed to elucidate the mechanisms through which weight loss confers improvements in physical function for

overweight and obese older adults. Additionally, although intentional weight loss remains a controversial issue for older adults (65+ y) due to concerns about potentially exacerbating sarcopenia and the loss of bone mass³⁵⁻³⁷, our findings provide additional evidence that dietary-induced weight loss may improve physical function in older adults if combined with an exercise intervention, especially resistance training^{38,39}.

While our findings provide novel evidence on the relative contributions of changes in muscle quality and body weight to changes in physical function in overweight and obese older women, there are several limitations to this study that should be addressed. Primarily, the lack of a single-treatment control group precludes inferences regarding the independent effects of exercise training and dietary-induced weight loss on the changes in LEPF. However, this study was not designed to compare the effects of exercise training versus weight loss as multiple clinical trials have demonstrated that a combination of these intervention strategies is effective for improving physical function in older adults^{9,12,40}. In addition, our sample was comprised of relatively healthy white women aged 65-77 y and the relationships between body composition, muscle quality and LEPF may not be generalizable to other populations of older adults. For example, previous cross-sectional studies have provided evidence of a sexual dimorphism with regard to predictors of physical function in older adults^{8,14}. Thus, it is possible that predictors of a change in physical function are different for older men compared to women, but additional research is needed in this area. Likewise, this study was not designed to elucidate the underlying physiologic mechanism responsible for the increase in muscle quality following the intervention. It is important to note that there was a modest, but significant, decrease in mineral-free lean mass of the upper leg (-0.3 kg or -2.2%) over the course of the 6-month intervention. However, despite a small reduction in the size of the leg muscles, there was a significant increase in force

production (+16.5 N-m/kg), resulting in greater strength per unit of muscle mass (e.g., muscle quality). It is plausible, and highly likely, that neurological mechanisms accounted for the greater leg muscle strength in the presence of less lean mass, but future research is needed to characterize the physiologic changes responsible for improvements in muscle quality during concomitant exercise training and weight loss.

In conclusion, this study characterized the relative importance of changes in body weight, adiposity, and muscle quality for changes in physical function following exercise and intentional diet-induced weight loss in overweight and obese older women. Increased muscle quality is the strongest independent predictor of a change in physical function, although a reduction in overall body weight is also a significant contributor. Intervention strategies that increase muscle quality in the presence of dietary-induced weight loss may confer substantial improvements in physical function for overweight and obese older women.

3.6 References

1. Villareal DT, Apovian CM, Kushner RF, Klein S. Obesity in older adults: technical review and position statement of the American Society for Nutrition and NAASO, The Obesity Society. *Am J Clin Nutr.* 2005;82:923-934.
2. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of childhood and adult obesity in the United States, 2011-2012. *JAMA.* 2014;311:806-814.
3. Davison KK, Ford ES, Cogswell ME, Dietz WH. Percentage of body fat and body mass index are associated with mobility limitations in people aged 70 and older from NHANES III. *J Am Geriatr Soc.* 2002;50:1802-1809.
4. Zamboni M, Turcato E, Santana H, et al. The relationship between body composition and physical performance in older women. *J Am Geriatr Soc.* 1999;47:1403-1408.
5. Zoico E, Di Francesco V, Guralnik JM, et al. Physical disability and muscular strength in relation to obesity and different body composition indexes in a sample of healthy elderly women. *Int J Obes Relat Metab Disord.* 2004;28:234-241.
6. Friedmann JM, Elasy T, Jensen GL. The relationship between body mass index and self-reported functional limitation among older adults: a gender difference. *J Am Geriatr Soc.* 2001;49:398-403.
7. Riebe D, Blissmer BJ, Greaney ML, Garber CE, Lees FD, Clark PG. The relationship between obesity, physical activity, and physical function in older adults. *J Aging Health.* 2009;21:1159-1178.
8. Straight CR, Brady AO, Evans E. Sex-specific relationships of physical activity, body composition, and muscle quality with lower-extremity physical function in older men and women. *Menopause.* 2014; In Press.
9. Anton SD, Manini TM, Milsom VA, et al. Effects of a weight loss plus exercise program on physical function in overweight, older women: a randomized controlled trial. *Clin Interv Aging.* 2011;6:141-149.
10. Messier SP, Loeser RF, Mitchell MN, et al. Exercise and weight loss in obese older adults with knee osteoarthritis: a preliminary study. *J Am Geriatr Soc.* 2000;48:1062-1072.
11. Villareal DT, Banks M, Sinacore DR, Siener C, Klein S. Effect of weight loss and exercise on frailty in obese older adults. *Arch Intern Med.* 2006;166:860-866.
12. Villareal DT, Chode S, Parimi N, et al. Weight loss, exercise, or both and physical function in obese older adults. *N Engl J Med.* 2011;364:1218-1229.

13. Beavers KM, Beavers DP, Houston DK, et al. Associations between body composition and gait-speed decline: results from the Health, Aging, and Body Composition study. *Am J Clin Nutr.* 2013;97:552-560.
14. Fragala MS, Clark MH, Walsh SJ, et al. Gender differences in anthropometric predictors of physical performance in older adults. *Gen Med.* 2012;9:445-456.
15. Misic MM, Rosengren KS, Woods JA, Evans EM. Muscle quality, aerobic fitness and fat mass predict lower-extremity physical function in community-dwelling older adults. *Gerontology.* 2007;53:260-266.
16. Straight CR, Brady AO, Evans EM. Muscle quality and relative adiposity are the strongest predictors of lower-extremity physical function in older women. *Maturitas.* 2015;80:95-99.
17. Beavers KM, Miller ME, Rejeski WJ, Nicklas BJ, Krichevsky SB. Fat mass loss predicts gain in physical function with intentional weight loss in older adults. *J Gerontol A Biol Sci Med Sci.* 2013;68:80-86.
18. Mojtahedi MC, Thorpe MP, Karampinos DC, et al. The effects of a higher protein intake during energy restriction on changes in body composition and physical function in older women. *J Gerontol A Biol Sci Med Sci.* 2011;66:1218-1225.
19. Marsh AP, Miller ME, Rejeski WJ, Hutton SL, Kritchevsky SB. Lower extremity muscle function after strength or power training in older adults. *J Aging Phys Act.* 2009;17:416-443.
20. Pinto RS, Correa CS, Radaelli R, Cadore EL, Brown LE, Bottaro M. Short-term strength training improves muscle quality and functional capacity of elderly women. *Age (Dordr).* 2014;36:365-372.
21. Sun F, Norman IJ, While AE. Physical activity in older people: a systematic review. *BMC Public Health.* 2013;13:449.
22. Jankowski CM, Gozansky WS, Van Pelt RE, et al. Relative contributions of adiposity and muscularity to physical function in community-dwelling older adults. *Obesity (Silver Spring).* 2008;16:1039-1044.
23. Newman AB, Haggerty CL, Goodpaster B, et al. Strength and muscle quality in a well-functioning cohort of older adults: the Health, Aging and Body Composition Study. *J Am Geriatr Soc.* 2003;51:323-330.
24. Holmes J, Powell-Griner E, Lethbridge-Cejku M, Heyman K. Aging differently: Physical limitations among adults aged 50 years and over: United States, 2001-2007. *NCHS Data Brief.* 2009:1-8.
25. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res.* 1975;12:189-198.

26. Rikli RE, Jones CJ. The reliability and validity of a 6-minute walk test as a measure of physical endurance in older adults. *J Aging Phys Act.* 1998;6:363-375.
27. Rikli RE, Jones CJ. *Senior Fitness Test Manual.* 2nd ed. Champaign, IL: Human Kinetics; 2013.
28. Rikli RE, Jones CJ. Development and validation of a functional fitness test for community-residing older adults. *J Aging Phys Act.* 1999;7:129-161.
29. Jones CJ, Rikli RE, Beam WC. A 30-s chair-stand test as a measure of lower body strength in community-residing older adults. *Res Q Exerc Sport.* 1999;70:113-119.
30. Garber CE, Blissmer B, Deschenes MR, et al. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Med Sci Sports Exerc.* 2011;43:1334-1359.
31. Nelson ME, Rejeski WJ, Blair SN, et al. Physical activity and public health in older adults: recommendation from the American College of Sports Medicine and the American Heart Association. *Circulation.* 2007;116:1094-1105.
32. Bandura A. Health promotion by social cognitive means. *Health Educ Behav.* 2004;31:143-164.
33. Vincent HK, Vincent KR, Lamb KM. Obesity and mobility disability in the older adult. *Obes Rev.* 2010;11:568-579.
34. Ko S, Stenholm S, Ferrucci L. Characteristic gait patterns in older adults with obesity--results from the Baltimore Longitudinal Study of Aging. *J Biomech.* 2010;43:1104-1110.
35. Waters DL, Ward AL, Villareal DT. Weight loss in obese adults 65years and older: a review of the controversy. *Exp Gerontol.* 2013;48:1054-1061.
36. Darmon P. Intentional weight loss in older adults: useful or wasting disease generating strategy? *Curr Opin Clin Nutr Metab Care.* 2013;16:284-289.
37. Bales CW, Buhr G. Is obesity bad for older persons? A systematic review of the pros and cons of weight reduction in later life. *J Am Med Dir Assoc.* 2008;9:302-312.
38. Delmonico MJ, Lofgren IE. Resistance training during weight loss in overweight and obese older adults: what are the benefits? *Am J Lifestyle Med.* 2010;4:309-313.
39. Frimel TN, Sinacore DR, Villareal DT. Exercise attenuates the weight-loss-induced reduction in muscle mass in frail obese older adults. *Med Sci Sports Exerc.* 2008;40:1213-1219.

40. Messier SP, Loeser RF, Miller GD, et al. Exercise and dietary weight loss in overweight and obese older adults with knee osteoarthritis: the Arthritis, Diet, and Activity Promotion Trial. *Arthritis Rheum.* 2004;50:1501-1510.

Table 3.1. Participant characteristics (n=38)

Characteristic	Mean \pm SD	Range
Age (y)	69.3 \pm 4.1	65-77
Height (m)	1.6 \pm 0.1	1.4-1.8
Weight (kg)	79.6 \pm 10.3	53.7-100.2
Body Mass Index (kg/m ²)	30.0 \pm 4.4	25.0-44.4
Waist Circumference (cm) ^a	101.0 \pm 12.1	82.2-141.9
Mini-Mental State Examination (0-30)	29.1 \pm 1.1	26-30
Number of Medications (total)	3.8 \pm 2.7	0-10
Physical Activity (steps/d)	5155.9 \pm 2019.4	1680.9-9108.5

MFLM = mineral-free lean mass

^an=37

Table 3.2. Characteristics of the multicomponent exercise training intervention

		Week 8	Week 12	Week 16	Week 20	Week 24
<i>Cardiorespiratory Training</i>	HR (beats/min)	119.6 ± 15.2	123.4 ± 14.2	121.7 ± 13.6	120.5 ± 13.1	121.0 ± 12.7
	RPE (6-20)	12.9 ± 0.9	13.0 ± 1.0	13.2 ± 1.0	13.3 ± 0.9	13.1 ± 0.9
<i>Resistance Training</i>	Leg Press (lbs)	137.3 ± 32.3	142.8 ± 29.9	150.2 ± 28.7	154.1 ± 27.5	157.1 ± 27.7
	Knee Extension (lbs)	59.8 ± 17.4	62.0 ± 16.2	64.9 ± 16.2	68.0 ± 15.1	68.2 ± 15.5
	Knee Curl (lbs)	52.3 ± 10.1	54.2 ± 11.3	56.6 ± 11.2	58.0 ± 10.3	59.7 ± 10.8
	Chest Press (lbs)	35.3 ± 12.8	37.7 ± 13.6	40.9 ± 13.1	43.8 ± 14.4	44.9 ± 14.6
	Back Row (lbs)	62.1 ± 10.5	64.8 ± 10.8	66.4 ± 11.3	67.7 ± 12.3	68.4 ± 12.6
	Overhead Press (lbs)	22.1 ± 11.1	25.3 ± 12.0	27.7 ± 11.2	29.0 ± 11.4	29.2 ± 11.8
	Abdominal Crunch (lbs)	59.7 ± 11.5	63.0 ± 10.4	66.0 ± 10.4	66.9 ± 13.3	68.4 ± 13.3
<i>Functional Activities</i>	Chair stands (total)	17.2 ± 4.0	18.1 ± 4.9	19.1 ± 4.8	19.1 ± 5.7	19.9 ± 6.1
	Transfer task (total)	5.6 ± 1.7	5.8 ± 1.8	5.9 ± 1.9	6.7 ± 3.6	6.0 ± 2.0
	Lift-and-carry task (lbs)	22.8 ± 3.6	23.5 ± 4.7	24.3 ± 4.8	23.3 ± 6.0	24.8 ± 5.2
	Wall push-ups (total)	17.0 ± 3.3	18.3 ± 4.3	19.2 ± 4.8	19.5 ± 4.8	20.7 ± 5.1

Data are presented as mean ± SD.

HR = heart rate; RPE = rating of perceived exertion

Table 3.3. Baseline and post-intervention values for body composition, muscle quality and lower-extremity physical function (n=38)

Characteristic	Baseline	Post-Intervention	<i>P</i>
Relative Adiposity (%)	47.8 ± 3.8	42.9 ± 4.9	< 0.01
Fat Mass (kg)	37.1 ± 7.2	30.2 ± 7.0	< 0.01
Upper-Leg MFLM (kg)	13.7 ± 1.6	13.4 ± 1.5	< 0.01
Isokinetic Knee Torque (N-m)	272.6 ± 49.0	289.2 ± 50.8	< 0.01
Muscle Quality (N-m/kg)	20.1 ± 3.7	21.7 ± 3.6	< 0.01
6-Minute Walk (m)	521.6 ± 67.8	580.5 ± 62.2	< 0.01
8-Foot Up-and-Go (s)	6.44 ± 1.25	5.59 ± 0.78	< 0.01
30-S Chair Stand (total)	13.7 ± 2.3	21.4 ± 5.9	< 0.01
Transfer Task (s)	9.11 ± 6.59	4.85 ± 1.75	< 0.01

Data are presented as mean ± SD.

MFLM = mineral-free lean mass

Muscle quality (N-m/kg) = isokinetic knee torque (N-m) / upper-leg mineral-free lean mass (kg)

Table 3.4. Relative contributions of percent changes in body composition and muscle quality to a change in lower-extremity physical function Z-score (n=38)

	Predictor	β	Partial R^2	P
Model 1	% Δ Body Weight	-0.30	0.130	<0.05
	% Δ Muscle Quality	0.64	0.336	<0.01
Model 2	% Δ Fat Mass	-0.26	0.090	0.08
	% Δ Muscle Quality	0.63	0.314	<0.01
Model 3	% Δ Relative Adiposity	-0.20	0.044	0.23
	% Δ Muscle Quality	0.62	0.303	<0.01

Analysis controlled for baseline values

% Δ = [(Post-intervention – baseline) / baseline] x 100

Muscle quality (N-m/kg) = isokinetic knee torque (N-m) / upper-leg mineral-free lean mass (kg)

LEPF Z-score = sum of Z-scores from 6-minute walk, 8-foot up-and-go, 30-second chair stand and transfer task

Betas represent standardized regression coefficients

Partial R^2 is the explained variance of each parameter in the model

Figure 3.1. Percent changes from baseline to 6 months for measures of body composition and muscle quality; %Fat = relative adiposity; MQ = muscle quality; values represent mean \pm SE.

*Indicates a significant change from baseline at $p < 0.01$

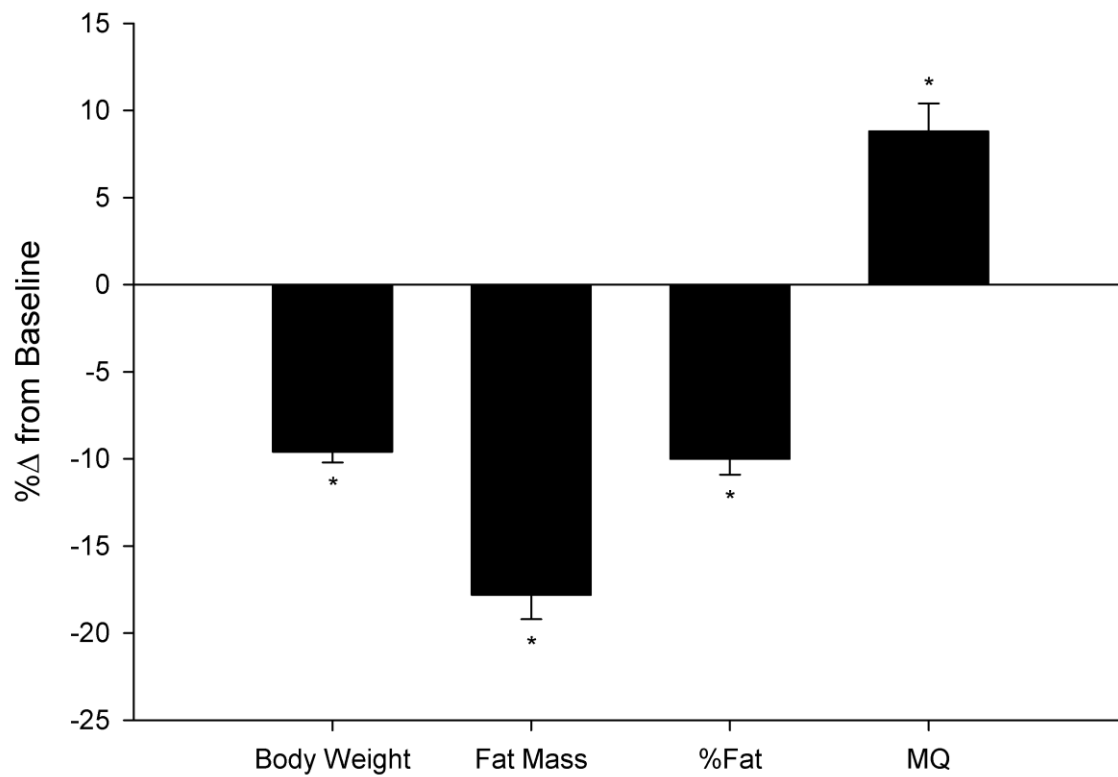


Figure 3.2. Percent changes from baseline to 6 months in measures of lower-extremity physical function (LEPF); 6MWT = 6-minute walk; UPGO = 8-foot up-and-go; CHAIR = 30-s chair stand; TRANSFER = transfer task; values represent mean \pm SE.

*Indicates a significant change from baseline at $p < 0.01$

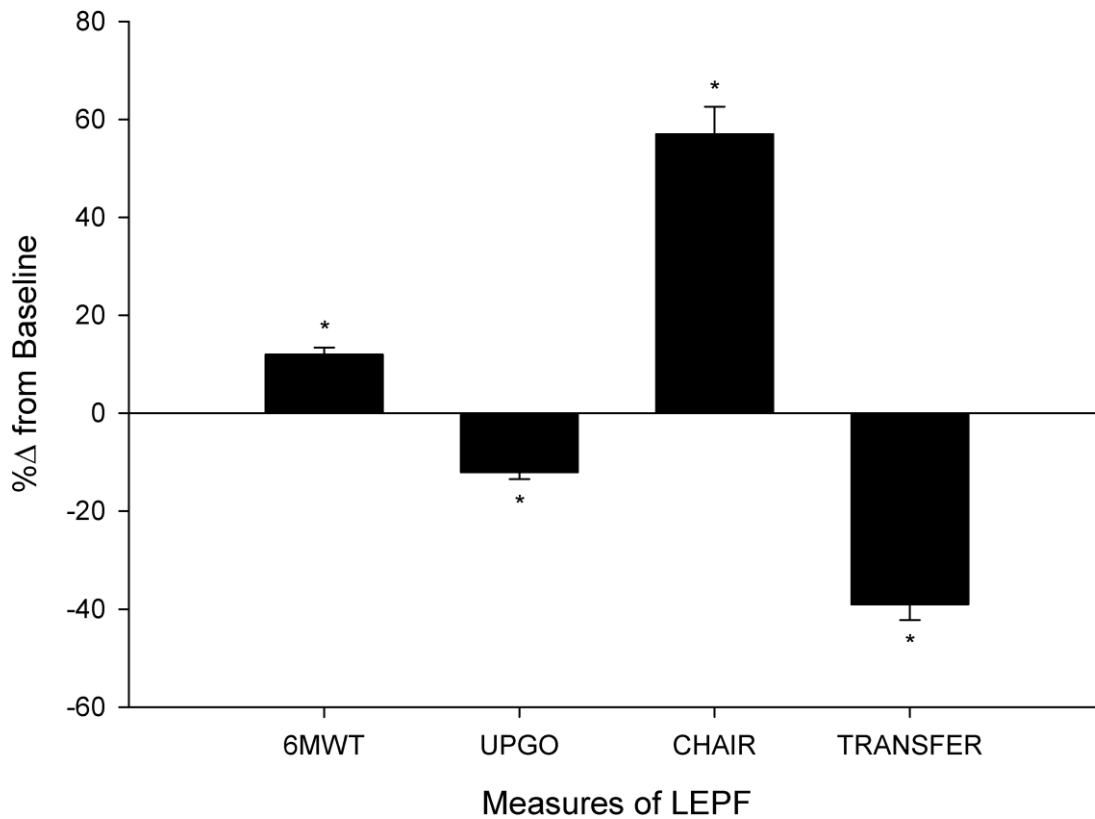


Figure 3.3. Comparison of change from baseline in LEPF Z-score between participants who increased muscle quality by $\geq 10\%$ (n=12) and those who did not (n=26); values represent estimated marginal means \pm SE, adjusted for percent change in body weight.

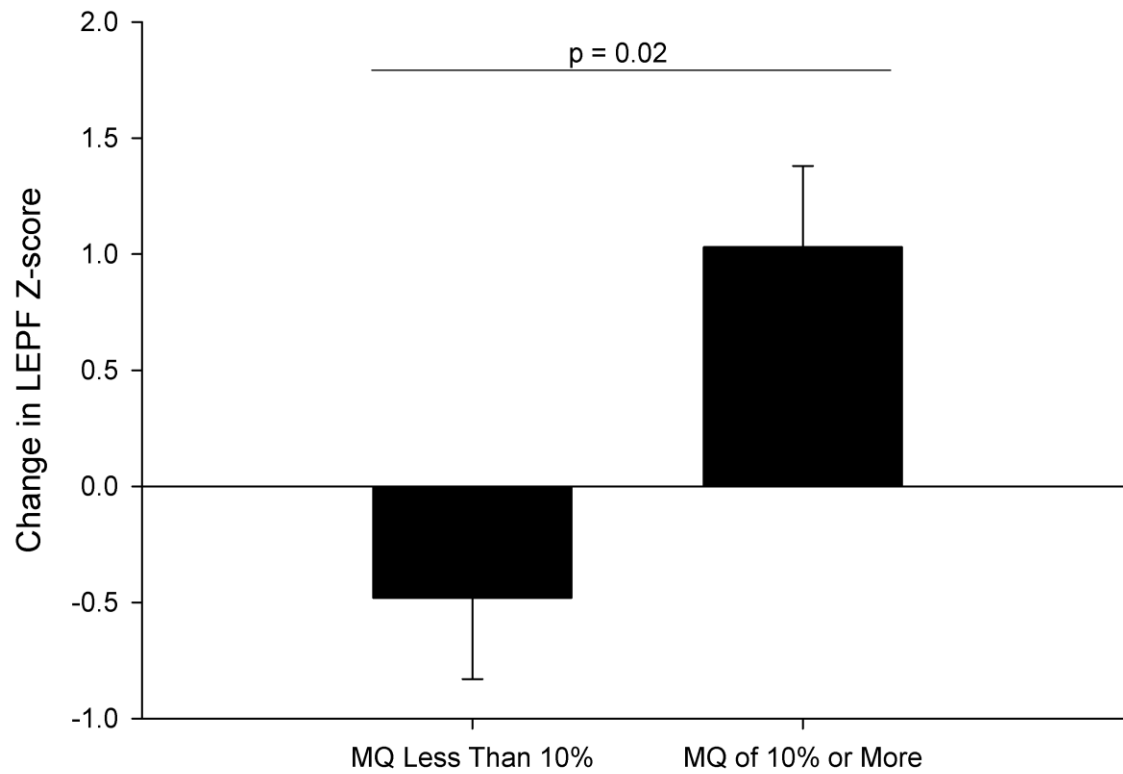
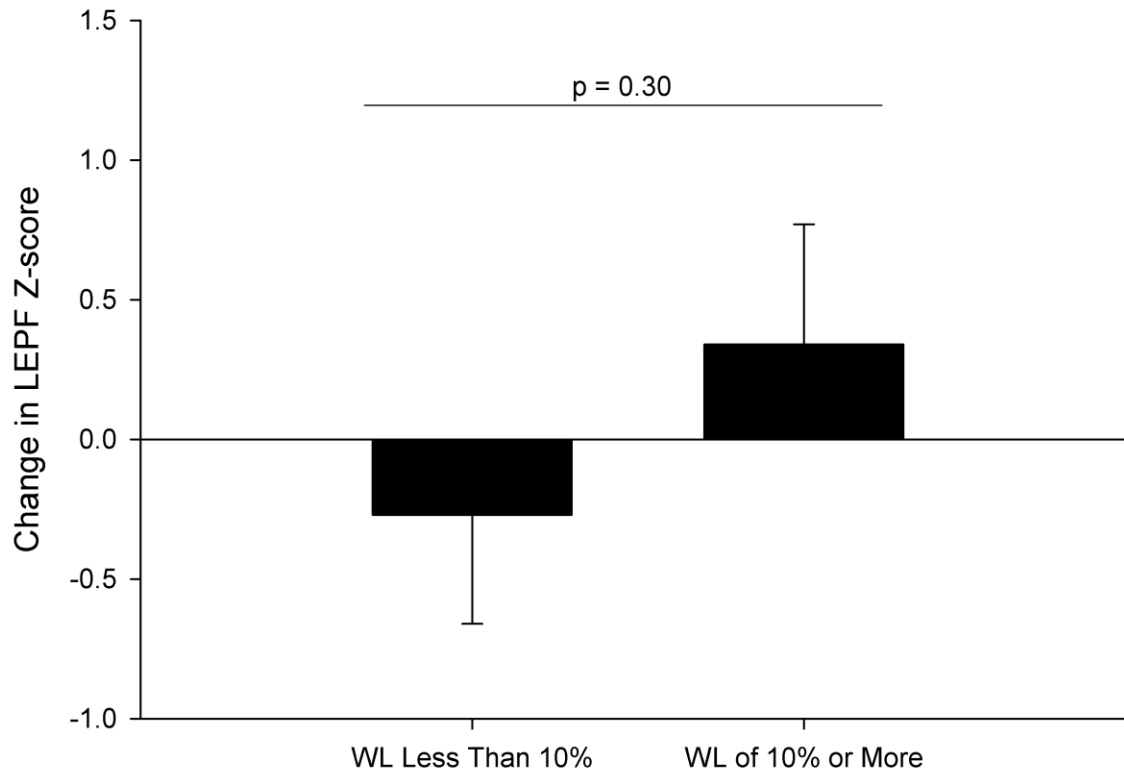


Figure 3.4. Comparison of change from baseline in LEPF Z-score between participants who achieved $\geq 10\%$ loss of initial body weight (n=17) and those who did not (n=21); values represent estimated marginal means \pm SE, adjusted for percent change in muscle quality.



CHAPTER 4

**SPECIFIC FUNCTIONAL IMPROVEMENTS ASSOCIATED WITH INCREASES IN
WHOLE-MUSCLE PERFORMANCE IN OVERWEIGHT AND OBESE OLDER
WOMEN FOLLOWING 6 MONTHS OF EXERCISE AND WEIGHT LOSS¹**

¹Straight, C.R., Johnson, M.A., and Evans E.M. To be submitted to *European Journal of Applied Physiology*.

4.1 Abstract

Purpose: The purpose of this study was to examine the relationships between changes in whole-muscle contractile performance and objective measures of physical function following 6 months of exercise and intentional dietary-induced weight loss in overweight and obese older women.

Methods: Thirty-eight overweight and obese ($BMI = 30.0 \pm 4.4 \text{ kg/m}^2$) postmenopausal women (age = $69.3 \pm 4.1 \text{ y}$) completed a 6-month exercise and weight loss intervention. Whole-muscle contractile performance of the leg was measured via isokinetic dynamometry at different testing velocities (isometric, $60^\circ/\text{s}$) and a leg extension power rig. Lower-extremity physical function was assessed using four objective measurements (6-minute walk, 8-foot up-and-go, 30-s chair stand and transfer task).

Results: Linear regression models indicated that changes in isokinetic knee torque and leg power consistently predicted improvements in 6-minute walk distance (unstandardized β range = 0.310 to 0.505, $p < 0.05$). Additionally, a 1 N-m increase in isometric knee torque ($\beta = -0.010$, $p < 0.01$) and isokinetic knee torque at $60^\circ/\text{s}$ ($\beta = -0.012$, $p < 0.05$) predicted a decrease in time on the 8-foot up-and-go. In contrast, only changes in absolute and relative leg extension power significantly predicted improvements on tests measuring sit-to-stand performance, including the 30-s chair stand and transfer task, at the 6-month follow-up.

Conclusion: Increases in muscle strength, power and quality consistently predicted improvements in widely-used indicators of physical function, including the 6-minute walk and 8-foot up-and-go, although leg power may be more important for tasks requiring the transfer of body weight (e.g., sitting-to-standing).

4.2 Introduction

The loss of skeletal muscle mass with age, known as sarcopenia, is one of the prominent changes in body composition experienced by older adults¹. The loss of muscle is accompanied by more precipitous declines in strength and power, suggesting an age-related decrease in muscle quality²⁻⁴. This is concerning as a considerable body of evidence suggests lower-body muscle strength, power and quality are all important determinants of physical function in the older adult cohort⁵⁻¹⁰. Thus, exercise is prescribed as an intervention strategy for improving muscle capacity, and subsequently physical function, in older adults¹¹.

While a positive association between strength, power and quality of the major lower-extremity muscles (quadriceps, hamstrings, gluteals) with physical function has consistently been reported in cross-sectional studies involving older adults^{5,7,8}, there is a paucity of data regarding whether improvements in muscle capacity are associated with commensurate improvements in physical function following exercise interventions^{12,13}. Moreover, the relationships between changes in whole-muscle performance and physical function are not adequately characterized following exercise interventions during concomitant intentional weight loss. Importantly, this represents a void in the scientific literature as the combination of exercise and diet-induced weight loss is widely recommended as a safe and effective interdisciplinary therapy for improving physical function among overweight and obese older adults¹⁴.

Randomized controlled trials have shown that interventions combining these strategies can improve various indexes of physical function in older adults¹⁵⁻¹⁷, but the relationship with changes in muscle strength, power or quality has not been thoroughly examined. Villareal et al.¹⁶ reported a positive association (partial $r = 0.42$) between changes in knee strength and physical function following 6 months of exercise and weight loss in overweight and obese older adults.

However, to our knowledge, no other study has attempted to characterize the improvements in specific measures of physical function associated with changes in different measures of whole-muscle contractile performance following exercise training and dietary-induced weight loss in overweight and obese older women. In addition, the relationship between measures of muscle capacity (strength vs. power) and physical function may be predicated upon the nature of the functional task; muscle power may be more important for activities requiring rapid vertical displacement (getting up from the floor) than it is for activities with a greater reliance on muscle endurance (walking ¼ mile). Although research has suggested that muscle power may be more important for physical function than muscle strength⁶, it remains unclear whether increases in muscle strength and power promote improvements in different aspects of function in older adults, especially under conditions of weight loss.

In this context, the aim of the present study was to examine the association between changes in measures of muscle strength (isometric vs. isokinetic torque), power (leg extension power) and quality (specific strength vs. specific power) and changes in performance on a battery of objectively-measured lower-extremity physical function (LEPF) tests after a 6-month multicomponent exercise and weight loss intervention in overweight and obese older women. Based on previous studies that have reported a higher relative importance of muscle power compared to muscle strength for physical function^{6,7}, it was hypothesized that a change in specific power (muscle power per unit of mass) would consistently be the strongest predictor of changes in various LEPF tests following the intervention.

4.3 Methods

Study Design and Participants

This study is a secondary analysis of a larger project that was designed to determine the effects of a 6-month exercise and weight loss intervention on body composition and LEPP in overweight and obese older women. For this analysis, only participants who 1) were enrolled in the exercise and weight loss arms of the trial and, 2) achieved $\geq 3\%$ loss of baseline body weight, were included. All participants obtained medical clearance from their physician and provided written informed consent prior to enrollment. All procedures of this study were approved by the university's Institutional Review Board.

Thirty-eight community-dwelling overweight and obese older women were included in the present analysis. Women aged 65-80 y were eligible for inclusion in the study if they met the following criteria: body mass index $\geq 25.0 \text{ kg/m}^2$, stable body weight during the previous six months (within 2 kg), sedentary (defined as $< 1 \text{ hr/wk}$ of physical activity or < 2 exercise sessions per week in the past six months), non-smoking or tobacco using, and free of any chronic disease or condition that would have precluded safe participation in exercise training or dietary restriction. Self-reported use of prescription medications was ascertained via a questionnaire and cognitive state was measured using the Mini-Mental State Examination¹⁸.

Body Composition

Standing height and weight were measured with participants wearing light-weight clothing and no shoes. Height was obtained using a stadiometer (Seca, Model 242) with measures obtained to the nearest 0.1 cm. Weight was measured on a calibrated digital scale (Tanita, Model WB-110A). Whole-body and regional soft tissue composition (relative adiposity and mineral-free lean mass) was assessed via dual-energy X-ray absorptiometry (iDXA, GE

Healthcare-Luna, Madison, WI). Mineral-free lean mass of the upper leg (e.g., quadriceps and hamstrings) was determined via bisecting the femoral neck and patella according to manufacturer guidelines. Lower-body mineral-free lean mass (e.g., quadriceps, hamstrings and lower leg) was quantified as total mineral-free lean mass below the superior border of the iliac crest.

Whole-Muscle Performance

Maximal isometric and isokinetic (60°/s) knee extension and flexion torque was measured via isokinetic dynamometry (System 4 Pro, Biodex Medical Systems Inc, Shirley, NY). For isometric strength, participants performed 2 sets of 4-s isometric extension and flexion contractions with the knee positioned at 60° of knee flexion, and the greatest torque values were used for analysis. Concentric isokinetic knee strength was assessed at 60°/s using 2 sets of 4 extension and flexion repetitions. The greatest extension and flexion peak torque values for each leg were summed to calculate maximal concentric isokinetic knee torque. For each measure of absolute knee strength (isometric and isokinetic at 60°/s), a corresponding measure of concentric muscle quality (Isometric-MQ and Isokinetic-MQ) was calculated by dividing maximal knee torque (N-m) by mineral-free lean mass of the upper leg (kg).

Unilateral leg extension power was assessed using the Nottingham power rig (University of Nottingham Medical School, Model NG7 2UH, Nottingham, UK). The participant was seated in an adjustable seat and instructed to push against a foot pedal as hard and quickly as possible until their knee was extended. Ten trials were performed for each leg, and maximal leg extension power was determined by summing the peak power values of the left and right legs. Specific muscle power (LEP-MQ) was calculated by normalizing maximal leg extension power (watts) for total lower-body mineral-free lean mass (kg).

Lower-Extremity Physical Function

Objective LEPF was measured using the 6-minute walk, 8-foot up-and-go, 30-s chair stand and transfer task. The 6-minute walk measures the greatest distance that an individual can walk in 6 minutes, and is a valid and reliable test of physical endurance in community-dwelling older adults¹⁹. The 8-foot up-and-go test requires a person to stand up from a chair, walk around a cone located 8 feet away and return to the chair as quickly as possible²⁰. This assessment is valid and reliable, and provides a measurement of dynamic balance, agility and speed in older adults²¹. Each participant completed two trials of the 8-foot up-and-go test and the shortest time was used for analysis. The 30-second chair stand measured the number of times that an individual could rise to a full stand from a seated position without using their arms in 30 seconds²⁰, and has been identified as a valid and reliable instrument in older adults²². Lastly, participants completed a transfer task, which required them to sit down on the floor and then return to a standing position as quickly as possible²³.

Exercise Intervention

All participants were expected to complete three 75-minute sessions of supervised exercise on nonconsecutive days during each week of the intervention for six months. All exercise sessions were conducted by trained graduate students in the Department of Kinesiology. The exercise intervention was a multicomponent program that integrated cardiorespiratory training, resistance training, balance, flexibility and functional activities, and was designed to be congruent with physical activity recommendations from the American College of Sports Medicine^{11,24}. Cardiorespiratory training included 30 minutes of continuous exercise (walking on a treadmill, cycling or using an elliptical) at 70-80% of age-predicted maximal heart rate. Exercise intensity during the cardiorespiratory training was monitored throughout each session

by recording heart rate and rating of perceived exertion at 10, 20, and 30 minutes of exercise. Participants performed three upper-body (chest press, shoulder press, and back row), three lower-body (leg press, knee extension, and knee curl), and one core (abdominal crunch) resistance training exercise during every session. Participants performed 2 sets of 8-10 repetitions at 65% of one-repetition maximum (1-RM) for each exercise until volitional muscle fatigue. In addition, 4-RM testing for each exercise was conducted every 6 weeks during the intervention to reassess muscle strength and adjust training load accordingly. In addition to cardiorespiratory and resistance training, two 30-s sets of four different functional activities (chair rises, wall push-ups, lift-and-carry, and transfer task) were performed during every training session. Finally, ~5-10 minutes of balance and flexibility exercises were performed at the end of every training session.

Diet Intervention

All participants were prescribed a diet that was designed to facilitate ~10% loss of initial body weight at the end of the 6-month intervention via reduction of estimated energy needs by ~500 kcal/d. To ensure participants were meeting micronutrient needs during the intervention, all participants were provided with a multivitamin mineral supplement formulated for older women (Centrum® Silver® Women, Pfizer, Inc. Madison, NJ) that provided 800 IU of vitamin D and 500 mg of calcium.

During the initial phase of the intervention, all participants attended at least two individual sessions with a registered dietitian nutritionist or supervised nutrition graduate student for instruction regarding topics such as energy restriction and self-monitoring methods. For the remainder of the 6-month intervention, participants attended weekly educational/motivational group sessions (45-60 min) with the registered dietitian nutritionist or graduate student, as well

as individual sessions in order to meet weight loss goals. Dietary records for all participants were monitored weekly and individual written feedback from the registered dietitian nutritionist or supervised graduate student was provided at each group session. The curriculum for the group sessions was designed according to Social Cognitive Theory²⁵ and included topics such as general nutrition education and behavioral strategies for weight management. In addition, all participants were instructed to use a free online dietary intake monitoring application (MyFitnessPal.com). Trained staff monitored entries weekly and participants were provided individualized feedback throughout the intervention to help meet weight loss and nutrient goals.

Statistical Analysis

All statistical analyses were conducted using SPSS for Windows version 22.0 (SPSS Inc., Chicago, IL). Data were examined for normality via distribution statistics (skewness and kurtosis) and visual inspection of histograms. Paired samples t-tests were used to determine within-group changes for all measures of muscle strength, power, quality and LEPF. Change variables were calculated (post – baseline value) for all outcomes, and linear regression analyses were performed to examine the contributions of changes in different measures of whole-muscle contractile performance to changes in individual measures of LEPF following the intervention. Previous investigations in this area have varied in duration, type of intervention and study cohort, and the correlation between changes in muscle strength or power and physical function has varied from $r = -0.71$ to 0.42 ^{12,13,16}. Thus, in order to detect an association between change in muscle quality and change in LEPF ($r = 0.45$), assuming $\alpha = 0.05$ and power of 0.80, a sample size of 36 was necessary. Statistical significance was set at $p < 0.05$ for all tests.

4.4 Results

Participant Characteristics

Baseline characteristics for the sample are presented in Table 1. The mean age of the participants was 69.3 ± 4.1 y and all participants were white. Participants were categorized as obese according to BMI (30.0 ± 4.4 kg/m²) and percent body fat ($47.7 \pm 3.8\%$). As expected based on enrollment criteria, the participants were sedentary with a mean step count of 5155.9 ± 2019.4 at baseline. With regard to the exercise intervention, mean attendance was 60.8 ± 5.1 training sessions, which corresponded to $75.6 \pm 5.7\%$ of total possible sessions. Data from the exercise intervention at different time points of the study for each mode of training (cardiorespiratory, resistance and functional activities) are presented in Table 2.

Body Composition

The overall loss of body weight was 7.6 ± 2.9 kg, which corresponded to a percent weight loss of $9.6 \pm 3.5\%$. For anthropometric measurements, there were significant reductions in BMI (2.9 ± 1.2 kg/m², $p < 0.01$) and waist circumference (8.0 ± 6.1 cm, $p < 0.01$). With regard to body composition, there were significant decreases in relative adiposity ($4.9 \pm 2.1\%$, $p < 0.01$) and absolute fat mass (6.8 ± 2.4 kg, $p < 0.01$) following the intervention. Additionally, there was a modest, but significant, reduction in mineral-free lean mass of the upper-leg (quadriceps and hamstrings) from baseline to post-intervention (-0.3 ± 0.5 kg, $p < 0.01$). Likewise, lower-body mineral-free lean mass (e.g., below the superior border of the iliac crest) was significantly decreased at 6 months (-0.3 ± 0.6 kg, $p < 0.01$).

Whole-Muscle Performance and LEPF

Baseline, post and absolute change values for indices of whole-muscle contractile performance and LEPF are presented in Table 3. Despite a small decrease in leg lean mass, there

were significant increases in all measures of muscle strength, power and quality. A comparison of the percent changes for the different measures of whole-muscle performance from baseline to post-intervention is presented in Figure 1. Following the intervention, there were also significant improvements in all measures of LEPF. A negative percent change in the timed tests (8-foot up-and-go and transfer task) is indicative of a faster time to complete the test and thus represents an improvement. The greatest percent changes were evident in performance on the 30-s chair stand ($+57.0 \pm 34.4\%$) and transfer task ($-39.0 \pm 19.8\%$), while the magnitude of improvement was smaller for the 6-minute walk ($+12.0 \pm 8.7\%$) and 8-foot up-and-go ($-12.1 \pm 8.4\%$).

Relationships between Changes in Muscle Strength, Power, Quality and LEPF

Linear regression analyses were performed to examine the association between changes in absolute muscle strength and power and changes in LEPF following the intervention (Table 4). Simple linear regression models were created to examine the unadjusted association between changes in muscle strength, power and quality with LEPF. Additionally, a second model was examined to control for the influence of baseline value in whole-muscle contractile performance. In the unadjusted model, change in isometric knee torque was a significant predictor of changes in the 6-minute walk ($\beta = 0.499$, $p < 0.01$) and the 8-foot up-and-go ($\beta = -0.010$, $p < 0.01$) tests. Likewise, change in isokinetic torque at $60^\circ/\text{s}$ was a significant predictor of change in 6-minute walk ($\beta = 0.505$, $P < 0.05$) and change in the 8-foot up-and-go ($\beta = -0.012$, $p < 0.05$). In contrast, change in leg extension power was the only significant predictor of change in performance on the transfer task ($\beta = -0.066$, $p < 0.05$) and no associations were observed between changes in absolute muscle strength or power and change in performance on the 30-s chair stand. Adjustment for baseline values did not appreciably alter interpretation of the results, except for the relationship between change in leg extension power and the transfer task, which was no

longer significant ($\beta = -0.052$, $p = 0.12$). One outlier was identified for change in the transfer task (change > 3 SD from mean change) and excluding this participant from the unadjusted model slightly attenuated the relationship with leg extension power ($\beta = 0.029$, $p = 0.05$).

The relationships between changes in measures of muscle quality and measures of LEPF are shown in Table 5. In general, the associations between changes in muscle quality and LEPF were similar to the relationships observed for changes in absolute leg muscle strength and power. However, there was a strong trend for LEP-MQ to predict a change in performance on the 30-s chair stand in the unadjusted model ($\beta = 0.850$, $p = 0.06$), and this relationship was significant when controlling for baseline LEP-MQ ($\beta = 1.205$, $p < 0.05$). Again, excluding the one outlier from the linear regression analysis of the transfer task attenuated the unadjusted model for LEP-MQ ($\beta = -0.520$, $p = 0.09$) but did not alter the interpretation of results.

4.5 Discussion

The purpose of this study was to examine the relative strength of the relationships between changes in whole-muscle contractile performance and objective measures of LEPF following 6 months of exercise and diet-induced weight loss in overweight and obese older women. Our study expands upon the current body of literature by characterizing the predictive value of changes in muscle strength, power and quality for improvements in physical function tasks with different biomechanical and metabolic properties following a multicomponent exercise and weight loss intervention.

We found that changes in muscle strength, power and quality predicted changes in some tests of LEPF; however, the strength of association varied across functional tasks. For example, our linear regression models indicated that changes in leg muscle strength, power and quality were all independent predictors of a change in 6-minute walk performance. For isokinetic knee

torque at 60°/s, which is the most commonly used clinical measure of whole-muscle contractile performance, every 1 N-m improvement predicted an increase of 0.505 m in distance covered during the 6-minute walk. Similar improvements in performance on the 6-minute walk were observed with a 1 N-m increase in isometric knee torque ($\beta = 0.499$) and leg extension power ($\beta = 0.301$). Improvements in physical endurance (e.g., 6-minute walk) may have translational importance as recent evidence indicates that the 6-minute walk is independently associated with all-cause mortality in community-dwelling older adults from the Cardiovascular Health Study²⁶. Therefore, the notion that increased leg muscle strength or power can predict improvements in a critical marker of overall health suggests this association has clinical relevance for older adults. With regard to the 8-foot up-and-go, which assesses dynamic balance and agility and has distinctly different biomechanical and bioenergetic properties from the 6-minute walk, a 1-N-m increase in isometric knee torque and isokinetic torque at 60°/s predicted decreases of 0.010 and 0.012 s, respectively, in duration required to complete the test. Importantly, performance on the 8-foot up-and-go is a predictor of falls in community-dwelling older adults²⁷, and improving dynamic balance and agility in overweight and obese older women may translate to a decreased risk of falling. In general, changes in muscle strength significantly predicted improvements on the 6-minute walk and 8-foot up-and-go, both of which are associated with important clinical outcomes in older adults.

In contrast, none of the indices of muscle strength predicted a change in the ability to sit down on the floor and then rise to a standing position, whereas the change in leg extension power was a significant predictor. In our unadjusted regression model, an improvement in leg extension power by 1 watt predicted a reduction of 0.066 s in time required to sit down on the floor and rise to a standing position. Although the transfer task is a simple test to administer, the ability to

sit down and rise from the floor is a functionally relevant movement for older adults, and has been identified as a significant predictor of all-cause mortality in adults aged 51-80 y²⁸, suggesting that improving this skill is critical. Similarly, the only measure of muscle quality that predicted a change in performance on the 30-s chair stand was LEP-MQ (Table 5). These findings are in accordance with our hypothesis, and provide preliminary evidence that changes in muscle power may be more important than changes in strength for physical function tasks that require rapid production of force (e.g., sit-to-stand), and are also congruent with data from cross-sectional studies comparing muscle power and strength in older adults^{6,7}. In addition, although the relative intensity of the functional tasks administered in our study (6-minute walk, 8-foot up-and-go, 30-s chair stand and transfer task) has not been characterized, previous research suggests that the relation between maximal knee strength or power and performance on functional tasks in older adults is dependent upon the intensity of the task^{29,30}. Salem et al.³⁰ reported that maximal knee strength explained 41-54% of the variance in higher-intensity activities compared to 31-33% of the variance in lower-intensity activities in a cohort of community-dwelling older adults. Likewise, others have hypothesized that the relationship between maximal leg power and physical function is similarly influenced by the intensity of the functional task²⁹. Thus, the variability in strength of relation between our measures of contractile performance and physical function may be attributable, in part, to differences in the intensity of the functional tasks. Additional research is necessary to determine if intensity of functional task influences the relationship with whole-muscle contractile performance, especially under conditions of change (e.g., exercise training and/or weight loss).

Interestingly, aside from changes in leg power, improvements in contractile performance did not consistently predict changes in the 30-s chair stand test or transfer task following the

intervention. However, it is important to highlight that the 30-s chair stand (standing up from a chair) and transfer task (standing up from the floor) require the greatest vertical displacement during the testing movement. It has been shown that sit-to-stand performance is influenced by a variety of sensorimotor, balance and psychological factors, in addition to lower-body muscle strength (knee extension, knee flexion and ankle dorsiflexion), among community-dwelling older men and women³¹. Thus, it is plausible that our intervention elicited changes in several of the above variables, which were not measured in our study, but that may have confounded the relationship between changes in muscle strength/power and the ability to transfer from a sitting to a standing position. Further research is necessary to characterize the relative importance of changes in the most pertinent variables for improved sit-to-stand performance following interventions in older adults. However, overall, our findings do suggest that improvements in muscle strength, power and quality have an instrumental role in promoting improvements on some widely-used assessments of physical function (e.g., 6-minute walk and 8-foot up-and-go), but that changes in additional factors (such as psychological, sensorimotor and biomechanical) should be accounted for as they may help explain improvements in particular functional tasks (e.g., sit-to-stand).

In addition to characterizing the relationships between changes in muscle strength, power, quality and LEPF, our study indicates that the combination of exercise training and diet-induced weight loss can attenuate the marked age-related decline in physical function among older adults. To aid in interpretation of the clinical significance of our findings, we compared changes in LEPF following our intervention to previous literature that has reported criteria for identifying meaningful changes in common measures of physical performance for older adults. For example, Perera et al.³² demonstrated that an improvement of 20 m in the 6-minute walk

constitutes a small meaningful change, while an improvement of 50 m represents a substantial meaningful change. In the present study, the mean change in distance for 6-minute walk was ~59 m, suggesting our intervention elicited a substantial meaningful change. Additionally, we found that 25 of the 38 participants (~66% of the sample) exceeded a change of 50 m in the 6-minute walk. This is noteworthy in the context of relatively steep age-related decrements in physical function among older adults. For instance, Onder et al.³³ reported that various measures of lower-extremity performance (walking speed, balance and chair stand tests) declined 16-27% over 3 years among women aged 65+ y involved in the Women's Health and Aging Study. In light of those findings, the magnitude of change observed in our measures of LEPF (+12-57%) after 6 months underscores the notion that exercise and weight loss is an efficacious intervention strategy for improving physical function in overweight and obese older women, which is a subgroup of older adults at particular risk for poor functional health outcomes, such as frailty³⁴.

While our findings help elucidate the relationships between changes in muscle contractile performance and LEPF in overweight and obese older women undergoing weight loss, there are limitations to the present study that warrant consideration. First, the lack of a control group or a parallel arm design (e.g., diet-only group) does not allow us to examine whether the associations between changes in muscle strength, power, quality and LEPF vary according to the intervention strategy (exercise vs. weight loss). However, a recent systematic review reporting the effects of energy restriction on fat-free mass in adults aged 50 y and older indicated that 81% of energy restriction groups lost $\geq 15\%$ of body weight as fat-free mass³⁵, and it is intuitive that a decrease in muscle mass (in the absence of exercise training) would contribute to lower muscle strength, power and quality. In addition, our own work determined that a reduction in total body mass significantly predicts a decrease in isokinetic quadriceps torque after 6 months of dietary-induced

weight loss among overweight and obese older women²³. Thus, from a clinical standpoint, it was most relevant to examine the relationships among changes in muscle strength, power, quality and LEPF in the presence of two widely recommended behavioral interventions (exercise and weight loss) for overweight and obese older adults¹⁴. A second consideration is our relatively homogeneous sample, which was comprised of community-dwelling overweight and obese white women. Likewise, all the participants in our sample had the capacity to ambulate independently, and extrapolating our findings to other subgroups of older adults, such as those with mobility-related disability, should be done so cautiously. Findings from one randomized controlled trial indicate that a 12-week resistance training intervention can improve lower-extremity muscle power and quality in mobility-limited older adults³⁶. However, that study did not include intentional weight loss, and whether or not muscle power changes predict improvements in physical function among mobility-limited older adults undergoing weight loss has not been well-characterized and future research is necessary. Therefore, examining these changes under conditions of diet-induced intentional weight loss during longer interventions is also needed to advance our understanding of these relationships.

In conclusion, we present novel evidence that increases in muscle strength and power consistently predicted improvements on the 6-minute walk and 8-foot up-and-go tests following exercise and weight loss in overweight and obese older women. However, increases in leg power were more important than strength for tasks requiring the transfer of body weight (e.g., sitting-to-standing). Overweight older women undergoing intentional weight loss may derive specific functional benefits by engaging in a concurrent exercise program designed to improve muscle strength or power.

4.6 References

1. Fielding RA, Vellas B, Evans WJ, et al. Sarcopenia: an undiagnosed condition in older adults. Current consensus definition: prevalence, etiology, and consequences. International working group on sarcopenia. *J Am Med Dir Assoc.* 2011;12:249-256.
2. Clark BC, Manini TM. Sarcopenia \neq dynapenia. *J Gerontol A Biol Sci Med Sci.* 2008;63:829-834.
3. Clark DJ, Pojednic RM, Reid KF, et al. Longitudinal decline of neuromuscular activation and power in healthy older adults. *J Gerontol A Biol Sci Med Sci.* 2013;68:1419-1425.
4. Delmonico MJ, Harris TB, Visser M, et al. Longitudinal study of muscle strength, quality, and adipose tissue infiltration. *Am J Clin Nutr.* 2009;90:1579-1585.
5. Bean JF, Kiely DK, Herman S, et al. The relationship between leg power and physical performance in mobility-limited older people. *J Am Geriatr Soc.* 2002;50:461-467.
6. Bean JF, Leveille SG, Kiely DK, Bandinelli S, Guralnik JM, Ferrucci L. A comparison of leg power and leg strength within the InCHIANTI study: which influences mobility more? *J Gerontol A Biol Sci Med Sci.* 2003;58:728-733.
7. Foldvari M, Clark M, Laviolette LC, et al. Association of muscle power with functional status in community-dwelling elderly women. *J Gerontol A Biol Sci Med Sci.* 2000;55:M192-199.
8. Misisic MM, Rosengren KS, Woods JA, Evans EM. Muscle quality, aerobic fitness and fat mass predict lower-extremity physical function in community-dwelling older adults. *Gerontology.* 2007;53:260-266.
9. Straight CR, Brady AO, Evans EM. Muscle quality and relative adiposity are the strongest predictors of lower-extremity physical function in older women. *Maturitas.* 2015;80:95-99.
10. Suzuki T, Bean JF, Fielding RA. Muscle power of the ankle flexors predicts functional performance in community-dwelling older women. *J Am Geriatr Soc.* 2001;49:1161-1167.
11. Nelson ME, Rejeski WJ, Blair SN, et al. Physical activity and public health in older adults: recommendation from the American College of Sports Medicine and the American Heart Association. *Circulation.* 2007;116:1094-1105.
12. Marsh AP, Miller ME, Rejeski WJ, Hutton SL, Kritchevsky SB. Lower extremity muscle function after strength or power training in older adults. *J Aging Phys Act.* 2009;17:416-443.

13. Pinto RS, Correa CS, Radaelli R, Cadore EL, Brown LE, Bottaro M. Short-term strength training improves muscle quality and functional capacity of elderly women. *Age (Dordr)*. 2014;36:365-372.
14. Villareal DT, Apovian CM, Kushner RF, Klein S. Obesity in older adults: technical review and position statement of the American Society for Nutrition and NAASO, The Obesity Society. *Am J Clin Nutr*. 2005;82:923-934.
15. Nicklas BJ, Chmelo E, Delbono O, Carr JJ, Lyles MF, Marsh AP. Effects of resistance training with and without caloric restriction on physical function and mobility in overweight and obese older adults: a randomized controlled trial. *Am J Clin Nutr*. 2015;101:991-999.
16. Villareal DT, Banks M, Sinacore DR, Siener C, Klein S. Effect of weight loss and exercise on frailty in obese older adults. *Arch Intern Med*. 2006;166:860-866.
17. Villareal DT, Chode S, Parimi N, et al. Weight loss, exercise, or both and physical function in obese older adults. *N Engl J Med*. 2011;364:1218-1229.
18. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12:189-198.
19. Rikli RE, Jones CJ. The reliability and validity of a 6-minute walk test as a measure of physical endurance in older adults. *J Aging Phys Act*. 1998;6:363-375.
20. Rikli RE, Jones CJ. *Senior Fitness Test Manual*. 2nd ed. Champaign, IL: Human Kinetics; 2013.
21. Rikli RE, Jones CJ. Development and validation of a functional fitness test for community-residing older adults. *J Aging Phys Act*. 1999;7:129-161.
22. Jones CJ, Rikli RE, Beam WC. A 30-s chair-stand test as a measure of lower body strength in community-residing older adults. *Res Q Exerc Sport*. 1999;70:113-119.
23. Mojtahedi MC, Thorpe MP, Karampinos DC, et al. The effects of a higher protein intake during energy restriction on changes in body composition and physical function in older women. *J Gerontol A Biol Sci Med Sci*. 2011;66:1218-1225.
24. Garber CE, Blissmer B, Deschenes MR, et al. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Med Sci Sports Exerc*. 2011;43:1334-1359.
25. Bandura A. Health promotion by social cognitive means. *Health Educ Behav*. 2004;31:143-164.

26. Yazdanyar A, Aziz MM, Enright PL, et al. Association Between 6-Minute Walk Test and All-Cause Mortality, Coronary Heart Disease-Specific Mortality, and Incident Coronary Heart Disease. *J Aging Health*. 2014;26:583-599.
27. Rose DJ, Jones JC, Lucchese N. Predicting the probability of falls in community-residing older adults using the 8-foot up-and-go: a new measure of functional mobility. *J Aging Phys Act*. 2002;10:466-475.
28. Brito LB, Ricardo DR, Araujo DS, Ramos PS, Myers J, Araujo CG. Ability to sit and rise from the floor as a predictor of all-cause mortality. *Eur J Prev Cardiol*. 2014;21:892-898.
29. Puthoff ML, Nielsen DH. Relationships among impairments in lower-extremity strength and power, functional limitations, and disability in older adults. *Phys Ther*. 2007;87:1334-1347.
30. Salem GJ, Wang MY, Young JT, Marion M, Greendale GA. Knee strength and lower- and higher-intensity functional performance in older adults. *Med Sci Sports Exerc*. 2000;32:1679-1684.
31. Lord SR, Murray SM, Chapman K, Munro B, Tiedemann A. Sit-to-stand performance depends on sensation, speed, balance, and psychological status in addition to strength in older people. *J Gerontol A Biol Sci Med Sci*. 2002;57:M539-543.
32. Perera S, Mody SH, Woodman RC, Studenski SA. Meaningful change and responsiveness in common physical performance measures in older adults. *J Am Geriatr Soc*. 2006;54:743-749.
33. Onder G, Penninx BW, Lapuerta P, et al. Change in physical performance over time in older women: the Women's Health and Aging Study. *J Gerontol A Biol Sci Med Sci*. 2002;57:M289-293.
34. Blaum CS, Xue QL, Michelon E, Semba RD, Fried LP. The association between obesity and the frailty syndrome in older women: the Women's Health and Aging Studies. *J Am Geriatr Soc*. 2005;53:927-934.
35. Weinheimer EM, Sands LP, Campbell WW. A systematic review of the separate and combined effects of energy restriction and exercise on fat-free mass in middle-aged and older adults: implications for sarcopenic obesity. *Nutr Rev*. 2010;68:375-388.
36. Reid KF, Callahan DM, Carabello RJ, Phillips EM, Frontera WR, Fielding RA. Lower extremity power training in elderly subjects with mobility limitations: a randomized controlled trial. *Aging Clin Exp Res*. 2008;20:337-343.

Table 4.1. Participant characteristics (n=38)

Characteristic	Mean \pm SD	Range
Age (y)	69.3 \pm 4.1	65-77
Height (m)	1.6 \pm 0.1	1.4-1.8
Weight (kg)	79.6 \pm 10.3	53.7-100.2
Body Mass Index (kg/m ²)	30.0 \pm 4.4	25.0-44.4
Waist Circumference (cm) ^a	101.0 \pm 12.1	82.2-141.9
Percent Body Fat (%)	47.7 \pm 3.8	40.9-56.0
Fat Mass (kg)	37.0 \pm 7.1	23.5-51.0
Upper-Leg MFLM (kg)	13.7 \pm 1.6	8.8-17.1
Lower-Body MFLM (kg)	20.5 \pm 2.7	13.4-25.0
Mini-Mental State Examination (0-30)	29.1 \pm 1.1	26-30
Number of Medications (total)	3.8 \pm 2.7	0-10
Physical Activity (steps/d)	5155.9 \pm 2019.4	1680.9-9108.5

MFLM = mineral-free lean mass

^an=37

Table 4.2. Characteristics of the multicomponent exercise training intervention

		Week 8	Week 12	Week 16	Week 20	Week 24
<i>Cardiorespiratory Training</i>	HR (beats/min)	119.6 ± 15.2	123.4 ± 14.2	121.7 ± 13.6	120.5 ± 13.1	121.0 ± 12.7
	RPE (6-20)	12.9 ± 0.9	13.0 ± 1.0	13.2 ± 1.0	13.3 ± 0.9	13.1 ± 0.9
<i>Resistance Training</i>	Leg Press (lbs)	137.3 ± 32.3	142.8 ± 29.9	150.2 ± 28.7	154.1 ± 27.5	157.1 ± 27.7
	Knee Extension (lbs)	59.8 ± 17.4	62.0 ± 16.2	64.9 ± 16.2	68.0 ± 15.1	68.2 ± 15.5
	Knee Curl (lbs)	52.3 ± 10.1	54.2 ± 11.3	56.6 ± 11.2	58.0 ± 10.3	59.7 ± 10.8
	Chest Press (lbs)	35.3 ± 12.8	37.7 ± 13.6	40.9 ± 13.1	43.8 ± 14.4	44.9 ± 14.6
	Back Row (lbs)	62.1 ± 10.5	64.8 ± 10.8	66.4 ± 11.3	67.7 ± 12.3	68.4 ± 12.6
	Overhead Press (lbs)	22.1 ± 11.1	25.3 ± 12.0	27.7 ± 11.2	29.0 ± 11.4	29.2 ± 11.8
	Abdominal Crunch (lbs)	59.7 ± 11.5	63.0 ± 10.4	66.0 ± 10.4	66.9 ± 13.3	68.4 ± 13.3
<i>Functional Activities</i>	Chair stands (total)	17.2 ± 4.0	18.1 ± 4.9	19.1 ± 4.8	19.1 ± 5.7	19.9 ± 6.1
	Transfer task (total)	5.6 ± 1.7	5.8 ± 1.8	5.9 ± 1.9	6.7 ± 3.6	6.0 ± 2.0
	Lift-and-carry task (lbs)	22.8 ± 3.6	23.5 ± 4.7	24.3 ± 4.8	23.3 ± 6.0	24.8 ± 5.2
	Wall push-ups (total)	17.0 ± 3.3	18.3 ± 4.3	19.2 ± 4.8	19.5 ± 4.8	20.7 ± 5.1

Data are presented as mean ± SD
 HR = heart rate; RPE = rating of perceived exertion

Table 4.3. Baseline, post and change values for indices of whole-muscle contractile performance and lower-extremity physical function (n=38)

Measure	Baseline	Post	Δ	<i>P</i>
Isometric Knee Torque (N-m)	296.8 \pm 57.5	316.5 \pm 56.0	19.7 \pm 35.4	< 0.01
Isometric-MQ (N-m/kg)	21.9 \pm 4.5	23.8 \pm 4.3	1.9 \pm 2.4	< 0.01
Isokinetic Knee Torque at 60/s (N-m)	272.7 \pm 49.0	289.2 \pm 50.8	16.5 \pm 25.5	< 0.01
Isokinetic-MQ (N-m/kg)	20.1 \pm 3.7	21.7 \pm 3.6	1.6 \pm 1.8	< 0.01
Leg Extension Power (watts) ^a	200.6 \pm 56.5	223.9 \pm 43.4	23.3 \pm 39.1	< 0.01
LEP-MQ (watts/kg) ^a	9.8 \pm 2.6	11.2 \pm 2.3	1.4 \pm 1.9	< 0.01
6-Minute Walk (m)	521.6 \pm 67.8	580.5 \pm 62.2	58.9 \pm 33.7	< 0.01
8-Foot Up-and-Go (s)	6.44 \pm 1.25	5.59 \pm 0.78	-0.84 \pm 0.74	< 0.01
30-S Chair Stand (total)	13.7 \pm 2.7	21.4 \pm 5.9	7.8 \pm 5.0	< 0.01
Transfer Task (s)	9.11 \pm 6.59	4.85 \pm 1.75	-4.26 \pm 5.67	< 0.01

Data are presented as mean \pm SD

Δ = post - baseline

^an=34

Table 4.4. Associations between changes in muscle capacity and lower-extremity physical function using linear regression analysis (n=38)

Predictor	Δ 6-Minute Walk				Δ 8-Foot Up-and-Go				Δ 30-S Chair Stand				Δ Transfer Task			
	β	SE	P	R ²	β	SE	P	R ²	β	SE	P	R ²	β	SE	P	R ²
Δ Isometric Knee Torque	0.499	0.135	<0.01	0.28	-0.010	0.003	<0.01	0.22	0.011	0.024	0.65	0.01	-0.011	0.027	0.69	0.01
Adjusted	0.480	0.146	<0.01	0.28	-0.008	0.003	<0.05	0.29	0.009	0.026	0.73	0.01	0.007	0.028	0.81	0.09
Δ Isokinetic Knee Torque	0.505	0.203	<0.05	0.15	-0.012	0.004	<0.01	0.19	0.040	0.032	0.22	0.04	-0.055	0.036	0.14	0.06
Adjusted	0.509	0.210	<0.05	0.15	-0.011	0.004	<0.05	0.22	0.040	0.033	0.24	0.04	-0.041	0.035	0.25	0.16
Δ Leg Extension Power ^a	0.310	0.148	<0.05	0.12	-0.004	0.003	0.22	0.05	0.027	0.022	0.23	0.04	-0.066	0.024	<0.05	0.19
Adjusted	0.526	0.187	<0.01	0.20	-0.003	0.005	0.57	0.06	0.021	0.029	0.47	0.05	-0.052	0.032	0.12	0.20

Δ = Post-intervention – baseline

Adjusted model is controlled for baseline values

^an=34

Table 4.5. Associations between changes in muscle quality and lower-extremity physical function using linear regression analysis (n=38)

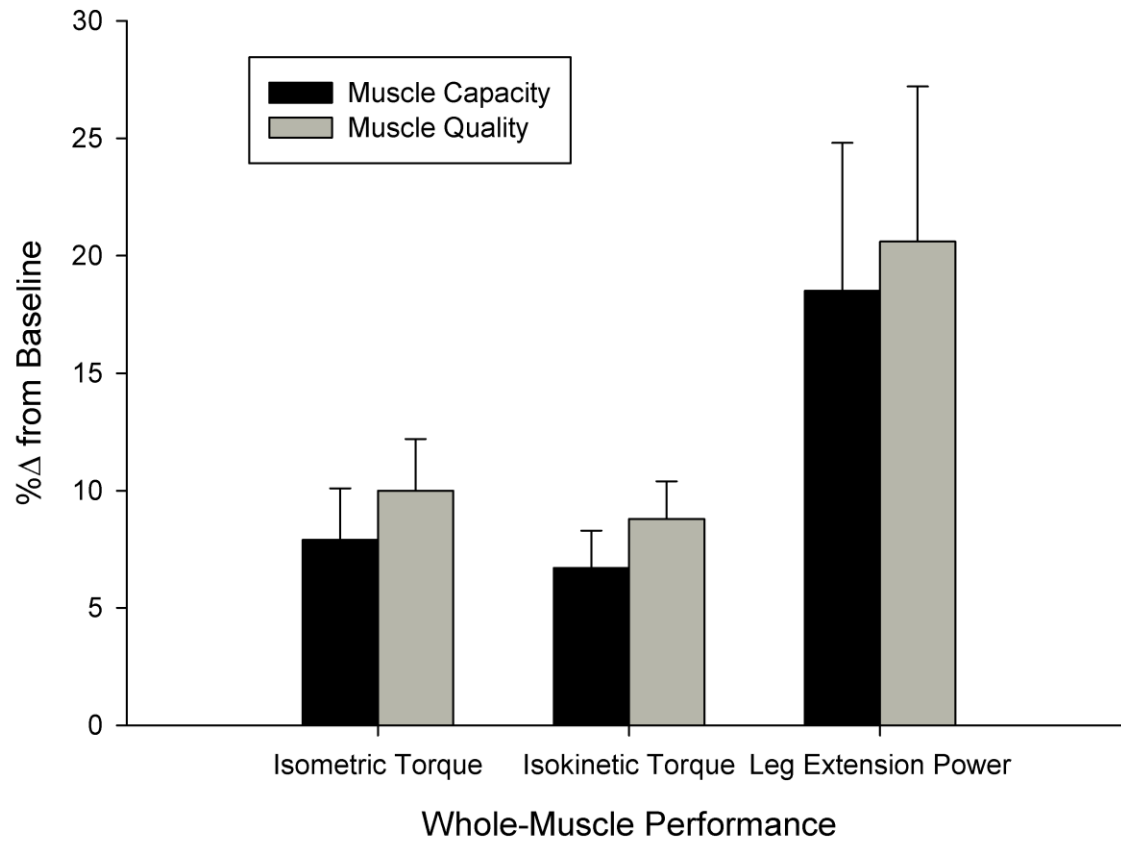
Predictor	Δ 6-Minute Walk				Δ 8-Foot Up-and-Go				Δ 30-S Chair Stand				Δ Transfer Task			
	β	SE	P	R ²	β	SE	P	R ²	β	SE	P	R ²	β	SE	P	R ²
Δ Isometric-MQ	7.064	2.050	<0.01	0.25	-0.136	0.046	<0.01	0.19	0.180	0.352	0.61	0.01	-0.244	0.396	0.54	0.01
Adjusted	7.040	2.237	<0.01	0.25	-0.094	0.047	0.05	0.31	0.365	0.374	0.34	0.06	0.043	0.412	0.92	0.10
Δ Isokinetic-MQ	6.047	2.952	<0.05	0.10	-0.158	0.063	<0.05	0.15	0.509	0.458	0.27	0.03	-0.972	0.499	0.06	0.10
Adjusted	6.462	3.114	<0.05	0.11	-0.127	0.064	0.06	0.21	0.742	0.465	0.12	0.11	-0.676	0.498	0.18	0.20
Δ LEP-MQ ^a	6.080	2.986	0.05	0.12	-0.077	0.069	0.27	0.04	0.850	0.431	0.06	0.11	-1.205	0.497	<0.05	0.16
Adjusted	8.342	3.530	<0.05	0.15	-0.010	0.080	0.91	0.11	1.158	0.511	<0.05	0.14	-0.651	0.572	0.26	0.24

Δ = Post-intervention – baseline

Adjusted model is controlled for baseline values

^an=3

Figure 4.1. Percent changes in muscle strength, power and quality from baseline to post-intervention; values represent mean \pm SE; all measures of whole-muscle performance significantly improved at $p < 0.01$



CHAPTER 5

MIDTHIGH INTERMUSCULAR ADIPOSE TISSUE AND MUSCLE QUALITY

DIFFERENTIALLY PREDICT IMPROVEMENTS IN PHYSICAL FUNCTION

FOLLOWING EXERCISE AND WEIGHT LOSS IN OVERWEIGHT AND OBESE

OLDER WOMEN¹

¹Straight, C.R., Johnson, M.A., and Evans, E.M. To be submitted to *Preventive Medicine*.

5.1 Abstract

Background: To examine the effects of exercise and weight loss on thigh composition, muscle quality and physical function, and the relationships between changes in these outcomes, in overweight and obese older women.

Methods: Twenty-five overweight and obese ($BMI = 29.0 \pm 3.2 \text{ kg/m}^2$) postmenopausal (age = $68.5 \pm 3.8 \text{ y}$) women completed a 6-month exercise and weight loss intervention. Whole-body and regional composition was measured via dual-energy X-ray absorptiometry and magnetic resonance imaging. Muscle quality ($\text{N}\cdot\text{m}/\text{cm}^2$) was defined as isokinetic knee torque divided by muscle cross-sectional area and physical function was measured using the 6-minute walk and 30-s chair stand.

Results: At 6 months, overall weight loss was $7.6 \pm 3.1 \text{ kg}$ ($-9.9 \pm 3.9\%$, $p < 0.01$). There was a $16.3 \pm 8.8\%$ reduction in thigh intermuscular adipose tissue ($-2.9 \pm 2.0 \text{ cm}^2$, $p < 0.01$) and $18.0 \pm 7.7\%$ decrease in subcutaneous adipose tissue area ($-18.3 \pm 8.4 \text{ cm}^2$, $p < 0.01$), while muscle area did not change ($-1.0 \pm 2.7 \text{ cm}^2$, $p = 0.12$). Additionally, muscle quality ($+0.11 \pm 0.20 \text{ N}\cdot\text{m}/\text{cm}^2$, $p < 0.01$) and measures of physical function improved ($+9.7\text{-}58.7\%$, $p < 0.01$). Reduction in thigh IMAT area was the strongest independent predictor of a change in performance on the 30-s chair stand (standardized $\beta = -0.80$, $p < 0.01$) and explained 34% of the variance. In contrast, change in muscle quality was a significant predictor of change in 6-minute walk distance ($\beta = 0.48$, $p < 0.05$) and independently accounted for 24% of the variance.

Conclusion: Changes in midthigh IMAT and muscle quality are both independent predictors of improved physical function following exercise and weight loss in overweight and obese older women; however, their relative importance may vary according to the functional task.

5.2 Introduction

In 2010, the prevalence of obesity was 42.3% among older women living in the United States¹. In addition to a myriad of well-known cardiometabolic consequences², obesity is related to adverse functional outcomes, such as decrements in walking, stair ascent and rising from a chair³. Due to the well-known and numerous health effects of overweight and obesity, lifestyle therapies involving weight loss are a contemporary research interest and public health priority.

While obesity represents disordered body composition at the whole-body level, it also results in unfavorable composition of regional tissue compartments. Thigh composition is of particular interest because of the critical role thigh musculature (e.g., quadriceps and hamstrings) has in determining physical function among older adults^{4,5}. In addition to loss of skeletal muscle, another prominent change in thigh composition among overweight and obese older adults is an increase in intermuscular adipose tissue (IMAT). Traditionally defined as adipose located beneath the fascia of the thigh muscles⁶, IMAT increases with advancing age⁷⁻⁹ and with greater fat mass and relative adiposity in older adults¹⁰. This is concerning because studies have shown that thigh IMAT is associated with insulin resistance^{11,12}, systemic inflammation¹³, poor muscle strength and quality¹⁰, and mobility function¹⁴⁻¹⁶. Whether or not IMAT can be reduced without an accompanying decline in muscle size is critical for overweight and obese older adults who may have low muscle mass relative to body weight. Moreover, it is unclear if reductions in thigh IMAT are associated with improvements in physical function, independent of changes in overall fat mass, among overweight and obese older women.

In addition to unfavorable thigh composition, overweight and obesity also appear to negatively impact muscle quality, or strength per unit of muscle size, which has emerged as a salient indicator of functional health among older adults^{4,5,17-21}. Cross-sectional studies have

shown that older women who are overweight or obese have significantly lower muscle quality than their normal weight counterparts, and this finding has been consistent across studies that have estimated adiposity using body mass index²² and measured relative adiposity, expressed as percent body fat²³. Although weight loss reduces adiposity and confers a more favorable body composition, it is unlikely to improve muscle quality in the absence of an exercise program due to an unintentional concomitant decline in lean mass^{24,25}.

In this context, the aim of the present study was to investigate the effects of exercise plus weight loss on thigh composition, muscle quality and objective physical function in overweight and obese older women. It was hypothesized that midthigh IMAT, subcutaneous adipose tissue (SAT) and muscle cross-sectional area would all decrease, but that muscle quality and physical function would improve, following the intervention. As a secondary aim, we examined the associations among changes in whole-body adiposity, thigh composition, muscle quality and physical function.

5.3 Methods

Participants

This study is a secondary analysis of data from overweight and obese older women (n=25) who completed a 6-month exercise and weight loss intervention. Women were eligible for inclusion in the study if they met the following criteria: body mass index ≥ 25.0 kg/m², stable body weight during the previous six months (within 2 kg), sedentary (defined as < 1 hr/wk of physical activity or < 2 exercise sessions per week in the past six months), non-smoking or tobacco using, and free of any chronic disease/condition that would preclude safe participation in exercise training or dietary restriction. Self-reported use of prescription medications was ascertained via a questionnaire and cognitive state was measured using the Mini-Mental State

Examination²⁶. All participants obtained medical clearance and provided written informed consent prior to enrollment, and the procedures of this study were approved by the Institutional Review Board at the University of Georgia.

Whole-Body and Thigh Composition

Standing height and weight were measured with participants wearing light-weight clothing and no shoes. Height was obtained using a stadiometer (Seca, Model 242) with measures obtained to the nearest 0.1 cm. Weight was measured on a calibrated digital scale (Tanita, Model WB-110A). Whole-body and regional soft tissue composition was assessed via dual-energy X-ray absorptiometry (iDXA, GE Healthcare-Luna, Madison, WI).

Thigh composition was determined via magnetic resonance imaging (MRI) scans obtained at baseline and following completion of the 24-week intervention using a 3.0-Tesla superconducting magnet (Signa HDx, GE Healthcare, Waukesha, WI). Eight T1-weighted axial images, with a 10-mm slice thickness and a 5-mm interslice distance, were acquired 50 mm superior to the proximal border of the patella using a fast spin echo-XL sequence. All images were obtained in DICOM format and tissues of interest were quantified using Analyze Direct software (Analyze Direct, Overland Park, KS). Cross-sectional area (cm²) of the midthigh muscle, SAT, and IMAT was determined via semi-automatic and manual segmentation tools. Intermuscular adipose tissue was defined as adipose tissue located beneath the deep fascia and between the quadriceps and hamstrings muscle groups.

Muscle Strength and Quality

Maximal concentric isokinetic knee extension and flexion torque was measured at 60°/s via isokinetic dynamometry to provide a measurement of lower-body muscle strength (System 4 Pro, Biodex Medical Systems Inc, Shirley, NY). Participants performed 2 sets of 4 extension and

flexion repetitions for the left and right legs. The greatest extension and flexion peak torque values for each leg were summed to calculate maximal concentric isokinetic knee torque at 60°/s. Muscle quality (N-m/cm²) was calculated by dividing maximal isokinetic knee torque (N-m) by mean cross-sectional area (cm²) of the thigh muscle.

Physical Function

Performance-based physical function was determined using the 6-minute walk and the 30-s chair stand tests. The 6-minute walk measures the greatest distance that an individual can walk in 6 minutes, and is a valid and reliable test of physical endurance in community-dwelling older adults^{27,28}. The 30-second chair stand measured the number of times that an individual could rise to a full stand from a seated position without using their arms in 30 seconds²⁸, and is a valid and reliable instrument in older adults²⁹. These tests were selected as they assess distinctly different aspects of physical function (physical endurance vs. sit-to-stand performance), which was necessary to determine whether the nature of the functional task influenced the relationship with changes in IMAT and muscle quality.

Exercise Intervention

All participants were expected to complete three 75-minute sessions of supervised exercise on nonconsecutive days during each week of the intervention for six months. The exercise intervention was a multicomponent program that integrated cardiorespiratory training, resistance training, balance, flexibility and functional activities, and was congruent with physical activity guidelines set forth by the American College of Sports Medicine^{30,31}. Cardiorespiratory training included 30 minutes of continuous exercise (walking on a treadmill, cycling or using an elliptical) at 70-80% of age-predicted maximal heart rate. Exercise intensity during the cardiorespiratory training was monitored throughout each session by recording heart rate and

rating of perceived exertion at 10, 20, and 30 minutes of exercise. Participants performed three upper-body (chest press, shoulder press, and back row), three lower-body (leg press, knee extension, and knee curl), and one core (abdominal crunch) resistance training exercise during every session. For each exercise, participants performed 2 sets of 8-10 repetitions at 65% of one-repetition maximum (1-RM) until volitional fatigue. In addition, 4-RM testing for each exercise was conducted every 6 weeks during the intervention to reassess muscle strength and adjust training load accordingly. In addition to cardiorespiratory and resistance training, two 30-s sets of four different functional activities (chair rises, wall push-ups, lift-and-carry, and transfer task) were performed during every training session. Finally, ~5-10 minutes of balance and flexibility exercises were performed at the end of every training session.

Diet Intervention

All participants were prescribed a diet that was designed to facilitate ~10% loss of initial body weight at the end of the 6-month intervention via reduction of estimated energy needs by ~500 kcal/d. To ensure participants were meeting micronutrient needs during the intervention, all participants were provided with a multivitamin mineral supplement formulated for older women (Centrum® Silver® Women, Pfizer, Inc. Madison, NJ) that provided 800 IU of vitamin D and 500 mg of calcium.

During the initial phase of the intervention, all participants attended at least two individual sessions with a registered dietitian nutritionist or supervised nutrition graduate student for instruction regarding topics such as energy restriction and self-monitoring methods. For the remainder of the 6-month intervention, participants attended weekly educational/motivational group sessions (45-60 min) with the registered dietitian nutritionist or graduate student, as well as individual sessions in order to meet weight loss goals. Dietary records for all participants were

monitored weekly and individual written feedback from the registered dietitian nutritionist or supervised graduate student was provided at each group session. The curriculum for the group sessions was designed according to Social Cognitive Theory³² and included topics such as general nutrition education and behavioral strategies for weight management. In addition, all participants were instructed to use a free online dietary intake monitoring application (MyFitnessPal.com). Trained staff monitored entries weekly and participants were provided individualized feedback throughout the intervention to help meet weight loss and nutrient goals.

Statistical Analysis

All statistical analyses were conducted using SPSS for Windows version 22.0 (SPSS Inc., Chicago, IL). Data were examined for normality via distribution statistics (skewness and kurtosis) and visual inspection of histograms. Paired samples t-tests were used to determine within-group changes in all measures of thigh composition, muscle quality and physical function. Pearson correlations were performed to examine the bivariate associations between changes in measures of whole-body adiposity and thigh composition. Multivariate linear regression models were created to examine the relative contributions of changes in fat mass, IMAT and muscle quality to changes in physical function. Statistical significance was set at $p < 0.05$.

5.4 Results

Participant characteristics for the sample are presented in Table 1. The study cohort (68.5 ± 3.8 y) was relatively healthy, but as expected due to study design, they were overweight/obese, with a mean BMI of 29.0 ± 3.2 kg/m² and relative adiposity of $47.1 \pm 3.8\%$ at baseline. Additionally, according to step count measured via accelerometry, our sample was considered sedentary (5466.2 ± 1780.3 steps/d). With regard to the exercise intervention, mean attendance was 59.8 ± 5.0 training sessions, which corresponded to $75.3 \pm 6.5\%$ of total possible sessions.

Data from the exercise intervention at different time points of the study for each mode of training (cardiorespiratory, resistance and functional activities) are presented in Table 2.

Overall, mean weight loss for the sample was 7.6 ± 3.1 kg, which corresponded to a percent decrease of $9.9 \pm 3.9\%$. With regard to whole-body composition, there were significant reductions in BMI (2.8 ± 1.2 kg/m²), absolute fat mass (6.6 ± 2.4 kg) and relative adiposity ($4.9 \pm 2.3\%$). Additionally, there was also a small decline in upper-leg mineral-free lean mass (0.3 ± 0.6 kg, $p < 0.01$).

Table 3 presents baseline and post-intervention values for thigh composition, muscle quality and physical function. There were significant reductions in cross-sectional area of thigh SAT (-18.3 ± 8.4 cm², $p < 0.01$) and IMAT (-2.9 ± 2.0 cm², $p < 0.01$) following the intervention. In contrast, thigh muscle cross-sectional area (-0.9 ± 2.7 cm², $p = 0.12$) did not significantly change at 6 months. The percent changes in each midthigh composition variable are shown in Figure 1. When each tissue was expressed relative to total thigh area, there was a significant increase in the percent of total thigh area occupied by muscle ($+4.6 \pm 2.4\%$, $p < 0.01$), while the relative area occupied by SAT ($-4.0 \pm 2.1\%$, $p < 0.01$) and IMAT ($-0.6 \pm 0.6\%$, $p < 0.01$) both significantly decreased following the intervention (Figure 2). With regard to muscle function, there was a significant improvement in isokinetic knee torque at 60°/s ($+15.2 \pm 28.3$ N-m, $p = 0.01$) and leg muscle quality ($+0.11 \pm 0.20$ N-m/cm², $p < 0.01$) (Table 3). Finally, there were significant improvements in performance on the 6-minute walk ($+9.7\%$) and 30-s chair stand tests ($+58.2\%$).

Figures 3 and 4 show that the change in overall body mass was significantly associated with changes in midthigh SAT and IMAT cross-sectional area ($r = 0.53$ and 0.73 , respectively; both, $p < 0.01$). Similarly, change in absolute fat mass was significantly related to change in

thigh SAT ($r = 0.48$, $p < 0.05$) and IMAT ($r = 0.69$, $p < 0.01$) areas. Additionally, there was a significant association between the changes in midthigh SAT and IMAT cross-sectional area ($r = 0.71$, $p < 0.01$). Moreover, baseline thigh IMAT area was significantly related to change in IMAT (Figure 5) and accounted for 37.2% of the variance. We also examined the association between change in muscle quality and changes in thigh IMAT area ($r = 0.22$) and relative (%) IMAT area ($r = 0.32$); however, these associations did not reach statistical significance (both, $p > 0.05$).

Multivariate linear regression analyses were performed to examine the relative contributions of changes in whole-body adiposity, thigh IMAT area and muscle quality to changes in performance-based physical function following the intervention (Table 4). Change in muscle quality was the strongest independent predictor of a change in performance on the 6-minute walk (standardized $\beta = 0.48$, $p < 0.05$) and explained 24% of the variance. In contrast, change in thigh IMAT area had the strongest independent association with change in the 30-s chair stand test ($\beta = -0.80$, $p < 0.01$) and accounted for nearly 34% of the variance. In addition, change in absolute fat mass was also a significant contributor to the change in performance on the 30-s chair stand ($\beta = 0.70$, $p < 0.01$), with 28.1% of the variance in change in 30-s chair stand attributable to the change in fat mass.

5.5 Discussion

The present study investigated the effects of a 6-month multicomponent exercise and weight loss intervention on muscle quality and midthigh composition in overweight and obese older women. The major findings from this study are: a) there were significant reductions in midthigh IMAT and SAT, but maintenance of muscle cross-sectional area, b) muscle quality and

objective physical function significantly improved, and c) changes in muscle quality and IMAT area predicted improvements in different physical function tests.

In the present study, we observed a 16.3% (-2.9 cm²) reduction in mid thigh IMAT following 6 months of exercise and dietary-induced weight loss (-7.6 kg or 9.9%) in overweight and obese older women. Our results are in accordance with previous research that reported a comparable reduction in thigh IMAT (-2.0 cm²) following a similar duration (6 months) of physical activity and weight loss (-4.9 kg or 5.5%) in obese older adults³³. Similarly, our findings agree with other studies that found exercise and weight loss is effective for reducing IMAT in older adults, although the magnitude of reduction varies^{34,35}. In the larger context of body composition, we found that the overall loss of body mass was strongly correlated with the reduction in thigh IMAT ($r = 0.73$) and SAT ($r = 0.53$), and observed similar associations between the loss of whole-body fat mass and thigh adiposity ($r = 0.48$ to 0.69). From a clinical perspective, this finding is important in the context of a well-documented steep age-related increase in IMAT that occurs among older adults. For example, Delmonico et al.⁷ found that mid thigh IMAT increased 29% over 5 y in older women (70-79 y at baseline) from the Health, Aging and Body Composition Study cohort. Moreover, in the same study, there was a 3.1% annual increase in IMAT among women who lost $\geq 3\%$ of initial body mass over 5 y, suggesting that IMAT increases with age despite the presence of weight loss. Likewise, Goodpaster et al.³⁶ reported a ~18% increase in mid thigh IMAT among older adults in a control group during a 1-y randomized controlled trial. In light of these findings, the magnitude of reduction in mid thigh IMAT observed in our study (-16.3%) suggests that regular exercise and intentional weight loss is an effective interdisciplinary combination of therapies for attenuating, and potentially reversing, the marked age-related increase in muscle fat infiltration among older adults.

Another notable finding related to body composition was the maintenance of skeletal muscle mass/tissue in the presence of significant weight loss. Prescribing weight loss for older adults (e.g., 65+ y) remains a controversial issue due to the potential for accelerating age-related declines in skeletal muscle mass and bone mineral density^{2,24,25}. However, the results of our study suggest that the addition of multicomponent exercise training to a weight loss intervention has the capacity to maintain muscle mass/tissue relative to changes in whole-body and regional adiposity. Traditionally, ~75% of weight loss in older adults is a loss of fat mass and 25% is due to a loss of lean mass². In the present study, nearly 87% of the decrease in overall body weight was due to a reduction in total fat mass (6.6 kg of the 7.6 kg), indicating that our intervention positively impacted the proportion of adiposity lost. With regard to regional thigh composition, we found that midthigh muscle cross-sectional area did not significantly change (-1%), despite considerable reductions in IMAT (-16.3%) and SAT (-18.0%) area. Likewise, expressed in relative terms, we found that the percentage of total thigh area occupied by SAT and IMAT decreased by 4% and 0.6%, respectively, while the relative thigh area occupied by muscle tissue increased 4.6%. Our study contributes to a growing body of literature that suggests exercise can attenuate the weight loss-induced reduction in DXA-measured lean body mass^{37,38}, by providing evidence that MRI-derived thigh muscle tissue can be maintained.

Cross-sectional and prospective studies have indicated that thigh IMAT^{14-16,39} and muscle quality^{18,20,40} are related to physical function in older adults. However, no known studies have attempted to delineate the relative contributions of changes in thigh IMAT and muscle quality for physical function following exercise and/or weight loss in overweight and obese older adults. We created multivariate linear regression models to examine the relative importance of changes in whole-body adiposity, thigh IMAT and muscle quality for changes in objective measures of

physical function following the intervention. Our analyses indicated that changes in IMAT and muscle quality both predicted improvements in lower-extremity physical function; however, their importance varied according to the nature of the functional task. For example, we found that a reduction in IMAT area accounted for nearly 34% of the variance in change in ability to rise from a chair ($\beta = -0.80$), and this association was independent of changes in whole-body absolute fat mass or muscle quality. In contrast, the decrease in IMAT did not predict improved walking distance during the 6-minute walk test. Because the 30-s chair stand and 6-minute walk have distinctly different mechanical and bioenergetic properties, it is possible that the benefits of reducing IMAT are influenced by the requirements of the functional task. It is physiologically plausible that IMAT would be a stronger predictor of sit-to-stand performance (e.g., rising from a chair or floor), which requires a greater degree of rapid force generation from quadriceps and hamstrings muscles compared to the 6-minute walk. While previous research has suggested that IMAT interferes with whole-muscle contractile performance⁶, and that this may impair ability to complete functional tasks, our results suggest an independent benefit of reducing IMAT for one particular domain of physical function (sit-to-stand performance) that is heavily reliant on thigh musculature. Future intervention trials should address the potential benefits of reducing IMAT for other aspects of function, including more global indices, as well as whether or not mid thigh IMAT operates independent of known covariates (whole-body adiposity, muscle quality, etc.).

Study Strengths and Limitations

This study has both strengths and weaknesses that should be acknowledged. Notable strengths of our study include an interdisciplinary intervention with comprehensive exercise and weight loss regimens, use of magnetic resonance imaging for mid thigh composition changes, objective measures of lower-extremity physical function, and quantification of cardiorespiratory

exercise intensity and resistance training load throughout the intervention. The primary limitation to this study is a relatively small sample size, which reduced our statistical power for detecting a significant association between changes in IMAT and muscle quality. We also did not include a single-treatment control group, such as an exercise- or diet-only condition, and therefore we are unable to determine the independent effects of exercise and diet-induced weight loss on our outcomes. In addition, although our sample was comprised of overweight and obese older women, the participants in our study were relatively healthy, especially with regard to mobility function. Indeed, the participants needed to be healthy enough to engage in resistance training exercises designed to progressively overload their lower-extremity muscle groups. Therefore, research is needed to determine the safety and efficacy of these intervention strategies for other populations of older women, such as those with mobility-disability, sarcopenic-obesity and various chronic health conditions (e.g. diabetes, cancer).

Conclusion

In conclusion, whole-body and midthigh adiposity significantly decreased, but muscle mass/tissue was maintained, following 6 months of exercise and weight loss in overweight and obese older women. Our findings also indicate that changes in thigh IMAT and muscle quality independently predict improvements in lower-extremity physical function, although their relative contributions may be predicated upon the nature of the functional task. Additional intervention trials are needed to characterize the relationship between changes in IMAT and muscle quality under conditions of exercise and/or weight loss, and to determine whether or not improvements in these outcomes positively impact physical function in overweight and obese older adults.

5.6 References

1. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of obesity in the United States, 2009-2010. *NCHS Data Brief*. 2012;1-8.
2. Villareal DT, Apovian CM, Kushner RF, Klein S. Obesity in older adults: technical review and position statement of the American Society for Nutrition and NAASO, The Obesity Society. *Am J Clin Nutr*. 2005;82:923-934.
3. Vincent HK, Vincent KR, Lamb KM. Obesity and mobility disability in the older adult. *Obes Rev*. 2010;11:568-579.
4. Barbat-Artigas S, Rolland Y, Zamboni M, Aubertin-Leheudre M. How to assess functional status: a new muscle quality index. *J Nutr Health Aging*. 2012;16:67-77.
5. Straight CR, Brady AO, Evans EM. Muscle quality in older adults: what are the health implications? *Am J Lifestyle Med*. 2015;9:130-136.
6. Addison O, Marcus RL, Lastayo PC, Ryan AS. Intermuscular fat: a review of the consequences and causes. *Int J Endocrinol*. 2014;2014:309570.
7. Delmonico MJ, Harris TB, Visser M, et al. Longitudinal study of muscle strength, quality, and adipose tissue infiltration. *Am J Clin Nutr*. 2009;90:1579-1585.
8. Song MY, Ruts E, Kim J, Janumala I, Heymsfield S, Gallagher D. Sarcopenia and increased adipose tissue infiltration of muscle in elderly African American women. *Am J Clin Nutr*. 2004;79:874-880.
9. Marcus RL, Addison O, Kidde JP, Dibble LE, Lastayo PC. Skeletal muscle fat infiltration: impact of age, inactivity, and exercise. *J Nutr Health Aging*. 2010;14:362-366.
10. Goodpaster BH, Carlson CL, Visser M, et al. Attenuation of skeletal muscle and strength in the elderly: The Health ABC Study. *J Appl Physiol*. 2001;90:2157-2165.
11. Albu JB, Kovera AJ, Allen L, et al. Independent association of insulin resistance with larger amounts of intermuscular adipose tissue and a greater acute insulin response to glucose in African American than in white nondiabetic women. *Am J Clin Nutr*. 2005;82:1210-1217.
12. Goodpaster BH, Thaete FL, Kelley DE. Thigh adipose tissue distribution is associated with insulin resistance in obesity and in type 2 diabetes mellitus. *Am J Clin Nutr*. 2000;71:885-892.
13. Beasley LE, Koster A, Newman AB, et al. Inflammation and race and gender differences in computerized tomography-measured adipose depots. *Obesity (Silver Spring)*. 2009;17:1062-1069.

14. Marcus RL, Addison O, Dibble LE, Foreman KB, Morrell G, Lastayo P. Intramuscular adipose tissue, sarcopenia, and mobility function in older individuals. *J Aging Res.* 2012;2012:629637.
15. Visser M, Goodpaster BH, Kritchevsky SB, et al. Muscle mass, muscle strength, and muscle fat infiltration as predictors of incident mobility limitations in well-functioning older persons. *J Gerontol A Biol Sci Med Sci.* 2005;60:324-333.
16. Tuttle LJ, Sinacore DR, Mueller MJ. Intramuscular adipose tissue, sarcopenia, and mobility function in older individuals. *J Aging Res.* 2012;2012:172957.
17. Fragala MS, Kenny AM, Kuchel GA. Muscle quality in aging: a multi-dimensional approach to muscle functioning with applications for treatment. *Sports Med.* 2015; 45:641-658.
18. Fragala MS, Clark MH, Walsh SJ, et al. Gender differences in anthropometric predictors of physical performance in older adults. *Gend Med.* 2012;9:445-456.
19. Cawthon PM, Fox KM, Gandra SR, et al. Do muscle mass, muscle density, strength, and physical function similarly influence risk of hospitalization in older adults? *J Am Geriatr Soc.* 2009;57:1411-1419.
20. Barbat-Artigas S, Rolland Y, Cesari M, Abellan van Kan G, Vellas B, Aubertin-Leheudre M. Clinical relevance of different muscle strength indexes and functional impairment in women aged 75 years and older. *J Gerontol A Biol Sci Med Sci.* 2013;68:811-819.
21. Shin S, Valentine RJ, Evans EM, Sosnoff JJ. Lower extremity muscle quality and gait variability in older adults. *Age Ageing.* 2012;41:595-599.
22. Brady AO, Straight CR, Schmidt MD, Evans EM. Impact of body mass index on the relationship between muscle quality and physical function in older women. *J Nutr Health Aging.* 2014;18:378-382.
23. Newman AB, Haggerty CL, Goodpaster B, et al. Strength and muscle quality in a well-functioning cohort of older adults: the Health, Aging and Body Composition Study. *J Am Geriatr Soc.* 2003;51:323-330.
24. Bales CW, Buhr G. Is obesity bad for older persons? A systematic review of the pros and cons of weight reduction in later life. *J Am Med Dir Assoc.* 2008;9:302-312.
25. Waters DL, Ward AL, Villareal DT. Weight loss in obese adults 65 years and older: a review of the controversy. *Exp Gerontol.* 2013;48:1054-1061.
26. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res.* 1975;12:189-198.
27. Rikli RE, Jones CJ. The reliability and validity of a 6-minute walk test as a measure of physical endurance in older adults. *J Aging Phys Act.* 1998;6:363-375.

28. Rikli RE, Jones CJ. *Senior Fitness Test Manual*. 2nd ed. Champaign, IL: Human Kinetics; 2013.
29. Jones CJ, Rikli RE, Beam WC. A 30-s chair-stand test as a measure of lower body strength in community-residing older adults. *Res Q Exerc Sport*. 1999;70:113-119.
30. Garber CE, Blissmer B, Deschenes MR, et al. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Med Sci Sports Exerc*. 2011;43:1334-1359.
31. Nelson ME, Rejeski WJ, Blair SN, et al. Physical activity and public health in older adults: recommendation from the American College of Sports Medicine and the American Heart Association. *Circulation*. 2007;116:1094-1105.
32. Bandura A. Health promotion by social cognitive means. *Health Educ Behav*. 2004;31:143-164.
33. Santanasto AJ, Glynn NW, Newman MA, et al. Impact of weight loss on physical function with changes in strength, muscle mass, and muscle fat infiltration in overweight to moderately obese older adults: a randomized clinical trial. *J Obes*. 2011.
34. Christiansen T, Paulsen SK, Bruun JM, et al. Comparable reduction of the visceral adipose tissue depot after a diet-induced weight loss with or without aerobic exercise in obese subjects: a 12-week randomized intervention study. *Eur J Endocrinol*. 2009;160:759-767.
35. Murphy JC, McDaniel JL, Mora K, Villareal DT, Fontana L, Weiss EP. Preferential reductions in intermuscular and visceral adipose tissue with exercise-induced weight loss compared with calorie restriction. *J Appl Physiol*. 2012;112:79-85.
36. Goodpaster BH, Chomentowski P, Ward BK, et al. Effects of physical activity on strength and skeletal muscle fat infiltration in older adults: a randomized controlled trial. *J Appl Physiol*. 2008;105:1498-1503.
37. Frimel TN, Sinacore DR, Villareal DT. Exercise attenuates the weight-loss-induced reduction in muscle mass in frail obese older adults. *Med Sci Sports Exerc*. 2008;40:1213-1219.
38. Villareal DT, Banks M, Sinacore DR, Siener C, Klein S. Effect of weight loss and exercise on frailty in obese older adults. *Arch Intern Med*. 2006;166:860-866.
39. Visser M, Kritchevsky SB, Goodpaster BH, et al. Leg muscle mass and composition in relation to lower extremity performance in men and women aged 70 to 79: the health, aging and body composition study. *J Am Geriatr Soc*. 2002;50:897-904.

40. Mistic MM, Rosengren KS, Woods JA, Evans EM. Muscle quality, aerobic fitness and fat mass predict lower-extremity physical function in community-dwelling older adults. *Gerontology*. 2007;53:260-266.

Table 5.1. Participant characteristics (n=25)

Characteristic	Mean \pm SD	Range
Age (y)	68.5 \pm 3.8	65-77
Height (m)	1.6 \pm 0.1	1.4-1.7
Weight (kg)	77.0 \pm 8.8	53.7-94.2
Body Mass Index (kg/m ²)	29.0 \pm 3.2	25.0-35.8
Waist Circumference (cm) ^a	97.7 \pm 8.2	75.7-134.7
Relative Adiposity (%)	47.1 \pm 3.8	40.9-56.0
Fat Mass (kg)	35.4 \pm 6.3	23.5-49.7
Leg Mineral-Free Lean Mass (kg)	13.5 \pm 1.6	8.8-16.0
Mini-Mental State Examination (0-30)	29.0 \pm 1.2	26-30
Number of Medications (total)	3.1 \pm 2.4	0-9
Physical Activity (steps/d) ^a	5466.2 \pm 1780.3	2635.4-9108.5

^an=24

Table 5.2. Characteristics of the multicomponent exercise training intervention

		Week 8	Week 12	Week 16	Week 20	Week 24
<i>Cardiorespiratory Training</i>	HR (beats/min)	119.3 ± 11.9	121.0 ± 9.9	120.8 ± 12.6	121.1 ± 11.5	120.4 ± 12.2
	RPE (6-20)	12.9 ± 0.9	13.1 ± 0.8	13.2 ± 0.9	13.4 ± 1.0	13.2 ± 1.0
<i>Resistance Training</i>	Leg Press (lbs)	136.8 ± 37.1	141.1 ± 34.7	150.7 ± 32.8	154.4 ± 30.9	158.5 ± 30.4
	Knee Extension (lbs)	62.0 ± 14.6	63.0 ± 14.0	66.3 ± 13.5	68.3 ± 15.4	68.2 ± 16.0
	Knee Curl (lbs)	51.9 ± 10.5	52.6 ± 12.9	55.0 ± 12.1	56.3 ± 11.7	58.2 ± 11.8
	Chest Press (lbs)	38.0 ± 12.1	40.2 ± 13.3	43.2 ± 12.4	46.1 ± 14.5	47.2 ± 14.8
	Back Row (lbs)	62.0 ± 11.3	63.9 ± 11.5	65.6 ± 11.9	66.7 ± 13.7	67.1 ± 14.1
	Overhead Press (lbs)	24.5 ± 10.4	28.2 ± 10.9	30.8 ± 10.0	31.3 ± 10.9	32.3 ± 10.6
	Abdominal Crunch (lbs)	60.0 ± 10.7	62.3 ± 10.6	65.3 ± 11.1	65.3 ± 15.2	67.1 ± 15.5
<i>Functional Activities</i>	Chair stands (total)	17.6 ± 3.8	19.1 ± 5.4	20.3 ± 5.0	20.0 ± 6.1	20.4 ± 6.9
	Transfer task (total)	5.7 ± 1.7	6.3 ± 1.8	6.3 ± 1.8	6.5 ± 1.7	6.2 ± 2.1
	Lift-and-carry task (lbs)	23.1 ± 3.3	23.3 ± 3.9	24.7 ± 4.6	23.0 ± 6.3	24.5 ± 5.3
	Wall push-ups (total)	17.4 ± 3.5	18.6 ± 5.0	19.8 ± 5.2	19.3 ± 5.3	20.5 ± 5.8

Data are presented as mean ± SD

HR = heart rate; RPE = rating of perceived exertion

Table 5.3. Baseline and post-intervention values for midthigh composition, muscle quality and physical function following exercise and weight loss in overweight and obese older women (n=25)

Characteristic	Baseline	Post	<i>P</i>
Subcutaneous Adipose Tissue (cm ²)	103.6 ± 32.9	85.4 ± 31.1	<0.01
Intermuscular Adipose Tissue (cm ²)	17.6 ± 4.4	14.7 ± 3.6	<0.01
Thigh Muscle (cm ²)	80.5 ± 7.8	79.6 ± 7.5	0.12
Isokinetic Knee Torque (N-m)	272.6 ± 39.9	287.8 ± 50.1	<0.01
Muscle Quality (N-m/cm ²)	1.70 ± 0.22	1.81 ± 0.28	<0.01
6-Minute Walk (m)	543.9 ± 46.7	596.2 ± 57.3	<0.01
30-s Chair Stand (total)	14.1 ± 2.1	22.3 ± 6.1	<0.01

Data are presented as mean ± SD

Muscle quality (N-m/cm²) = isokinetic knee torque (N-m) / muscle cross-sectional area (cm²)

Table 5.4. Multivariate linear regression analysis of changes in whole-body fat mass, mid thigh intermuscular adipose tissue and muscle quality for changes in physical function following exercise and weight loss in overweight and obese older women (n=25)

	Predictor	β	Partial R^2	P
Δ 6-Minute Walk	Δ Fat Mass	-0.42	0.123	0.11
	Δ IMAT	0.12	0.010	0.64
	Δ Muscle Quality	0.48	0.240	<0.05
Δ 30-s Chair Stand	Δ Fat Mass	0.70	0.281	<0.01
	Δ IMAT	-0.80	0.336	<0.01
	Δ Muscle Quality	0.14	0.029	0.45

IMAT = intermuscular adipose tissue

Muscle quality ($\text{N}\cdot\text{m}/\text{cm}^2$) = isokinetic knee torque ($\text{N}\cdot\text{m}$) / mid thigh muscle cross-sectional area (cm^2)

Betas represent standardized regression coefficients

Partial R^2 is the explained variance of each parameter in the model

Figure 5.1. Percent changes from baseline to 6 months in mid thigh composition; IMAT = intermuscular adipose tissue; SAT = subcutaneous adipose tissue; values represent mean \pm SE.

*Indicates a significant change from baseline at $p < 0.01$

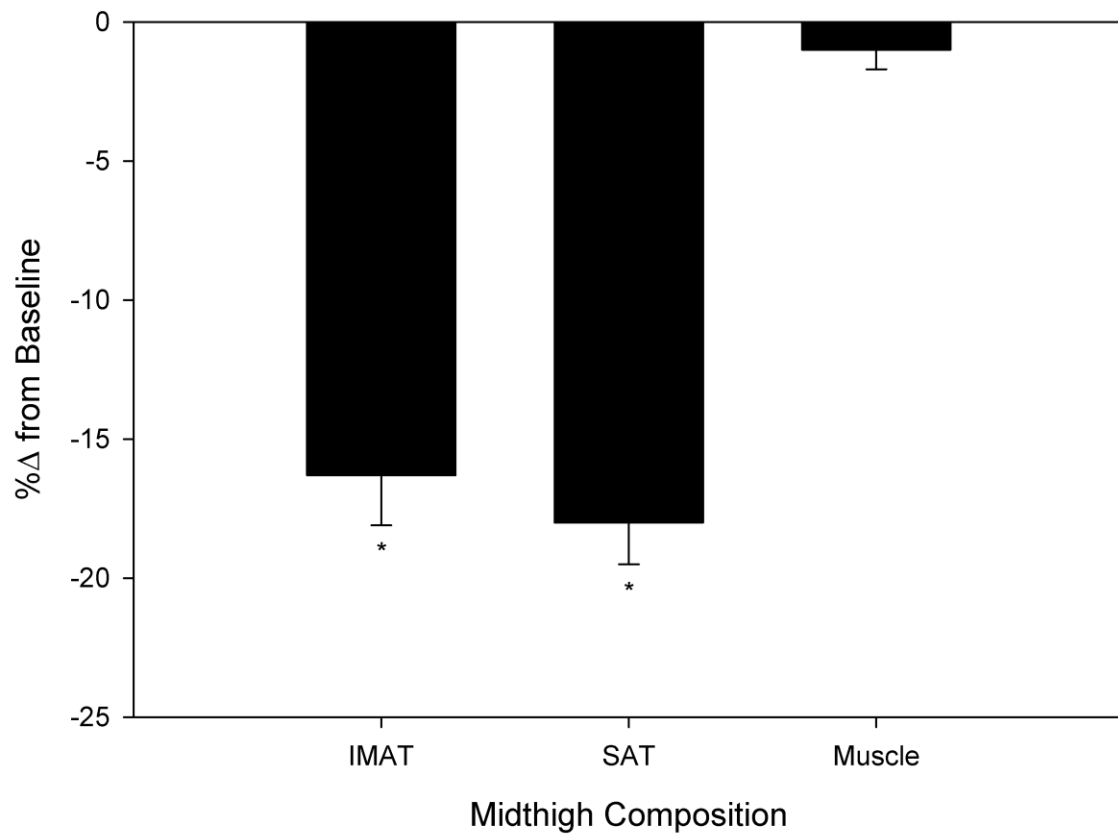


Figure 5.2. Change from baseline to 6 months in percent of total thigh area occupied by intermuscular adipose tissue (IMAT), subcutaneous adipose tissue (SAT) and muscle; values represent mean \pm SE.

*Indicates a significant change from baseline at $p < 0.01$

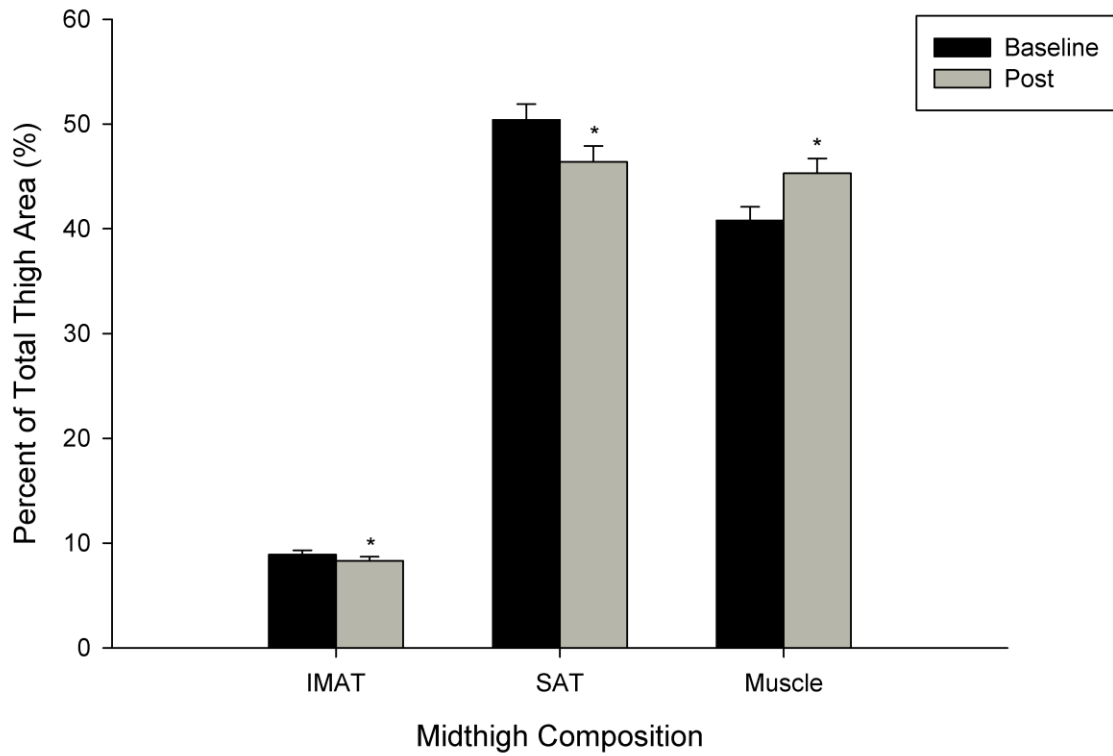


Figure 5.3. Bivariate association between changes in overall body mass and mid thigh subcutaneous adipose tissue (SAT) cross-sectional area.

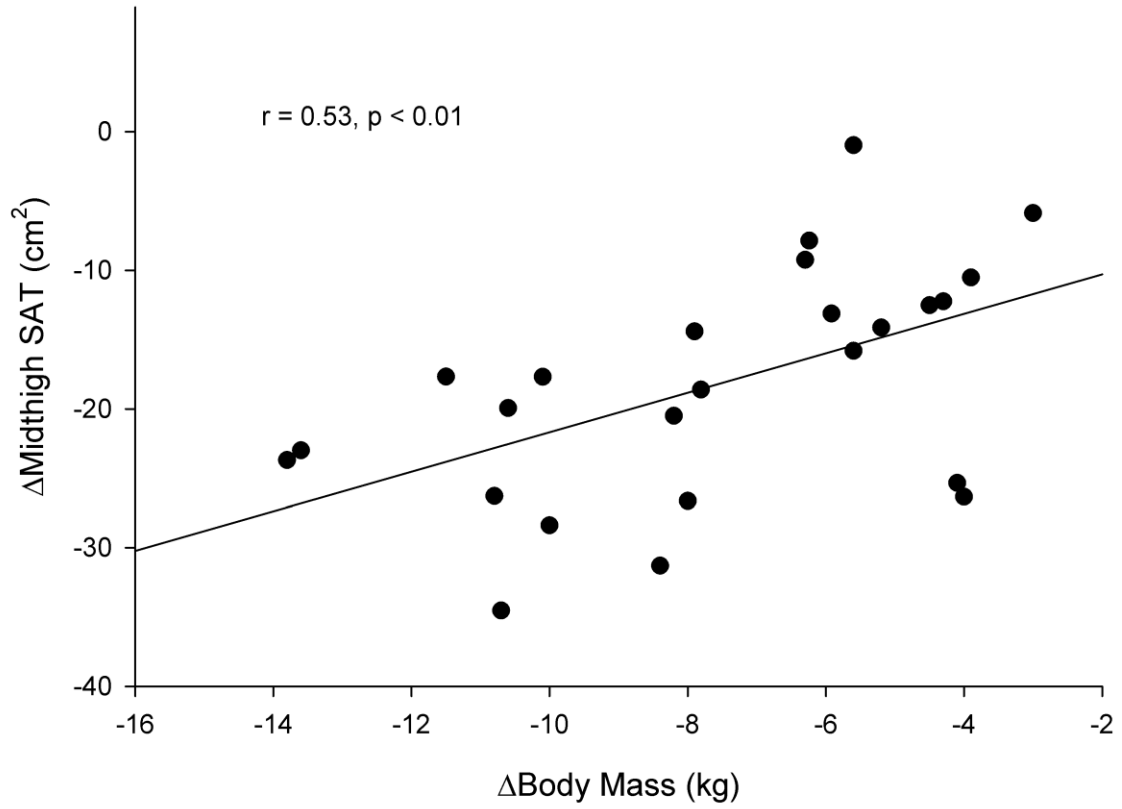


Figure 5.4. Bivariate association between changes in overall body mass and midhigh intermuscular adipose tissue (IMAT) cross-sectional area.

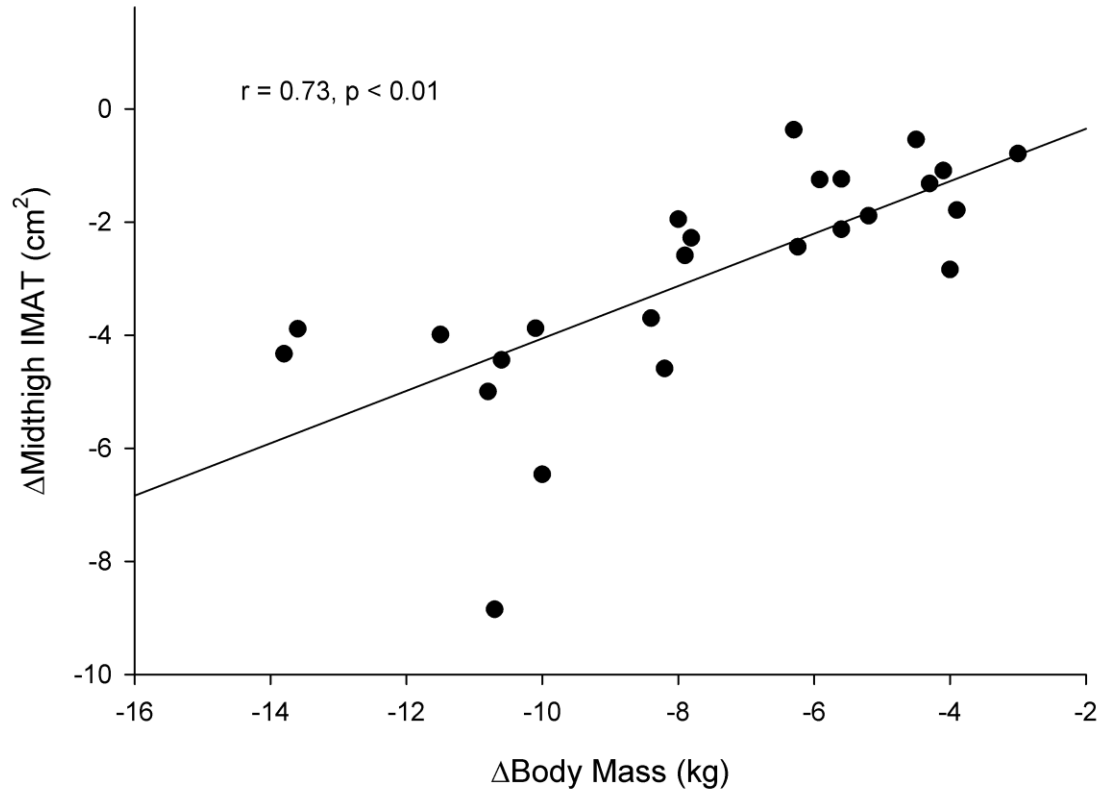
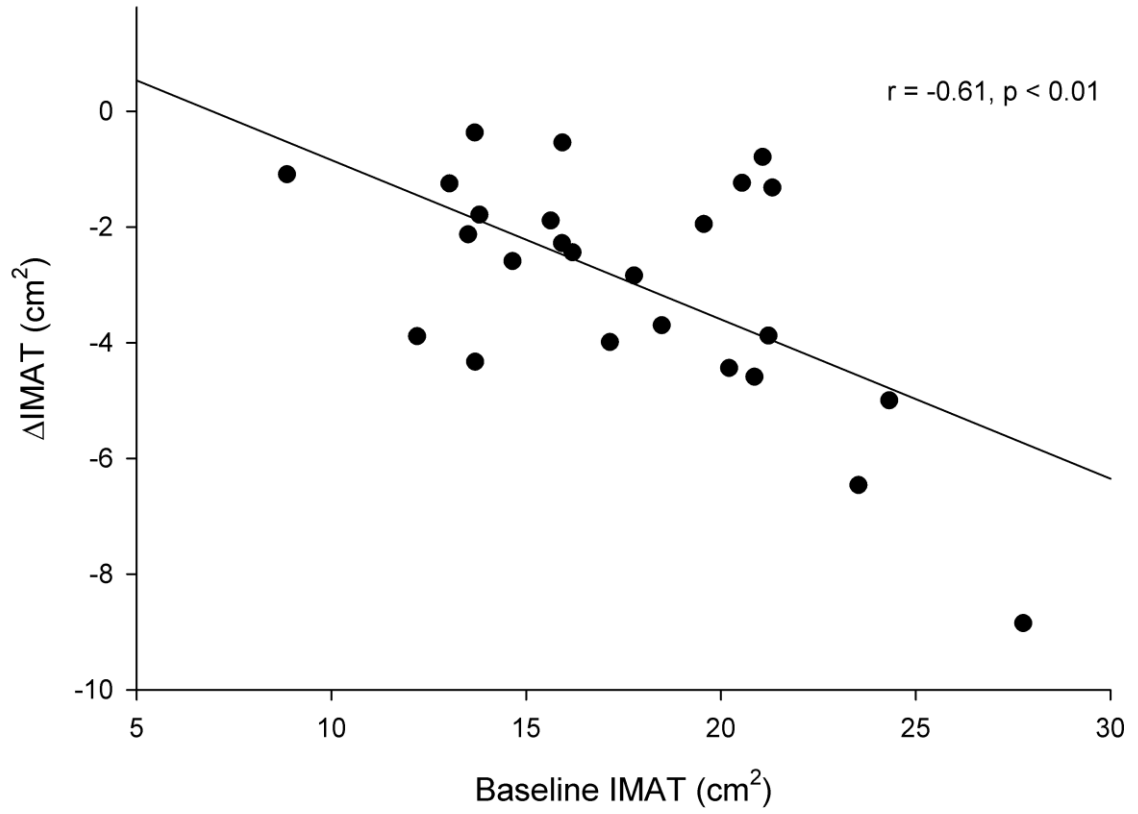


Figure 5.5. Bivariate association between baseline intermuscular adipose tissue (IMAT) cross-sectional area and absolute IMAT change at 6 months.



CHAPTER 6

SUMMARY AND CONCLUSIONS

In conclusion, the purpose of this dissertation was to characterize the role of improving muscle quality for a subsequent improvement in lower-extremity physical function (LEPF) following a 6-month exercise and diet-induced weight loss intervention for overweight and obese older women. The primary aims of this dissertation were three-fold: 1) to examine the relative contributions of changes in muscle quality and body composition for changes in LEPF, 2) to determine the functional improvements associated with increasing muscle strength, power and quality after exercise training under conditions of weight loss, and 3) to examine whether changes in mid-thigh composition, specifically intermuscular adipose tissue (IMAT), predicted changes in muscle quality or LEPF.

Following 6 months of exercise and weight loss, there were significant reductions in whole-body mass, absolute fat mass, relative adiposity, and lean mass. However, there were significant increases in muscle quality and selected measures of objective LEPF. Our analysis indicated that the percent improvement in muscle quality was the strongest independent predictor of a change in a composite measure of LEPF. Additionally, percent change in whole-body mass was also a significant contributor to change in LEPF. In contrast, changes in absolute or relative adiposity did not predict improvements in LEPF at 6 months. Intervention strategies that increase muscle quality in the presence of weight

loss may confer improvements in objective physical function for overweight and obese older women.

It was also determined that various indices of whole-muscle contractile performance significantly improved following the intervention, and that changes in muscle strength, power and quality significantly predicted changes in specific measures of LEPF. Increases in muscle strength consistently predicted an increase in distance covered during the 6-minute walk and a reduction in time to complete the 8-foot up-and-go, while a change in leg power appeared to be more important for tasks requiring the transfer of body weight (e.g., sit-to-stand performance). These findings add to the current body of literature by characterizing the predictive value of changes in muscle strength, power and quality for improvements in LEPF tasks with different biomechanical and metabolic properties following an exercise and weight loss intervention.

In addition, significant improvements in mid thigh composition following the intervention, including considerable reductions in IMAT and subcutaneous adipose tissue and maintenance of muscle area, were also observed. A reduction in IMAT area and an increase in muscle quality were both independent predictors of improvements in specific LEPF tasks, although the strength of the association with LEPF varied. Thus, mid thigh composition and muscle quality significantly improved at 6 months; however, their relative importance for LEPF may be predicated upon the nature of the functional task.

This dissertation examined the effects of exercise training and weight loss on LEPF, which included tasks such as walking, rising from a chair and getting up off the floor. Lower-extremity physical function was of particular interest as it is a significant predictor of subsequent disability, nursing home admission and mortality in older adults.

In our analyses, we found that a reduction in body weight, as well as particular regional depots of adiposity (e.g., thigh IMAT), were associated with significant improvements in selected LEPF tasks. This makes physiologic sense as performance on all four LEPF tests is largely determined by the lower-body musculature (gluteals, quadriceps and hamstrings) and an older adult's ability to transfer body weight (especially the 30-s chair stand and standing up from the floor). Conversely, it has not been well-characterized whether a reduction in body weight or adiposity confers improvements in other physical function tasks that more heavily rely on upper-body musculature, such as lifting heavy objects (e.g., groceries) or reaching overhead. Therefore, additional intervention research is necessary to determine if the loss of body weight predicts improvements in other domains of physical function among overweight and obese older women.

It is also important to note that this dissertation had constraints because it was aligned with a larger parent project funded by the National Cattlemen's Beef Association (NCBA). In the parent project, participants were randomly assigned to one of three intervention groups: 1) a high-protein diet without exercise (HP), 2) a high-protein diet with exercise (HP+EX) and, 3) a conventional normal or standard protein diet with exercise (NP+EX). The primary aim of the NCBA grant was to compare the effects of these different exercise and weight loss interventions on body composition, physical function and fatigue following 6 months of treatment. In contrast to the parent project, the purpose of this dissertation was to characterize the relationships between changes in muscle quality, body composition and physical function among participants who were randomized into one of the exercise training groups (HP+EX and NP+EX). Therefore, we collapsed the two training groups into a single sample and conducted all statistical

analyses using this cohort. For this reason, we did not examine whether HP+EX or NP+EX was more effective for improving our outcomes of interest following the intervention, as this was the primary aim of the parent project. Although it is plausible that protein intake influenced our results as the two exercise groups in our collapsed sample received different diet interventions (differences in macronutrient composition), controlling for group assignment in all primary analyses within this dissertation project did not alter the results or conclusions suggesting that the effects are likely minimal. A comparison of the three treatment groups will be examined in future analyses designed to address the primary aims of the NCBA grant.

In conclusion, we provide novel evidence that changes in muscle quality and body composition are both significant predictors of improvements in physical function following 6 months of exercise and intentional weight loss in overweight and obese older women. Thus, intervention strategies that improve muscle quality and body composition may translate to better physical function among overweight and obese older women, and ultimately result in a reduced likelihood of future physical disability.