

OBESITY, MODERATE KNEE OSTEOARTHRITIS, AND KNEE JOINT
DYNAMICS

by

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at

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DALHOUSIE UNIVERSITY
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Abstract

Knee osteoarthritis (OA) is a significant cause of pain and disability in adult populations. Obesity is a highly cited risk factor for knee OA that has been associated with increased risk of radiographic OA, symptomatic OA, and accelerated disease progression. Rates of obesity are increasing internationally, and while obesity is well established as a risk factor, the precise role of obesity in knee OA pathogenesis and progression is not as clearly understood.

Mechanical loading has been implicated as an important factor in knee OA initiation and progression. As walking is one of the activities of daily living that places the highest frequency load on the lower extremity, many studies have investigated biomechanical loading alterations associated with knee OA through the application of modern gait analysis techniques. Previous research has also investigated biomechanical alterations associated with obesity during walking in an effort to better characterize loading changes occurring in obese subjects. However, no studies have investigated the interacting biomechanical effects of knee OA disease presence and obesity together. The purpose of this thesis was to further examine the roles of moderate knee OA disease presence and obesity on knee joint mechanics during gait, and to characterize their mechanical interaction.

Two methods have been applied to investigate dynamic biomechanical effects of these two factors as well as effects of their interaction. In the first study, the method of principal component analysis has been applied to resultant waveforms from gait analysis. In the second study, a sagittal plane joint contact force model has been applied to further characterize the local loading experienced by tibio-femoral articular cartilage. Severe knee OA disease presence is associated with highly variable mechanical gait alterations and as such, this thesis has focused on the moderate stage of knee OA disease progression in order to better characterize simultaneous underlying alterations associated with obesity.

In both studies, statistical differences in biomechanical loading parameters have been found in association with obesity, moderate knee OA, and their interaction. In the first study the findings suggest that the mechanical process of knee OA development is different depending on body mass index (BMI), or that individuals with different BMI categories adapt differently to the early changes associated with knee OA. In the second study an absolute increase in loading for obese subjects both in compressive and anterior-posterior shear directions was found. In addition, the second study has shown that moderate knee OA disease presence and obesity interact and are related to alteration of the quadriceps force, demonstrating what may be a compensation strategy to manage shear forces. Given the increasing prevalence of obesity, these findings have important implications for knee OA disease management and the development of treatment strategies.

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Chapter 1 - Introduction

1.1 Introduction

Knee osteoarthritis (OA) is an increasingly common cause of pain and disability, but its pathogenesis remains unclear. The osteoarthritis disease process is highly complex, involving numerous metabolic and mechanical aspects and is highly variable in presentation of clinical symptoms. Many treatment strategies exist, although none have been shown to significantly impede the progression of the disease, and total knee replacement is ultimately necessary in most cases.

Obesity is the most significant modifiable risk factor associated with knee osteoarthritis, and increasing rates of obesity are therefore important contributors to this disease's societal burden. But, the role of obesity in knee osteoarthritis initiation and progression is not clearly established. Both metabolic and mechanical aspects of the disease process have been investigated, but researchers have presented arguments suggesting the importance of mechanical as opposed to systemic metabolic effects.

Indeed, the important role of dynamic mechanical loading during walking as a high frequency daily activity is underlined throughout the knee OA literature, and the focus of this research will be to study the effects of obesity on dynamic loading conditions early in the disease process. In this thesis, it is hypothesized that obesity will contribute to alterations in knee mechanics resulting in increased dynamic joint loads, which then play an important role in the articular cartilage wear and tear characteristic of OA. It is also hypothesized that the alterations in knee mechanics associated with

obesity will be affected by moderate knee osteoarthritis disease presence. These hypotheses will be examined through gait analysis and joint contact force modeling.

1.2 Objectives

Current conservative treatment options for knee osteoarthritis are not effective, leaving joint replacement as the outcome of knee OA for too many patients. With increasing rates of obesity, the need to understand the interaction between obesity and knee osteoarthritis is growing. Joint loading is believed to be a critical factor in the onset and progression of knee OA, and as such, loads at the knee will be considered through the multi-factor analysis of mechanical aspects of gait in obese subjects. To further develop the characterization of the dynamic loading environment at the knee, joint contact forces will also be determined through an empirical muscle model. Although TKR is effective in reducing pain and restoring function, results from this work may help to suggest conservative treatment options for knee OA patients preventing subjects from requiring this highly invasive procedure. Weight loss combined with other conservative strategies that may alter knee joint loading patterns during gait may be recommended as a preventative measure in knee OA based on knowledge of pathomechanics as opposed to observational studies. Treatment strategies that would be based on an evaluation of the dynamic function of the knee may be developed to complement the pain management strategies available for moderate knee OA subjects at this time. Knowledge of joint

biomechanics may also provide information regarding those obese individuals who may be at increased risk of knee OA development and progression and those who are not.

1.2.1 Objective 1: Alterations in Biomechanical Gait Patterns

In order to understand the relationship between obesity and knee OA, there is a need for better multi-factored consideration of the problem. An effort needs to be made to distinguish possible effects of obesity from those of knee OA and at the same time to better characterize their interaction. Also, there is a need to include alterations in gait mechanics which may not be described by peak parameters, but which are only captured when including waveform differences as measured by PCA. Therefore the first objective is: *to examine the interacting role of early to moderate knee osteoarthritis and overweight/obesity on the pattern of resultant mechanical aspects of gait.* It is hypothesized that biomechanical changes in gait will be associated with overweight and obesity and with the presence or absence of moderate knee OA. It is further hypothesized that biomechanical changes will occur in association with the interaction between moderate knee OA disease presence and increased body mass index.

1.2.2 Objective 2: Alterations in Knee Joint Contact Forces

The results of the first objective in this work are limited by the fact that conventional inverse dynamics gait analysis provides net joint forces and moments but not contact forces between articulating joint surfaces. In order to gain a more complete

picture of the dynamic loading environment at the knee and its role in moderate osteoarthritis disease development with obesity, a muscle model of walking will be used. Therefore the second objective is: *to examine the interacting role of early to moderate knee osteoarthritis and overweight/obesity on tibio-femoral joint contact forces during gait*. It is hypothesized that joint contact forces will be higher in obese subjects and that alterations to joint contact forces will occur in conjunction with alterations to forces in the quadriceps, hamstrings and gastrocnemius muscles. It is further hypothesized that moderate knee OA, and the interaction between moderate knee OA and obesity will be associated with alterations in knee joint contact forces.

1.3 Structure of Thesis

The structure of this thesis is broken into a literature review, two studies which have been written for journal publication, and a conclusions and future directions chapter. Chapter 2 of the thesis gives a general background and literature review on obesity, osteoarthritis, gait analysis, and joint contact force modeling. Chapter 3 addresses the first objective of the thesis and describes the methods of gait analysis and principal component analysis. Chapter 4 addresses the second objective of the thesis, and describes the contact force modeling method that has been applied. Chapters 3 and 4 have each been written as stand-alone submissions for journal publication and therefore include some redundancy with Chapter 2 and each other. Chapter 3 has already been submitted for publication in *Osteoarthritis and Cartilage* and we are currently submitting a revised version after a first review. Chapter 5 summarizes the thesis, discusses its implications and limitations, and provides concluding remarks including direction for future work.

Chapter 2 - Background

2.1 Introduction

2.2 Knee Osteoarthritis

Osteoarthritis is the most common type of degenerative joint disease and a leading cause of disability in the elderly worldwide¹². It is characterized by the gradual degradation and eventual loss of articular cartilage, sclerosis of underlying subchondral bone, osteophyte formation, joint laxity and joint space narrowing³. The etiology of initiation and progression of osteoarthritis are multifactorial and highly complex, as is evident in recent definitions depicting osteoarthritis as a group of distinct diseases overlapping in clinical symptoms – typically pain, stiffness, limitation of movement, crepitus, effusion, and local inflammation – as opposed to previous definitions which viewed osteoarthritis as a single pathological process⁴.

Presentation of clinically relevant symptoms in knee OA is highly variable. As a result, the majority of epidemiological studies focus on the prevalence of radiographic evidence of the disease – most commonly involving joint space narrowing, osteophyte formation, and subchondral sclerosis⁵. It is based on this radiographic evidence that osteoarthritis has been recognized as a leading cause of disability in elderly persons with a prevalence of greater than 50% in those aged 65 or older in western cultures⁵. The prevalence of arthritis in Canada for those aged fifteen years or older was 16% in the year 2000, and is projected to increase to above 20% by the year 2026 partly as a result of the rapidly aging Canadian population⁶. Given that osteoarthritis is the most common form

of arthritis and rheumatism¹, this implies a projected increase in the prevalence of OA among Canadians⁶. Also interestingly, residents of Nova Scotia report arthritis and rheumatism significantly more frequently than residents of other Canadian provinces and territories, at a rate of 23%⁶.

Most studies have shown that the knee is the most commonly affected joint⁷, with the rate of knee osteoarthritis being significantly greater than the rate of hip OA. Osteoarthritis is also the most common diagnosis made in older adults with knee pain⁸. Given the prevalence of OA in general, both in Canada and internationally, and given that the knee is the most commonly involved joint, knee OA stands to place an increasingly large burden on individuals and on social and health care systems in the years to come. In fact, knee OA is likely to become the fourth most important cause of disability in women and eighth most important in men around the globe⁹.

In spite of the prevalence of this disease, the causes of knee OA are not completely understood¹⁰. The disease process involves complex alterations in mechanical and metabolic properties of cartilage, subchondral bone and synovial mediators as well as changes in neuromuscular control making assessments of causality difficult. Secondary knee OA is a result of joint injury, trauma, surgery, or infection, either proximal or remote in time to the onset of the disease, but the pathogenesis of primary knee OA remains unclear¹¹.

Conservative treatment options are available for osteoarthritis, but almost all of them are treatments of symptoms and do not have demonstrated effects on disease progression¹². Mechanical conservative treatment options are available, including valgus unloader braces, lateral shoe wedges, and deliberately altered gait patterns. Conservative

treatment through pharmaceuticals such as non-steroidal anti-inflammatory drugs (NSAIDS) and supplements including glucosamine and chondroitin are often only marginally beneficial in comparison to placebo, and this marginal benefit is questionable when considering their side effects. Pain relief also may not be beneficial to knee OA patients as it has been shown that compressive joint loading is in fact higher with less knee pain¹³. There is currently no effective structure modification treatment of osteoarthritis creating an irreversible progression of cartilage degradation with current medical treatments¹².

2.3 Obesity

It has been known for almost 25 years that rates of overweight and obesity are rising in Canada, but until much more recently the extent of the increase was uncertain because data were self-reported¹⁴, a method known to underestimate the prevalence of overweight and obesity^{15,16}. Based on measured height and weight, the prevalence of overweight and obesity combined is estimated to be 65.0% for men and 53.4% for women, indicating that the majority of Canadians are in a weight range that increases their risk of developing health problems¹⁴. The obese comprise 22.9% and 23.2% of the Canadian population of men and women respectively representing a sharp increase from obesity rates of 11.5% and 15.7% reported in 1978/79¹⁴.

The consequences of excess weight are well known. Obesity has been associated with increased risk of cardiovascular disease¹⁷, insulin resistance¹⁸, and most importantly to this work, knee osteoarthritis^{19,20,21,22,23,24}. In fact, obesity is the most significant modifiable risk factor for knee OA, having been associated with both radiographic and symptomatic OA³.

While obesity has been well established as a risk factor for knee OA, its role in knee OA pathogenesis and progression is not as clear. In general, two central hypotheses have been suggested in the literature to explain the role of obesity in knee OA. The first of these is that obesity interacts through the metabolically active aspect of OA. Gradual changes in joint homeostasis may be the result of the local effects of adipokines, particularly leptin, which has been found to be over expressed in OA cartilage²⁵. Also, it has recently been shown that not all obesity is equivalent in the risk for knee OA, with the co-existence of disordered glucose and lipid metabolism being particularly strongly linked to the development of knee OA²⁶. These metabolic perspectives are important in the identification of new targets for disease modifying OA drugs.

It is also hypothesized that obesity interacts with osteoarthritis through increased joint loading. Mechanical loading has been shown to be a significant factor in the wear and tear characteristic of OA, and loading is thought to increase due to greater body weight in the obese. This hypothesis is found widely in the literature^{27,28,29} where studies have shown a strong association between BMI and knee OA, but not as strong an association between BMI and osteoarthritis development of other joints, which lends support to a theory of increased mechanical loading at the knee as opposed to one involving the systemic metabolic pathway of the disease^{27,30}. There is also evidence to support behavioural changes to gait patterns associated with changes in body weight and BMI, including altered gait speed, stride length, and the duration of stance phase³¹. This thesis will focus on understanding the mechanical association of obesity and knee osteoarthritis rather than metabolic aspects of the association. Future work will be needed to understand the interaction between the two.

2.4 Gait Analysis

Modern gait analysis, using 3D motion capture and force platforms, provides a model for understanding the dynamic mechanical loading environment of the joint during activities of daily living³². Walking is one of the highest frequency activities of daily life placing loads on the lower extremity³³, and one of the most common functional deficits reported by those suffering from knee OA³⁴. As such, gait analysis has been broadly applied in studies of knee osteoarthritis, and mechanical alterations in gait have been hypothesized to be important factors in initiation and progression of the disease³⁵. Joint loading is often assessed using net joint moments calculated by inverse dynamics techniques³⁶, and information regarding muscle activity is also often incorporated through the collection of electromyographic data³⁷⁻³⁹.

Studies of gait have reported various findings in dynamic mechanical alterations related to knee osteoarthritis^{32, 33, 36, 40-45}. Common changes associated with knee OA include decreased stride lengths and slower walking speeds⁴⁶, as well as decreased knee flexion angles and moments⁴⁷. The kinetic finding reported most often in association with knee OA is an increased knee adduction moment during stance phase, with this higher knee adduction moment having been related to severity of the disease⁴⁸, as well as progression⁴⁸. As a surrogate measure of load in the medial compartment, this increase in the adduction moment is perhaps partly explanatory of the higher rate of medial compartment knee OA⁴.

The typical gait alterations associated with knee OA including reduced peak values of knee flexion angles and knee flexion moments, and increased peak values of the knee adduction moment have not been uniformly found in subjects with only mild-

moderate stage disease. Some studies have found that moderate knee OA subjects walk more slowly^{48, 49}, with longer stride times, longer stance times, and greater percentages of the gait cycle spent in stance⁴⁸. Others have not found such differences in stride characteristics, and have demonstrated that subjects with moderate OA walk at similar speeds to those who are asymptomatic^{43, 50, 51}. Decreased knee flexion angles were also described in association with moderate knee OA in some studies⁴⁸⁻⁵⁰ although this decrease was not found universally⁴³. Findings regarding decreased peak knee adduction moments have also been variable between studies of moderate stage knee OA. Mundermann et al. 2005, Landry et al. 2007, and Mundermann et al. 2004 did not detect significant differences in peak knee adduction moments between moderate OA and control subjects^{43, 50, 51}. However, Astephen et al. 2008 and Kaufman et al. 2001 have identified increases^{48, 49}. Three previous studies have also identified decreased knee flexion moments with moderate knee OA disease presence^{43, 48, 49}.

Andriacchi et al. (2006) have shown that ambulatory mechanics and alterations in dynamic loading are likely related to the initiation of knee OA. They argue that the disease process begins through the exposure of new areas of articular cartilage to increased mechanical load during walking as a result of altered kinematics³². These altered kinematics may result from either from a traumatic injury or a chronic condition. Indeed, it is possible that the biomechanical effect of obesity, due to both greater body weight and increased limb segment sizes, may cause kinematic alterations resulting in the exposure of previously unconditioned regions of articular cartilage to mechanical loading, creating the required conditions for disease initiation.

Given the well-established role of joint loading in the initiation and progression of knee osteoarthritis, and the increased risk of knee OA in the obese, modern gait analysis has also been used to investigate joint loading characteristics in the obese. Increased dynamic joint loading in the obese has been demonstrated, although not in all cases³⁰. In 2007, Browning and Kram showed through the application of a sagittal-plane inverse dynamic model that both the absolute ground reaction force and the peak flexion-extension moment were increased in obese subjects walking at their self selected speed⁵². This group has also demonstrated that in reducing their walking speed, the peak knee loading experienced by obese subjects throughout the gait cycle could be reduced to levels not significantly different from those of healthy weight subjects. Messier et al. (2005) found that after an 18-month clinical trial of diet and exercise, weight loss dramatically reduced peak compressive forces and peak knee adduction moments in the knees of overweight or obese older adults with knee OA³. For each unit of weight lost (1 kg or 9.8 N), knee joint loading was reduced by multiple units (~4 kg or 38.7-40.6 N), indicating that over time the knees of lighter weight subjects are exposed to an apparently clinically significant reduction in repetitive loading³. In the 2005 study, body mass in kg was reduced by 2.6% from baseline to follow-up. In a subsequent study in 2011 Messier et al. investigated the effects of higher weight loss. This study evaluated compressive, shear, and muscle forces in subjects with high (10.2% reduction in body mass), low (2.7% reduction in body mass), and no weight loss (increase of 1.5% body mass). Compressive forces were reduced in the high weight loss group as compared to the no weight loss group. This reduction in compressive force was largely mediated by a reduction in hamstring forces⁵³. Aaboe et al. have also studied the effects of weight loss

in obese subjects with knee OA. Given a 16 week dietary intervention resulting in an average weight loss of 13.5%, subjects demonstrated 13% lower peak compressive forces and 12% lower peak external knee adduction moments.

It is also important to consider in these studies that gait patterns could adjust to weight loss over time, and that these reduced loads could therefore be only temporary. That is, smaller segment masses could eventually allow a greater walking speed leading back to increased loading. However in this study the effects of walking speed were statistically controlled, which may mitigate this effect. Longitudinal data would be needed to determine the duration of this reduced loading. These results do however confirm the general hypothesis of increased knee joint loads in obese adults.

Further confirmation of increased dynamic loading can be found from the work of Gushue et al. (2005) on the gait patterns of obese children. The rate of overweight in children has quadrupled over the past 25 years, resulting in an estimated 30% of children now being overweight⁵⁴. They showed increased joint loading as a result of higher body weight in children. Obese children have been shown to walk with altered dynamic loading, in particular, with a higher external knee adduction moment. Once again, given that the development of medial compartment knee OA has been linked to increased dynamic loading of the medial compartment of the knee joint, this result suggests that obese children are at a higher risk of developing musculoskeletal disease. It also suggests the need for preventative tools targeted at children specifically.

Although there appears to be a majority of studies indicating a direct relationship between obesity and higher dynamic knee joint loads, not all studies have demonstrated this finding. In particular, a 2003 study by DeVita and Hortobagyi demonstrated

evidence of an adaptive mechanism serving to reduce knee loads in the obese. Having found no increases in loading at the knee (or hip) in obese subjects, this group argues that the kinematic adaptations characteristic of obese gait, including increased double support time, shorter step length, decreased velocity and reduced knee flexion angles, all serve to reduce muscle forces. Given that muscle forces contribute the majority of the total joint load⁵⁵ they conclude that in fact increased knee loading is not a characteristic of obese gait. This conflict in findings introduces an important consideration. We must recognize that not all obese subjects develop knee OA, and that mediating factors are therefore important in the relationship between these variables. As indicated by DeVita, some obese individuals may be able to adapt neuromuscular function and resulting gait biomechanics to maintain musculoskeletal health, while other may not. It may be this inability to adapt which is a more accurate risk indicator for disease than body weight or body composition alone, suggesting the need to biomechanically differentiate between obese ‘adapters’ and ‘non-adapters’.

Another important consideration in reviewing the studies of gait related to obesity is that studies compare varying levels of body mass index or weight loss between obese subject groups and healthy weight subject groups. Devita et al. 2003 and Hortobagyi et al. 2011 compared gait parameters between obese but otherwise healthy subjects with average BMI greater than 40 to control subjects with average BMI of less than 23. Browning and Kram compared gait parameters between otherwise healthy subjects with average BMI of 37.0 to subjects with average BMI of 21.0. Studies of gait alterations with weight loss in subjects who are obese and have knee OA have also investigated different BMI groups. Aaboe et al. 2011 studied weight loss from a BMI of 36.9 on

average at baseline to a BMI of 31.8 at 16 week follow-up. Messier et al. 2010 studied weight loss of 10.2% of baseline body weight, and compared biomechanical parameters in this high weight loss group both to a lower weight loss group who lost 2.7% of baseline body weight, and to a no weight loss group who gained 1.5% of baseline body mass at 18-month follow-up (BMI not shown for these groups). The diverse levels of body mass and BMI compared between groups in different studies may partly explain discrepancies in resulting biomechanical alterations.

Many of the results discussed so far are, unfortunately, limited due to a lack of multifactor analyses considering the resulting alterations in biomechanical characteristics with both the effects of knee osteoarthritis and obesity considered simultaneously. The work of Messier et al. (2005) provided results for subjects with both obesity and knee osteoarthritis, but the interaction effects between these variables were not considered. Also the results of previous studies have been limited by the lack of inclusion of dynamic waveform information in statistical analysis. In each of the gait studies mentioned above, peak values were selected for analysis from dynamic waveforms calculated throughout the gait cycle, a method that fails to include important information on the time dependence of movement. In our group, a multivariate statistical technique called principal component analysis has been applied to biomechanical^{36, 41, 48, 56} and neuromuscular^{37-39, 57} dynamic waveforms allowing separation between subject groups that includes this temporal information. Application of principal component analysis to the gait patterns and EMG of obese/healthy weight subjects with and without osteoarthritis may provide additional information regarding the complex relationship

between biomechanical changes associated with knee OA and those associated with obese gait.

2.5 Joint Force Modeling

The analysis of conventional gait variables given by inverse dynamics has proven to be a very useful tool in the estimation of joint loads, providing associations between altered gait mechanics and osteoarthritis as well as a number of other pathologies. However, we must be clear in interpreting the results. Three-dimensional gait kinetic variables that result from an inverse dynamics procedure are *net* joint forces and moments, and do not correspond to forces on individual anatomical structures. Although they provide us with information about the intensity of the actuation that is required to produce a given motion, we do not obtain information about the quantities of force being produced by individual muscles or acting through individual ligaments. Without this information, we also do not have a representation of forces acting between articulating surfaces of the joints, which is important to consider in knee OA initiation and progression. Joint forces are often underestimated with inverse dynamics as co-contracting muscles around the joints can increase contact forces, but are not reflected in the net forces and moments from inverse dynamics. Given that the onset and progression of knee OA, as well as surgical outcomes of knee replacement, has been so strongly linked to the local loading environment of the joint, estimation of contact forces during gait may reveal further relationships between cartilage degradation and dynamic joint loading.

Taylor et al. (2004)⁵⁵ have shown that the majority of the net force experienced at the joints is a result of muscle activity and not reaction forces due to body weight, so

determination of muscle forces plays a key role in obtaining accurate contact force estimates. Muscle forces cannot be measured in vivo without the use of highly invasive techniques so these forces must be estimated from motion capture, external force data, and muscle activity data, all of which are available from non-invasive measurements in a gait lab.

A variety of mathematical modeling methods have been used to determine individual muscle, ligament, and contact loads during walking in vivo, although it should be noted that determination of these loads is difficult due to complex anatomy, complicated movement, and indeterminate muscle function⁵⁵. Regarding anatomy, the creation of an appropriate musculoskeletal anatomical model including estimation of locations and geometries of anatomical structures is included in any muscle model. Software packages are available for this purpose, most notably in the literature OpenSim and AnyBody. These allow the inclusion of muscle origin and insertion sites on bony anatomy as well as the paths of the muscles in between these locations. Muscles are often represented as straight lines travelling from origin to insertion⁵⁵, but in OpenSim, muscle wrapping has been included to maintain accurate estimates of moment arms lengths throughout movements⁵⁸. Information about pennation angles and wider attachment sites can also be included, for example the wider attachment site of the hip abductors, although this may involve the creation of additional lines of action⁵⁵. Musculoskeletal geometry is most often scaled to individual subjects, but it is possible to incorporate subject specific geometries from imaging modalities⁵⁵.

Indeterminate muscle function also adds to the complexity of muscle modeling. The human body is indeterminately actuated, that is, there are many more muscles than

there are degrees of freedom in the joints⁵⁹. For example, at the knee, a joint with 6 degrees of freedom, the following muscles contribute to its actuation: semimembranosus, semitendinosus, biceps femoris long head, biceps femoris short head, sartorius, tensor fascia latae, gracilis, vastus lateralis, vastus intermedius, vastus medialis, rectus femoris, medial gastrocnemius, lateral gastrocnemius, plantaris, and popliteus⁵⁸. This poses the problem of force-sharing⁵⁹. Which combination of forces through these many muscles produces a given movement, or a given net resultant moment at a given point in time? And what factors play a role in neuromuscular control of these force combinations?

One method for answering these questions is optimization. Static optimization models choose a combination of muscle forces to minimize an objective cost function, and this cost function is assumed to model some physiological criterion for a given activity⁵⁹. For example, Heintz et al. chose a cost function minimizing muscle stress – the force through the muscle divided by its physiological cross sectional area⁶⁰. A choice to minimize the metabolic cost of walking is also common in models of gait⁶¹. The method of static optimization is limited by the fact that it neglects muscle contraction and activation dynamics, but it is computationally efficient and has been more widely implemented⁵⁹. Also, in 2001 Anderson and Pandy argued that a static optimization was practically equivalent to the much more computationally costly dynamic optimization method in terms of resulting muscle and contact forces when simulating once cycle of gait during level walking in asymptomatic individuals⁶².

Static optimizations have been criticized in several ways. Kinematic data collection must be accurate in order to produce reliable results from the inverse dynamics problem. Also, as mentioned above, these models do not account for the physiology of

muscle. Dynamic optimization methods are not subject to these criticisms as they account for muscle contraction and activation dynamics, and are based on a forward dynamics approach to solving the kinetic equations of motion. The inclusion of force-length and force-velocity relationships for as many as thirty muscles in each leg does however come at an enormous computational cost, and given the apparently comparable results between these methods in the case of human gait, it is difficult to justify this additional computational cost and complexity⁶². In pathologic populations, neuromuscular activation patterns change significantly and the cost function used in static optimization may not be representative of underlying physiology.

An alternative solution that does not depend on a cost function and optimization routine is to determine muscle forces from electromyography (EMG). This method has the advantage of accounting for a subject's individual activation patterns without the need to satisfy a certain performance criterion that may or may not be representative of true physiology. For example, it has been shown through collection of dynamic EMG that co-contraction of quadriceps and hamstrings increases in subjects suffering from knee osteoarthritis³⁹. But this mechanism of neuromuscular control would not be accounted for by a cost function minimizing muscle stress, nor by one minimizing metabolic cost. EMG-to-force methods have been used to investigate pathologies because they account for individual muscle recruitment and co-contraction strategies.

Given that the results of conventional gait analysis calculations from inverse dynamics are limited to a relatively general representation of dynamic loading, a more specific representation may reveal additional relationships between obesity and knee osteoarthritis. Muscle modeling can be used to non-invasively estimate individual

muscle forces, thereby allowing calculation of the contact forces between articulating surfaces, but methods of muscle modeling are diverse and there is a trade-off between computational complexity and additional model accuracy which depends on the application of the model. If co-contraction is suspected, the additional complexity of an EMG-driven contact force modeling approach would be appropriate. Based on the available literature, the additional computational cost of dynamic optimization appears to be unjustified in gait analysis of asymptomatic subjects however, the method of EMG-to-force modeling is promising as it is capable of including important considerations such as muscular co-contraction around the knee during stance phase in pathologic gait.

Chapter 3 - PCA and Obesity

3.1 Introduction

Excessive mechanical loading has been implicated in the progression of knee OA⁶³, and since dynamic joint loading occurs more often during walking than other activities of daily life³³, gait analysis has proven to be an effective model for understanding the mechanical loading environment of the knee^{32, 35}. In particular, an increased magnitude of the knee adduction moment during gait has been associated with the pathological process of knee OA^{4, 40, 42, 48, 50, 64}.

Numerous risk factors for knee osteoarthritis (OA) incidence and progression have been identified, including, age, sex, heredity, and previous knee injury⁶⁵⁻⁶⁸. Obesity, as measured by BMI, is a highly cited and important modifiable⁶⁹ risk factor for knee OA^{19-21, 24, 29, 70-72}. While obesity is a well-established risk factor, its role in knee OA pathogenesis and progression is not as clear^{12, 73}. Excess weight may contribute to an increased mechanical burden and altered dynamic movement and loading patterns at the knee^{30, 63, 74}. However, there have not yet been any studies that have examined the interacting role of obesity and knee OA presence on joint movement and loading characteristics during gait.

Biomechanical alterations associated with knee OA are related to differing stages of clinical severity⁷⁵. While the majority of biomechanical gait studies in knee OA have focused on subjects with severe degenerative disease, some recent studies have focused

on investigations of dynamic loading alterations during gait between asymptomatic and moderate knee OA subjects in an effort to better understand the pathomechanics of the disease progression and to develop early treatment strategies^{43, 51, 64}. Moderate knee OA subjects have been found to walk more slowly^{48, 49}, with longer stance times, longer stride lengths, and spending a greater portion of the gait cycle in stance phase⁴⁸. Moderate stage OA disease presence is also associated with reduced peak knee flexion angles^{49, 50}, and reduced peak knee flexion moments^{43, 48}. Some studies have demonstrated increased knee adduction moments during stance in association with moderate knee OA^{43, 48, 49}.

Most gait studies on knee OA have examined peak values from biomechanical waveforms captured during gait which tell us little about the dynamic and temporal nature of changes over the gait cycle. More recently applied multivariate statistical techniques such as Principal Component Analysis (PCA) have been used to understand the dynamic changes in gait waveform patterns⁷⁶. PCA has been used to understand the changes in gait biomechanics and neuromuscular control with varying levels of knee OA severity^{38, 41, 57}. PCA has the advantage of identifying biomechanical alterations objectively based on variance in the data^{41, 43, 56} and features other than peak variables have been found to differ with severity. PCA has not yet been used to understand the biomechanical differences during gait between overweight/obese individuals and healthy weight individuals without and without knee OA. The objective of this study was therefore to examine the interacting role of early to moderate knee osteoarthritis presence and overweight/obesity (based on BMI) on knee joint movement and resultant moments during gait using PCA.

3.2 Methods

3.2.1 Subjects

This study included 104 asymptomatic subjects and 140 diagnosed with moderate knee OA. Asymptomatic subjects did not have any history of knee pain or surgery to their lower limbs and were recruited through university and hospital postings and advertisements. Subjects with moderate knee OA were recruited from the Orthopedic and Sports Medicine Clinic of Nova Scotia and the Orthopaedic Assessment Clinic at the QEII Halifax Infirmery site. A clinical diagnosis of knee OA was obtained from radiographic evidence (anterior-posterior and lateral views) as well as physical and clinical exam. Consistent with our previous work, subjects were included in the study if they had clinical and radiographic evidence of knee OA, but were *not* candidates for total knee replacement surgery^{37, 43}. To meet inclusion criteria, all subjects with moderate OA were able to walk a city block, jog 5 m, and walk upstairs in a reciprocal fashion. Subjects were excluded due to history of cardiovascular disease, stroke, neuromuscular disorders, other forms of arthritis, gout, or history of trauma or surgery to the lower limb. All subjects were over the age of 35 years, and informed consent was obtained prior to testing in accordance with the institutional ethics review board.

Asymptomatic and moderate knee OA subject groups were each divided into three body mass categories based on BMI as indicated by Health Canada: healthy weight (BMI<25), overweight (25<=BMI<=30), and obese (BMI>30)⁷⁷. The asymptomatic group included 58 healthy weight subjects, 38 overweight subjects, and 14 subjects who were obese, while the moderate knee OA group contained 16 healthy weight subjects, 57 overweight subjects, and 67 subjects who were obese.

3.2.2 Gait Analysis

Each subject visited the Dynamics of Human Motion Laboratory once for gait testing. Before gait testing, demographic and anthropometric data was collected including age, height, weight, thigh and calf circumference. Gait testing consisted of a minimum of five walking trials conducted at the subject's self-selected walking speed. During each walking trial, three-dimensional motion of the affected (or randomized in the case of asymptomatics) lower limb was recorded at 100 Hz using 2 Optotrak™ 3020 motion capture camera units (Northern Digital Inc., Waterloo, ON). Ground reaction forces were collected at 2000 Hz using an AMTI force platform (Advanced Mechanical Technology Inc., Watertown, MA). A triad of infrared light emitting diodes was placed on each of the pelvis, thigh, shank, and foot. Individual light emitting diodes were placed on the shoulder and three bony landmarks of the lower limb: the greater trochanter, lateral epicondyle, and lateral malleolus. In addition, virtual markers were defined during quiet standing located on the right and left anterior superior iliac spines, medial and lateral epicondyles, fibular head, tibial tubercle, medial malleolus, second metatarsal, and heel⁴³.

The thigh, shank and foot were modeled as rigid bodies in order to calculate kinematics and kinetics at the knee joint. The position and orientation of each segment was determined according to a least-squares optimization routine, minimizing the error between the position of each rigid body and the experimental marker data⁷⁸. The description of angles and moments at the knee followed the anatomically based joint coordinate system as defined by Grood and Suntay⁷⁹. Using an inverse dynamics method, implemented through custom Matlab (The Mathworks, Natick, MA, USA)

software, net external knee joint moments were calculated from three-dimensional positional data, ground reaction data, and from limb segment inertial properties⁸⁰. Only the knee flexion/extension angle and the three dimensions of the net knee joint reaction moment were analyzed in this particular study, and moments were normalized to ground contact with the foot of the affected leg to the subsequent contact with the same foot. Stride characteristics including walking speed, stride length, stance time, and stance percent were also calculated.

3.2.3 Statistical Methods

In order to objectively extract magnitude and timing information from the four gait waveforms (3D knee moments and knee flexion angle), principal component analysis (PCA) was applied separately to each. PCA is a multivariate statistical technique which has proven effective in the reduction and interpretation of gait waveform data⁴¹. For each gait waveform, a data matrix, \mathbf{X} , was created, which contained each subject's average waveform at each percentage of the gait cycle. These matrices were 244 (the total number of subjects) x 101 (the number of data points in one full gait cycle). PCA transforms these matrices, which are initially expressed in terms of 101 variables that may be correlated, into new matrices expressed in terms of 101 orthogonal (uncorrelated) variables or principal components (PCs). These PCs are the eigenvectors of the covariance matrix of \mathbf{X} , and each one represents an independent waveform feature. The first PC explains the largest portion of the variance in \mathbf{X} , the second PC the second largest portion, and so on. PC scores were calculated to measure the degree to which a particular feature was present in each subject's individual waveform, by projecting each subject's original data with mean removed onto the eigenvector ($PCscore_{ij} = PC_i * [x_j -$

x_{mean}], where $PCscore_{ij}$ is the i th PC score for subject j , PC_i is the vector pattern of the i th principal component, x_j is the original waveform data for subject i). Only the first three PCs were retained for each of the four gait waveforms analyzed to capture the primary modes of variability in the data. Differences in demographics, anthropometrics, PC scores, and stride characteristics were compared between the BMI-divided groups using a two-factor ANOVA with post-hoc Tukey tests. Statistical significance was set at 0.05.

3.3 Results

Table 3.1 summarizes the demographic, anthropometric, and stride characteristic results for the asymptomatic group, the moderate OA group, and all subjects together. Moderate OA subjects were slightly older, had higher BMI and mass, and a larger portion of them were male. Moderate OA subjects also walked significantly slower with a shorter stride length and a longer stance time, spending a larger proportion of the gait cycle in stance phase (Table 3.1). Table 3.1 also summarizes these data for the healthy weight, overweight, and obese subject groups. Obese subjects spent a greater portion of the gait cycle in stance phase (Table 1). An interaction between moderate OA and body mass index was found in stride length, where higher BMI was associated with shorter stride length in moderate knee OA subjects, but not in asymptomatic subjects ($p=0.027$). Table 3.2 summarizes the demographic, anthropometric, and stride characteristic results for the asymptomatic group and the moderate OA group each divided into 3 healthy weight, overweight and obese categories.

The first three PCs cumulatively explained 83.9%, 71.4%, 68.3%, and 77.0% of the variability in the original knee flexion/extension angle, knee ad/abduction moment, knee flexion/extension moment, and knee internal/external rotation moment data respectively.

3.3.1 Moderate OA Effects

Table 3.3 summarizes the significant principal component waveform differences associated with moderate knee OA, body mass index, and interaction effects. The first PC, PC1, of the knee flexion/extension angle represented the overall magnitude of the waveform throughout the gait cycle. The moderate knee OA group had lower overall magnitudes of the knee flexion/extension angle (i.e. lower PC1 scores) than the asymptomatic group ($p < 0.01$). PC1 of the knee adduction moment captured the overall magnitude of the moment during the stance phase of the gait cycle. The moderate knee OA group had higher magnitudes of the knee adduction moment during stance phase (i.e. higher PC1 scores) than asymptomatics ($p < 0.01$). Waveform alterations to the (net external) knee rotation moment were also associated with moderate knee OA as indicated by PC2 and PC3. Subjects with moderate OA demonstrated a higher magnitude of the knee rotation moment in late stance phase (i.e. more internal rotation moment) (PC2, $p = 0.02$), but less moment range throughout the stance phase (PC3, $p < 0.01$).

Table 3.1 – Demographics, anthropometrics, and stride characteristics of healthy weight (HW), overweight (OW), obese (OB), asymptomatic and moderate OA subject groups. P-values for ANOVA and post-hoc Tukey’s tests are included.

	Healthy Weight	Overweight	Obese	ANOVA p-value (obesity effects)	Multiple Comparisons		
					HW vs. OV	HW vs. OB	OV vs. OB
N	68	95	81	N/A			
Age (yrs)	51.0 (9.0)	53.7 (10.2)	55.9 (10.2)	0.99	0.99	0.99	0.999
Height (m)	1.70 (0.08)	1.72 (0.09)	1.71 (0.11)	0.65	0.71	0.998	0.75
Weight (kg)	66.0 (8.1)	82.7 (9.4)	102.6 (17.1)	<0.01*	<0.01*	<0.01*	<0.01*
BMI (kg/m ²)	22.8 (1.4)	27.6 (1.4)	34.9 (4.0)	<0.01*	<0.01*	<0.01*	<0.01*
Thigh Circ. (m)	0.50 (0.04)	0.54 (0.04)	0.57 (0.05)	<0.01*	<0.01*	<0.01*	<0.01*
Calf Circ. (m)	0.36 (0.03)	0.38 (0.03)	0.41 (0.04)	<0.01*	<0.01*	<0.01*	<0.01*
Sex (F/M)	42/26	37/58	35/46	0.31	0.008*	0.051	0.83
<i>Stride Characteristics</i>							
Speed (m/sec)	1.35 (0.18)	1.32 (0.18)	1.22 (0.21)	0.23	0.97	0.27	0.28
Stride Len (m)	1.44 (0.13)	1.44 (0.14)	1.35 (0.16)	0.12	0.98	0.24	0.11
Stance (%)	62.4 (1.6)	63.4 (1.5)	64.8 (1.8)	<0.01*	<0.01*	<0.01*	<0.01*
Stance Time (sec)	0.67 (0.06)	0.70 (0.07)	0.73 (0.08)	0.094	0.37	0.077	0.49
	All	Asym	Mod OA	p-value			
N	244	104	140	N/A			
Age (yrs)	53.7 (10.0)	48.3 (9.2)	57.6 (8.8)	<0.01*			
Height (m)	1.71 (0.10)	1.69 (0.09)	1.72 (0.10)	0.082			
Mass (kg)	84.7 (18.8)	74.6 (14.8)	92.1 (18.1)	<0.01*			
BMI (kg/m ²)	28.7 (5.4)	25.7 (4.1)	30.9 (5.3)	<0.01*			
Thigh Circ. (m)	0.53 (0.05)	0.53 (0.05)	0.54 (0.05)	0.23			
Calf Circ. (m)	0.38 (0.04)	0.37 (0.04)	0.39 (0.04)	0.68			
Sex (F/M)	114/130	66/38	48/92	<0.01*			
<i>Stride Characteristics</i>							
Speed (m/sec)	1.30 (0.20)	1.37 (0.17)	1.24 (0.20)	<0.01*			
Stride Length (m)	1.41 (0.15)	1.45 (0.13)	1.38 (0.16)	0.02*			
Stance Time (sec)	0.70 (0.07)	0.67 (0.06)	0.72 (0.08)	<0.01*			
Stance (%)	63.6 (1.9)	62.7 (1.5)	64.2 (1.9)	<0.01*			

*represents statistically significant difference at $\alpha = 0.05$ level

Table 3.2 – Demographics, anthropometrics, and stride characteristics of asymptomatic and moderate OA subjects divided by BMI into healthy weight (HW), overweight (OW), and obese (OB) categories.

	Asymptomatic			Moderate OA		
	Healthy Weight	Overweight	Obese	Healthy Weight	Overweight	Obese
N	52	38	14	16	57	67
Age (yrs)	49.3 (9.1)	47.3 (8.8)	47.6(10.6)	56.2 (6.7)	58.0 (9.0)	57.6 (9.3)
Height (m)	1.69 (0.08)	1.71 (0.09)	1.71 (0.10)	1.73 (0.10)	1.74 (0.09)	1.71 (0.11)
Weight (kg)	64.6 (7.6)	80.1 (9.3)	97.1 (15.0)	70.6 (8.4)	84.4 (9.0)	103.7 (17.4)
BMI (kg/m ²)	22.6 (1.5)	27.4 (1.6)	33.1 (3.4)	23.5 (0.7)	27.8 (1.2)	35.2 (4.0)
Thigh Circ. (m)	0.50 (0.04)	0.55 (0.05)	0.57 (0.04)	0.48 (0.03)	0.52 (0.04)	0.57 (0.05)
Calf Circ. (m)	0.36 (0.03)	0.38 (0.03)	0.40 (0.06)	0.36 (0.02)	0.37 (0.02)	0.41 (0.03)
Sex (F/M)	35/17	23/15	8/6	7/9	14/43	27/40
<i>Stride Characteristics</i>						
Speed (m/sec)	1.36 (0.18)	1.39 (0.16)	1.37 (0.16)	1.31(0.18)	1.28(0.19)	1.19 (0.20)
Stride Length (m)	1.43 (0.12)	1.47 (0.14)	1.46 (0.14)	1.45 (0.15)	1.42 (0.14)	1.33 (0.15)
Stance (%)	62.4 (1.7)	62.9 (1.1)	63.6 (1.1)	62.4 (1.6)	63.7 (1.6)	65.0 (1.8)

Table 3.3 – P-values for statistically significant ($\alpha=0.05$) moderate OA, body mass, and interaction effects and descriptions of the waveform feature that each PC explains. In the Direction of Effect column, p-values for multiple comparisons are given in parentheses. OB = obese, OV = overweight, and HW = healthy weight.

Waveform	PC	Feature Description	Effect	Direction of Effect	ANOVA p-value
Knee Flexion Angle	1	overall magnitude	OA	OA < asym	<0.01
	3	range during stance	Interaction	Interaction	0.03
Knee Adduction Moment	1	stance phase magnitude	OA	OA > asym	<0.01
	3	1 st peak to mid-stance diff.	BMI	OB < HW (p<0.001), OV < HW (p=0.003)	<0.01
Knee Flexion Moment	1	late stance magnitude	BMI	OB > OV (p<0.001), OB > HW (p<0.001)	0.02
	2	range during stance	Interaction	Interaction	<0.01
Knee Rotation Moment	2	late stance magnitude	OA	OA > asym	0.02
	3	range during stance	OA	OA < asym	<0.01
	3	range during stance	BMI	OB < OV (p<0.001), OB < HW (p<0.001)	<0.01

3.3.2 Body Mass Index Effects

Three gait waveform alterations were found to be associated with different BMI category. In PC3 of the knee adduction moment, which represented the difference between the first peak and mid-stance value, healthy weight subjects had a larger range in the moment from the first peak to mid-stance than both the obese and overweight subject groups (Figure 1). That is, a BMI>25 (both overweight and obese groups) was associated with a more constant knee adduction moment during the stance phase (p<0.01). In PC1 of the knee flexion/extension moment, which represented the late stance extension moment magnitude, obese subjects had lower extension moment magnitudes than both overweight and healthy weight subjects (p=0.02). Finally, in PC3 of the knee rotation moment, which represented the range of the moment during stance phase, obese subjects

had a small range (i.e. lower PC3 scores) than overweight and healthy weight subjects ($p < 0.01$) (Figure 2), similar to the moderate OA effect of this PC described above.

3.3.3 Interaction Effects

Two significant gait waveform interaction effects were found. In PC3 of the knee flexion angle, which represented the range in the angle between late stance and swing phase, higher BMI category had the effect of reducing the range more for OA subjects than for asymptomatic subjects ($p = 0.03$) (Figure 3). Similarly, in PC2 of the knee flexion moment, which represented the range in the moment during stance phase, higher BMI category had the effect of reducing this range for subjects with moderate OA, but it did not have this effect in asymptomatic subjects ($p < 0.01$) (Figure 4).

Table 3.4 - Within Group P-values for Knee Flexion Angle PC3 Scores

	HW vs. OW	OW vs. OB	HW vs. OB
Asymptomatic Group	1.0000	0.9954	0.9974
Moderate OA Group	0.8532	<0.0001*	0.0002*

*refers to statistically significant difference between groups at $\alpha = 0.05$ level of significance.

Table 3.5 - Within Group P-values for Knee Flexion Moment PC2 Scores

	HW vs. OW	OW vs. OB	HW vs. OB
Asymptomatic Group	0.8734	0.9912	0.7199
Moderate OA Group	0.4523	0.0239*	0.0019*

*refers to statistically significant difference between groups at $\alpha = 0.05$ level of significance.

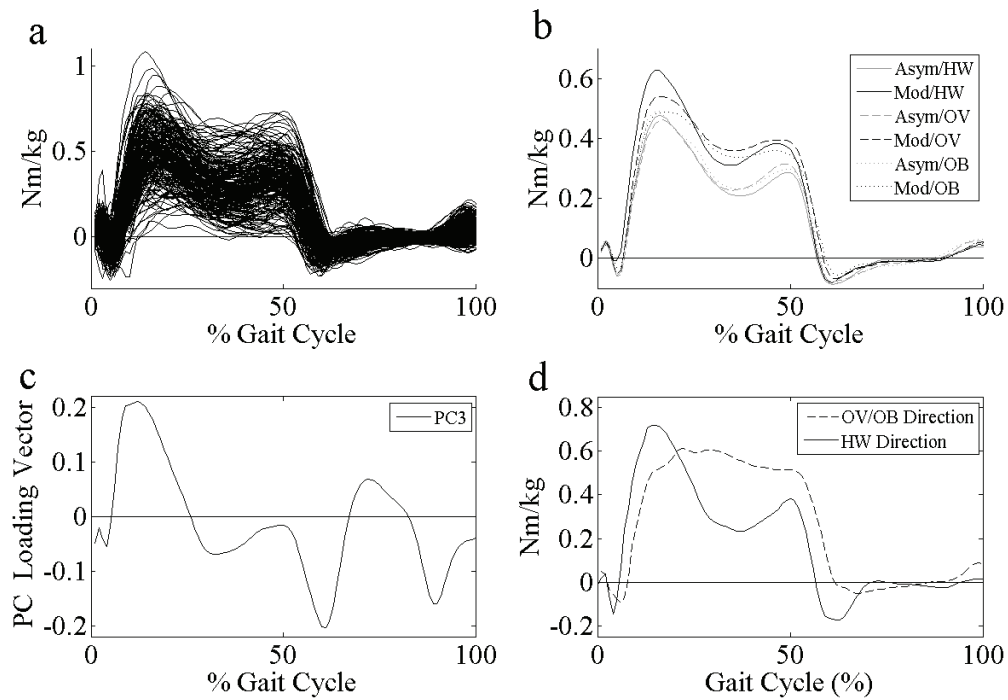


Figure 3.1 - Knee adduction moment PC3. (a) The knee adduction moment waveforms for all subjects are shown. (b) Mean knee adduction moment waveforms for each of the six subject groups based on BMI category and moderate OA disease presence. (c) PC3 of the knee adduction moment represented the range in the waveform during stance phase, high PC3 scores indicated high first peak adduction moments relative to mid-late stance values. (d) Representative high (HW direction) and low (OV/OB direction) subject waveforms (95th and 5th percentiles) demonstrate the interpretation of PC3.

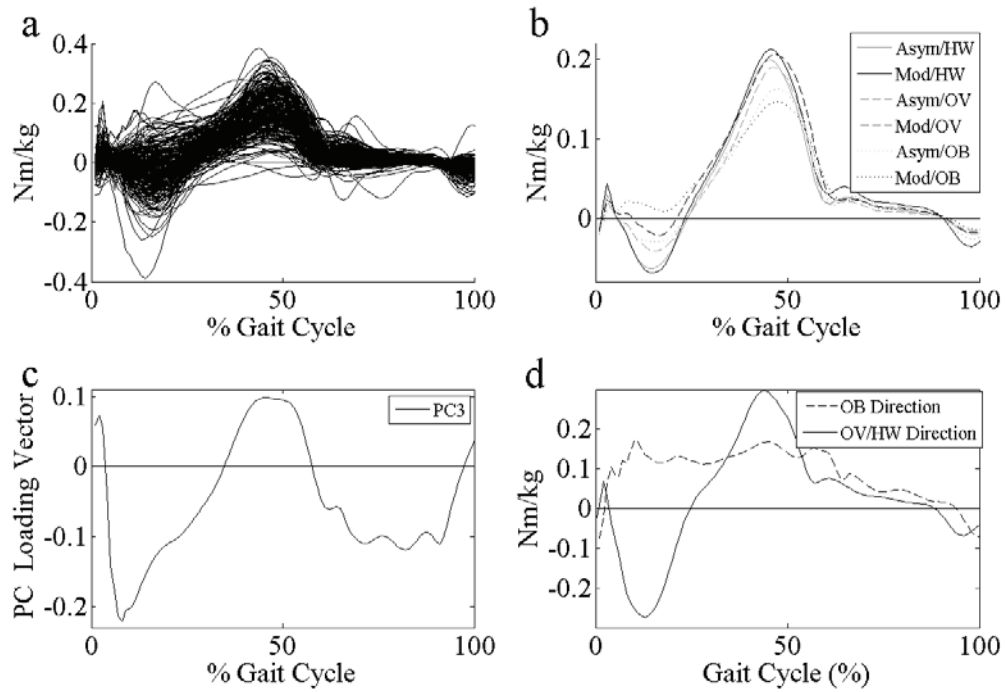


Figure 3.2- Knee rotation moment PC3. (a) The knee internal rotation moment waveforms for all subjects are shown. (b) Mean knee internal rotation moment waveforms for each of the six subject groups based on BMI category and moderate OA disease presence. (c) PC3 of the knee internal rotation moment represented the range in the waveform during stance phase. (d) Representative high (OV/HW direction) and low (OB direction) subject waveforms (95th and 5th percentiles) demonstrate the interpretation of PC3.

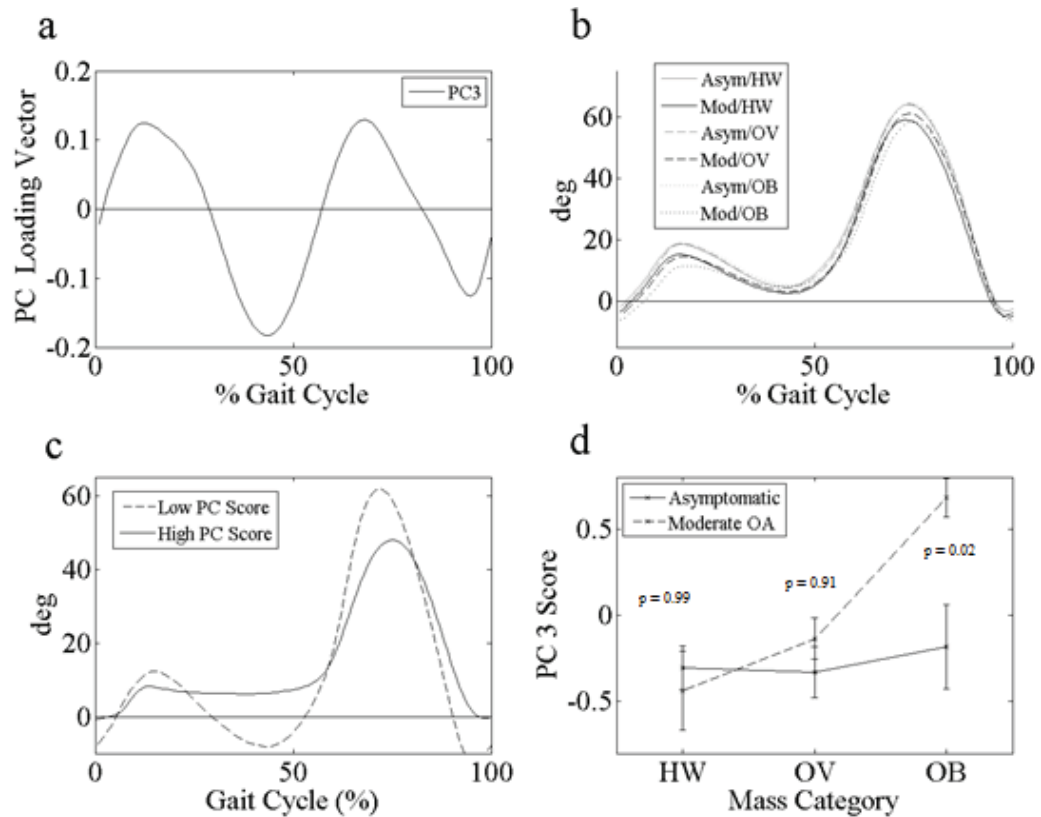


Figure 3.3- Knee flexion angle interaction effect. (a) PC3 of the knee flexion angle represented the range during the stance phase. (b) Mean knee flexion angle waveforms for each of the six subject groups based on BMI category and moderate OA disease presence. (c) Representative high and low subject waveforms (95th and 5th percentiles) demonstrate the interpretation of PC3. (d) Interaction between obesity and moderate knee OA in PC3 of the knee flexion angle.

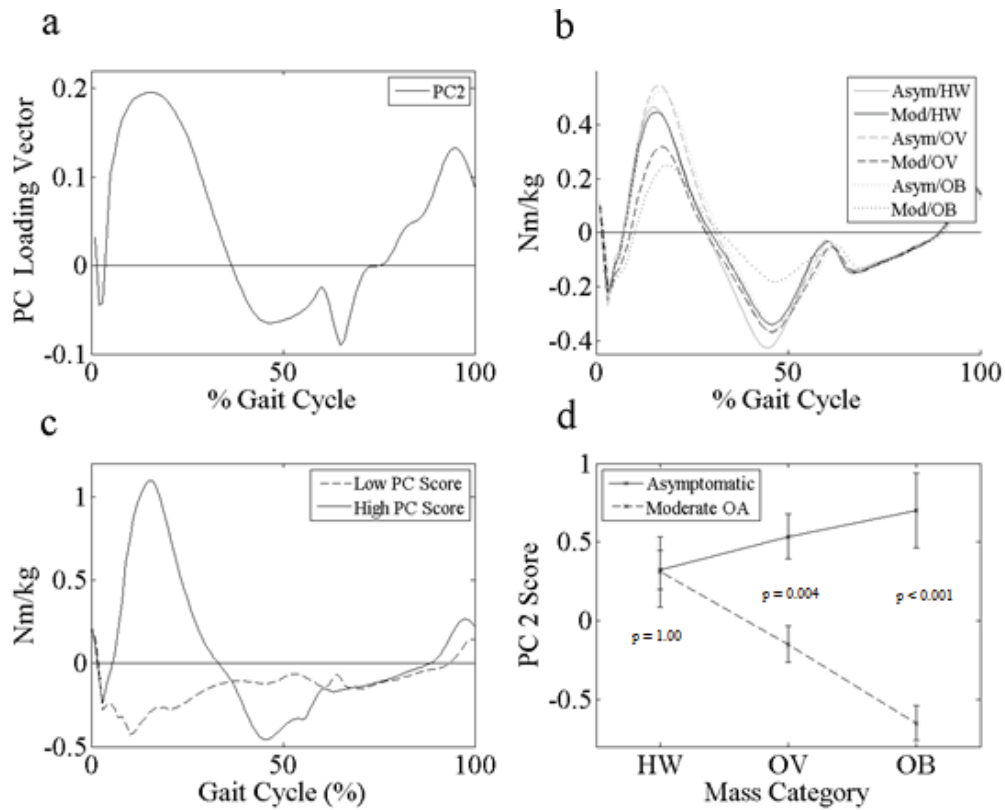


Figure 3.4 - Knee flexion moment interaction effect. (a) PC2 of the knee flexion moment represented the range during the stance phase. (b) Mean knee flexion moment waveforms for each of the six subject groups based on BMI category and moderate OA disease presence. (c) Representative high and low subject waveforms (95th and 5th percentiles) demonstrate the interpretation of PC2. (d) Interaction between obesity and moderate knee OA in PC2 of the knee flexion moment.

3.4 Discussion

The results of this study show a number of gait alterations associated with moderate knee OA, BMI category, and their interaction. The moderate knee OA group walked with altered stride characteristics, having shorter stride lengths, longer stance times, and spent a greater portion of the gait cycle in stance phase. These stride characteristic differences, as well as the overall reduction in the magnitude of the knee flexion angle associated with the moderate knee OA group (Table 3.3), are typical of individuals with knee OA. Successively smaller knee flexion angles during stance phase are associated with increasing knee OA severity, and decreased knee flexion angles during swing phase have been associated with severe knee OA⁴⁸. The OA subject group in our study walked with decreased knee flexion angles throughout the entire gait cycle, which may indicate that the subject group included in this study may be somewhat more functionally impaired and further progressed than those of some previous studies of moderate OA^{50,43}.

Higher knee adduction moments during the stance phase were also observed in the moderate knee OA subject group compared to the asymptomatic group, a finding that has been frequently associated with knee OA^{40, 47, 64, 81}. Higher knee adduction moments have been associated both with radiographic OA severity and progression of OA^{48, 82}. As it has been correlated with medial compartment forces⁸³, this increase in the adduction moment may be intrinsically associated with the pathogenesis of knee OA⁴⁰ and perhaps partly explains the higher rate of medial compartment knee OA⁴.

Less range in knee rotation moments was associated with increased BMI category in this study. There has been very little investigation into changes in the rotational loading patterns of the knee joint with knee OA; a few studies have associated reduced transverse plane loading with knee OA^{43, 48, 69}. Changes in transverse plane kinematics after ACL injury have been described as a mechanism for the development of knee OA⁸⁴, and so changes in transverse plane moments may be important in the development and progression of knee OA and should be further explored.

The obese subject group spent a greater portion of the gait cycle in stance phase, which is consistent with previous studies⁸⁴. Scores for PC3 of the knee adduction moment were reduced in the overweight and obese groups, reflecting more constant knee adduction moment curves during stance in these groups as compared to healthy weight subjects. This result demonstrates that alterations of the biomechanical loading environment with obesity are not limited to the effects of purely increased body mass alone, and highlights the added value of extracting temporal information from gait waveforms for analysis. Obesity had an effect on the temporal nature of the adduction moment rather than the magnitude, and obese individuals loaded their joints more constantly in the frontal plane than healthy weight individuals. This would correspond to more cumulative load on the joint which had been suggested as being detrimental to joint integrity⁸⁵. Also, further support for potentially increased cumulative load in obese subjects is found in combining this altered loading pattern and the fact that obese subjects spent a greater proportion of the gait cycle in stance phase, when the greatest loading occurs. A few studies have examined the effect of obesity on peak values of the adduction moment. Segal et al. (2009) compared peak values of the knee adduction

moment normalized to body mass (Nm/kg) between obese and healthy weight subjects, and did not demonstrate a significant difference in peak moments between the groups²². However, Aaboe et al. (2011) showed a 12% decrease in the peak value of the moment (in Nm not normalized to body mass) after a weight loss program which decreased the BMI of the group from 36.9 to 31.9 kg/m².⁸⁶ Messier et al (2005) also found a direct association between obesity and knee adduction moments, but this occurred in the presence of knee OA, a factor which has been shown to increase the knee adduction moment³. They showed that in subjects with knee OA as well, decreased peak internal knee abduction moments (equivalent to peak external knee adduction moments), could be explained by weight loss.

PCA also identified an alteration to the knee flexion moment associated with obesity. During late stance, the magnitude of the net external knee extension moment was reduced in obese subjects. Most previous studies have identified no significant alterations to the sagittal plane knee moments in obese subjects^{69, 74, 86, 87}. However, DeVita et al. (2003) demonstrated that “when scaled for body mass, the peak extensor torque at the knee was severely reduced in obese compared to lean participants.” Our finding, while not directly comparable to the findings of DeVita et al., may further the suggestion made by DeVita that in obese subjects, “there is a reorganization of neuromuscular function in order to maintain knee loading at a level observed in healthy weight subjects.” This may be true for some obese individuals who do not develop knee OA. However, our results suggest that this may be a characteristic of obesity in general regardless of whether or not they have knee OA.

A number of previous studies have demonstrated the biomechanical effects of obesity^{22, 30, 74}, of moderate knee OA^{43, 51, 64}, or of both at once during gait^{69, 86}, but few have investigated the mechanical interactions between these two factors. To our knowledge, this is the first study to investigate the interaction of these factors during dynamic gait. In this study, two alterations have been associated with the interaction of obesity and moderate knee OA, both occurring in the sagittal plane. In PC3 of the knee flexion angle, representing the range between late stance and swing phase, obesity has the effect of reducing this range more for moderate OA subjects than for asymptomatics. Obese subjects have been shown to have poorer pain and function with OA than healthy weight subjects⁸⁸, and so the added reduction of knee flexion angles with obesity in the moderate OA group suggest a more functionally impaired group of individuals with knee OA. A similar interaction pattern was also seen in stride length, where stride lengths were reduced for the obese group with OA, but not in the asymptomatic group. Shorter stride lengths are a further indication of increased functional impairment in the group of obese individuals with knee OA. The second interaction effect occurred in PC2 of the knee flexion moment, representing the moment range during stance phase. Obesity had the effect of reducing this range in the moderate OA group, but not in the asymptomatic group. Reduced knee flexion moment ranges have been observed in more severe knee OA populations⁵⁷. It is unlikely that this sagittal plane alteration is related to avoidance of weak quadriceps muscles, as previous work has demonstrated increased quadriceps muscle activity in moderate knee OA subjects³⁷. In particular this work has shown overall increased activity of vastus lateralis and longer duration of activity in rectus femoris in subjects with moderate knee OA than in subjects who are asymptomatic³⁷.

Increased quadriceps muscle activity leading to increased force generation in the quadriceps would tend to reduce the knee flexion moment, so it is possible that subjects with moderate knee OA and increased BMI recruit the quadriceps muscles to greater extent than asymptomatic subjects do.

Whether or not these alterations are protective or detrimental is unclear. These patterns could be adopted by those with knee OA and obesity to avoid further joint loading and further OA progression, or they could represent gait patterns in obese individuals that may have contributed to their development of knee OA. Longitudinal data is needed to explore potential initiation models in these populations, and electromyography data should also be examined to provide the added insight into neuromuscular adaptation strategies that would allow these groups to affect joint loading. Joint contact forces obtained through muscle modeling may further develop the characterization of the dynamic loading environment at the knee in these populations. BMI is a useful measure of obesity that has been clearly linked to knee OA in longitudinal epidemiological studies; however it lacks specificity in terms of body composition and body fat percentage. Further study may be enhanced by exploring improved metrics of body mass and body adiposity that may better correlate with knee OA presence and progression.

3.5 Conclusion

In conclusion, this study has identified biomechanical factors during gait that are altered with knee OA, with obesity classification and those that interact between OA and obesity. This suggests either that the pathomechanical process of knee OA development

is different depending on BMI, or that individuals with different BMI categories adapt differently to the early changes associated with knee OA. Further longitudinal study of these interactions should be performed to understand whether these adaptations may cause or be the result of the knee OA process and to develop appropriate conservative and early treatment strategies for knee OA that may be specific to body mass category.

Chapter 4 - Effects of Obesity and Moderate Knee Osteoarthritis on Tibio-femoral Contact Forces during Gait

4.1 Introduction

Osteoarthritis (OA) is a disease characterized by degradation of the structural and functional integrity of articular cartilage⁸⁹. Its initiation and progression are complex and not fully understood⁹⁰, involving interacting effects of biomechanical and metabolic factors⁸⁹. OA is the most common of all joint diseases⁹¹ and results in varying degrees of joint pain, stiffness, swelling, and disability for approximately 10% of the adult Canadian population greater than 18 years of age⁹². The knee is the joint most commonly affected by osteoarthritis⁹³, and the medial compartment of the knee in particular is more commonly affected than the lateral compartment⁹⁴. Risk factors related to the development and progression of knee OA include age, female gender, heredity, previous knee injury, and obesity. Obesity is an important risk factor both for the development of symptomatic knee OA and for the eventual need of total replacement surgery⁹⁵, and the rapidly increasing proportion of adults who are overweight or obese has played an important role in the dramatic increase in rates of knee replacement in recent years⁹⁶.

The precise etiology of knee OA development remains unclear¹⁰, but alterations to dynamic mechanical loading are implicated in the knee OA disease process^{40, 87, 97}.

While moderate mechanical loading is necessary for maintenance of homeostasis in cartilage cellular components⁸⁹, alteration to the local loading environment due to joint laxity⁹⁸, mal-alignment⁹⁹ or obesity^{19, 20, 70, 72} is related to increased knee OA incidence or

progression. The role of obesity in the pathogenesis of knee OA has traditionally been attributed to increased axial joint loading and increased wear and tear that is characteristic of knee OA⁶³. More recently the role of obesity has been described as a complex combination of altered dynamic joint loading and altered cartilage metabolism, but biomechanical factors play a critical role in events leading to OA initiation and progression⁹⁰. Although the epidemiologic association between obesity and knee osteoarthritis incidence and progression is strong⁹⁵, the precise mechanical role of obesity in development and progression of knee OA remains to be fully characterized.

Walking is one of the most frequent activities of daily living placing loads on the lower extremity³³, and gait analysis has proven an effective method of characterizing the dynamic mechanical loading environment of the knee^{32, 35}. Many studies have demonstrated that alterations to the dynamic loading environment during walking occur with knee OA^{32, 33, 36, 40, 42, 47, 100}. In particular, an increase in the knee adduction moment is associated with knee OA disease presence, severity, and progression⁹⁴. Obesity has also been associated with alterations of dynamic knee loading⁵², as well as with increased knee adduction moments in particular²². These studies have shown the importance of both knee OA disease presence, and increased body mass as distinct factors related to loading of articular cartilage during walking and development of knee OA. In the previous chapter of this thesis, dynamic alterations to the mechanical loading environment associated with obesity and moderate knee OA separately, and with their have also been described.

The loading alterations characterized by these studies have been demonstrated in terms of alterations to net knee joint moments obtained by the method of inverse

dynamics⁸⁰. While net joint moments reflect overall knee joint loading, it is not as clear how alterations to net joint moments may contribute to the pathologic osteoarthritis process. Ultimately, it is tibio-femoral joint contact forces which represent the load repetitively placed on the articulating cartilage surfaces during walking. In-vivo tibio-femoral joint contact forces are not directly measurable during dynamic tasks (unless by instrumented total knee replacement¹⁰¹) and therefore tibio-femoral contact forces must be estimated mathematically. Previous studies have also investigated tibio-femoral contact forces and weight loss in obese subjects with knee OA^{3, 53, 86}. These studies have shown that weight loss can be effective in reducing compressive joint loading, and that for each unit of weight lost compressive force is reduced by multiple units³. Net joint moments are effective as surrogate measures of dynamic knee joint load, and are associated with knee OA disease presence, but joint contact forces may bear a stronger relationship to the underlying pathomechanics of knee OA. Both knee OA disease presence and obesity are important factors associated with altered knee joint loading, and previous work has investigated tibio-femoral joint contact forces in subjects with knee OA before and after a program of weight loss. However, to our knowledge, no study has investigated the interaction between obesity and knee OA disease presence on joint contact forces. The purpose of this study was to examine the separate and interacting roles of early to moderate knee osteoarthritis and overweight/obesity on tibio-femoral joint contact forces during gait.

4.2 Methods

4.2.1 Subjects

The study included 204 subjects in total, 115 asymptomatic subjects and 89 with moderate knee OA. The asymptomatic study participants were recruited through institutional postings and advertisements in public locations at the university and hospitals. Asymptomatic subjects had to meet inclusion criteria including that they have no history of knee pain, and that they had never had surgery to their lower limbs. Two clinics, the Orthopaedic Assessment Clinic at the Halifax Infirmary and the Orthopedic and Sports Medicine Clinic of Nova Scotia, were used to recruit moderate knee OA subjects. An orthopaedic surgeon made a diagnosis of moderate knee OA based on radiographic evidence and the results of a clinical physical exam. Subjects were only included in the study if they were moderate in knee osteoarthritis severity which was defined as having evidence of knee OA clinically and radiographically, but not yet being candidates for total knee replacement. This categorization assumed that any subject considered a candidate for knee replacement surgery was farther advanced in clinical severity of knee OA than any subject who was not. This assumption has been made in other studies conducted by our group^{43,48}. All subjects included in the study were able to jog 5 metres, walk stairs reciprocally, and walk a city block without a walking aid. Any subject with a past history of cardiovascular disease, stroke, neuromuscular disorders, other forms of arthritis, gout, or history of trauma or surgery to the lower limb, was excluded from the study. The minimum age for inclusion in the study was 35 years. Informed consent was obtained for each subject before laboratory testing began, in accordance with the ethics review board of the institution.

According to definitions described by Health Canada, asymptomatic and moderate knee OA subject groups were each divided into three categories based on their

BMI: healthy weight ($BMI < 25$), overweight ($25 \leq BMI \leq 30$), and obese ($BMI > 30$)⁷⁷.

The asymptomatic group contained 44 healthy weight subjects, 32 overweight subjects, and 13 subjects who were obese, while the moderate knee OA group contained 13 healthy weight subjects, 45 overweight subjects, and 57 subjects who were obese.

4.2.2 Gait Analysis

Gait testing was conducted once with each subject. Demographic and anthropometric data was collected including age, height, weight, thigh and calf circumference. Three-dimensional motion of the lower limb was recorded at 100 Hz using 2 Optotrak™ 3020 motion capture sensors (Northern Digital Inc., Waterloo, ON) during each walking trial, and a minimum of 5 walking trials were conducted for each subject. Ground reaction forces were collected at 1000 Hz using an AMTI force platform (Advanced Mechanical Technology Inc., Watertown, MA). The right or left lower limb was selected randomly for asymptomatic subjects and for moderate knee OA subjects the motion and ground reaction forces of the affected limb were recorded. Subjects all walked at their self-selected speed, with no knowledge of their speed. The pelvis, thigh, shank and foot were modeled as rigid bodies in order to calculate kinematics and kinetics at the ankle, knee, and hip joints, although this particular study focused on the knee joint. As such, triads of infrared light emitting diodes were placed on the pelvis, thigh, shank and foot. Individual diodes were placed on the shoulder and three bony landmarks of the lower limb: the greater trochanter, lateral epicondyle, and lateral malleolus. Subjects were asked to stand still while virtual markers were defined on the right and left anterior superior iliac spines, medial epicondyle, fibular head, tibial tubercle, medial malleolus, second metatarsal, and heel⁴³. A least-squares optimization routine, minimizing the error

between the position of each rigid body and the experimental marker data was used to determine the relative position and orientation of the 4 rigid bodies⁷⁸. Angles and moments at each joint followed an anatomically based joint coordinate system⁷⁹. According to this system, flexion/extension occurs about the medial lateral axis of the thigh, internal/external rotation occurs about the distal proximal axis of the shank, and adduction/abduction occurs about a floating axis perpendicular to both previously described axes. An inverse dynamics method was implemented through custom Matlab software (The MathWorks, Natick, MA, USA). Three dimensional position data, ground reaction forces, and limb inertial properties were used to calculate net external inter-segmental joint reaction moments⁸⁰. Resulting waveforms were time normalized to a single gait cycle, which occurs from heel strike with one foot to the next heel strike with the same foot. Walking speed, stride length, stance time, and stance percent were also calculated. In addition, electromyography was collected from 7 muscle sites, the lateral and medial hamstrings, vastuslateralis, vastusmedialis, rectus femoris, and the lateral and medial gastrocnemii³⁹, although this data is not presented in the current study.

4.2.3 Contact Force Model

The model developed by DeVita and Hortobagyi has been used to estimate compressive and shear tibio-femoral joint contact forces at the knee¹⁰². As described above, a 3D inverse dynamics analysis of the lower limb was used to produce net external inter-segmental joint reaction torques. The contact force model used in this step is a 2D sagittal plane torque driven model, as it determines the tibio-femoral contact forces based on the resultant joint torques at the ankle, knee, and hip in the sagittal plane from inverse dynamics. There are two steps involved in this model. Step one is to calculate the forces

in the three largest force producing muscle groups in the lower limb, the quadriceps, hamstrings, and gastrocnemii. Step two is the application of these to the tibia along with net joint reaction forces from inverse dynamics. Gastrocnemius forces were determined from the net plantar flexor moment at the ankle and the lever arm of the Achilles tendon. The lever arm was assumed to vary depending on the flexion angle of the ankle¹⁰³. The plantar flexor moment was divided by the Achilles tendon moment arm, to produce the triceps surae force. This value was then multiplied by the ratio of the gastrocnemius physiological cross-sectional area (PCSA) to the overall PCSA of the triceps surae muscles which was assumed to be 0.319 (Equation 1)¹⁰⁴.

$$G = \frac{A_t}{A_d} \cdot 0.319$$

Equation 1 – G is force in the gastrocnemii, A_t is ankle plantarflexor torque (or moment), and A_d is the lever arm of the Achilles tendon.

Hamstrings force was calculated in a similar fashion based on the net extensor moment at the hip joint. The proportion of the net extensor moment generated by the hamstrings was determined based on the ratio of the hamstring PCSA to the combined PCSA of the hamstrings and gluteus maximus, as well as on the ratio of the hamstrings moment arm to the gluteus maximus moment arm (Equations 2 and 3).

$$H_p = \left[\frac{H_{PCSA}}{H_{PCSA} + GM_{PCSA}} \right] \cdot \left[\frac{H_d}{GM_d} \right]$$

Equation 2 – H_{PCSA} and GM_{PCSA} are the physiological cross-sectional area of the hamstrings and gluteus maximus, H_d and GM_d are the hamstrings and gluteus maximus lever arms.

$$H = \frac{H_p \cdot H_t}{H_d}$$

Equation 3 – H is force in hamstrings, H_p is proportion of hamstrings, H_t is hip extension torque (or moment), and H_d is the hamstrings lever arm.

Given that the net flexion/extension moment at the knee is assumed to be a result of the hamstrings, gastrocnemius, and quadriceps muscles acting on their respective moment arms, the quadriceps force could be calculated. Quadriceps force was determined based on the hamstrings and gastrocnemius forces, their moment arms, and the net flexion/extension torque at the knee from inverse dynamics (Equation 4). The moment arm of the quadriceps tendon given the flexion angle of the knee was derived from the literature¹⁰⁵.

$$Q = \frac{K_t + H \cdot H_d + G \cdot A_d}{Q_d}$$

Equation 4 - Q is quadriceps force, K_t is the net knee flexion torque (moment), H is hamstrings force, H_d is hamstrings lever arm, G is gastrocnemius force, A_d is Achilles tendon lever arm, and Q_d is quadriceps tendon lever arm.

The three predicted muscle forces, and the net joint reaction forces resulting from inverse dynamics were then applied to the tibia, with the predicted forces occurring along their respective lines of action (Equation 5 and Figure 4.1).

$$K_s = G \sin \alpha - H \sin \beta + Q \sin \varphi - K_z \sin \lambda + K_y \cos \lambda$$

$$K_c = G \cos \alpha - H \cos \beta + Q \cos \varphi - K_z \cos \lambda + K_y \sin \lambda$$

Equation 5 – K_s is knee shear force, α, β, φ , and λ are shown in Figure 4.1, G is gastrocnemius force, H is hamstrings force, and Q is quadriceps force, K_z is vertical net reaction force, and K_y is horizontal net reaction force. K_s is knee shear force, and K_c is knee compressive force.

Compressive forces were positive when directed into the tibia, and shear forces were positive when applied anteriorly. Muscle forces (quadriceps, hamstrings and gastrocnemius) and knee joint compressive and anterior-posterior shear forces were calculated both in absolute units (in Newtons), and normalized units (expressed as multiples of the subject's body weight).

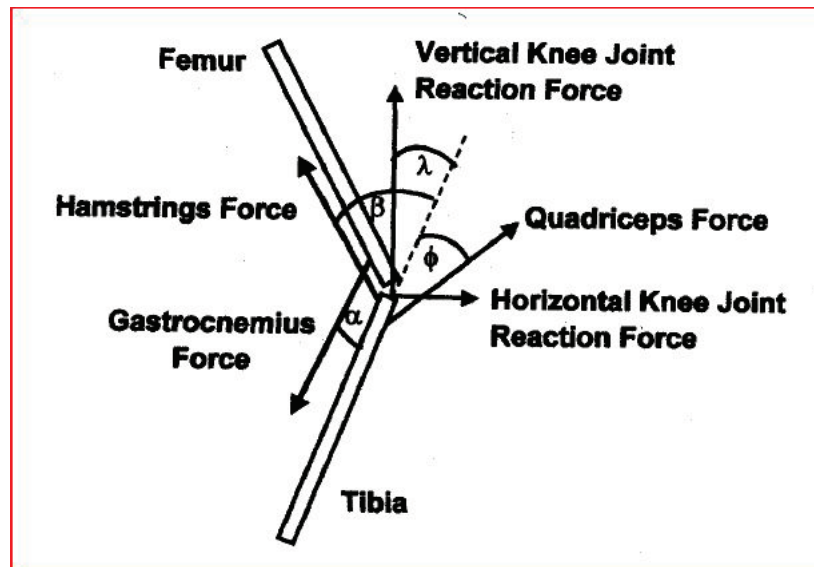


Figure 4.1 - Diagram of sagittal plane tibio-femoral joint contact force model from DeVita and Hortobagyi, 2001

4.2.4 Statistical Methods

Two peak values were extracted from the compressive and shear knee joint forces and a single peak value was extracted from the muscle force curves (Table 2).

Differences in demographics, anthropometrics, stride characteristics, and the peak values extracted from compressive, shear, and muscle force curves were compared between groups using a two-factored ANOVA and post-hoc Tukey tests with moderate knee OA disease presence as one factor, and BMI category as the other. Statistical significance was set at 0.05.

4.3 Results

Anthropometrics, demographics, and stride characteristics for asymptomatic and moderate knee OA subjects are given in Table 4.1. Moderate OA subjects were older ($p < 0.001$), heavier ($p = 0.006$), had higher BMI ($p = 0.008$), larger thigh ($p = 0.009$) and calf circumferences ($p = 0.003$), and a greater percentage were male than the asymptomatic group. This is consistent with previous moderate OA groups for our laboratory^{43, 48} Table 4.2 summarizes anthropometric, demographic and stride characteristic results by BMI category. Subjects with higher BMI were heavier and had larger thigh and calf circumferences (see Table 4.2). The portion of the gait cycle spent in the stance phase increased progressively from healthy weight to obese body mass categories (see Table 4.2). Walking speed, stride length, and stance time were not significantly different between BMI groups (also see Table 4.2). Table 4.3 shows the demographics,

anthropometrics, and stride characteristics of the asymptomatic and moderate OA groups each divided into healthy weight, overweight, and obese groups.

Peak values of normalized AP shear, compressive, and muscular forces were not different across normal weight, overweight or obese BMI categories as shown in Table 4.4. However, significant differences in normalized forces were associated with moderate knee OA. Subjects with moderate knee OA had lower first peak normalized shear forces, lower normalized quadriceps forces, and lower normalized gastrocnemius forces (Table 4.5). Tibio-femoral shear, quadriceps and gastrocnemius force waveforms for subjects with and without moderate knee OA are shown in Figure 4.2. No significant interactions between moderate OA disease presence and body mass were found in normalized muscle and joint contact forces (Table 4.4).

In contrast, absolute tibio-femoral contact forces and muscle forces measured in Newtons were not significantly different based on moderate knee osteoarthritis disease presence (Table 4.6). However, anterior-posterior shear force, compressive force, gastrocnemius, and hamstrings muscle forces were all significantly different across BMI categories (Table 4.6). Multiple comparisons between healthy weight, overweight and obese subjects are shown in Table 4.7. Four of these peak forces were progressively increased from healthy weight, to overweight, to obese subjects: the second peaks of anterior-posterior shear force and compressive force, the peak hamstrings force and the peak gastrocnemius force. These progressive increases can be seen in Figures 4.3 and 4.4. Overweight and obese subjects also had higher first peak anterior-posterior shear and compressive contact forces than healthy weight subjects (Table 4.7 and Figure 4.4).

A significant interaction between moderate knee OA disease presence and body mass category was found in absolute peak quadriceps forces (Table 4.6). This interaction is shown in Figure 4.5, which demonstrates that asymptomatic subjects increased their peak absolute quadriceps force more than moderate knee OA subjects did as body mass category increased from healthy weight to obese.

Overweight subjects exhibited approximately 30% higher first peak shear forces than normal weight subjects, and obese subjects exhibited a further increase of 18% in the second peak of shear force compared to overweight subjects (Table 4.8). Similarly, overweight subjects exhibited approximately 29% higher first peak compressive force than healthy weight subjects, with obese subjects showing a further increase of 20% in the second peak of compressive force compared to overweight subjects. Increased absolute AP shear and compressive forces with increasing BMI is also apparent in Figure 1. Gastrocnemius and hamstring forces were significantly increased across the BMI categories, and quadriceps forces were significantly higher for obese subjects than for healthy weight subjects (Table 5, Figure 3).

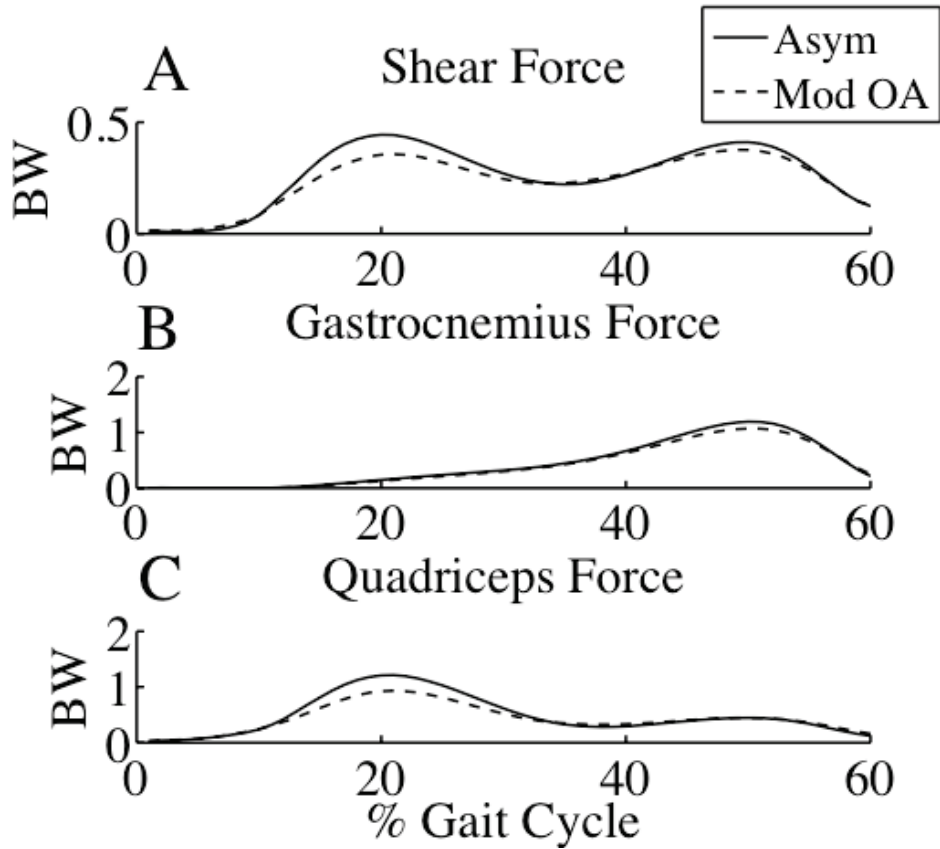


Figure 4.2 – Anterior-posterior shear contact force, quadriceps force, and gastrocnemius force waveforms normalized to body mass for subjects with and without moderate knee osteoarthritis.

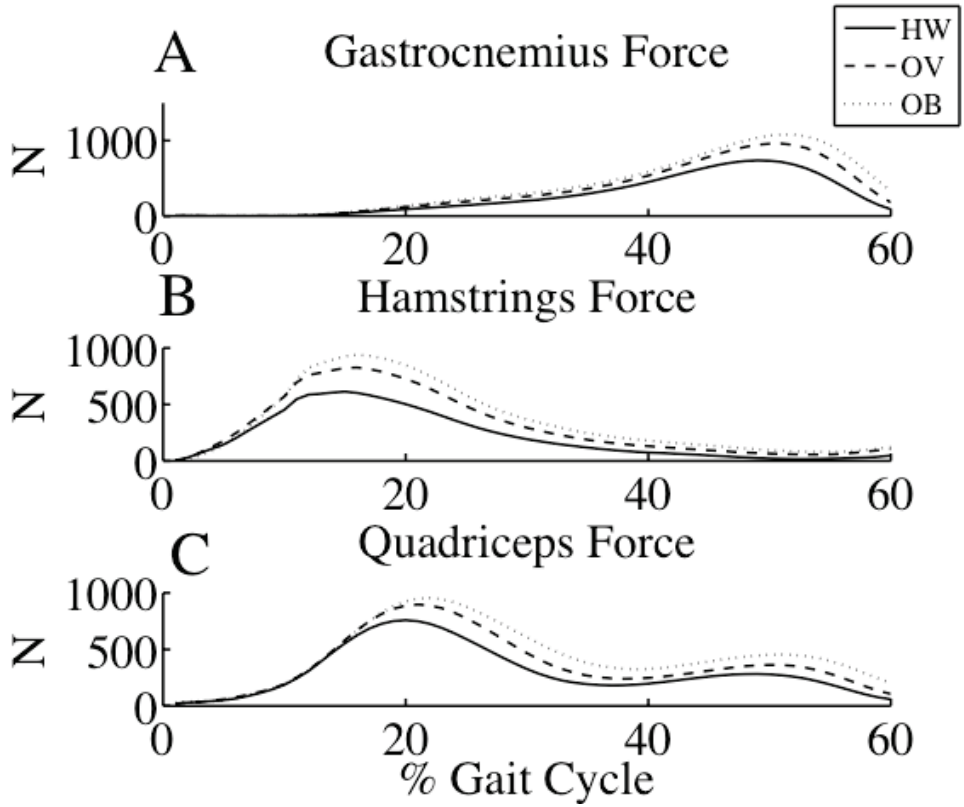


Figure 4.3 – Absolute gastrocnemius, hamstrings, and quadriceps force waveforms during stance phase of gait for healthy weight (HW), overweight (OV), and obese (OB) subjects.

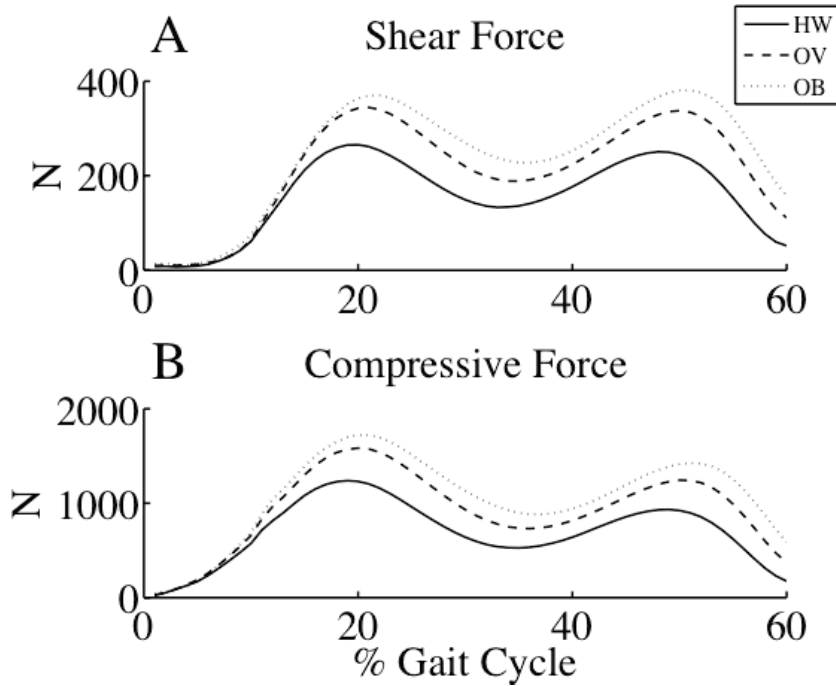


Figure 4.4 – Absolute tibio-femoral anterior-posterior shear force and compressive force during the stance phase of gait for healthy weight (HW – solid line), overweight (OW – dashed line), and obese (OB – dotted line) subjects.

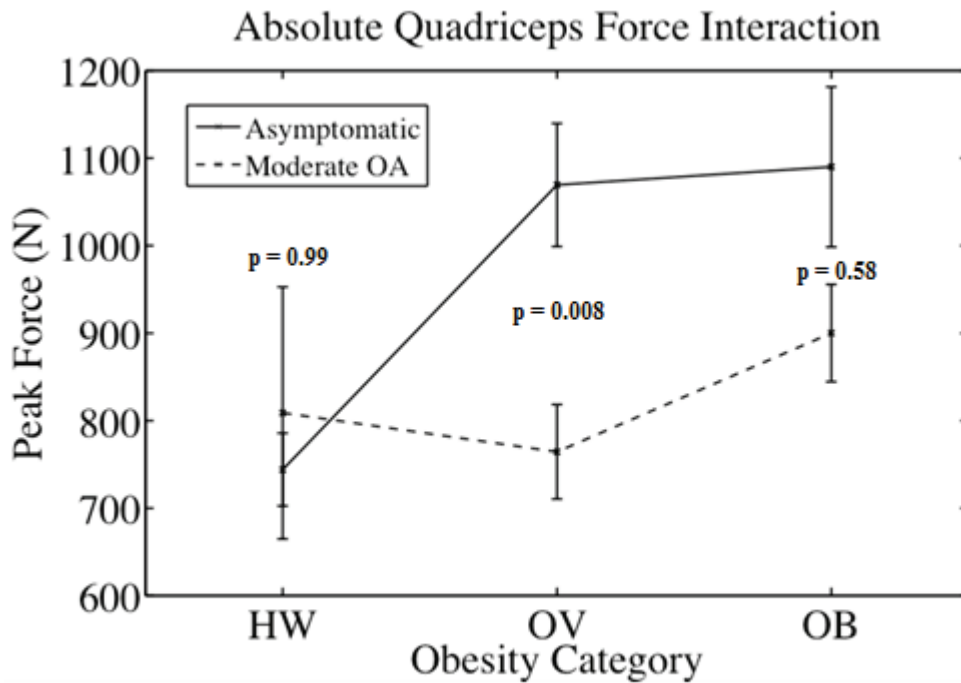


Figure 4.5 – Interaction between moderate knee osteoarthritis disease presence and body mass category (healthy weight – HW, overweight – OW, and obese – OB) in peak quadriceps forces not normalized to body mass (unit = Newtons).

Table 4.1 – Demographics, anthropometrics, and stride characteristics of asymptomatic and moderate knee OA subjects. P-values resulting from two-way ANOVA are shown.

	Asymptomatic	Moderate OA	p-value
N	89	115	-
Age (yrs)	48.1 (9.0)	57.5 (9.0)	<0.001*
Height (m)	1.70 (0.09)	1.72 (0.10)	0.14
Weight (kg)	74.6 (14.4)	91.3 (17.9)	0.006*
BMI	25.8 (4.0)	30.7 (5.0)	0.008*
Thigh Circ. (m)	0.53 (0.05)	0.54 (0.05)	0.009*
Calf Circ. (m)	0.37 (0.04)	0.39 (0.04)	0.006*
Sex (F/M)	56/33	41/74	0.003*
<i>Stride Characteristics</i>			
Speed (m/sec)	1.39 (0.17)	1.24 (0.20)	<0.001*
Stride Length (m)	1.46 (0.13)	1.38 (0.16)	0.019
Stance Time(sec)	0.66 (0.06)	0.73 (0.08)	<0.001*
Stance (%)	62.6 (1.5)	64.0 (1.9)	0.006*

*refers to statistically significant difference between asymptomatic and moderate OA group at $\alpha = 0.05$ level of significance.

Table 4.2. – Demographics, anthropometrics, and stride characteristics of healthy weight, overweight, and obese subjects. P-values for ANOVA and post-hoc Tukey tests are included.

	Healthy Weight	Overweight	Obese	ANOVA p-value (obesity effects)	Multiple Comparisons		
					HW vs. OV	HW vs. OB	OV vs. OB
N	57	77	70	N/A			
Age (yrs)	50.8 (9.2)	53.8 (10.2)	55.2 (10.6)	0.81	-	-	-
Height (m)	1.69 (0.09)	1.72 (0.09)	1.71 (0.10)	0.54	-	-	-
Weight (kg)	65.5 (8.10)	82.0 (9.01)	101.2 (16.3)	<0.001*	<0.001*	<0.001*	<0.001*
BMI	22.8 (1.4)	27.6 (1.4)	34.4 (3.8)	<0.001*	<0.001*	<0.001*	<0.001*
Thigh Circ. (m)	0.50 (0.04)	0.53 (0.04)	0.57 (0.05)	<0.001*	<0.001*	<0.001*	0.004
Calf Circ. (m)	0.35 (0.02)	0.38 (0.03)	0.40 (0.04)	<0.001*	<0.001*	<0.001*	<0.001*
Sex (F/M)	36/21	31/46	31/39	0.23	-	-	-
<i>Stride Characteristics</i>							
Speed (m/sec)	1.37 (0.19)	1.33 (0.19)	1.22 (0.21)	0.13	-	-	-
Stride Length (m)	1.45 (0.13)	1.45 (0.14)	1.35 (0.16)	0.07	-	-	-
Stance Time(sec)	0.66 (0.06)	0.70 (0.07)	0.73 (0.08)	0.085	-	-	-
Stance (%)	62.3 (1.6)	63.2 (1.4)	64.6 (1.8)	<0.001*	0.021	<0.001	0.0028

*refers to statistically significant difference between groups at $\alpha = 0.05$ level of significance.

Table 4.3 - Demographics, anthropometrics, and stride characteristics of asymptomatic and moderate OA subjects divided by BMI into healthy weight (HW), overweight (OW), and obese (OB) categories.

	Asymptomatic			Moderate OA		
	Healthy Weight	Overweight	Obese	Healthy Weight	Overweight	Obese
N	44	32	13	13	45	57
Age (yrs)	49.0 (9.0)	47.6 (8.7)	46.5 (10.3)	56.9 (7.2)	58.2 (8.8)	57.2 (9.7)
Height (m)	1.68 (0.08)	1.72 (0.09)	1.70 (0.09)	1.73 (0.10)	1.73 (0.09)	1.72 (0.11)
Weight (kg)	64.2 (7.5)	80.9 (9.5)	94.6 (12.0)	70.1 (8.5)	83.0 (8.6)	102.7 (16.9)
BMI (kg/m ²)	22.6 (1.5)	27.3 (1.5)	32.7 (3.2)	23.5 (0.80)	27.7 (1.2)	34.8 (3.8)
Thigh Circ. (m)	0.50 (0.04)	0.72 (0.97)	0.57 (0.04)	0.48 (0.04)	0.52 (0.04)	0.56 (0.05)
Calf Circ. (m)	0.35 (0.02)	0.38 (0.03)	0.40 (0.06)	0.35 (0.02)	0.37 (0.02)	0.40 (0.03)
Sex (F/M)	30/14	18/14	8/5	6/7	12/33	23/34
<i>Stride Characteristics</i>						
Speed (m/sec)	1.38 (0.18)	1.40 (0.16)	1.35 (0.16)	1.32 (0.19)	1.27 (0.19)	1.19 (0.21)
Stride Len (m)	1.44 (0.12)	1.49 (0.13)	1.45 (0.13)	1.46 (0.17)	1.42 (0.15)	1/34 (0.16)
Stance Time (sec)	0.65 (0.06)	0.67 (0.07)	0.68 (0.05)	0.70 (0.05)	0.71 (0.08)	0.74 (0.08)
Stance (%)	62.2 (1.6)	62.8 (1.1)	63.5 (1.1)	62.4 (1.7)	63.5 (1.6)	64.8 (1.9)

Table 4.4 – P-values from ANOVA for normalized (x body weight) tibio-femoral contact forces, and muscle forces.

Force Name	Peak	OA Effect	Body Mass Effect	Interaction Effect
Shear	1	0.010*	0.434	0.222
	2	0.067	0.129	0.413
Compressive	1	0.199	0.368	0.229
	2	0.062	0.207	0.143
Gastrocnemius	1	0.003*	0.178	0.522
Hamstrings	1	0.206	0.495	0.226
Quadriceps	1	0.001*	0.400	0.084

*refers to statistically significant difference between groups at $\alpha = 0.05$ level of significance.

Table 4.5 – Peak values of normalized tibio-femoral contact forces and muscle forces for subjects with and without moderate knee osteoarthritis.

Force (% body mass)	Peak	Asymptomatic	Moderate OA	Difference	ANOVA p-value
Shear	1	0.46 (0.20)	0.37 (0.17)	-0.09	0.01*
	2	0.43 (0.11)	0.40 (0.11)	-0.03	0.067
Compressive	1	1.99 (0.68)	1.81 (0.63)	-0.17	0.199
	2	1.61 (0.35)	1.52(0.42)	-0.09	0.062
Gastrocnemius	1	1.23 (0.21)	1.12 (0.26)	-0.11	0.003*
Hamstrings	1	1.01 (0.37)	1.10 (0.40)	0.09	0.206
Quadriceps	1	1.24 (0.43)	0.93 (0.44)	-0.31	0.001*

*refers to statistically significant difference between groups at $\alpha = 0.05$ level of significance.

Table 4.6 – P-values from ANOVA for absolute (N) tibio-femoral contact forces and muscle forces.

Force Name	Peak	OA Effect	Body Mass Effect	Interaction Effect
Shear	1	0.174	0.004*	0.163
	2	0.919	<0.001*	0.232
Compressive	1	0.948	0.001*	0.116
	2	0.985	<0.001*	0.116
Gastrocnemius	1	0.48	<0.001*	0.943
Hamstrings	1	0.29	<0.001*	0.081
Quadriceps	1	0.23	0.031	0.046*

*refers to statistically significant difference between groups at $\alpha = 0.05$ level of significance.

Table 4.7 – Peak values of absolute tibio-femoral contact forces and muscle forces for healthy weight (HW), overweight (OW) and obese (OB) subjects with multiple comparisons.

Force (N)	Peak	HW	OW	OB	ANOVA p-value	Multiple Comparisons		
						HW vs. OW	HW vs. OB	OV vs. OB
Shear	1	273.5 (137.7)	355.4 (150.2)	382.1 (187.5)	0.004	0.015	0.0048	>0.05
	2	272.5 (82.3)	356.1 (89.1)	420.5 (135.8)	<0.001	0.002	<0.0001	0.0239
Compressive	1	1227.3 (521.3)	1586.0 (543.7)	1812.9 (703.8)	0.001	0.0088	0.0005	>0.05
	2	980.6 (257.9)	1264.1 (321.5)	1528.2 (516.2)	<0.001	0.002	<0.0001	0.0238
Gastrocnemius	1	769.4 (168.1)	978.6 (227.4)	1107.9 (324.2)	<0.001	<0.0001	<0.0001	0.0241
Hamstrings	1	645.4 (309.7)	876.4 (266.2)	1096.5 (506.2)	<0.001	0.0139	0.0003	0.2155
Quadriceps	1	758.9 (341.8)	891.2 (403.9)	935.4 (409.3)	0.031	>0.05	0.0254	>0.05

*refers to statistically significant difference between groups at $\alpha = 0.05$ level of significance.

Table 4.8 – Peak values of absolute AP shear, compressive, and muscle forces for healthy weight (HW), overweight (OV), and obese (OB) subjects with percent change from health weight to overweight and from overweight to obese. P-values represent results of two-way ANOVA statistical testing.

Force	Peak	HW	OV	OB	p-value	% Change (HW to OW)	% Change (OV to OB)
AP Shear (N)	1	273.5 (137.7)	355.4 (150.2)	382.1 (187.5)	0.004*	29.9%	7.5%
	2	272.5 (82.3)	356.1 (89.1)	420.5 (135.8)	<0.001*	30.7%	18.1%
Compressive (N)	1	1227.3 (521.3)	1586.0 (543.7)	1812.9 (703.8)	0.001*	29.2%	14.3%
	2	980.6 (257.9)	1264.1 (321.5)	1528.2 (516.2)	<0.001*	28.9%	20.9%
Gastrocnemius (N)	1	769.4 (168.1)	978.6 (227.4)	1107.9 (324.2)	<0.001*	27.2%	13.2%
Hamstrings (N)	1	645.4 (309.7)	876.4 (266.2)	1096.5 (506.2)	<0.001*	35.8%	25.1%
Quadriceps (N)	1	758.9 (341.8)	891.2 (403.9)	935.4 (409.3)	0.031*	17.4%	5.0%

*refers to statistically significant difference between groups at $\alpha = 0.05$ level of significance.

Table 4.9 – Within Group P-values for Peak Absolute Quadriceps Muscle Forces

	Healthy Weight vs. Overweight	Overweight vs. Obese	Healthy Weight vs. Obese
Asymptomatic Group	0.0038*	1.0000	0.0476*
Moderate OA Group	0.9991	0.4695	0.9698

*refers to statistically significant difference between groups at $\alpha = 0.05$ level of significance.

4.4 Discussion

Previous studies have demonstrated decreased walking speed, decreased stride lengths and increased stance times with higher body mass index^{30, 52, 106, 107}. Groups with higher body mass index tended to walk more slowly, with shorter stride lengths and longer stance times, but these stride characteristic alterations were not statistically significant in the current study. The average BMI of our obese group was 34.4 which is lower than in previous studies^{30, 31, 52}. This may partially explain the lack of significant changes in stride characteristics associated with obesity.

The mean normalized compressive contact force of 1.99 x BW for asymptomatic subjects calculated by the sagittal plane knee model is within the range of previously calculated tibio-femoral joint contact forces during gait. These forces have been found to be between 1.7 x BW and 2.4 x BW during level walking when similar models were applied¹⁰⁸. Mean normalized compressive contact forces were not significantly different in subjects with moderate knee OA than in subjects who were asymptomatic. Individuals with knee OA have frequently been shown to have higher knee adduction moments, reflecting increased medial compartment loading relative to lateral compartment loads⁹⁴. The model applied did not demonstrate increased compressive loading in either the first or the second peak normalized value for subjects with moderate knee OA.

Also, early stance phase anterior-posterior shear forces were reduced in subjects with moderate knee OA, reflecting a potential compensatory reorganization of neuromuscular function. This decrease in anterior-posterior shear force may have been produced through the corresponding decrease in quadriceps muscle force, as the

quadriceps contribute to anterior shear force generation during the early stance phase of the gait cycle. Decreased quadriceps muscle activity or quadriceps avoidance gait has been observed in subjects with ACL deficiency¹⁰⁹ where reduced activity of the quadriceps counteracts the potential for excess anterior tibial translation during stance phase. However, decreased quadriceps muscle activity has not been associated with moderate knee OA. In fact, overall quadriceps muscle activity in vastus lateralis and the duration of rectus femoris activity have both been demonstrated to be increased in moderate knee OA subjects³⁷. Results of this study suggest that a neuromuscular reorganization may be occurring as a result of symptomatic knee OA disease presence, but as muscle activity in individual muscles obtained from surface EMG measurements was not included in this analysis, it is not known whether decreased quadriceps muscle activity corresponded to the reduced quadriceps forces and anterior-posterior shear forces observed in association with moderate knee OA. This highlights the additional benefit of EMG-driven muscle modeling techniques in analyzing alterations to joint contact forces in pathologic gait.

Mean normalized gastrocnemius forces were also significantly reduced in subjects with moderate knee OA. Force generation and muscular activity in the gastrocnemii occurs later in stance phase than quadriceps and hamstrings activity, and contributes to posterior shear in the sagittal plane knee model. However, no significant alteration was found to the peak value of anterior-posterior shear force occurring later in stance phase between subjects with and without moderate knee OA. Although the difference in peak normalized hamstrings force between asymptomatic and moderate knee OA groups did not reach statistical significance ($p=0.206$).

Decreased anterior-posterior shear force in subjects with moderate knee OA may have been produced in part through decreased walking velocity, as subjects with moderate knee OA walked on average 0.15 m/s more slowly than subjects who were asymptomatic. Speed was not however included as a covariate in the analysis, as reduction in walking velocity was assumed to be intrinsic to the knee osteoarthritis disease process¹¹⁰. Neuromuscular feedback related to symptomatic knee OA disease presence resulting in slower self-selected walking speed and decreased shear force delivery to articular cartilage may be one mechanism for explaining that moderate knee OA subjects choose to walk more slowly.

There were no significant differences observed between body mass index categories in normalized tibio-femoral contact forces or muscle forces. In contrast, there were significant differences in all of these forces associated with body mass index category when they were not normalized to body mass (absolute forces in Newtons). The lack of significant differences detected in normalized contact and muscle forces indicates that overall dynamic knee joint loading in obese subjects was maintained at a level consistent with the increase in body mass. That is, the lack of differences in normalized forces indicates that increased loading of the lower limb did not occur over and above the effects created by increased body mass alone. This finding supports the argument that obesity alone, in the absence of symptomatic knee OA, may be associated with behavioural gait alterations including neuromuscular reorganization to maintain overall knee loading and musculoskeletal health³⁰.

Compressive and shear forces were increased across BMI categories, as were quadriceps, hamstrings and muscle forces. A similar effect, a correspondence between

weight loss and decreased compressive force has been previously shown^{3, 53, 86}. Aaboe et al. showed that when obese subjects with knee osteoarthritis reduced their BMI from a mean of 36.9 to a mean of 31.9, that peak compressive tibio-femoral joint contact force was reduced by 7%, along with lower axial impulse and decreased peak values of the external knee adduction moment⁸⁶. For each Newton of weight loss, compressive loading was reduced by 2.2 Newtons. Similarly, Messier et al. have demonstrated the direct relationship between reduced body mass and reduced compressive tibio-femoral joint contact forces with each pound of weight loss corresponding to a reduction of approximately 4 pounds of joint load^{3, 53}. Results of the current study further emphasize this direct relationship and indicate that higher compressive and shear loading is associated with higher BMI category. This study also demonstrates that forces generated by the three major force generating muscle groups acting at the knee are all significantly increased. The higher hamstrings and quadriceps muscle forces both occur during the early stance phase, and may be acting to counter act instability in response to excess body weight.

Muscular co-activation of the quadriceps and hamstrings determined through analysis of surface electromyography (EMG) data has also been associated with knee OA³⁹. In subjects with knee OA, increased co-activation of the muscle groups surrounding the knee has been consistently reported^{64, 111, 112}. In the current study, the model applied does not account for individual differences in neuromuscular activation directly, but instead determines hamstrings, quadriceps, and gastrocnemius muscle forces through net joint moments from inverse dynamics.

The significant interaction effect between moderate knee OA disease presence and body mass index category shows that absolute quadriceps forces are increased in asymptomatic subjects with higher body mass, but that in subjects with moderate OA the same increase in peak quadriceps forces was not generated across body mass categories. In the contact force model applied here, reduced quadriceps force generation should reduce anterior-posterior shear force. Given the contribution of quadriceps force to anterior-posterior shear force generation, the relative decrease in quadriceps force in moderate knee OA subjects may again represent a compensation strategy for subjects with symptomatic and radiographic knee OA.

Limitations of the current study include the fact that the model is two-dimensional and torque driven, relying on net joint moments calculated at the ankle, knee, and hip, instead of determining muscle forces through measured muscular activity as in an EMG-driven model⁵⁸. Neuromuscular alterations are an important aspect of the gait alterations associated with the knee osteoarthritis disease process, and the model applied does not directly take into account these alterations. As such, an EMG-driven contact force analysis of obese gait in subjects with and without knee OA would serve to more accurately characterize the relationship between neuromuscular or behavioural alteration of dynamic gait and the generation of tibio-femoral joint contact forces. A further limitation of the model is that it applies tibio-femoral contact forces at a single point, and does not take into account the distribution of these contact forces across the articular joint surface or between medial and lateral joint compartments¹¹³. Finally, regression models that utilize subject-specific anthropometric measurements may not as accurately predict body segment inertial parameters in the presence of excess body mass¹¹⁴.

Previous studies of the relationship between obesity, knee osteoarthritis, and knee joint loading have focused in general of the process of weight loss. A recent study of gait alterations associated with massive weight loss in morbidly obese metabolic surgery subjects demonstrated that behavioural adaptations in gait may occur subsequent in time to the period of weight loss³¹. In distinction to these studies, this study is cross-sectional in design and indicates the current dynamic loading environment of the knee joint across a wide range of BMI which has not been experimentally altered by weight loss. Cross-sectional study is however limited by its inability to temporally characterize the relationship between alteration of body mass and changes to knee joint loads. These limitations indicate the need for future longitudinal study of the association between alteration of body mass index, initiation and progression of knee osteoarthritis, and characterization of the dynamic loading environment of the knee.

In conclusion, results of the present study underline the association between increased body mass index and increased absolute force delivery to the articular surfaces of the knee. The effects of higher BMI and presence of moderate knee OA in absolute quadriceps forces emphasizes that these two factors which are often present simultaneously interact. These results also demonstrate that neuromuscular alterations may exist which allow the maintenance of knee loading in obese subjects to correspond with increased body weight but not exceed it. These should be further examined in electromyography studies of similar populations. Also, further work should examine mechanical alterations at the hip and ankle in association with BMI category and moderate knee OA disease presence as this work suggests reorganization of loading between the joints of the lower extremity. Moderate knee OA subjects did not increase

absolute quadriceps forces to the same extent that asymptomatic subjects do in response to higher body mass. This may be compensatory to reduce shear forces, or it may be pathologic and one aspect of the multifactorial pathogenesis of knee OA. This study supports the role for treatment options targeted to the management of healthy body mass index in subjects with and without moderate knee OA.

Chapter 5 - Conclusion

5.1 Thesis Summary

Rates of obesity have risen dramatically in Canada¹¹⁵ and around the globe¹¹⁶ in recent years. The epidemiologic association between increased body mass and risk of development of symptomatic knee OA is well established,⁹⁵ and in the absence of conservative treatment options affecting disease progression¹², the rates of total knee replacement are rising dramatically also⁹⁶. Although obesity is a well-established risk factor for the development of symptomatic knee OA, and although alteration to mechanical loading is known to be an important factor in knee OA pathogenesis, the precise role of obesity in the pathomechanics of knee OA remains to be fully characterized¹². This thesis has analyzed the mechanical loading environment at the knee using modern gait analysis and a torque driven joint contact force modeling to better characterize the mechanical interactions between knee OA disease presence and increased body mass index.

Two primary objectives were addressed. First, the interacting role of early to moderate knee osteoarthritis and overweight/obesity on mechanical aspects of gait acquired from inverse dynamics were analyzed using PCA. The results of this study, described in Chapter 3 of the thesis, demonstrated that obese individuals do load their knee joints differently during walking, particularly in the sagittal plane, depending on the presence of moderate knee OA. This study also demonstrated that the gait patterns of subjects with moderate knee OA change depending on their body mass category. Given

the results of the analysis from the first study (Chapter 3), a second study was also conducted. Extending the methodology of Chapter 3 to include a more detailed tibio-femoral contact force and muscle force model, a second study was conducted to examine the interacting role of early to moderate knee osteoarthritis and overweight/obesity on estimated tibio-femoral joint contact and muscle forces during gait. This study, presented in Chapter 4 of the thesis has demonstrated an absolute increase in loading for obese subjects both in compressive and anterior-posterior shear directions. It has also demonstrated that along with modification of quadriceps forces, a decreased anterior-posterior shear force was obtained in subjects with moderate knee OA. In addition, similar to the results of the first study, the second study has shown that moderate knee OA disease presence and obesity interact in the amount of muscle force produced during gait. In this case, these factors interacted and were related to alteration of the quadriceps force, again demonstrating what may be a compensation strategy to manage shear forces in subjects with moderate knee OA and obesity. These alterations may be compensatory, in response to the symptoms of knee OA, or they may be part of the intrinsic and pathologic mechanical loading process which may be contributing to the development of knee OA in these subjects.

5.2 Implications of Thesis Results

The results of this thesis have potential implications for future management of knee osteoarthritis based on body mass index. They have shown that mechanical loading differs based on body mass index, and the effectiveness of conservative treatment options such as gait alteration, footwear alteration, lateral wedge insoles, or knee braces might be enhanced through more objective and better informed application of these strategies.

Some individuals who are obese develop knee OA, and others do not. Similarly, some healthy weight individuals develop knee OA, and others do not. The analysis presented in this thesis, based both on net joint moments and on tibio-femoral joint contact forces, indicates that the relationship between these two factors is complex. Ideally, given a more complete understanding of the loading environment at the knee and its relationship to osteoarthritis disease progression, gait and contact force analysis could be conducted for individual subjects, and tailored physical therapy or conservative treatment strategies could then be developed. These results suggest that gait patterns of those with moderate OA do differ depending on body mass index category, and therefore the development of guidelines and potential gait-modifying strategies for knee OA treatment should incorporate these differences based on body mass category.

In addition, the direct relationship between increased body mass index category and increased absolute compressive and shear forces described in Chapter 4 has provided further objective evidence in support of weight loss as a strategy for the management of knee joint loading. Although the precise connection between increased mechanical load and the initiation and progression of knee OA is not fully understood, it is accepted that mechanical loading plays an important role, and weight loss to manage this loading can be objectively recommended based on the results of this study.

5.3 Limitations

The limitations of this work are related to the limitations of conventional gait analysis, the contact force model applied, and the cross-sectional nature of the study designs. Conventional gait analysis is limited in its modeling of the lower limb as a

series of connected rigid bodies, and by the error associated with determining rigid body positions based on reflective marker motion during dynamic tasks. In obese subjects error in the determination of rigid body positions due to skin marker motion may have been increased¹¹⁴. Because they are of similar magnitude to the error caused by skin marker motion and kinematic cross-talk, the kinematics in the transverse and frontal planes have not been fully explored in this thesis^{117, 118}. Given that kinematic alterations are associated with initiation of OA through the exposure to load of previously unloaded regions of articular cartilage, these kinematic alterations should be further investigated in future. Also, the conclusions drawn from PCA are limited by the percentage of variability which the principal components cumulatively describe. The contact force model applied was two-dimensional and did not account for individual muscle activation patterns as in an EMG-driven model. Tibio-femoral contact forces were applied and analyzed at a single point, and did not account for distribution of forces across the articular surfaces or between medial and lateral compartments. Finally, both the study in Chapter 3 and the study in Chapter 4 are limited by the cross-sectional nature of their design. Cross-sectional study represents a given point in time, and so lacks information about the changes to the knee's dynamic loading environment depending on changing BMI in a single individual, or changing severity of the knee OA disease state. It is not possible to draw conclusions about the causal associations between biomechanical variables and the pathological osteoarthritis disease process based on cross-sectional data.

5.4 Recommendations for Future Work

The interacting alterations to muscle and joint contact forces described using the methods of this thesis indicates the potential existence of neuromuscular reorganization

occurring in association with moderate knee OA and obesity. This indicates the potential for exploration of the EMG profiles in these groups and for the application of an EMG-driven musculoskeletal model of the lower limb to describe the knee joint loading environment based on individualized muscular activation patterns. A model such as this would take into account factors such as increased muscular co-contraction to stabilize the knee, and would effectively characterize how this co-contraction is related to loads delivered to the articular cartilage. Future work should also focus on the application of calculated contact forces to the complex morphology of the articular surfaces. A first step might be the calculation and application of tibio-femoral joint contact forces to the medial and lateral compartments. Eventually, application of contact forces to the individual's own articular morphology might be made through three-dimensional image acquisition and integration into the contact force model. Integration of the understanding of the biomechanical loading environment of the knee during walking should also be integrated with the cartilage homeostasis alterations that are characteristic of knee OA disease pathogenesis and progression.

The need for future longitudinal study of obesity and its interaction with moderate knee OA is also suggested by the results of this thesis. Although the thesis has succeeded in demonstrating that these factors do indeed interact, and that individualized loading information may be a key factor determining future risks of OA initiation and progression, the temporal relationships between changes in body mass, behavioural modification of gait parameters, and subsequent alterations to joint loading, would be better illuminated through longitudinal study. Given the results of longitudinal study, risk stratification for knee OA disease initiation or progression could be based on obesity

and individual joint loading characteristics.

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