THE SEVERITY OF OBESITY AND KNEE OSTEOARTHRITIS: EFFECTS ON
STRENGTH AND GAIT

By

BENJAMIN D. PIERCE

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Approved By:

Stephen P. Messier, Ph.D., Advisor

Examining Committee:

Shannon L. Mihalko, Ph.D.

Floyd H. Chilton, Ph.D.
DEDICATION

To my parents, John and Millie, and my sister Maggie. For encouraging me, believing in me, talking with me and listening to me, and being my three biggest supporters as I navigate this journey called life. Your love, laughter, and steadying influence have guided my every day, and I am truly grateful to call you my family. This is for you, with appreciation and love.
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ABSTRACT

PURPOSE: The purposes of this investigation were to examine the relationships between severity of obesity (defined by BMI) and radiographic evidence of knee OA and their associations with abnormal joint loading, muscular weakness, knee pain, and function in older adults.

METHODS: Baseline data from participants (n= 30) enrolled in the Fatty acids, Arthritis, and Inflammation in the Elderly clinical trial were utilized for this study. Presence of knee OA was confirmed by a K-L score ≥ 1, and participants had to have a BMI ≥ 27.0 kg/m². Internal knee moments, knee joint forces, and quadriceps and compressive forces were calculated using 3-D gait analysis with a 37-reflective marker set arranged in a Cleveland Clinic full-body configuration, a 6-Camera Motion Analysis System set to sample data at 60 Hz, and a torque-driven musculoskeletal model. Quadriceps and hamstrings strength were assessed using an isokinetic dynamometer. Pair-wise Pearson correlations were computed between the outcome and explanatory variables. Generalized linear modeling was used to look for associations between the outcome and explanatory measures controlling for gender, race, and weight.

RESULTS: Significant associations were found such that tall, heavy males were associated with greater internal knee extension moments and greater compressive forces and quadriceps forces. Height and weight were associated with increased quadriceps strength; however, only height was associated with increased hamstring strength. We also found a K-L score > 1 to be associated with an increased internal knee abduction moment. After adjusting for race, gender, and weight, increased pain and decreased function explained a significant amount of the variance with quadriceps force, while
walking speed explained a significant amount of the variance with compressive and quadriceps force.

**CONCLUSION:** It is well known that obesity is a major risk factor for knee OA. These data confirm associations between the internal knee extension moment and compressive forces which may accelerate disease progression. Other associations confirmed previous relationships identified in the literature.
CHAPTER 1

REVIEW OF LITERATURE

Introduction

Arthritis is the leading cause of disability among Americans and is a primary factor leading to work limitation. Data from the National Health Interview Survey (NHIS) reported that 46.4 million American adults over the age of 18 (21.6% of that population) had physician diagnosed arthritis, with one out of every two adults 65 years and older having the condition. The prevalence of arthritis is expected to increase, and by the year 2030 an estimated 67 million American adults will report physician-diagnosed arthritis—a 40 percent increase in a span of 25 years. The NHIS showed that nearly 9% of American adults over age 18 years (19 million persons) reported arthritis-attributable activity limitations. This figure was even higher in adults over the age of 65, as 22% of this population was limited due to their arthritis. By 2030, an estimated 25 million American adults will report activity limitations attributed to their arthritis, or just under 10% of the United States population.

Osteoarthritis (OA) is the most common form of arthritis, affecting 27 million American adults over the age of 25 years. The prevalence of OA is increasing due to an increase in the average lifespan. Sixty-percent of men and 70% of women over age 65 years are affected by this condition. OA is the number one cause of chronic disability in older adults, with 13% of Americans between the ages of 55 and 64, and 17% of Americans aged 65 to 74 reporting pain and functional limitations as a result of OA.
By definition, OA results from mechanical and biologic events that destroy articular cartilage and subchondral bone. This breakdown leads to softening, fibrillation, loss of articular cartilage, and the formation of osteophytes and subchondral cysts that cause joint pain, movement limitations, crepitus, and varying degrees of inflammation. OA commonly affects the hands, feet, knees, and hips, with the knee being the most affected weight bearing joint. Principal risk factors include advanced age, female sex, obesity, and joint trauma. OA typically presents itself in the form of symptoms that include joint pain, morning stiffness, instability, and loss of function, as well as signs such as boney enlargements, range of motion limitations, pain and/or crepitus during motion, tenderness, and malalignment or joint deformity. OA is the leading cause of total hip and knee replacements, and is responsible for the most pain and difficulty with activities of daily living (ADL’s) such as walking, kneeling, and climbing stairs.

Obesity is the most modifiable risk factor for OA, and contributes to the development and progression of osteoarthritis via three critical pathways. First, excess weight increases the loads upon the knee joint, and second, there is an inflammatory pathway whereby obesity increases the size and number of human fat cells, resulting in a corresponding increase in circulating inflammatory markers, especially tumor necrosis factor-α (TNF-α), C-reactive protein, and interleukin’s 1 and 6 (IL-1, IL-6). The third mechanism is that elements of the diet that lead to obesity adversely affect bone, cartilage, and other joint structures. An increase in joint loads and inflammation leads to cartilage loss, subchondral tissue damage, bone cysts and synovitis.

The association between obesity and knee OA has been well established. Davis et al. found that obese persons (BMI ≥30 kg/m²) were 3.5 times as likely to develop
unilateral knee OA, and nearly 8 times as likely to develop bilateral knee OA compared to individuals with a BMI less than 30. Anderson and Felson\textsuperscript{3} showed that the risk of knee OA is increased by 15\% for every additional unit increase in BMI above 27 kg/m\textsuperscript{2}, and Leach et al.\textsuperscript{62} found that 83\% of their female sample who had knee OA were obese compared to 42\% of their normal-weight controls. Although obesity as a risk factor for knee OA is well documented, and the impact of obesity upon gait and strength variables has been previously reported\textsuperscript{9, 13, 28, 57, 72}, the severity of obesity (defined by BMI) and its association with gait and strength variables is not well understood.

There is little literature that examines the impact that OA severity has on gait and strength. Huang et al.\textsuperscript{47} found that mild and severe knee OA groups had a peak knee extensor moment during gait that was 48\% and 56\% less than controls. Liikavainio and colleagues\textsuperscript{64} showed a significant association between OA severity and isometric knee extensor torque, but Brandt et al.\textsuperscript{10} failed to find a significant relationship between the two. Such minimal and conflicting evidence warrants further investigation into the relationships between severity of obesity (defined by BMI) and radiographic evidence of knee OA, and their associations with abnormal joint loading, muscular weakness, knee pain, and function.

We hypothesize that:

1) There is an association between higher levels of obesity and abnormal joint loads during gait and reduced strength, and;

2) There is an association between more severe levels of radiographic OA with abnormal joint loads during gait and reduced strength.
Anatomy of the Knee Joint

The knee joint is a condyloid joint with two degrees of freedom whereby flexion and extension occur with a small amount of rotation. The muscles and ligaments surrounding the knee are loaded in tension, and bone provides support and resistance to compressive loads.40, 68, 78

Three articulations comprise the knee joint, the tibiofemoral joint, the patellofemoral joint, and the superior tibiofibular joint. The tibiofemoral joint is commonly referred to as the actual knee joint, because it is the articulation of the femur and the tibia. The distal end of the femur comprises the medial and lateral condyles that are separated by the intercondylar notch posteriorly, and by the trochlear groove anteriorly. The condyles rest on the tibial plateau that is separated by the intercondylar eminence. The intercondylar eminence serves as an attachment site for ligaments, centers the joint, and stabilizes the bones during weight bearing.40, 112

The joint is protected by articular cartilage that is made from hyaline cartilage. Typically 2 to 5 mm thick, articular cartilage is maintained by chondrocytes that facilitate a balance between matrix synthesis and destruction central to healthy tissue metabolism.109 Articular cartilage serves a dual purpose of deforming under mechanical load and providing a smooth load bearing surface to permit minimal amounts of friction when the joint moves. Cartilage is composed of a unique structure of chondrocytes that are embedded in a matrix of collagen and proteoglycan. Type II collagen is the major structural protein, while proteoglycan is commonly presented as a large macromolecule known as aggrecan.21
Two menisci separate the tibia and the femur. The lateral meniscus is more mobile than the medial meniscus, able to move more than twice the distance of the medial meniscus in the anteroposterior direction.\textsuperscript{112} The menisci are important to the knee joint given that they improve joint stability by deepening the contact surface of the tibia. The menisci participate in shock absorption by transmitting loads across the joint surface, thus reducing the pressure on the tibiofemoral contact sites.\textsuperscript{35} When the menisci are missing, the contact area of the joint is reduced by two-thirds, and the pressure increases threefold thereby increasing the risk of injury.\textsuperscript{79}

Four main ligaments support the tibiofemoral joint, two collateral and two cruciate.\textsuperscript{79} The collateral ligaments are located on the sides of the joint. The medial collateral ligament (MCL) supports the knee against valgus forces (a medially directed force that causes the distal tibia to move laterally), and offers some resistance to both internal and external rotation. The MCL is taut when the leg is extended, and is reduced in length by 17\% when the leg is in full flexion.\textsuperscript{113} The lateral collateral ligament (LCL) offers the primary resistance to the varus force (a lateral force that causes the distal tibia to move medially) at the knee. The LCL is also taut in leg extension and is reduced by roughly 25\% in full flexion.\textsuperscript{113}

The cruciate ligaments lie inside the intercondylar space, and control both anteroposterior and rotational motion in the joint. The anterior cruciate ligament (ACL) provides 85\% of the primary restraint for anterior movement of the tibia relative to the femur, and is approximately 40\% larger than the posterior cruciate ligament (PCL). The PCL provides approximately 95\% of the restraint to posterior movement of the tibia on the femur.\textsuperscript{80}
The patellofemoral joint is formed by the articulation of the patella with the trochlear groove on the femur. The patellar ligament connects the patella to the tibial tuberosity, and the primary role of the patella is to increase the mechanical advantage of the quadriceps femoris.

The tibiofibular joint is the smallest and most superior of the three knee joint articulations, and it is formed by the articulation between the head of the fibula and the posterolateral and inferior aspect of the tibial condyle. Its primary purpose is to disperse the stresses applied by the movements of the foot and to assuage lateral tibial bending.87

The quadriceps femoris muscle group is one of the strongest in the body and is responsible for extension at the knee. The quadriceps femoris is formed by the rectus femoris and the vastus intermedius in the middle of the muscle group, with the vastus lateralis and the vastus medialis on the lateral and medial sides, respectively.8 The vastus lateralis applies lateral force to the patella and is the largest and strongest of the four muscles, while the vastus medialis pulls medially.

The hamstrings are the major muscle group contributing to knee flexion, and these three muscles include the biceps femoris and the semimembranosus and semitendinosus. The hamstrings are two joint muscles working to extend the hip, and they also rotate the knee joint due to their insertions on the sides of the knee. The hamstrings generate the greatest force from a flexed position of 90°, but at full extension, flexion strength is reduced by 50%. Besides the hamstrings muscle group, the sartorius, gracilis, popliteus, and the two-joint gastrocnemius contribute to knee flexion.81
Internal and external rotations are necessary movements associated with the knee joint. The sartorius, gracilis, semitendinosus, semimembranosus, and popliteus produce internal rotation of the tibia, and this rotation is greatest at 90° of hip flexion.83, 84

Diagnosis of Knee OA

OA may be diagnosed by radiographs, symptoms, or a combination of the two. In 1957, Kellgren and Lawrence (K-L) concluded that the following features were evidence of radiographic osteoarthritis: 1) the formation of osteophytes, 2) periarticular ossicles, 3) narrowing of joint space, and 4) sclerosis of subchondral bone.56 With these criteria, a 0-4 scale was proposed to grade the severity of an individual’s disease. A score of 0 indicated that there is no radiologic evidence of OA, a score of 1 conferred doubtful OA (questionable presence of osteophytes and joint space narrowing), a score of 2 confirmed that OA is present but not severe (definite osteophytes with possible joint space narrowing), a score of 3 showed that OA is present and moderately severe (joint space narrowing of 50% with cysts or sclerosis), and a score of 4 indicated severe OA (complete lack of joint space and sclerosis of subchondral bone).21, 31, 56

The most important symptom of OA is pain that usually occurs with joint use during walking and climbing stairs. Acute morning stiffness is a common complaint, as is joint instability that may cause a decrease in function. As the disease progresses, limited motion is a common symptom and crepitus (cracking or grating sound as the joint is moved) may result due to loss of cartilage and joint surface irregularity. Joint enlargement may develop due to an increase in synovial fluid, and late stages of the disease may cause deformity and subluxation associated with cartilage loss, destruction
of subchondral bone, and bony overgrowth.\textsuperscript{21,92} Included in Table A are the classification criteria of idiopathic OA as determined by the American College of Rheumatology.\textsuperscript{1}

**Table A:** American College of Rheumatology classification criteria of idiopathic OA

<table>
<thead>
<tr>
<th>Clinical and Laboratory</th>
<th>Clinical and radiographic</th>
<th>Clinical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee pain + at least 5 of 9 of the following:</td>
<td>Knee pain + at least 1 of 3 of the following:</td>
<td>Knee pain + at least 3 of 6 of the following</td>
</tr>
<tr>
<td>Age &gt; 50 yrs</td>
<td>Age &gt; 50 yrs</td>
<td>Age &gt; 50 yrs</td>
</tr>
<tr>
<td>Stiffness &lt; 30 min</td>
<td>Stiffness &lt; 30 min</td>
<td>Stiffness &lt; 30 min</td>
</tr>
<tr>
<td>Crepitus</td>
<td>Crepitus + osteophytes</td>
<td>Crepitus</td>
</tr>
<tr>
<td>Bony tenderness</td>
<td>Bony enlargement</td>
<td>Bony tenderness</td>
</tr>
<tr>
<td>No palpable warmth</td>
<td>ESR &lt; 40 mm/hr</td>
<td>No palpable warmth</td>
</tr>
<tr>
<td>ESR &lt; 40 mm/hr</td>
<td>RF &lt; 1:40</td>
<td></td>
</tr>
<tr>
<td>SF OA</td>
<td>92% sensitive</td>
<td>95% sensitive</td>
</tr>
<tr>
<td>75% specific</td>
<td>86% specific</td>
<td>69% specific</td>
</tr>
</tbody>
</table>

ESR = erythrocyte sedimentation rate; RF = rheumatoid factor; SF OA = synovial fluid signs of OA; sensitivity = probability of a positive test result correctly identifying people with disease; specificity = probability of a negative test result correctly identifying people without disease.

**Pathogenesis of Knee OA**

OA is commonly viewed as a disease of articular cartilage in combination with changes to subchondral bone. Progressive articular cartilage loss coupled with changes to the subchondral bone (including osteophytes, and increased thickness of subchondral bone) is the primary culprit in the pathology of OA.\textsuperscript{44} Human articular cartilage is constantly remodeled as a result of anabolic and catabolic processes. In healthy cartilage,
there is a balance between the synthesis and breakdown of extracellular matrix components. In OA, however, new matrix synthesis is outweighed by the breakdown of matrix components. Increased matrix catabolism has largely been attributed to upregulation of proteinase activities, especially those of metalloproteinase’s (MMPs). The MMPs are enzymes that include collagenases, gelatinases, and stromelysin. These enzymes target collagen and degrade other matrix components. MMPs play an important role in the destruction of cartilage, with analysis of synovial fluid showing higher concentrations of MMPs in OA subjects compared to controls. OA synovial fluid also demonstrates higher levels of the tissue inhibitor metalloproteinase's (TIMPs), a fact that may reflect chondrocyte attempts to balance excessive proteinase activities.

Risk Factors of OA

Principal risk factors for OA include increasing age, female sex, obesity, and joint trauma. Age is the strongest risk factor for the development of OA, as it is believed that aging cartilage is more susceptible to damage and degradation. The prevalence of OA increases to 50% of the population aged 65 and older, and moves above 85% of adults 75 and older. Women tend to be at greater risk of OA than men, especially after the onset of menopause.

Overweight and obese people commonly suffer from knee OA. Three common hypotheses have been proposed that attempt to explain the relationship between obesity and the onset of knee OA. The first is that obesity increases the load across the knee joint resulting in abnormal stress and deterioration of joint structures. The second is that obesity works through metabolic changes associated with increased fatness such as
inflammation, glucose intolerance, hyperlipidemia, or changes in bone density. The third mechanism is that elements of the diet that lead to obesity adversely affect bone, cartilage, or other joint structures.\textsuperscript{24} In 1990, using data from NHANES I, Davis et al.\textsuperscript{24} showed a significant relationship between unilateral and bilateral knee OA and obesity. Obese individuals (BMI $\geq 30$) were 3.45 times more likely to develop unilateral knee OA, and 7.92 times as likely to develop bilateral knee OA. Anderson and Felson\textsuperscript{3} provided further evidence that showed the association between obesity and OA is stronger for bilateral disease than unilateral disease. They found that the risk of knee OA is increased approximately 15\% for every additional unit increase in BMI above $27 \text{ kg/m}^2$.\textsuperscript{3,24}

Furthermore, several longitudinal studies have shown that increased weight precedes the presentation of knee OA and is not a consequence of the OA. Manninen et al.\textsuperscript{67} found a significant correlation between BMI and risk of developing knee OA when following participants over a 10 year period.\textsuperscript{67} Additionally, overweight and obese persons are at a greater risk of having the disease progress compared to persons who are not overweight.\textsuperscript{100} Felson examined data from the Framingham study and concluded that being overweight was a strong predictor of future radiographic knee OA. In women, those in the heaviest fifth of the group had a relative risk of 3.16 for developing knee OA of grade 2 or worse than those women in the lightest 60\% of the group. The risk of radiographic knee OA was also increased in men if they were obese at baseline; however, their relative risk was only 1.86 times greater than men of healthy weight. These data offer confirmation that obesity is an important risk factor for knee OA, and also supports reports that knee OA is more common in women than in men.\textsuperscript{31}
Inflammation is another risk factor for knee OA and obesity contributes to this phenomenon. As individuals gain weight, fat cells first increase in size then increase in number. Larger fat cells are more active than smaller ones, and so fat cells in obese persons produce more inflammatory messengers compared to an individual of healthy weight.\textsuperscript{17} Obesity, therefore, increases the quantity of circulating inflammatory markers, especially tumor necrosis factor-\(\alpha\) (TNF-\(\alpha\)), C-reactive protein, and interleukin’s 1 and 6 (IL-1, IL-6).\textsuperscript{17, 21, 102} Excess inflammation contributes to knee OA as a greater quantity of TNF-\(\alpha\) and IL-1 are found in the chondrocytes of healthy human cartilage. Chondrocytes produce matrix metalloproteinase's (MMPs) that breakdown and maintain cartilage homeostasis. Under normal conditions, tissue inhibitors of matrix metalloproteinase's (TIMPs) bind to MMPs in a 1:1 ratio, however, when inflammation increases, chondrocytes produce MMPs in a quantity that the TIMPs can not inhibit. Thus, cartilage breakdown results leading to OA.\textsuperscript{15}

Evidence is varied in terms of explaining the relationship between ethnicity and OA. Spector et al.\textsuperscript{101} suggested that black women have a higher prevalence of knee OA then men, while the Johnston County OA project concluded that there was no difference in the prevalence of knee disease, but black men were 35\% more likely to have hip OA compared to whites.\textsuperscript{18}

The influence of exercise or physical activity as a risk factor for OA may depend on the intensity of the activity and gender. Rogers et al.\textsuperscript{90} showed that, compared to men and women who did not participate in regular physical activity, men engaging in physical activity with moderate to high joint stress decreased their risk for OA by 38\%, while women decreased their risk by 76\% with moderate to high joint stress, and by 42\% with
low joint stress activities.\textsuperscript{90} Conversely, Imeokparia et al.\textsuperscript{50} demonstrated that women involved in high physical activity had a 74\% increased risk of knee OA\textsuperscript{50}, while Vingard et al.\textsuperscript{111} reported that men with a high exposure to sport were 4.5 times more likely to develop hip osteoarthritis and men exposed to high levels of sport and occupational physical activity had an OR of 8.5 for the development of hip OA.\textsuperscript{111} Interestingly, while Vingard et al.\textsuperscript{111} reported that high exposure to sport and occupational physical activity increased the risk of developing hip OA, Imeokparia showed this relationship was present only in women.

In a population based longitudinal study by Cooper et al.\textsuperscript{20}, regular sports participation and a high BMI increased the individual’s incidence of knee OA; however, these factors did not have a significant influence upon the progression of knee OA.\textsuperscript{20} In contrast, Lane et al.\textsuperscript{60} performed a cross-sectional study and found that members of a running club aged 52-74 had an increased progression of knee and lateral spine bone spurs.\textsuperscript{60} These results suggest that repetitive stress on the knee and spine via running increased the progression of osteophytes, one of the hallmark indicators of osteoarthritis.

Not all studies have found that increased physical activity worsens knee OA. Cooper et al.\textsuperscript{20} found that physical activity did not cause joint space narrowing although it may play a role in osteophytes formation. Additionally, Ettinger et al.\textsuperscript{30} determined that adults that either walked or resistance trained for 18 months exhibited no difference in radiographic progression of OA compared to a health education control group.\textsuperscript{30}

Finally, a community based prospective cohort and a population based cohort study both provided evidence that physical activity neither increased nor decreased an individual’s risk for osteoarthritis. Felson et al.\textsuperscript{32} concluded that older men and women
walking more or less than six miles per week and working up a sweat more or less than three times per week had no increased or decreased chance of developing OA, although they did have slightly more joint space loss compared to less active individuals.\(^{32}\) Similarly, Hannan et al.\(^{42}\) found that women who were slightly more active, defined by an FEV\(_1\) of 1.36-1.51 L/min, had a significantly increased risk for knee OA, however, men and women in all other levels of physical activity (assessed by FEV\(_1\) and resting pulse rate) were not more prone to knee injury or eventual development of OA.\(^{42}\)

Brouwer et al.\(^{12}\) demonstrated that more varus knee alignment was associated with both the progression and the development of knee OA. Using data from 1,501 participants randomly selected from the Rotterdam study, Brouwer and colleagues\(^{12}\) assessed knee OA using the K-L scale at baseline and an average follow up of 6.6 years.\(^{12}\) They concluded that malalignment at baseline was associated with an increased risk in the development of knee OA—the first study to demonstrate such results. Among knees with a K-L score of 0 or 1 at baseline, OA developed in 45 of the 819 knees with valgus alignment, 43 of the 579 knees with varus alignment, and in 35 of the 892 knees with normal alignment. Compared to normal alignment, valgus alignment provided an odds ratio (OR) of 1.54 for the development of knee OA (K/L grade 2 or higher), while varus alignment showed an OR of 2.06.\(^{12}\)

The relationship between baseline alignment and progression of knee OA was also analyzed, and was assessed by an increase in K-L score of \(\geq 1\) from a score of at least 2 at baseline. In knees with a varus alignment, a significant risk emerged for progression of OA, with an OR of 2.90 compared to knees with normal alignment.\(^{12}\) Additionally, when the analyses were stratified according to BMI, a non-significant OR of 1.42
emerged between valgus and normal individuals with a BMI $\geq 25$ kg/m$^2$ but $< 30$ kg/m$^2$. However, a significant OR of 3.25 existed for participants with valgus alignment and a BMI $\geq 30$ kg/m$^2$. When varus alignment was compared to normal alignment, a significant OR of 2.02 appeared for persons with a BMI $\geq 25$ kg/m$^2$ but $< 30$ kg/m$^2$, and in individuals with a BMI $\geq 30$ kg/m$^2$, the OR increased to 5.06.  

Obesity and Gait

Obese individuals make modifications to their gait in an attempt to reduce the load on their knees. In an obese population, Devita et al.\textsuperscript{28} found that the greater an individual’s BMI, the shorter their stride length and the lower their knee-joint extensor torque. Consequently, the cohort exhibited a shift to a dominant flexor torque at high BMI’s, thus the hamstrings rather than the quadriceps provided knee stability. Subjects with low BMI’s exhibit no relationship between BMI, stride length, and knee torques.\textsuperscript{28}

Abnormal gait is characteristic of obese people, as is greater force generation. Messier et al.\textsuperscript{72} found that higher BMI values were significantly associated with decreased knee kinematics, stride length, and walking velocity. Additionally, the authors concluded that BMI was significantly correlated with vertical, anteroposterior, and mediolateral force variables. As BMI increased, vertical force and vertical impulse values increased significantly; braking and propulsive forces and impulses significantly increased; and medial and lateral maximum forces tended to increase.\textsuperscript{72}

Browning and Kram,\textsuperscript{13} examining the effects of obesity on gait biomechanics at different walking speeds, found that obese adults had greater ground reaction forces (GRF), stance-phase sagittal-plane net muscle moments, and step width. At each of 6
different walking speeds, peak vertical GRF was approximately 60% greater and peak mediolateral GRF was approximately 85% greater for the obese subjects compared to normal weight controls. Absolute GRF and mediolateral GRF decreased significantly at slower walking speeds in both groups, however the difference between groups remained consistent.

Browning and Kram\textsuperscript{13} did not observe a difference in stride length and stride frequency between the two groups, but step width was about 30% greater in the obese versus normal weight subjects and did not change significantly with walking speed. Absolute net muscle moments were significantly greater in the obese versus normal weight subjects, suggesting that the obese subjects walked with greater joint loads. These values decreased significantly at slower walking speeds in both groups. Whereas Browning and Kram\textsuperscript{13} concluded that sagittal-plane net muscle moments are greater in obese individuals, Devita and Hortobagyi\textsuperscript{28} found the absolute peak knee moments at the same walking speed were identical for obese and normal-weight subjects. Consequently, the required net muscle moments and sagittal-plane knee forces were likely not different between the groups.\textsuperscript{28} Additionally, Browning and Kram\textsuperscript{13} concluded that the peak external knee adduction moment increased with walking speed, and was significantly greater in obese versus normal-weight subjects.\textsuperscript{13}

Obese individuals exert greater forces than individuals of normal-weight during gait, and as obesity worsens modifications are made to minimize the load on their knees.\textsuperscript{69} Since obesity is strongly associated with knee OA, the relationship between obesity, gait, and OA severity merits further investigation.
Pain and Gait

Joint pain is the cardinal symptom of knee OA, and pain reduction is a prime objective in the treatment of the disease. Radin et al.\textsuperscript{88} reported that subjects with activity-related knee pain exhibit inefficient gait mechanics, strike the ground with greater impact, and display larger angular accelerations during the swing phase of gait.\textsuperscript{88}

Knee pain is not always accompanied by joint damage and radiographic evidence of OA. In 2006, Teichtahl et al.\textsuperscript{107} examined the relationship between knee adduction moment and self-reported knee pain in 20 women without knee OA. An inverse relationship between the peak knee adduction moment and knee pain during the late stance phase of gait was observed. This observation suggests that women experiencing knee pain adopt a compensatory gait pattern to reduce their knee adduction moment and, consequently, their medial tibiofemoral load. The inverse relationship between the knee adductor moment and knee pain was observed during the late, but not the early stance phase of gait, causing the authors to hypothesize that pain may be more prominent during late stance when body mass becomes concentrated over the medial tibiofemoral compartment of the knee.\textsuperscript{107} Similarly, upon the development of radiographic evidence of knee OA, Hurwitz et al.\textsuperscript{49} showed that increased knee pain results in a significantly reduced peak external knee adduction moment, while Schnitzer et al.\textsuperscript{94} showed that reductions in pain via NSAID use leads to increased walking speed, and greater adduction and quadriceps moments.

In 2008, Maly et al.\textsuperscript{65} determined that mechanical variables explain 29% of the variance in pain intensity during gait, and found pain intensity to be significantly related to the dynamic range of flexion-extension knee motion while walking. The authors
concluded that a 5° increase in flexion-extension knee range of motion resulted in lower reported pain (assessed by the WOMAC), by 14.5 points. Additionally, Maly and colleagues found no relationship between pain and the mean peak knee adduction moment.

Amin et al. studied 132 older adults who had undergone kinetic and kinematic motion analysis while standing, walking, rising from a chair, and descending stairs. Eighty of these older adults (mean age=75 years) reported no pain at baseline, but at 3-4 year follow-up, 7 reported a development of chronic knee pain. Those who developed chronic knee pain exhibited higher baseline adduction moments for all four activities, ranging from 8% higher during the chair rise to 39% higher while descending stairs. Thus, the authors concluded that a higher knee adduction moment contributes to the onset of chronic knee pain.

Research suggests that OA patients may cope with two pain-related cognitions: pain catastrophizing and pain-related fear. Pain catastrophizing refers to a tendency to focus upon and magnify pain sensations while feeling helpless in the face of pain, whereas pain-related fear results from a feeling of vulnerability to pain and thus an excessive and debilitating fear of physical activity. Somers et al. examined the relationship between pain catastrophizing and pain-related fear in knee OA subjects walking at normal speed, fast speed, and intermediate speed. They found that pain catastrophizing and pain-related fear accounted for 7% of the variance at normal walking speed, 11% of the variance at fast walking speed, and 9% of the variance at intermediate walking speed. Pain catastrophizing was a significant individual predictor of walking at all three speeds, while pain-related fear was an individual predictor at only the fast
walking pace. The variance in walking speed explained by pain catastrophizing and pain-related fear is important because these pain cognitions may discourage OA patients from engaging in exercise and other physical activities that are important in managing pain and disability.\textsuperscript{76,99}

**Knee OA and Gait**

Gait analysis is a reliable and quantifiable measure used to assess physical function in older adults with knee OA.\textsuperscript{70} In a study using age-, mass-, and gender-matched controls, Messier et al.\textsuperscript{75} found that older adults with knee OA had a lower mean knee angular velocity, a slower maximum knee extension velocity, and a shorter stride length than the control group. Additionally, when comparing the affected and unaffected legs of the OA group, the authors found the affected leg’s knee velocity, knee range of motion, and mean hip angular velocity were significantly less than in the unaffected leg. The OA subjects also had a slightly greater, but non-significant increase in loading rate in the unaffected leg.\textsuperscript{75}

In a review, Messier\textsuperscript{70} noted a significant difference between the walking patterns of older adults with knee OA and healthy adults. Previous studies observed that adults with knee OA walked with a reduced velocity, stride length, and cadence, and also exhibited reduced knee range of motion, stance phase knee flexion and extension, and less internal and external knee rotation when compared to a control group.\textsuperscript{38,104} A more recent study, however, found no significant differences in gait speed, cadence, stride length, and step width between an OA and healthy control group.\textsuperscript{47}
Messier\textsuperscript{70} concluded that persons with knee OA may make gait modifications to minimize pain and maximize stability. Stauffer and colleagues\textsuperscript{104} noted that OA subjects exhibit an initial peak force that is less than 100\% of their body weight, and a slower rate of vertical loading after heel strike.\textsuperscript{104} However, Messier et al.\textsuperscript{75} found no difference in peak vertical force between individuals with knee OA and healthy controls that walked at similar speeds, while a significant difference remained in initial vertical peak loading rate. Persons that make such modifications may display an aided or shuffling gait, and are attempting to decrease the forces across their affected knee while walking.\textsuperscript{70}

Baliunas et al.\textsuperscript{6} and Landry and colleagues\textsuperscript{59} provided further evidence that subjects with knee OA have a decreased flexion moment and a more pronounced external extension moment during early and mid-stance phase of gait. Such a pattern has been termed “quadriceps avoidance” gait and is adopted by OA patients to relieve pain while walking. Twenty-six percent of knee OA subjects in the Baliunas et al.\textsuperscript{6} study walked with this pattern.

The medial compartment of the knee absorbs a peak force during walking that is 2.5 times greater than the force absorbed by the lateral compartment. This contributes to a higher prevalence of medial tibiofemoral osteoarthritis.\textsuperscript{49,93} The external knee adduction moment relates to the distribution of forces between the medial and lateral knee joint, and is a measure of the varus torque at the knee that adducts the knee during gait. Increased loads on the medial compartment of the knee indicate greater external knee adduction moments that accelerate progression of medial tibiofemoral OA.\textsuperscript{49} Previous studies demonstrated a positive correlation between pain and the magnitude of the knee adduction moment.\textsuperscript{6,93,107} In a study comparing 31 subjects with radiographic
evidence of knee OA and medial compartment cartilage damage to 31 asymptomatic control subjects, Baliunas et al.\textsuperscript{6} found that subjects with knee OA and medial compartment cartilage damage walked with a significantly greater peak external knee adduction moment than controls. This suggests that subjects with knee OA walk with increased joint loads across the medial compartment of their knee joint.\textsuperscript{6}

**Obesity and Strength**

Muscle strength, as a function of body weight, tends to decrease with increasing body fat. Thus, those who are obese have lower relative muscular strength compared to those who are normal-weight. Kitagawa and Miyashita\textsuperscript{57} found that much of the muscle strength per kilogram of body weight tends to decrease as percent body fat increases. The authors formed a composite score for total strength after measuring hand-grip strength, elbow flexion, trunk extension, and knee extension, and found that obese men display lower scores per kilogram of lean body mass compared to their non-obese counterparts.\textsuperscript{57}

Reduced physical activity levels in obese persons may also contribute to declines in muscular strength. Blimkie et al.\textsuperscript{9} concluded that excess fat mass combined with reduced neuromuscular activation may be responsible for the reduction in strength per kilogram of body mass ratio evident in obese people.\textsuperscript{9} Similarly, Jadelis et al.\textsuperscript{52} found that higher BMI values were associated with poorer dynamic balance across multiple levels of knee strength. Because obese individuals tend to be weaker than normal-weight individuals, and the muscular strength required to correct loss of balance increases with increasing BMI\textsuperscript{63}, muscular weakness places obese individuals at greater risk of falling
The fact that obesity is strongly associated with knee OA merits further investigation into the relationship between obesity, disease severity, and strength.

**Pain and Strength**

Lower limb function is strongly associated with quadriceps strength in the elderly, and quadriceps weakness has been demonstrated in both subjects with knee OA and knee pain, but is greater in those with both. Hall et al. measured maximum voluntary contractions (MVC) during isometric knee extension. Subjects without knee pain and knee OA (n=55) generated an average force of 26.58 N and had a force to body weight ratio of 0.38 N/kg. The group with knee pain and no knee OA (n=28) generated significantly less force with an average value of 20.67 N and a force to body weight ratio of 0.28 N/kg. Additional observations were made in individuals with knee OA and no knee pain, and in individuals with both knee OA and knee pain. Compared to healthy subjects, all subgroups exhibited significantly lower strength values.

O’Reilly et al. found similar results to those of Hall and colleagues. Subjects with knee pain generated mean quadriceps strength that was significantly lower than the mean force generated by pain-free controls. Quadriceps activation was also significantly lower in knee pain subjects (77.1%) compared to controls (80.4%).

Hassan and colleagues investigated the effect of pain alleviation on quadriceps function as assessed by isometric MVC of the quadriceps. All subjects had signs and symptoms consistent with knee OA, as well as radiographic evidence and reported knee pain of at least 20mm on a visual analog scale (VAS) where 0mm = no pain, and 100mm = worst pain imaginable. In a crossover, double blind design, each patient received an
intra-articular injection of either 5 ml 0.5% bupivacaine or 5 ml 0.9% saline (placebo) into one or both knees. Subjects received the other injection 2 weeks later. Both agents resulted in decreased pain one hour following injection, with bupivacaine giving a median pain reduction of 56.85%, and the placebo a median reduction of 41.94%. MVC significantly improved for both interventions, with the placebo resulting in a 7.64% improvement in quadriceps strength and the bupivacaine leading to an 18.83% improvement in quadriceps strength. The difference between placebo and bupivacaine approached, but did not reach, statistical significance. The reduction in knee pain following injection allowed subjects to generate more force and increase quadriceps MVC. The authors concluded that subjects might push harder when their pain is less severe, and that reduction in pain may reduce pain-induced reflex inhibition of the quadriceps.43

Knee OA and Strength

Quadriceps weakness is common to persons with symptomatic knee OA, and increases their risk for disability. The quadriceps assists in decelerating the knee at the end of the swing phase of the gait cycle, and provides anteroposterior support to the knee. If quadriceps weakness is present, the sites of mechanical loading on the joint surface may be changed, thus promoting damage to articular cartilage in the knee.5,97,98 Quadriceps weakness may be exacerbated by a “quadriceps avoidance” gait pattern, where individuals walk with a decreased flexion moment and an increased external extension moment during the early and mid-stance phase of gait. This pattern is adopted to relieve pain and limits the contraction of the quadriceps while walking.6
It is widely thought that the weakness associated with knee OA results from joint pain that leads to disuse and muscle atrophy.\textsuperscript{5, 97, 98} Slemenda et al.\textsuperscript{97} concluded that men and women with knee OA had 20\% less quadriceps strength than men and women without the disease. There was no significant difference in flexor strength between the two groups.\textsuperscript{97} Although extensor weakness in older adults is frequently associated with knee pain, Slemenda et al.\textsuperscript{98} found that women with knee OA who did not have knee pain or muscle atrophy also had a decrease in quadriceps strength. Additionally, the authors found baseline quadriceps strength was a predictor of incident radiographic knee OA in women, but not in men. Women who had normal findings at baseline but who developed radiographic knee OA at follow up (mean follow up 31.3 months) had 15\% to 18\% less quadriceps strength at baseline than women whose knee radiographs remained normal.\textsuperscript{98}

Messier et al.\textsuperscript{75} found that OA patients have less leg strength in their dominant and non-dominant legs when compared to age and gender matched healthy adults. They found older adults with knee OA had 22\% to 39\% less quadriceps strength than their peers.\textsuperscript{75} In a sample of 480 adults aged \( \geq 65 \) years with chronic knee pain, Messier et al.\textsuperscript{73} showed that individual’s with the weakest leg strength at baseline experienced the greatest declines in balance after 30 months when compared to their stronger peers. In the cohort, quadriceps extensor strength decreased by an average of 12.1\% in a span of 2.5 years.\textsuperscript{73} By comparison, Aniansson et al.\textsuperscript{4} showed isokinetic knee strength declines of 18\% and 13\% over a 5 year period in a healthy population of men and women ages 70-75 years, respectively.\textsuperscript{4} Strength accounts for 28\% of the variability associated with balance, hence rapid declines in strength can foster the onset of disability and injury.\textsuperscript{52, 73}
**OA Severity and Gait and Strength**

In a comparison of adults with mild OA (K/L grade 1 or 2), severe OA (K/L grade 3 or 4), and healthy controls, Huang et al.\(^47\) found that the severe OA group had a more extended knee, plantar-flexed ankle, and abducted hip at heel-strike compared to the healthy controls. In addition, all patients with knee OA exhibited a greater hip extensor moment during single-leg stance, and smaller flexor moments at take-off compared to the control group. During early stance phase, the mild and severe OA groups had a peak knee extensor moment that was 48% and 56% less than the control group. The authors also noted that the mild knee OA subjects maintained a normal abductor moment by shifting their body’s center of mass towards the stance leg, thus decreasing the forces across the medial tibiofemoral cartilage of their stance limb. Such an action reduced the load on the knee and may have provided pain relief. By contrast, the severe OA group tried to increase standing hip abduction, however they did not successfully achieve that goal.\(^47\)

Thorpe et al.\(^108\) sought to determine the relationship between knee pain and joint load in patients with symptomatic and asymptomatic mild knee OA (K/L grade 2) and with an asymptomatic control group (K/L grade 0-1). She and her colleagues found that the symptomatic K/L grade 2 group had a peak knee adduction moment that was 19% greater than both asymptomatic groups, and knee adduction angular impulses that were 30% greater than the two asymptomatic groups. The symptomatic grade 2 patients had a greater degree of varus alignment than the asymptomatic subjects with the same grade, and the authors concluded that mechanical factors may be closely tied to symptoms in persons who have radiographic evidence of degeneration of the knee.\(^108\)
In a study by Liikavainio et al.\textsuperscript{64} it was observed that 54 males with knee OA had 19.6\% and 12.8\% reduced extension and flexion strength compared to 53 healthy, age- and sex-matched controls. Moreover, a significant negative linear trend was observed such that as the severity of knee OA increased, the subjects maximal voluntary isometric knee extension torque decreased.\textsuperscript{64} Brandt and colleagues\textsuperscript{10} analyzed 79 women with knee OA, and found that peak knee extensor strength decreased by 9\% as the disease condition progressed. Although this decrease was not statistically significant compared to women with stable OA\textsuperscript{10}, the reduction in extensor strength with worsening severity of OA supports the finding of Liikavainio et al.\textsuperscript{64}

**Knee OA and Pain and Function**

Pain is a trademark symptom of knee OA and treatments often aim to reduce pain and improve physical function. The Framingham Osteoarthritis study revealed that adults with knee OA had significant increases in disability while performing activities of daily living such as house cleaning and carrying objects.\textsuperscript{31} The Western Ontario and McMaster University Osteoarthritis Index (WOMAC) is a self-administered questionnaire used to assess a person’s physical function, pain, and stiffness. The WOMAC contains 17 function, 5 pain, and 2 stiffness questions, and all questions are rated on a 5 point Likert scale (0-4), with higher scores indicating more pain and stiffness, and decreased function.\textsuperscript{7, 97} Bellamy and colleagues\textsuperscript{7} established the WOMAC as a valid and reliable self-administered assessment of pain, function, and stiffness in hip and knee OA subjects.\textsuperscript{7}
Creamer et al.\textsuperscript{23} found a significant association between self-reported disability and pain and obesity, and this association was greater than that between self-reported disability and the severity of radiographic evidence of knee OA. Additionally, WOMAC disability was greater when participants exhibited swelling of the joint. Participants with swelling had a mean disability score of $44.8 \pm 21.7$, while participants without swelling had a disability score of $30.6 \pm 22.8$.\textsuperscript{23}

Gait is a common measure of physical function. Hurwitz et al.\textsuperscript{49} demonstrated that a decrease in pain was associated with an increase in knee adductor moments during walking, while an increase in pain was associated with a decreased adductor moment. This finding provides an inverse correlation between change in pain and knee adduction moment, suggesting that reducing pain inhibits the pain protective reflex and results in increased joint loads. The subjects who experienced the greatest decrease in pain had a significant average increase in knee adduction moment of 10\%.\textsuperscript{49} Furthermore, in 2006, Maly et al.\textsuperscript{66} concluded that pain, peak knee extension angle, and knee range of motion were significantly related to disability and current levels of physical performance in older adults with mild to moderate knee OA. However, in the same study the authors found the knee adduction moment to be unrelated to physical performance and disability.\textsuperscript{66}

The literature has identified abnormal joint loading during gait and muscular weakness as risk factors for OA progression and mechanisms for disability in persons with knee OA. The purposes of this study were to examine the relationships between severity of obesity (defined by BMI) and radiographic evidence of knee OA, and their associations with abnormal joint loading, muscular weakness, knee pain, and function.
CHAPTER 2

METHODS

Fatty acids, Arthritis, and inflammation in the Elderly (FAME) is a randomized, double-blind controlled crossover trial involving 30 overweight and obese adults (BMI ≥ 27.0 kg/m²) with mild to severe knee osteoarthritis (K-L grade 1-4). The purposes of the FAME study are 1) to compare the effects of gamma linolenic acid (GLA) plus stearidonic acid (SDA) supplementation to a placebo on markers of inflammation, and 2) to compare the effects of GLA and SDA supplementation to a placebo on gait, mobility, thigh strength, self-reported physical function, and pain. This manuscript describes the relationship between the severity of obesity and knee osteoarthritis and the effects on gait and strength using baseline data only.

Criteria for participating in the FAME study include: 1) ambulatory persons aged 55 years and older, 2) radiographic evidence of knee OA (K-L grade 1-4), 3) BMI ≥ 27 kg/M² and 4) not currently participating in another intervention study. Exclusion criteria include: 1) presently taking an omega-3 fatty acid supplement, 2) previous lower extremity joint replacement, 3) dementia (3MSE < 70), 4) active cancer (non-skin or prostatic), 5) anemic (HCT < 32), 6) hepatic disease, 7) excess alcohol use (>21 alcoholic beverages a week), 8) inability to walk unsupported, 9) requires transportation or lives more than a one hour drive from Wake Forest University, and 10) inability to read or speak English. The primary method of recruitment consisted of calling participants deemed ineligible for the IDEA (Intensive Diet and Exercise for Arthritis) study.
Screening Visits

Pre-Screen: Individuals who do not meet the eligibility criteria for the IDEA study were informed of the FAME trial and its eligibility criteria. If interested, they were asked a series of brief questions that focused on major eligibility criteria. A screening visit appointment was made for participants who met major eligibility criteria. A medical history form and a medication form were mailed to the participants for them to complete.

Screening Visit (SV): Individuals came to the Geriatric General Clinical Research Center (GGCRC) at Wake Forest University Baptist Medical Center. SV included an explanation of the study and obtaining informed consent. Other assessments included medical history and medication use (previously mailed). The 3MSE and CES-D were administered, and individuals who scored <70 on the 3MSE and/or a score >20 on the CES-D were not eligible to participate in the study. All subjects who met the eligibility criteria completed bilateral standing (semi-flexed view) and sunrise view knee x-rays. X-rays were completed at Outpatient Radiology at Wake Forest University Baptist Medical Center and were graded on the 0-4 Kellgren-Lawrence scale (0 = no radiologic evidence of OA, 1 = doubtful OA (questionable presence of osteophytes and joint space narrowing), 2 = OA is present but not severe (definite osteophytes with possible joint space narrowing), 3 = OA is present and moderately severe (50% joint space narrowing with cysts or sclerosis), and 4 = severe OA (complete lack of joint space and sclerosis of subchondral bone)). Subjects with a score of 1-4 were eligible for participation. After the knee x-rays were evaluated, those who remained eligible were scheduled for a baseline visit (BV1).
Baseline Visit 1 (BV1): Individuals then visited Reynolds Gymnasium at Wake Forest University. The following tests and measures were performed: height, weight, knee strength, six-minute walk, gait analysis, and questionnaires including demographic information and the WOMAC.

Randomization Visit (RV): If the participant was eligible upon completion of the screening visit (SV) and first baseline visit (BV1), a randomization number was assigned for data entry and management. The participants were blinded to group assignment.

Gait Analysis

Each participant underwent a 3-D gait analysis using a 37-reflective marker set arranged in a Cleveland Clinic full-body configuration, and a 6-Camera Motion Analysis System set to sample data at 60 Hz. Kinematic data were collected, tracked, edited, and smoothed, using Evart 4.6 software (Motion Analysis Corp, Santa Rosa, CA), and a Butterworth low pass filter with a cut-off frequency of 6 Hz on a PC (Gateway GT5220, Gateway, Inc., Irvine, CA). The processed data were compiled using OrthoTrak 6.0 β4 clinical gait analysis software (Motion Analysis Corp, Santa Rosa, CA) to generate lower extremity kinematic and kinetic data. For placement of the reflective markers refer to Appendix B.

A 6-channel force platform (OR6-5-1, Advanced Mechanical Technologies, Inc., Newton, MA) was integrated with the motion capture system and allowed simultaneous kinetic data collection at 480 Hz. A biomechanical knee model developed by Devita and
Hortobagyi\textsuperscript{29,46} was used to calculate internal knee extension and abduction moments, knee joint muscle forces and knee joint compressive and shear forces.

The musculoskeletal torque-driven model used in this study has two basic components. The first component involves calculating joint moments and joint reaction forces from kinematic, physiological, and force plate data using Ortho Trak version 6.0. The joint moments and reaction forces were then used to calculate the muscular forces of the quadriceps, hamstrings, and gastrocnemius, as well as the force of the lateral collateral ligament. The muscle and ligament forces were then used to calculate the compressive and anterior-posterior shear forces about the knee. (Detailed explanation in Appendix A)

Participants walked on a 16.8 m walkway located in the J.B Snow Biomechanics Laboratory at a self selected walking speed. The speed was monitored using infrared photocells (Model 63501 IR, Lafayette Instrument Co., Lafayette, IN) set 7.3 m apart at waist level and interfaced with a digital timer (Model 54035, Lafayette Instrument Co., Lafayette, IN). A trial consisted of starting on the platform approximately 2 meters behind the initial timer and walking past the first beam of light to activate the timer. As the participant walked past the second beam of light the timer was stopped and the time was recorded. The participant turned around and performed the same test in the opposite direction. To determine freely chosen walking speed, participants made 6 round trip passes on the platform. The range of freely chosen walking speeds was calculated as the average ±3.5%. During actual testing, a successful trial was defined as one in which the participant’s entire foot was placed on the surface area of the force platform while
walking within the range of average walking speed (calculated earlier). Three successful trials were averaged for each side to provide a representative trial for each participant.

Reliability of the gait data was determined using 21 IDEA participants tested twice, one week apart. Intraclass-correlation coefficients were used to determine the between-day reliability of peak internal knee flexion/extension and internal abduction/adduction moments, peak knee compressive force, peak vertical ground reaction force, and stride length. Day to day reliability was excellent, with intraclass-correlation coefficients ranging from 0.86-0.98. The peak muscle force predictions from our model (in bodyweights, BW) compare well to the muscle force predictions from other studies. \(^{27,93}\) Values from the literature indicate a mean hamstrings force of 1.1 BW, quadriceps force of 2.3 BW, and gastrocnemius force of 1.3 BW. Our model predicts a mean hamstrings force of 1.3 BW, quadriceps force of 2.7 BW, and gastrocnemius force of 1.3 BW.

**Mobility**

The 6-minute walk test \(^{14,110}\) was used to assess mobility in each participant. Participants were asked to walk as many laps as they could in 6-minutes around an indoor track at Reynolds Gymnasium. Mobility was based on the distance that was covered in 6 minutes.

**Strength**

Strength was assessed in the participants most affected leg (self-reported) using the Kin-Com 125E isokinetic dynamometer. Knee flexor and extensor strength was
assessed both concentrically and eccentrically. The Kin-Com was set so that the axis of the dynamometer was in line with the mid-point of the knee joint center with the resistance pad positioned 2 cm above the lateral maleolous. Participants were secured in the chair with straps across their upper body, torso, and working leg. The dynamometer was calibrated and gravity was corrected by weighing the subject’s leg at a 30° angle.

Isometric testing was first performed to assess the participant’s maximal strength in their flexor and extensor muscle groups. A maximum of 6 trials were performed of each muscle group, and 50% of their maximal isometric strength was used as the activation point for isokinetic testing. This higher starting force results in higher total force.\textsuperscript{53, 58}

Knee flexors and extensors were assessed through a range of motion from 30° to 90°. Participants were asked to give a maximal effort, with 30-60 seconds between trials for a maximum of 6 trials. The first and last 10° of each trail was deleted to account for the acceleration and deceleration of the joint and to eliminate inconsistencies. The average of each trial was taken between the joint angles of 40° and 80°. Reliability was assessed using 5 males and 5 females tested twice, one week apart. The intraclass-correlation coefficient for peak concentric knee extension was 0.97.

Physical Function and Pain

The Western Ontario and McMaster University Osteoarthritis Index (WOMAC) is a self-administered questionnaire that was used to assess pain and physical function.\textsuperscript{7} Developed for participants with hip or knee OA, the WOMAC consists of 24 items which allow researchers to evaluate the participant’s perception of pain, joint stiffness, and
physical function. The WOMAC has 5 specific questions for pain that address sitting, lying in bed, walking, and ascending and descending stairs. Each question was answered on a 5-point Likert scale (0=none, 1=mild, 2=moderate, 3=severe, 4=extreme).\textsuperscript{7} Scores for function range from 0-68, with higher scores indicating poorer function; scores for pain range from 0-20, with higher scores indicating more pain; and scores for stiffness range from 0-8, with higher scores indicating more stiffness.

**X-Ray**

Bilateral standing (semi-flexed view) and sunrise view knee x-rays were used to identify the presence of knee osteoarthritis. Kellgren and Lawrence (K-L) score was used to assess the severity of knee OA, as described previously in this paper.\textsuperscript{56} A single view of each knee was obtained with the subject standing and facing the Bucky or cassette holder. The subject stood on the positioning guide with the index foot aligned with the foot angulation support and the great toe of each foot in contact with the front edge of the positioning guide. The index foot was fixed in 10 degree external rotation against the V-shaped support on the base of the Plexiglas frame. Body weight was distributed evenly between both legs, and the knee of interest was centered on the film. Participants flexed their knees until they came in contact, along with the anterior thigh, with the Bucky or cassette holder. The source image distance was 100 cm and the x-ray beam centered on the joint line of the knee of interest and was angled to 10°.

Image evaluation criterion included: 1) each knee was radiographed individually on a separate film, 2) the joint spaces of the knees were radiographically open, 3) the long axis of the tibia was vertical, 4) there was no rotation of the knee, 5) all of the joints,
including osteophytes, were captured on film, 6) left and right markers identified each leg on film, 7) film was neither over or under exposed, and 8) the metallic beads in the center of the positioning guide were visible on film. X-rays were graded on the 0-4 Kellgren-Lawrence (K-L) scale, with scores of 1-4 meeting the eligibility criteria.

**Height and Weight Measurement**

Participant’s height was measured with a vertically mounted metal ruler while participants stood erect with no shoes and was recorded to the nearest 0.1 cm. Weight was measured to the nearest 0.1 kg on an electronic scale after participants removed their shoes and wore only light clothing. BMI was calculated as mass (kg) divided by height squared (m²).

**Statistical Analysis**

Statistical analyses were conducted using the software package SAS 9.1 (Cary, NC). Distribution and simple statistics such as means, medians, standard deviations, and histograms were calculated on the descriptive variables and force, moment, and strength measures. Pair-wise Pearson correlations were computed to assess the relationship between the outcome measures and explanatory variables that included race, gender, height, weight, BMI, walking speed, 6-minute walk distance, K-L score and WOMAC pain and function scores. Linear regression modeling was used to look for associations between the outcome measures and explanatory variables after adjusting for gender, race, and weight. Natural log transformation was used for skewed measures and significance was determined if a p value was less than 0.05.
CHAPTER 3

RESULTS

Descriptive Characteristics

The purposes of this study were to examine the relationships between severity of obesity (defined by BMI) and radiographic evidence of knee OA and their associations with abnormal joint loading, muscular weakness, knee pain, and function. Means, standard deviations, and ranges of age, race, sex, height, weight, and BMI are listed in Table 1. Mean values, standard deviations, and ranges for affected knee K-L score, dichotomous affected knee K-L score (>1), WOMAC pain and function scores, walking speed, and 6-minute walk distance are summarized in Table 2.

Table 1: Descriptive characteristics (n=30).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
<th>SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>63.3</td>
<td>5.4</td>
<td>55-74</td>
</tr>
<tr>
<td>% White (n)</td>
<td>0.67 (20)</td>
<td>0.48</td>
<td></td>
</tr>
<tr>
<td>% Female (n)</td>
<td>0.80 (24)</td>
<td>0.41</td>
<td></td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.66</td>
<td>0.09</td>
<td>1.50-1.94</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>113.1</td>
<td>26.7</td>
<td>68.9-177.5</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>40.7</td>
<td>7.8</td>
<td>26.8-57.7</td>
</tr>
</tbody>
</table>
Table 2: Descriptive characteristics of Kellgren-Lawrence score, WOMAC Pain and Function score, walking speed, and 6-minute walk distance.

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Affected side knee K-L score (0-4)</td>
<td>29</td>
<td>2.66</td>
<td>1.37</td>
<td>1-4</td>
</tr>
<tr>
<td>Dichotomous affected side K-L score (&gt;1)</td>
<td>29</td>
<td>0.76</td>
<td>0.44</td>
<td></td>
</tr>
<tr>
<td>WOMAC pain score (0-20)</td>
<td>30</td>
<td>7.8</td>
<td>3.2</td>
<td>1-14</td>
</tr>
<tr>
<td>WOMAC function score (0-68)</td>
<td>30</td>
<td>26.9</td>
<td>10.3</td>
<td>11-51</td>
</tr>
<tr>
<td>Average walk speed (m/sec)</td>
<td>30</td>
<td>1.12</td>
<td>0.21</td>
<td>0.70-1.55</td>
</tr>
<tr>
<td>6 minute walk distance (m)</td>
<td>30</td>
<td>419</td>
<td>93</td>
<td>249-631</td>
</tr>
</tbody>
</table>

Baseline measures of compressive and quadriceps force, quadriceps and hamstring strength, and knee internal abduction and extension moments are shown in Table 3. Mean peak compressive force was 2.7 times mean body weight (BW) and quadriceps muscle force was 1.1 times mean BW. Figure 1 provides graphical representation of the mean knee extension moment for all 30 participants, while Figure 2 provides the mean graph of the participants’ knee abductor moment. The participants’ most affected leg displayed greater extension and abduction moments during the gait cycle.
Table 3: Means (SD) of peak compressive and quadriceps forces, mean quadriceps and hamstring strength, and peak knee abductor and extension moments. Mean body weight was 1108 N.

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compressive force (N)</td>
<td>30</td>
<td>3039</td>
<td>1293</td>
<td>1609-6410</td>
</tr>
<tr>
<td>Quadriceps force (N)</td>
<td>30</td>
<td>1188</td>
<td>784</td>
<td>0-3220</td>
</tr>
<tr>
<td>Knee abductor moment (Nm)</td>
<td>30</td>
<td>30.81</td>
<td>15.93</td>
<td>7.37-64.02</td>
</tr>
<tr>
<td>Knee extension moment (Nm)</td>
<td>30</td>
<td>25.03</td>
<td>26.47</td>
<td>-25.96-86.01</td>
</tr>
<tr>
<td>Quadriceps strength (Nm)</td>
<td>30</td>
<td>62.5</td>
<td>30.2</td>
<td>17.9-140.1</td>
</tr>
<tr>
<td>Hamstrings strength (Nm)</td>
<td>30</td>
<td>28.0</td>
<td>13.9</td>
<td>7.8-59.9</td>
</tr>
</tbody>
</table>

Figure 1: Mean (n=30) knee internal extension/flexion moments for the most affected and least affected legs. Positive values are extension moments and negative values are flexion moments.
Figure 2: Mean (n=30) internal knee abduction/adduction moments for most affected and least affected legs.

Relationship of Descriptive Characteristics With Knee Moments, Forces, and Strength

Unadjusted modeling showed significant associations between the following: race, sex, height, and weight with knee extension moment; sex, height, weight, and BMI with knee compression force; height and weight with quadriceps force; sex, height, and weight, with quadriceps strength; and race, sex, and height with hamstrings strength (Table 4). Correlation coefficients were strongest between height and knee extension moment \((r=0.49)\), quadriceps and hamstrings strength \((r=0.55 \text{ and } r=0.65)\), and between weight and compression and quadriceps forces \((r=0.71 \text{ and } r=0.47)\). Knee abductor moment was...
not significantly associated with any of the descriptive characteristics. Interestingly, height and weight were both significantly associated with knee extension moment and quadriceps force, while BMI was not.

**Table 4:** Unadjusted modeling results between participant descriptive characteristics and knee abduction and extension moments, knee forces, and knee strength. (p ≤ .05)

<table>
<thead>
<tr>
<th></th>
<th>Age</th>
<th>White</th>
<th>Female</th>
<th>Height</th>
<th>Weight</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Knee Abductor Moment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Nm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>r</td>
<td>-0.13</td>
<td>-0.04</td>
<td>-0.07</td>
<td>0.25</td>
<td>0.14</td>
<td>0.03</td>
</tr>
<tr>
<td>P-value</td>
<td>0.48</td>
<td>0.81</td>
<td>0.73</td>
<td>0.12</td>
<td>0.48</td>
<td>0.89</td>
</tr>
<tr>
<td><strong>Knee Extension Moment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Nm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>r</td>
<td>0.93</td>
<td>0.48*</td>
<td>-0.39*</td>
<td>0.49*</td>
<td>0.41*</td>
<td>0.19</td>
</tr>
<tr>
<td>P-value</td>
<td>0.63</td>
<td>0.008</td>
<td>0.03</td>
<td>0.005</td>
<td>0.03</td>
<td>0.32</td>
</tr>
<tr>
<td><strong>Compression Force</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(N)</td>
<td>-0.17</td>
<td>0.03</td>
<td>-0.61*</td>
<td>0.65*</td>
<td>0.71*</td>
<td>0.48*</td>
</tr>
<tr>
<td>P-value</td>
<td>0.37</td>
<td>0.88</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td>0.008</td>
</tr>
<tr>
<td><strong>Quadriceps Force</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(N)</td>
<td>-0.11</td>
<td>0.18</td>
<td>-0.20</td>
<td>0.46*</td>
<td>0.47*</td>
<td>0.27</td>
</tr>
<tr>
<td>P-value</td>
<td>0.57</td>
<td>0.34</td>
<td>0.31</td>
<td>0.01</td>
<td>0.01</td>
<td>0.15</td>
</tr>
<tr>
<td><strong>Quadriceps Strength</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Nm)</td>
<td>-0.13</td>
<td>0.32</td>
<td>-0.51*</td>
<td>0.55*</td>
<td>0.41*</td>
<td>0.17</td>
</tr>
<tr>
<td>P-value</td>
<td>0.53</td>
<td>0.09</td>
<td>0.005</td>
<td>0.003</td>
<td>0.03</td>
<td>0.39</td>
</tr>
<tr>
<td><strong>Hamstrings Strength</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Nm)</td>
<td>-0.16</td>
<td>0.41*</td>
<td>-0.50*</td>
<td>0.65*</td>
<td>0.31</td>
<td>-0.01</td>
</tr>
<tr>
<td>P-value</td>
<td>0.41</td>
<td>0.03</td>
<td>0.006</td>
<td>&lt;.001</td>
<td>0.11</td>
<td>0.95</td>
</tr>
</tbody>
</table>

* Indicates significant values

**Relationship of walking speed, 6-minute walk distance, K-L score, and WOMAC Pain and Function with Knee Moments, Forces, and Strength**

Table 5 presents the unadjusted (r) and adjusted (r^2) correlations between walking speed, 6-minute walk distance, affected knee K-L score, and WOMAC pain and function with knee moments, forces, and strength.
Table 5: Modeling results between walking speed, 6-minute walk distance, K-L score, and WOMAC pain and function. $r^2$ values were adjusted for race, gender, and weight. ($P \leq 0.05$)

<table>
<thead>
<tr>
<th></th>
<th>Speed</th>
<th>Distance</th>
<th>Affected knee K-L score</th>
<th>Dichotomous affected knee K-L $&gt;1$</th>
<th>WOMAC pain</th>
<th>WOMAC function</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Knee Abductor Moment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Nm)</td>
<td>r</td>
<td>0.02</td>
<td>0.07</td>
<td>0.35</td>
<td>0.40*</td>
<td>0.19</td>
</tr>
<tr>
<td></td>
<td>$r^2$</td>
<td>0.02</td>
<td>0.03</td>
<td>0.14</td>
<td>0.18</td>
<td>0.06</td>
</tr>
<tr>
<td><strong>Knee Extension Moment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Nm)</td>
<td>r</td>
<td>0.28</td>
<td>0.25</td>
<td>-0.11</td>
<td>-0.13</td>
<td>-0.32</td>
</tr>
<tr>
<td></td>
<td>$r^2$</td>
<td>0.63</td>
<td>0.63</td>
<td>0.66</td>
<td>0.66</td>
<td>0.64</td>
</tr>
<tr>
<td><strong>Compression Force</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(N)</td>
<td>r</td>
<td>0.42*</td>
<td>0.24</td>
<td>-0.04</td>
<td>0.07</td>
<td>-0.29</td>
</tr>
<tr>
<td></td>
<td>$r^2$</td>
<td>0.74†</td>
<td>0.65</td>
<td>0.64</td>
<td>0.60</td>
<td>0.64</td>
</tr>
<tr>
<td><strong>Quadriceps Force</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(N)</td>
<td>r</td>
<td>0.39*</td>
<td>0.31</td>
<td>-0.26</td>
<td>-0.12</td>
<td>-0.35</td>
</tr>
<tr>
<td></td>
<td>$r^2$</td>
<td>0.60†</td>
<td>0.56*</td>
<td>0.54</td>
<td>0.48</td>
<td>0.56*</td>
</tr>
<tr>
<td><strong>Quadriceps Strength</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Nm)</td>
<td>r</td>
<td>0.31</td>
<td>0.41*</td>
<td>-0.28</td>
<td>-0.13</td>
<td>-0.29</td>
</tr>
<tr>
<td></td>
<td>$r^2$</td>
<td>0.45</td>
<td>0.48</td>
<td>0.54*</td>
<td>0.44</td>
<td>0.44</td>
</tr>
<tr>
<td><strong>Hamstrings Strength</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Nm)</td>
<td>r</td>
<td>0.39*</td>
<td>0.53†</td>
<td>-0.26</td>
<td>-0.12</td>
<td>-0.30</td>
</tr>
<tr>
<td></td>
<td>$r^2$</td>
<td>0.45</td>
<td>0.52*</td>
<td>0.50</td>
<td>0.43</td>
<td>0.43</td>
</tr>
</tbody>
</table>

*indicates $p \leq 0.05$

†indicates $p \leq 0.01$

Unadjusted modeling showed that dichotomous affected knee K-L score greater than 1 was significantly associated with knee abductor moment ($r=0.40$), walking speed was significantly associated with compression and quadriceps forces ($r=0.42$ and $r=0.39$) and hamstrings strength ($r=0.39$), and 6-minute walk distance was significantly associated with quadriceps and hamstrings strengths ($r=0.41$ and $r=0.53$).

After adjusting for race, gender, and weight, significant associations were observed between walking speed and compression force; walking speed, 6-minute walk distance, WOMAC pain and WOMAC function with quadriceps force; affected knee K-L
score and quadriceps strength; and 6-minute walk distance and hamstrings strength. In Table 5, $r^2$ values describe the percentage of variance explained for each outcome after adjusting for race, sex, and weight. For example, walking speed explains 74% of the variance in compression force. R-squared significance was established at $p \leq 0.05$. 
CHAPTER 4

DISCUSSION

The purposes of this study were to examine the relationships between severity of obesity (defined by BMI) and radiographic evidence of knee OA and their associations with abnormal joint loading, muscular weakness, knee pain, and function.

Relationship between Obesity and Knee Joint Loads

Knee joint loads may be classified as either forces that act directly upon the knee or as moments that influence the direction of the force about the knee joint. Common knee joint loads include compressive and shear forces, and internal abductor/adductor and extension/flexion moments. The internal abductor moment is equivalent to the external adductor moment, that tends to cause stress on the medial compartment of the knee. The ground reaction force is directed to the medial side of the knee during walking, and its lever arm is the perpendicular distance from this force to the knee joint center. See Figure 3.

![Figure 3: External knee adduction moment](image)
The internal abductor moment counters the external adduction moment and is equal in magnitude to the adduction moment.\textsuperscript{36, 95} The internal extension moment is the response of the quadriceps muscles to the external knee flexion moments caused by the hamstrings.\textsuperscript{71, 55}

For a relatively small sample size, the cohort was heterogeneous in weight (68.9 kg-177.5 kg) and BMI (26.8 kg/m\textsuperscript{2}-57.7 kg/m\textsuperscript{2}). High BMI is associated with increased knee joint loads during walking.\textsuperscript{13, 74} Our participants had a mean BMI of 40.7 kg/m\textsuperscript{2}, indicating class III obesity (severe obesity), and we found a significant, positive association between BMI and knee compression force. Messier et al.\textsuperscript{72} found a significant association between larger forces relative to BMI (a ratio of body mass to body height) such that at a given walking velocity, a higher BMI increased the magnitude of the ground reaction forces. Obesity is an established risk factor for knee OA,\textsuperscript{3, 24, 56, 62} and our work supports previous findings that high BMI’s are associated with increased joint loads.\textsuperscript{72}

BMI was not associated with knee abduction or extension moments, or quadriceps force. This differs from the findings of Browning and Kram\textsuperscript{13} who, in a population with a mean BMI of 35.5 kg/m\textsuperscript{2}, concluded that obese subjects were walking with greater knee abduction moments compared to normal weight controls. Conversely, in a population where 50\% of the participants had a BMI value greater than 40 kg/m\textsuperscript{2}, Devita and Hortobagyi\textsuperscript{28} observed a lower average absolute knee net muscle moment (Nm) compared to lean controls. They tested 21 obese adults (mean BMI 42.3 kg/m\textsuperscript{2}) and 18 lean adults (mean BMI 22.7 kg/m\textsuperscript{2}) at self-selected and standard walking speeds, and found that obese subjects increased their knee flexion by 12\% in early stance, and
increased their ankle plantarflexion at toe off by 11%. Interestingly, they found that the joint torques and powers at the hip and knee were similar between lean and obese participants walking at the same velocity. When scaled for body mass, obese participants had a peak extensor torque that was 46% lower than the lean participants. The authors concluded that reduced knee flexion in early stance and the concurrent low extensor torque at the knee in obese participants suggested that their quadriceps force was either lower than, or equivalent to that in the lean participants. Furthermore, there was no significant difference between the total knee joint load in the obese and lean participants. In our analysis, high BMI was not associated with knee abduction or extension moments or quadriceps force, similar to the findings of Devita and Hortobagyi. It is possible that knee moments, which are surrogate measures of knee joint forces, are less sensitive than our observed knee joint loads that were derived from a torque-drive musculoskeletal model. These results suggest that as obesity increases above a certain threshold, individuals try to modify their gait to reduce knee-joint loads, and are partially successful, decreasing joint moments but not joint compressive forces.

Although we found a singular association between BMI and knee compressive force, body weight was positively associated with knee extension moment, compressive force, and quadriceps force. Indeed, there was a strong association between weight and compressive force (r = 0.71), whereas the association between BMI and compressive force was moderate (r = 0.48). Although Messier and colleagues and Browning and Kram both showed positive associations between ground reaction forces with higher BMI values, our significant associations between weight and knee extension moment, compressive force, and quadriceps force implies that weight may be a stronger predictor
of knee joint loads than BMI; although obesity, and not height or weight, is a risk factor for knee OA.

Greater walking speed was significantly associated with increased knee compressive and quadriceps forces. Walking speed accounted for 74% of the variance with compressive force, and 60% of the variance in quadriceps force. The high degree of variance in compressive and quadriceps force explained by walking speed was expected, given the Newtonian equation that force is equal to mass times acceleration. As our subjects walked faster, their knees were subjected to greater compressive and quadriceps forces. Repeated over time, these large forces may exacerbate the rate of cartilage destruction and ultimately influence the progression of knee OA. It has been previously demonstrated that people with OA walk slower to decrease the forces on their knee.\textsuperscript{11, 38, 104} We did not find an association between walking speed and knee abduction or extension moments. However, Browning and Kram\textsuperscript{13} found that peak external knee adduction moment increased with walking speed. This difference may be due to the fact that Browning and Kram\textsuperscript{13} analyzed their subjects at 6 different walking speeds, whereas we asked our subjects to walk at a self selected pace. Thus, their range of walking speeds was greater. Another possibility is that our participants may have modified their gait to walk slower and avoid increased stress and pain. Finally, there is the chance that a number of our obese participants may have had a valgus knee alignment (knock-knee), which acts to reduce the external knee adduction moment.\textsuperscript{48}

Our significant associations between height and increased knee extension moment, and increased compression and quadriceps forces suggests that taller people are placing more stress on their lower extremity and therefore may be more susceptible to OA.
progression. Taller people have longer lever arms, and because moments are a product of force and the distance this force travels, it follows that taller people (especially those who are overweight) would exhibit greater moments about their knees. Riyazi et al. found that taller (>180 cm vs. <160 cm) persons had a lower risk of familial OA, while Cerhan et al. found increasing height was inversely associated with OA progression in a cohort of older women. Cerhan et al. graded 6 radiographs for each participant (hands, cervical spine, lumbar spine, pelvis, knees, and feet) and measured full body OA using the criteria established by Kellgren and Lawrence (generalized OA in 3 or more joint groups with K-L score 2-4). Progression was defined as an increase in the number of sites with OA. After 1-9 years or 10-19 years follow-up, Cerhan and colleagues noted that shorter height in women was an independent risk factor for OA progression to new sites or joint groups. However, by measuring progression in all joints, they did not account for the fact that leg length would not affect upper body or trunk OA. We did not measure progression, only factors that have been associated with greater joint load, but we found height to be associated with an increase in joint loads. This association may not be detrimental if an individual is not obese, but further investigation into the independent association between height and knee OA progression is warranted.

In our sample, being tall and having knee OA, and being heavy and having knee OA were associated with a greater extension moment and compressive force; however, being obese and having knee OA was only associated with a greater compressive force. We speculate that our obese participants were trying to alter their walking mechanics to compensate for their larger forces, and while they adjusted their extension moments, they were less successful in lowering their compressive forces.
Being female was significantly associated with lower knee extension moments and compressive forces. These differences are surprising given that females are at a greater risk for knee OA compared to males.\textsuperscript{21, 22, 25} Males may have increased their extension moment and compressive force as an adaptation to stabilize the knee. Messier et al.\textsuperscript{71} and Schipplein and Andriacchi\textsuperscript{93} found associations between internal knee extension moments and compressive forces. The internal knee extension moment is a response to the external knee flexion moment, and may increase knee joint loading. At the same walking speed, Schipplein and Andriacchi\textsuperscript{93} found that osteoarthritic patients had a peak internal knee extension moment that was twice the magnitude of those of their healthy controls, as well as 16\% greater peak compressive force. Similarly, after adjusting for walking speed, Messier and colleagues\textsuperscript{71} noted a non-significant trend of 33\% higher peak internal knee extension moments in OA participants versus controls, coupled with an 8\% greater knee compressive force. An increased internal knee extension moment is an adaptive mechanism to stabilize the knee, but if it is too large, compressive forces also increase that can foster disease progression. The trends in our data (eg. tall, heavy males are associated with greater internal extension moments and compressive forces) support the work of others\textsuperscript{71, 93}, but more conclusive evidence is needed to adequately explain the relationship between higher extension moments and increased knee forces.

Caucasian participants had a significant, positive association with knee extension moment, but there was no association with knee abduction moment, or compressive and quadriceps forces. The larger knee extension moment may suggest that white participants adjusted their gait to improve stability, but this was not accompanied by an
increase in compression forces.\textsuperscript{71, 74, 93} Jordan and colleagues\textsuperscript{54} identified African Americans as being twice as likely as Caucasians to have OA progression, but the mechanism by which African American ethnicity increases progression is not well understood.

**Relationship between Obesity and Strength**

Previous research has shown that muscle strength tends to decrease with increasing body fat after adjusting for body weight.\textsuperscript{9, 57, 77} In our study, increased weight was associated with increased strength, as was increased height. There was no association between BMI, our measure of obesity, and quadriceps or hamstring strength. The independent associations between height and weight with strength were attenuated by obesity, as BMI was not associated with increased strength.

Being female was associated with decreased quadriceps and hamstrings strength, and because leg strength is associated with the compressive and quadriceps forces used to stabilize the knee, it may be surmised that muscular weakness contributes to the greater risk of knee OA in women. Schipplein and Andriacchi\textsuperscript{93} found that additional stability offered by compressive forces may exacerbate disease condition, however, failure to provide stability may also contribute to inefficient gait mechanics and accelerated disease state. Herein lies a “catch-22,” such that joint loads are needed to provide stability; however, excessive loads are a risk factor for OA incidence and progression.

Caucasian ethnicity was associated with greater hamstrings strength, and although not statistically significant, there was also an association between the Caucasian participants and quadriceps strength. Quadriceps weakness is common to persons with
knee OA and increases their risk for disability. Muscular weakness may promote damage to articular cartilage in the knee, leading to progression of the disease. Stronger leg muscles can improve gait, preventing uneven distribution of loads across the knee. Jordan and colleagues established African American ethnicity as a risk factor associated with radiographic progression of knee OA, and muscular weakness may be a factor which contributes to a greater risk of progression in African Americans. The role muscular weakness plays in this association merits further investigation.

**Relationship between Knee OA and Knee Joint Loads**

The internal knee abduction moment (equivalent to the external adduction moment) is a measure of the varus torque at the knee that adducts the knee during gait. Increased loads on the medial compartment of the knee indicate greater internal knee abduction moments that accelerate progression of medial tibiofemoral OA. Our results support this work, as participants with a dichotomous K-L score greater than 1 had a significantly greater internal abduction moment (r=0.40). When analyzing the non-dichotomous K-L scores, the abduction moment increased with increasing K-L scores, but this relationship was not significant.

After heel strike, gravity and inertia create a moment that tends to flex the knee. The quadriceps muscles act eccentrically to control the downward movement of the body, and thus a decrease in the extension moment suggests a decrease in quadriceps muscle force. Such a pattern is termed “quadriceps avoidance,” and knee OA patients frequently display this pattern to avoid increased stress on the knee during gait. Baliunas et al. and Landry et al. found that subjects with knee OA have a decreased extension moment and
an increased internal flexion moment during gait. This pattern avoids pain-inducing compressive and quadriceps forces by relying upon the hamstrings during the gait cycle to maintain stability. We showed no significant correlation between K-L score and knee extensor moment, indicating that in our small sample, higher K-L scores were not related to knee extensor moments.

Joint pain is the cardinal symptom of knee OA and pain reduction is a prime objective for those suffering from the disease. To avoid pain, OA patients often adopt inefficient gait mechanics. Teichtahl et al.\textsuperscript{107} observed an inverse relationship between peak external knee adduction moment and knee pain during the late stance phase of gait in 20 women with knee pain, but without radiographic evidence of knee OA. These results may be attributed to the heterogeneity of knee alignments, but they suggest that women with knee pain adopt a gait pattern that reduces their external knee adduction moment and, as a result, their medial tibiofemoral load. In our examination of the first 50\% of the gait cycle, no significant associations were found between knee pain and the external adduction moment.

African American ethnicity was related to smaller extension moments, suggesting that they walked with a pattern more indicative of quadriceps avoidance. As previously mentioned, this pattern is linked to OA progression and African Americans are more prone to OA progression.\textsuperscript{54} To our knowledge, no previous study has associated African American ethnicity with quadriceps avoidance gait. Our data also showed that African Americans tended to be weaker in their hamstrings and quadriceps. Muscular weakness and decreased extension moments may be mechanisms that contribute to the greater risk of OA progression in African Americans. We used an unadjusted, linear regression
model for this analysis, and it is possible that these relationships may not have existed had we adjusted for co-variants such as weight or BMI. We can not imply cause and effect based on associations, but it would be interesting to examine these relationships in a larger data set.

Increased pain and decreased function assessed by the WOMAC were negatively associated with quadriceps force. Both variables explained 56% of the variance in quadriceps force, respectively, suggesting that as pain increases and function decreases, participants make an effort to reduce the load on their knee by altering their gait. Hurwitz et al.49 showed that increased knee pain (suggesting worse disease severity) results in a significantly reduced external knee adduction moment (equivalent to an internal knee abduction moment). We found the opposite was true, as a K-L score greater than 1 was associated with a greater internal abduction moment. The relationship between increased pain and greater internal abduction moments was moderately significant, suggesting that greater internal abduction moments could exacerbate pain and disease progression.

**Relationship between Knee OA and Strength**

Older adults with knee OA consistently demonstrate reduced quadriceps strength compared to healthy, age-matched peers. Slemenda et al.97 showed that men and women with knee OA had 20% less quadriceps strength than individuals without the disease, while Messier and colleagues75 found that older adults with knee OA had 22% to 39% less quadriceps strength than their peers. Strength accounts for 28% of the variability associated with balance, and rapid declines in strength can foster the onset of disability
and injury.\textsuperscript{52, 75} Our results agree. In the present sample, we found that knee extensor strength was negatively associated with affected knee K-L score, such that increased K-L score was related to reduced strength.

There was a significant, positive association between walking speed and 6-minute walk distance with hamstrings strength. With increased walking speed, it was observed that hamstrings strength increased ($r=0.39$), and increased hamstring strength was positively associated with distance walked in 6-minutes ($r=0.53$), explaining 52\% of the variance. Increased quadriceps strength was significantly associated with 6-minute walk distance, such that stronger quadriceps produced a greater distance walked in 6-minutes ($r=0.41$). We expected to see these relationships, as these underscore the importance of muscular strength in maintaining activities of daily living in older adults with knee OA.\textsuperscript{66, 82, 97}

Greater forces are required to increase walking speed. People with OA often walk slower in an attempt to decrease the forces across the knee. Brinkman and Perry\textsuperscript{11} compared healthy and arthritic subjects, and found that healthy subjects ambulate at 1.33 m/s (2.98 mph), while the osteoarthritic subjects walked at 0.63 m/s (1.5 mph). Although not statistically significant, the difference in walking speed between groups was substantial. We found increased walking speed was associated with increased compressive and quadriceps forces and the slow mean walking speed in our cohort (1.13 m/s) may have been an attempt to reduce these forces.
Inter-subject Gait Variability

While mean values provide insight into group tendencies, examining inter-subject variability provides additional information on how people with knee OA adjust to their disease. Average peak knee extension moment for the population was 25.03 Nm, with a range of -25.96 Nm to 86.01 Nm. The mean BMI for the population was 40.7 kg/m$^2$, average K-L score was 2.66, and the average WOMAC pain score was 7.80 (0= no pain, 20= severe pain). The minimum peak knee extension value of -25.96 Nm indicates that at least one individual failed to exert an extension moment and used a flexion moment to stabilize their knee. Such a gait pattern is indicative of extreme quadriceps avoidance, and may have been adopted as a result of a high BMI. Indeed, this participant’s BMI was 41.7 kg/m$^2$, indicating severe obesity. Figure 3 displays the mean knee flexion/extension moment for both most affected and least affected legs of the population as compared to the flexion/extension moment for the most affected leg of the participant with a peak extension moment of -25.96 Nm. Here the absence of any extensor moment during the stance phase supports the work of Devita and Hortobagyi$^{28}$ that indicate as BMI increases, extensor moments decrease.
Figure 4: A) Mean knee extension moment of the population for most affected and least affected legs. B) Peak extension moment of the participant who was completely flexed in the first 50% of the gait cycle.

A)

B)
Limitations

Our study was limited by a small sample size (n=30) that contributes to low statistical power. Additionally, we did not determine knee alignment (varus or valgus), hence we could not control for a major risk factor for OA incidence and progression.12 Finally, although we used linear regression models to analyze our relationships, we have not yet subjected the data to a multiple regression analysis.

Conclusion

It is known that obesity is a major risk factor for OA, and that more severely obese people and individuals with more severe knee OA are at risk for poorer gait mechanics and decreased strength.72, 75 These factors may exacerbate the disease condition and impair function and mobility to an extent that may elevate risk of injury and disability.52, 73

Our results confirmed an association between high BMI and increased compression force, further emphasizing the clinical importance of obesity to incident knee OA. Body weight was significantly associated with the knee extension moment, compressive force, and quadriceps force, indicating that larger body weight is related to the need to exert more force to stabilize the knee.

Males were associated with higher extension moments and compressive forces, two factors that may accelerate the onset of knee OA and progression. This association in males was surprising given that females are at a greater risk of OA. African Americans were associated with a decreased extension moment that is indicative of quadriceps avoidance gait, and had significantly weaker hamstrings strength, and
borderline significantly weaker quadriceps strength. Because African Americans are more prone to OA progression, our work suggests that more quadriceps avoidance and lower strength are two factors that may contribute to their susceptibility to knee OA progression. Investigation of this relationship in a larger sample is needed.

Our finding that the internal abductor moment in individuals with K-L score greater than 1 supports the common association between internal knee abductor moment and an increased risk of incident and progressive knee OA. We further confirmed associations between walking speed and knee joint loads, as well as between knee strength and function. Future investigations are needed to determine the singular importance of each of these associations and their impact on OA incidence and progression.
Appendix A

Biomechanical knee model

The biomechanical model of the knee calculates compressive, anterior-posterior shear, and resultant joint forces within the tibio-femoral compartment of the knee. The model includes two basic components. The first component is a three dimensional inverse dynamics analysis of the lower extremity to obtain the joint torques and reaction forces at the hip, knee, and ankle. The second component uses these results along with the kinematic description of the person’s lower extremity and related anatomical and physiological characteristics to calculate knee muscle, lateral ligament, and joint forces during the stance phase of walking.

The lower extremity was modeled as a rigid, linked segment system. Magnitude and location of the segmental masses and mass centers in the lower extremity along with their moments of inertia were estimated from the position data using a mathematical model and relative segmental masses reported by Dempster. Inverse dynamics using linear and angular Newtonian equations of motion was used to calculate the joint reaction forces and torques at each joint. This process included applying the ground reaction forces to the foot at the center of pressure and calculating the three dimensional net joint reaction forces and torques at the ankle applied to the foot. The net forces and torques were then reversed and applied to the leg and the process was repeated for the knee net reaction forces and torques. The knee kinetics were then be used to calculate the hip forces and torques. This analysis is a standard biomechanical procedure.

The second component of the model calculates the forces in the three largest knee muscles and lateral soft tissue support structures (e.g. lateral collateral ligament) and
combines these with the knee joint reaction forces to determine the bone-on-bone forces. The model is a “torque-driven,” model in that it uses the joint torques from the inverse dynamic analysis to determine the muscle forces (Figure 4). This general technique has been successful in predicting forces in various joints and soft tissues in the lower extremity\textsuperscript{34,86}. The three basic steps in this component of the model are: 1) determine the forces in the gastrocnemius, hamstrings, and quadriceps muscles and in the lateral support tissues in the knee, 2) apply these forces along with the joint reaction forces onto the tibia and 3) determine the knee joint forces.

Figure 5: Planar representation of the biomechanical model of forces acting on the knee.

The gastrocnemius force is determined from the plantar flexor moment at the ankle joint during the stance phase of gait. It is assumed that the plantar flexor torque is produced by the triceps surae (gastrocnemius and soleus muscles) and the tibialis anterior, that is co-active with the gastrocnemius during the initial 25% of the stance phase\textsuperscript{21}. Triceps surae force was calculated as the quotient of the ankle joint torque and
the moment arm for the triceps surae at the observed angular position of the ankle joint
plus the additional 10% increase in force due to dorsiflexor coactivity. Muscle moment
arm values for each ankle position were from moment arm-ankle joint position curves
from the literature. Gastrocnemius force was then calculated from triceps surae force
based on its proportion of the total physiological cross sectional area (PCA) of the triceps
surae which is 0.319.

The direction of the gastrocnemius force was determined from the heel and knee
marker positions and is expressed as $\alpha$, the angle between the gastrocnemius force and
the tibia. The heel marker was used to represent the distal end of the gastrocnemius. The
proximal end was positioned 0.020 m superior and 0.023 m posterior to the knee joint,
along the line of the femur. This position accounted for the gastrocnemius wrapping
around the femoral condyles. The resultant direction of the gastrocnemius force was, on
average, about $\alpha = 3^\circ$ from parallel with the leg and so this force applied a relatively
large compressive load but small shear load on the knee.

Hamstrings force was calculated from the extensor torque at the hip joint
observed typically during the first half of stance. The predicted hamstrings force
accounted for both the hamstrings PCA (physiological cross-sectional area) relative to
the total PCA of the hamstrings and gluteus maximus and the hamstrings moment arm
at the hip relative to the gluteus maximus moment arm. The total hamstrings proportion
to the hip torque was calculated as:

$$ H_p = \left( \frac{\text{Ham PCA}}{\text{Ham PCA} + \text{GM PCA}} \right) \times (\text{Hd} \times \text{GMd}) \quad \text{Equation (5)} $$
where \( H_p \) is the proportion of the hip extensor torque generated by the hamstrings, \( \text{Ham PCA} \) and \( \text{GM PCA} \) are the hamstrings and gluteus maximus PCAs, and \( \text{Hd} \) and \( \text{GMd} \) are the hamstrings and gluteus maximus moment arms. Values for each of these constants are obtained from the literature \( (6; 24) \) and are: \( \text{Ham PCA} = 42.4 \text{ mm}^2 \), \( \text{GM PCA} = 17.36 \text{ mm}^2 \), \( \text{Ham d} = 0.042 \text{ m} \), and \( \text{GM d} = 0.047 \text{ m} \). The proportion of the hip extensor torque generated by the hamstrings \( (H_p) \) was equal to 0.63. The hamstrings force was then calculated as:

\[
H = H_p \frac{(H_{et})}{H_d} \quad \text{Equation (6)}
\]

where, \( H \) is the hamstrings force and \( H_{et} \) is the hip extensor torque. Hamstrings force is assumed to be zero when the hip torque is in the flexor direction. The direction of the hamstrings force is a line parallel to the femur and at angle \( \beta \) to the tibia.

The quadriceps force was calculated from the observed knee joint torque produced by the inverse dynamic analysis and the hamstrings and gastrocnemius forces. This calculation took into account co-contracting knee flexors. The observed knee torque was the net torque at the knee and is a function of all muscles crossing the joint:

\[
K_t = Q (Q_d) - H (H_d) - G (G_d) \quad \text{Equation (7)}
\]

where \( K_t \) is the net knee torque from inverse dynamics, \( Q \), \( H \), and \( G \) are the forces by the patellar tendon, hamstrings and gastrocnemius muscles, and \( Q_d \), \( H_d \), and \( G_d \) are the respective moment arms for the muscles at the knee. The force in the quadriceps, \( Q \), was then calculated as:
\[ Q = \frac{(Kt + H(Hd) + G(Gd))}{Qd} \quad \text{Equation (8)} \]

Moment arms at the knee were obtained from the literature by averaging the values from a number of studies and for each angular position of the knee joint\textsuperscript{37, 96, 103}. The mean values throughout the knee ROM for the three moment arms were, \( Qd = 0.035 \) m, \( Hd = 0.032 \) m, and \( Gd = 0.018 \) m. The direction of \( Q, \phi \), was determined from the literature\textsuperscript{74, 103} and is also a function of knee angle.

The methods of Schipplein et al.\textsuperscript{93} were used to determine the distribution of frontal plane loads and in particular the force in the lateral support structures at the knee during the stance phase. The external loads place an adductor torque on the knee that is resisted by a combination of abductor torques from the quadriceps and the lateral structures. The quadriceps exerts a small to moderate abductor torque during walking because the center of pressure between tibia and femur is located on the medial tibial plateau which is medial to the center of the patellar tendon. The moment arms for the quadriceps and lateral support structures to the center of pressure on the medial tibial plateau are estimated from the X-ray films for each subject. These distances average \(~2.5\) cm and \(~7.0\) cm, respectively. The quadriceps abductor torque (product of the quadriceps force and its frontal plane lever arm) is subtracted from the observed net internal abductor torque calculated by the inverse dynamic analysis. The remaining torque is distributed to the lateral knee tissues and the force in these tissues is calculated as the quotient of this torque and the lever arm. This force is considered to act parallel with the line of the tibia.
The final step was the calculation of knee joint forces. All muscle forces, the force in the lateral support structures and the joint reaction forces identified with inverse dynamics were partitioned into their compressive (parallel with the tibia) and anteroposterior shear (perpendicular to the tibia in the frontal plane) components and summed. The equations were:

\[
K_s = G \sin \alpha - H \sin \beta + Q \sin \phi - K_z \sin \lambda + K_y \cos \lambda \quad \text{Equation (9)}
\]

\[
K_c = G \cos \alpha - H \cos \beta + Q \cos \phi - K_z \cos \lambda + K_y \sin \lambda + L_{ss} \quad \text{Equation (10)}
\]

Where \(K_s\) and \(K_c\) are the shear and compressive forces at the knee, \(K_z\) and \(K_y\) are the vertical and horizontal knee joint reaction forces, and \(L_{ss}\) is the force in the lateral support structures. \(K_s\) is positive when the shear force applies an anterior load to the tibia and \(K_c\) is positive when the compressive force pushes into the tibia.

The primary limitation of the biomechanical knee model is the absence of most knee ligaments. The absence of cruciate and medial collateral ligaments would have increased the knee muscle force predictions since these tissues resist all external loads. The model does include the lateral collateral ligament, which is important and produces the principle, non-muscular restraint during the stance phase of walking.

A secondary limitation was the assumption of no coactivation by the hip flexors during stance. The assumption of no co-activity at the hip introduced some error due to missing force production in the rectus femoris which also applied force at the knee. This issue was relevant during the initial part of the stance phase when the hamstrings are active and producing force. Thus the predictions of hamstrings force and subsequently,
quadriceps and knee forces were probably underestimated. However, force in the rectus femoris during the first half of stance and relative EMG activation of this muscle among others, were relatively low. However, the model did include co-activation of knee flexors and extensors, and ankle dorsiflexors and plantar flexors during the stance phase.

The peak muscle force predictions from our model (in bodyweights, BW) compare well to the muscle force predictions from other studies.\textsuperscript{27, 93} Values from the literature indicate a mean hamstrings force of 1.1 BW, quadriceps force of 2.3 BW, and gastrocnemius force of 1.3 BW. Our model predicts a mean hamstrings force of 1.3 BW, quadriceps force of 2.7 BW, and gastrocnemius force of 1.3 BW.
## Appendix B

### Table 6: Reflective Markers Placement

<table>
<thead>
<tr>
<th>Description</th>
<th>Eva/EvoRT Marker Name</th>
<th>Static</th>
<th>Full Body</th>
<th>Min Head</th>
<th>Placement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left Lateral Knee</td>
<td>L.Knee Lateral</td>
<td>+</td>
<td></td>
<td></td>
<td>Along the flexion/extension axis of rotation at lateral femoral condyle</td>
</tr>
<tr>
<td>Right Lateral Knee</td>
<td>R.Knee Lateral</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left Medial Knee</td>
<td>L.Knee Medial</td>
<td></td>
<td></td>
<td></td>
<td>Along the flexion/extension axis of rotation at medial femoral condyle</td>
</tr>
<tr>
<td>Right Medial Knee</td>
<td>R.Knee Medial</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left Lateral Ankle</td>
<td>L.Ankle Lateral</td>
<td></td>
<td></td>
<td></td>
<td>Along the flexion/extension axis of rotation at lateral malleolus</td>
</tr>
<tr>
<td>Right Lateral Ankle</td>
<td>R.Ankle Lateral</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left Medial Ankle</td>
<td>L.Ankle Medial</td>
<td></td>
<td></td>
<td></td>
<td>Along the flexion/extension axis of rotation at medial malleolus</td>
</tr>
<tr>
<td>Right Medial Ankle</td>
<td>R.Ankle Medial</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper L. Thigh Array</td>
<td>L.Thigh Upper</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>On the lower thigh below the mid-point for best visibility by all cameras</td>
</tr>
<tr>
<td>Front L. Thigh Array</td>
<td>L.Thigh Front</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rear L. Thigh Array</td>
<td>L.Thigh Rear</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper R. Thigh Array</td>
<td>R.Thigh Upper</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Front R. Thigh Array</td>
<td>R.Thigh Front</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rear R. Thigh Array</td>
<td>R.Thigh Rear</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper L. Shank Array</td>
<td>L.Shank_upper</td>
<td>+</td>
<td></td>
<td></td>
<td>On the lower shank below the mid-point for best visibility by all cameras</td>
</tr>
<tr>
<td>Front L. Shank Array</td>
<td>L.Shank_front</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rear L. Shank Array</td>
<td>L.Shank_rear</td>
<td></td>
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</tr>
<tr>
<td>Upper R. Shank Array</td>
<td>R.Shank_upper</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Front R. Shank Array</td>
<td>R.Shank_front</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rear R. Shank Array</td>
<td>R.Shank_rear</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Left Toe</td>
<td>L.Toe</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Center of the foot between the 2nd and 3rd metatarsal</td>
</tr>
<tr>
<td>Right Toe</td>
<td>R.Toe</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left Heel</td>
<td>L.Heel</td>
<td>+</td>
<td></td>
<td></td>
<td>Posterior Calcaneus at same height form floor as toe marker</td>
</tr>
<tr>
<td>Right Heel</td>
<td>R.Heel</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left ASIS</td>
<td>L.ASIS</td>
<td>+</td>
<td></td>
<td></td>
<td>Anterior Superior Iliac Spine</td>
</tr>
<tr>
<td>Right ASIS</td>
<td>R.ASIS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sacrum</td>
<td>V.Sacral</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Superior Aspect at the L5-sacral Interface</td>
</tr>
<tr>
<td>Left Shoulder</td>
<td>L.Shoulder</td>
<td>+</td>
<td></td>
<td></td>
<td>Tip of the Acromion Process</td>
</tr>
<tr>
<td>Right Shoulder</td>
<td>R.Shoulder</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left Elbow</td>
<td>L.Elbow</td>
<td>+</td>
<td></td>
<td></td>
<td>Lateral Epicondyle of the Humerus</td>
</tr>
<tr>
<td>Right Elbow</td>
<td>R.Elbow</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Left Wrist</td>
<td>L.Wrist</td>
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<td></td>
<td></td>
<td>Centered between the styloid processes of the Radius and Ulna</td>
</tr>
<tr>
<td>Right Wrist</td>
<td>R.Wrist</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Back of the Head</td>
<td>Rear Head</td>
<td>+</td>
<td></td>
<td></td>
<td>On the front and back of the head at the same height above the floor</td>
</tr>
<tr>
<td>Front of the Head</td>
<td>Front Head</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Top of the Head</td>
<td>Top Head</td>
<td>+</td>
<td></td>
<td></td>
<td>On the center of the head, in line with the front and back markers</td>
</tr>
<tr>
<td>Left Scapula</td>
<td>L.Scapula</td>
<td>+</td>
<td></td>
<td></td>
<td>Inferior Aspect of the scapula</td>
</tr>
</tbody>
</table>
Figure 6: Reflective Marker Set


CURRICULUM VITA

BENJAMIN D. PIERCE

EDUCATION:  

Wake Forest University, Winston-Salem, NC

**B.S. Exercise/Sport Science**, May 2007  
Elon University, Elon, NC

HONORS:  
Omicron Delta Kappa National Leadership Fraternity, 2006

EXPERIENCE:  

**Project Coordinator**, August 2008–present  
Fatty acids, Arthritis, and inflammation in the Elderly (FAME)  
Wake Forest University, Winston Salem, NC

- Recruit, screen, and test 30 research participants using a 3-D motion analysis system and an isokinetic dynamometer.
- Develop and lead bi-weekly healthy lifestyle classes related to nutrition, fatty acids, and osteoarthritis for study participants.
- Author of research thesis titled: “The Severity of Obesity and Knee Osteoarthritis: Effects on Gait and Strength”

**Exercise Leader**, August 2007–present  
Healthy Exercise and Lifestyle Programs (HELPS)  
Wake Forest University, Winston Salem, NC

- Supervise 150 at-risk participants with cardiovascular disease during morning and afternoon exercise sessions.
- Perform submaximal treadmill exercise testing of participants while monitoring 12-lead ECG readings and blood pressure.

**Instructor, HES 101: Exercise for Health**, August 2007–present  
Wake Forest University, Winston Salem, NC

- Independently teach two, half semester sections of undergraduate students about exercising to prevent chronic disease.
- Administer homework assignments, papers, and exams. Report final grades to academic authorities.
Biomechanics Teaching Assistant, August 2008-December 2008  
J.B. Snow Biomechanics Lab  
Wake Forest University, Winston Salem, NC  
• Assisted in teaching first-year graduate students to collect data using 3-D motion analysis cameras and equipment, isokinetic dynamometer, analog data acquisition equipment (force plate), and goniometers.  
• Taught undergraduates to palpate joint locations and affix joint markers for motion analysis. Trained them to use ULead Video Studio 7 and Video Expert II software to analyze human movement.

Project Coordinator, February 2008-May 2008  
Intensive Dietary Restriction and Exercise in Arthritis (IDEA)  
Wake Forest University, Winston Salem, NC  
• Scheduled participant visits in cooperation with Wake Forest University Baptist Medical Center, Wake Forest University Clinical Research Center, and the Wake Forest University J.B. Snow Biomechanics Laboratory for a National Institute of Health R01 grant  
• Assisted in data collection of participant gait, strength, and balance data

Undergraduate Research Assistant, August 2006-December 2006  
Health and Human Performance Department  
Elon University, Elon, NC  
• Investigated the effects of various distraction stimuli on exercise efficiency, physiological responses, and perceived exertion.

Health and Wellness Coordinator Intern, June 2006-August 2006  
Verizon Wireless, Laurel, MD  
• Performed fitness assessments and interpreted results for clients.  
• Prescribed exercise programs and individually trained members.

SKILLS AND CERTIFICATIONS:  
BLS for Healthcare Providers (CPR and AED), American Heart Association  
Project management, 3D Motion Analysis (Force Plate), Isokinetic dynamometer testing.

COMPUTER SOFTWARE EXPERIENCE:  
MS Office, EvArt, EndNote, Orthotrak, SPSS