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## Dynamic Loading and Pain in Knee Osteoarthritis: Effects of Limb Realignment and Ligament Reconstruction Surgeries

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A thesis submitted in partial fulfillment of the requirements for the Doctor of Philosophy degree in Health and Rehabilitation Sciences

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## Abstract

Painful loading of the knee during walking is a key feature of knee osteoarthritis (OA). The external knee moments derived from three-dimensional gait analysis represent dynamic knee loads and may help evaluate surgical interventions. However, the relationships between knee moments and pain and the effects of surgery remain unclear. The overall purpose of this thesis was to investigate knee moments and pain during walking in patients with moderate medial knee OA, including the effects of limb realignment and ligament reconstruction surgeries. This thesis includes three studies investigating knee moments in patients with medial compartment tibiofemoral OA.

Chapter 2 describes a cross-sectional study examining the relationship between knee pain and knee moments during walking, while controlling for extraneous factors by comparing limbs within 265 patients with medial knee OA. Using conditional logistic regression, results indicated greater odds of an increase in pain during walking with increased knee adduction moment, adduction impulse and internal rotation moment, and decreased knee flexion moment. These findings suggest a strong relationship between knee moments (in all three planes of motion) and knee pain during walking when between-person confounding is lessened.

Chapter 3 describes a prospective cohort study evaluating the bilateral changes in knee moments in all three planes of motion in 33 patients undergoing combined medial opening-wedge high tibial osteotomy (HTO) and anterior cruciate ligament (ACL) reconstruction (HTO-ACLR). Patients underwent three-dimensional gait analysis, patient-reported outcomes and radiographic analysis preoperatively, 2 years postoperatively and a minimum 5 years postoperatively. Results indicated significant reductions in the knee adduction and internal rotation moments in the surgical limb, and a decrease in the knee flexion moment and an increase in the knee extension moment in both limbs. Changes in only the surgical limb suggest that HTO-ACLR reduces frontal and transverse plane knee moments. Bilateral changes suggest the passage of time, rather than the surgery, is responsible for the changes in sagittal plane knee moments.

Chapter 4 describes a retrospective matched cohort study comparing preoperative and 5-year postoperative changes in the knee adduction and flexion moments in 52 patients who underwent either combined HTO-ACLR or HTO-Alone. Results indicated that both groups experienced a significant reduction in the knee adduction moment in the surgical limb. However, the HTO-Alone group also experienced a significant decrease in the knee flexion moment while the HTO-ACLR group experienced no change in sagittal plane knee moments. These findings suggest that HTO-ACLR may lessen the long-term decrease in the knee flexion moment typically observed over time in patients with knee OA.

Overall, the results of this thesis support the use of investigating bilateral knee moments during walking in patients with medial knee OA, and provide rationale for future research examining whether the biomechanical changes observed in these individuals affects OA progression.

## Keywords

Knee osteoarthritis, High tibial osteotomy, Anterior cruciate ligament reconstruction, Gait biomechanics, Varus alignment

## Coauthorship Statement

This thesis contains material from one published manuscript (Chapter 3) and two manuscripts that will be prepared for submission (Chapters 2 and 4). Kendal Marriott was the primary author of all chapters contained in this thesis. Chapters were coauthored by T.B.

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## List of Abbreviations

|          |   |
|----------|---|
| 3D       | Three-Dimensional   |
| ACL      | Anterior Cruciate Ligament                                |
| ANOVA    | Analysis of Variance                                      |
| BMI      | Body Mass Index   |
| %BW×Ht   | Percent Body Weight Times Height                          |
| %BW×Ht×s | Percent Body Weight Times Height Times Seconds            |
| CI       | Confidence Interval                                       |
| GRF      | Ground Reaction Force                                     |
| CoM      | Center of Mass  |
| CoP      | Center of Pressure  |
| HTO      | High Tibial Osteotomy                                     |
| K/L      | Kellgren-Lawrence   |
| MAA      | Mechanical Axis Angle                                     |
| PTS      | Posterior Tibial Slope                                    |
| OA       | Osteoarthritis  |
| WBL      | Weightbearing Line  |
| KOOS     | Knee Osteoarthritis Outcome Score                         |
| WOMAC    | Western Ontario and McMaster Universities Arthritis Index |

# Chapter 1

## 1 Introduction: Background and Rationale

Knee osteoarthritis (OA) is a leading cause of pain, disability and healthcare-use globally. Pain during walking is the most common symptom for people with knee OA and is the most common reason people seek treatment. Additionally, aberrant loading of the knee during walking is widely accepted as an important risk factor for the onset and progression of knee OA. Accordingly, several biomechanical factors that contribute to knee loading during walking are thought to be involved in the OA disease process. These same factors are often the targets of various intervention strategies, including orthopaedic surgical procedures, which aim to improve the local biomechanical environment of the knee. Surprisingly, however, relatively little is known about the relationship between measures of knee pain and measures of joint loading, with even less known about the effects of surgeries on pain and walking (gait) biomechanics.

Two potent biomechanical risk factors for medial compartment knee OA are varus malalignment of the lower limb (e.g. bowed legs) and rupture of the anterior cruciate ligament (ACL). Furthermore, the risk for OA is thought to be even greater for individuals with both malalignment and ACL rupture. Medial opening-wedge high tibial osteotomy (HTO) is a surgical treatment option for individuals with varus malalignment of the lower limb and symptomatic OA primarily affecting the medial compartment of the tibiofemoral joint. Anterior cruciate ligament reconstruction is a separate surgical procedure that intends to restore ligamentous stability of the knee in individuals with ACL rupture/deficiency. These procedures can be combined in one operation with the goal of improving both stability and loading of the knee, ultimately improving gait biomechanics and pain. The relationship between pain and measures of knee loading (represented as external knee moments) during walking, and the results of combined medial opening wedge HTO with ACL reconstruction, are the foci of this thesis. The present chapter provides the relevant background and rationale for the thesis objectives.

## 1.1 Osteoarthritis

### 1.1.1 Demographics and Burden of Osteoarthritis

Osteoarthritis is a complex degenerative disease that involves the entirety of the joint as a consequence of multiple systemic and mechanical processes. OA most commonly affects weightbearing synovial joints. Risk factors for the development and progression of OA include an extensive number of factors and individuals often present with multiple physical and functional limitations. Pain during physical activity is the most frequently reported symptom.<sup>1</sup> However, the association between symptoms and objective measures of disease are typically not strong,<sup>2</sup> emphasizing the intricacy of the disease.

The reported prevalence of OA is estimated to vary between 1% and 40% of the general population.<sup>3</sup> Although the prevalence of OA tends to increase substantially in individuals greater than 60 years of age, younger individuals are not immune to its effects. In addition to age, sex discrepancies also exist. Prior to age 50, there is a higher prevalence of OA in men. However, past age 50, OA tends to affect more women than men.<sup>4</sup> OA ranks eleventh among the leading causes of years lost to disability with an overall prevalence of 3.64%.<sup>5</sup> The incidence of OA is increasing<sup>5,6</sup> and this rising incidence is related to an aging population and increasing obesity rates.<sup>7</sup> Therefore, limiting disease progression has become increasingly important.

### 1.1.2 Osteoarthritis of the Knee

OA can be classified either pathologically, radiographically or clinically<sup>8</sup> and is characterized by a number of hallmark features including focal degeneration of articular cartilage, subchondral bone sclerosis, osteophyte formation along joint margins and joint narrowing.<sup>2,9</sup> Additionally, there are changes to soft tissue structures surrounding the joint, including ligament laxity and muscle weakness.<sup>9</sup> Clinical problems associated with OA include pain related to joint use, stiffness with inactivity, joint crepitus and restricted joint range of motion.<sup>1,2</sup> Healthy articular cartilage requires regular, cyclical loading. However, with disease progression, abnormal joint biomechanics produce irregular patterns of cartilage degeneration.<sup>10</sup> Although OA can ultimately affect any synovial joint,<sup>2,9,11</sup> weightbearing joints are preferentially affected with the knee most commonly involved.<sup>6,12-14</sup> The overall

mechanism for disease development and progression rests within a combination of mechanical loading locally and a systemic response overall.<sup>11</sup>

OA is often defined according to the Kellgren and Lawrence (K/L) radiographic grading system. Disease severity is graded 1 through 4 with 1 indicating minimal OA and 4 indicating severe OA. Disease severity is determined according to the presence of various radiographic features including the size of osteophyte formation, degree of joint narrowing and the extent of subchondral bone sclerosis.<sup>15,16</sup>

In general, OA can be divided into two broad disorders including primary OA (insidious onset, idiopathic) and secondary OA (post-traumatic). In primary OA, the cause is unknown with no previous knee trauma identified. However, genetic predisposition may play a role. Conversely, in secondary OA, the cause is typically associated with a previous knee injury, such as an ACL or meniscal tear.<sup>11</sup> Degenerative meniscal tears are also recognized as a feature of OA<sup>17,18</sup> and are associated with an increased risk of developing OA.<sup>19</sup>

## 1.2 Anterior Cruciate Ligament Injuries

Tears of the anterior cruciate ligament (ACL) are the most common knee injury in adolescents.<sup>20</sup> Within a young, athletic population, females are at an increased risk of ACL injury<sup>21</sup> and undergoing ACL reconstruction.<sup>22</sup> However, within an older, athletic population, there is a higher incidence of ACL tears<sup>23</sup> and reconstruction<sup>22</sup> in males. Among nearly 20000 sports injuries observed over a ten year time period, approximately 40% were related to the knee and 20% of these knee injuries were ACL tears.<sup>24</sup> Although many individuals sustain their injuries while participating in sports, only 30% of the injuries are a direct result of contact with the knee while the other 70% of injuries are non-contact.<sup>25</sup> This large discrepancy in contact versus non-contact injuries suggests there are inherent risk factors related to anatomical, neuromuscular and biomechanical features that predispose certain individuals to ACL tears.

Approximately 10 to 20 years after ACL injury and reconstruction, 50% of individuals develop radiographic evidence of OA with reported knee pain and functional knee impairment.<sup>26,27</sup> Although current surgical techniques for ACL tears may provide substantial



improvements in patient reported outcomes,<sup>28</sup> there is a growing body of evidence that suggests ACL reconstruction may not restore normal ambulatory biomechanics.<sup>27,29-33</sup> Furthermore, evidence also suggests that ACL reconstruction may not provide additional benefits in patient-reported outcomes compared to conservative interventions, such as rehabilitation.<sup>34-36</sup> Overall, there is insufficient evidence to support superior outcomes with surgical interventions over conservative treatments.<sup>37</sup>

## 1.3 The Role of Lower Limb Alignment on Knee Joint Load

### 1.3.1 Static Alignment

Bilateral anterior-posterior radiographs are used to determine frontal plane lower limb alignment through measurement of the mechanical axis angle (MAA). The MAA is defined as the angle produced between the mechanical axis of the femur and the mechanical axis of the tibia. The mechanical axis of the femur is defined as a line extending from the center of the hip to the center of the knee and the mechanical axis of the tibia is defined as a line extending from the center of the ankle to the center of the knee.<sup>38,39</sup> A positive angle indicates valgus alignment and a negative angle indicates varus alignment.

Evidence suggests a positive relationship between varus malalignment and the development<sup>13</sup> and structural progression<sup>13,40,41</sup> of medial tibiofemoral OA. During stance, an adduction moment is created at the varus-aligned knee, placing increased load on the medial compartment and tension on the lateral structures. Data obtained from instrumented knee implants reveals a 5% increase in medial compartment load for every 1° increase in varus alignment.<sup>42</sup> Additionally, the odds of developing tibiofemoral OA 15 years after an ACL injury are 3.9 for individuals with varus alignment compared to individuals with neutral or valgus alignment.<sup>41</sup>

Lateral radiographs are used to determine sagittal plane knee alignment through measurement of the posterior tibial slope (PTS). The PTS is defined as the angle produced between a line perpendicular to the tibial diaphysis and a line parallel to the posterior inclination of the tibial plateau.<sup>43</sup> A larger value indicates greater anterior to posterior inclination relative to the transverse plane. Importantly, the magnitude of the PTS influences the degree of tension on the ACL<sup>43</sup> with a greater PTS leading to greater tension on the ACL.

### 1.3.2 Dynamic Alignment

Although static alignment measures obtained from radiographs are related to loads on the knee, dynamic measures derived from 3D motion analysis provide a more accurate representation of the loads on the knee sustained during physical activity and the risk associated with the development and progression of medial knee OA. For example, the external knee adduction moment is a valid proxy for mediolateral distribution of loads across the knee<sup>44-47</sup> and is also associated with increased progression of medial knee OA.<sup>48-51</sup> Specifically, there is a 6 fold increase in the risk of OA progression for every 1% BW×Ht increase in the external knee adduction moment.<sup>51</sup> Although the knee adduction moment has been identified as an important risk factor in the structural progression of medial tibiofemoral OA,<sup>48-51</sup> it is typically poorly correlated with pain and its clinical importance is often questioned.<sup>52-60</sup> The knee flexion moment is associated with medial contact force<sup>61</sup> and tibial cartilage thickness.<sup>62</sup> The knee internal rotation moment is associated with a greater degree of OA severity.<sup>63</sup> However, the relationship between these knee moments and pain is presently unclear. A thorough investigation of the relationship between pain and the external knee moments may allow us to identify patients who may benefit from interventions targeting knee biomechanics.

## 1.4 Surgical Interventions

### 1.4.1 Medial Opening-Wedge High Tibial Osteotomy

Although no cure for OA currently exists, there are various operative and non-operative treatment options available to address symptoms associated with pain and functional limitations. In addition to reducing symptoms, available treatments also intend to alter load distribution across the knee in an attempt to reduce disease progression. Medial opening-wedge HTO aims to improve the mediolateral distribution of loads across the knee for individuals with unicompartmental arthrosis<sup>64</sup> and varus deformity.<sup>65</sup> Therefore, medial opening-wedge HTO is typically reserved for relatively young individuals (mean age late 40s) with varus alignment and isolated degeneration of the medial compartment,<sup>66</sup> prior to the development of end-stage disease and the need for total joint arthroplasty.

From bilateral anterior-posterior radiographs, several important measures are obtained and used to estimate the required osteotomy correction, while considering other factors, such as disease severity in the lateral compartment. These measures include the weight-bearing line (WBL) which extends from the center of the hip to the center of the ankle and the MAA. Depending on the degree of deformity and health of the articular cartilage in the lateral knee compartment, the measures obtained from the radiographs are used to estimate the correction required to move the WBL laterally to a maximum position of 62.5% medial-to-lateral tibial width.<sup>67</sup>

### 1.4.2 ACL Injury and Reconstruction

There has been extensive research investigating the biomechanical factors associated with the initial rupture of the ACL, subsequent long-term effects related to the initial insult and the effectiveness of various treatment interventions. Although the literature evaluating the effects of ACL injury and reconstruction is quite comprehensive, discrepancies in experimental design between studies prove difficult in ascertaining the biomechanical effects of ACL injury, surgery and rehabilitation. Some studies evaluate the external knee moments at different points in stance during different tasks, such as walking, running and stair climbing. Some studies evaluate the kinematics and kinetics in only one plane while other studies investigate the biomechanical effects through two planes or all three planes. Research investigating the transverse plane is particularly scarce. However, despite these discrepancies, a number of studies have suggested that both ACL deficiency and ACL reconstruction results in a decreased external knee flexion moment.<sup>68-77</sup>

Approximately half of individuals who sustain an ACL injury develop post-traumatic OA, despite surgical intervention.<sup>27</sup> This high incidence of OA following ACL injury may indicate articular cartilage or subchondral bone disruption associated with the initial ligamentous tear.<sup>78</sup> Different methods of *in vivo* modeling have suggested an interaction between abnormal knee motion following ACL injury and a shift in load distribution. Specifically, a shift in load bearing from areas of conditioned cartilage to areas infrequently loaded, initiates degenerative changes by reducing the ability of the cartilage to withstand loads.<sup>29,79,80</sup> Additionally, this risk is higher for individuals with concomitant varus malalignment.<sup>41</sup> Variations in type of graft, graft tension, method of fixation and source of

tissue donation<sup>81</sup> have all been explored to determine whether the degree of anteroposterior laxity, functional outcomes and subsequent risk of knee OA are improved according to specific reconstruction techniques. Thus, the relationship between ligament integrity, normal ambulatory biomechanics and the risk of knee OA is complex and dynamic.

### 1.4.3 The Role of Combined HTO and ACL Reconstruction

Although valgus producing HTO creates a large change in frontal plane knee alignment, the procedure may also alter biomechanics in the sagittal plane, either inadvertently or as planned. Thus, alteration of both sagittal and frontal plane knee alignment combined with ligamentous reconstruction, may alter the biomechanical environment of the knee to favourably redistribute loads across the knee.<sup>82-84</sup>

Alterations in the external knee adduction<sup>48-51,62,85</sup> and flexion<sup>62,85</sup> moments have been identified as important risk factors in the progression of medial knee OA. However, these changes in knee biomechanics can potentially be corrected through realignment of the weightbearing axis laterally, decreasing contact pressure in the medial compartment.<sup>86</sup> Additionally, a greater PTS results in greater anterior tibial translation<sup>83,84,87,88</sup> and excessive strain on the ACL.<sup>89,90</sup> Thus, by reducing the PTS through corrective realignment of the sagittal plane, the degree of anterior tibial translation is minimized. This alteration of the PTS may favourably redistribute loads to areas of conditioned cartilage. Notably, an unintended increase in the PTS may occur with medial opening-wedge HTO.<sup>84</sup> Thus, care must be taken to reduce unwanted changes in the sagittal plane when completing the medial opening-wedge HTO, especially in individuals with compromised ligament integrity.

### 1.4.4 Combined HTO and ACL Reconstruction Literature Review

Although there is an abundance of literature examining lower extremity biomechanics following ACL injury and reconstruction and a growing body of evidence evaluating the effects of HTO, there is limited evidence exploring the role of combined HTO and ACL reconstruction. Additionally, large discrepancies between studies in time since injury and surgery, disease severity and the specific outcomes assessed has lead to inconsistent results and an inability to ascertain the long term effects of combined HTO and ACL reconstruction.

Kean et al. (2009)<sup>91</sup> evaluated 21 individuals with varus malalignment, medial compartment knee OA and ACL injury following simultaneous medial opening-wedge HTO and ACL reconstruction. Primary outcomes were obtained both preoperatively and one year postoperatively and included gait biomechanics in the sagittal and coronal planes in addition to muscle activity measured via electromyography. There was a decrease in both the external knee adduction and flexion moments along with an increase in the extension moment. However, there were no significant changes in muscle activation patterns. Although estimations of both external knee moments and muscle activity were assessed, only values for the sagittal and coronal planes were examined. Since several studies have reported an alteration in internal-external rotation following ACL injury that persists despite reconstruction,<sup>92-97</sup> the kinematics and kinetics in the transverse plane should be considered when evaluating the effects of the combined procedure. Additionally, individuals were only evaluated at one year postoperatively. Progressive, chronic diseases, such as OA, often develop over longer periods of time with repetitive loading. Thus, the efficacy of interventions designed to alter the disease course should be evaluated at multiple time points over several years. Although Kean et al. (2009)<sup>91</sup> investigated the effects of the combined procedure on gait biomechanics pre and postoperatively, continuous and persistent changes beyond one year were not evaluated.

Zaffagnini et al. (2013)<sup>98</sup> evaluated 32 individuals with varus malalignment, medial compartment knee OA and ACL injury who received simultaneous lateral closing-wedge HTO and primary ACL reconstruction or revision surgery. Pain and function, anteroposterior knee laxity and disease severity were evaluated at approximately 6.5 years after surgery. Following the combined surgery, pain and function significantly improved. Additionally, anteroposterior laxity remained in only two individuals. However, 22% of individuals developed severe OA (Grade D) in the medial compartment. Although Zaffagnini et al. (2013)<sup>98</sup> did evaluate the longer term effects of the combined procedure by following patients six years after surgery, outcomes were limited to clinical evaluation of symptoms. Thus, the long-term biomechanical effects of the combined surgery remain unknown, despite the recognized importance of abnormal biomechanics on the development and progression of medial knee OA.

Trojani et al. (2014)<sup>99</sup> retrospectively reviewed data from 29 individuals who underwent combined medial opening-wedge HTO and ACL reconstruction for chronic anterior knee laxity and early knee OA. Pain and function, knee stability and radiographic disease progression were evaluated six years after surgery. Following the combined surgery, 23 individuals resumed sporting activities, 28 individuals reported no instability and 21 individuals reported no pain. However, a clinically significant improvement in pain and function could not be determined as preoperative evaluations were not obtained. Most importantly, although the role of biomechanics in the onset and progression of OA is well established,<sup>48,51</sup> without evaluation of gait biomechanics in the current study, alterations in load distribution across the knee could not be determined. Furthermore, the duration of follow-up varied from just over two years (25 months) to 12 years. Thus, any time-dependent alterations in pain, function and radiographic measures remain unclear.

Schuster et al. (2016)<sup>100</sup> prospectively followed 23 individuals with varus malalignment, ACL deficiency, moderate to severe OA and full thickness cartilage defects who underwent combined HTO, ACL reconstruction and chondral resurfacing. Individuals were followed at a minimum five years after surgery. Primary outcomes included evaluation of survival (arthroplasty not required), pain, function and satisfaction, anteroposterior knee laxity and radiographic disease progression. There were significant improvements in pain and function. Additionally, good cartilage regeneration was seen in the majority of femoral condyles (~90%) and tibial plateaus (~56%). Although Schuster et al. (2016)<sup>100</sup> evaluated the long-term effects of the combined procedure at a minimum 5 years postoperatively, a relatively small cohort of individuals were included. Additionally, the effects of the combined procedure on knee biomechanics were not evaluated.

Li et al. (2015)<sup>101</sup> completed a systematic review on subjective and objective outcomes at a minimum two years following combined high tibial osteotomy and ACL reconstruction. An initial search retrieved a total of 712 articles. However, 11 studies remained after inclusion and exclusion criteria were applied. Of the 11 articles selected, 8 were case series and 3 were retrospective comparative studies, comprising 218 knees at a mean follow-up of 5.8 years (1-13 years). Overall, results indicated improvement in function and disease progression, however, there were some limitations identified. Although the inclusion and exclusion

criteria were fairly broad, a relatively small number of studies were included. Additionally, outcomes appeared to be limited to patient reported function and radiographic outcomes. Changes in knee biomechanics were not considered in any of the studies included. Although Li et al. (2015)<sup>101</sup> reported a tendency for individuals to return to most sporting activities, except for pivoting and jumping, objective measures evaluating return to sport were absent. Finally, outcome assessments among studies were not consistent. Different subjective scoring systems were used to evaluate function and return to sport. Additionally, some assessments were completed both preoperatively and postoperatively while other measures were only obtained at postoperative evaluation, increasing the difficulty of accurately establishing surgical changes.

## 1.5 Current Methods for the Evaluation of HTO and ACL Reconstruction

### 1.5.1 Three-Dimensional Gait Analysis

Quantitative gait analysis has been used extensively to evaluate the biomechanical profiles of a number of pathologies. Both kinematic and kinetic measures are combined to provide an estimate of the relative load distribution across the knee. During the stance phase of gait, the line of action of the ground reaction force (GRF) is directed towards the center of mass (CoM) from the center of pressure (CoP) under the foot. Depending on where the GRF vector passes relative to the center of the knee, different lever arms are created, producing different external moments about the knee in all three orthogonal planes. Although the GRF and lever arm largely impact the magnitude of the external knee moments, it is important to note that 3D gait analysis most often uses inverse dynamics to calculate knee moments. Inverse dynamics involves measures of external forces imposed on a system (i.e. GRF), net joint force and moment, linear and angular acceleration and anthropometric estimates in addition to lever arms. To calculate the net moments about a joint, these measures are incorporated into a musculoskeletal model that relies on the representation of the human body as a set of linked rigid segments.<sup>102-105</sup>

External knee moments provide indices that represent the loads on the knee during walking. The knee adduction moment is the most commonly reported moment in the knee OA

literature and is a valid proxy for the mediolateral distribution of knee load.<sup>46,106</sup> In the frontal plane, when the GRF passes medial to the center of the knee, an external knee adduction moment is created during stance. The knee adduction moment acts to adduct the tibia about the center of the knee, resulting in compression of the medial tibiofemoral compartment. The knee adduction moment typically demonstrates two peaks throughout stance with the greatest peak in early stance. This first peak corresponds to the loading response of the stance limb when the GRF is the greatest.

In the sagittal plane, when the GRF passes posterior to the center of the knee, an external knee flexion moment is created. The knee flexion moment is controlled through eccentric activation of the knee extensors (i.e. quadriceps).<sup>107</sup> The external knee flexion moment is suggested to represent net muscle contraction.<sup>108,109</sup> Conversely, when the GRF passes anterior to the center of the knee, an external knee extension moment is created. The knee extension moment is controlled through eccentric activation of the knee flexors (i.e. hamstrings).<sup>107</sup> The external knee moments in the sagittal plane typically demonstrate two peaks throughout stance. The first peak occurs during early stance and represents the knee flexion moment while the second peak occurs during late stance and represents the knee extension moment. The knee flexion moment corresponds to the loading response of the stance limb when the GRF is the greatest.

In the transverse plane, an internal rotation and external rotation moment act to internally rotate or externally rotate the tibia, respectively. The external knee moments in the transverse plane typically demonstrate two peaks throughout stance. The first peak occurs during early stance and represents the knee external rotation moment while the second peak occurs during late stance and represents the knee internal rotation moment. These moments are less commonly reported in the knee OA literature and their potential clinical importance is presently unclear. Overall, although clear limitations exist with respect to measuring the actual loads on the knee, quantitative gait analysis does provide the ability to represent dynamic knee loads and provides insight into the effects of different knee pathologies, disease progression and potential interventions.



### 1.5.2 Patient Reported Outcome Measures

There is an extensive array of patient reported outcome measures available to evaluate pain and functional limitations related to knee pathologies. The Knee Osteoarthritis Outcome Score (KOOS) was developed to assess individuals with various knee pathologies including ACL injuries, meniscal injuries, cartilage lesions and OA. This disease-specific questionnaire measures impairment and disability through a total of 42 items according to 5 domains and 5 response options per item. The 5 domains include pain (9 items), symptoms (7 items), activities of daily living (17 items), sport and recreation function (5 items) and knee-related quality of life (4 items). Domain scores are a standardized average of all items within the domain that vary between 0 (worst) and 100 (best).<sup>110,111</sup> The KOOS has been shown to have appropriate reliability and responsiveness for patients with knee OA or ACL deficiency.<sup>110</sup>

The Western Ontario and McMaster Universities Arthritis Index (WOMAC) was developed to assess individuals with knee and hip OA. This disease-specific questionnaire measures patient symptoms and function through 24 items divided into three subscales. The three subscales include pain (5 items), stiffness (2 items) and function (17 items). Responses are determined according to a Likert scale ranging from 0 to 4. Items within each subscale are summed. The overall scores within each subscale are also summed together to obtain a total WOMAC score. Importantly, to ensure content validity for older patients with knee OA, the developers of the KOOS included the original questions from the WOMAC subscales in the corresponding KOOS domains. By integrating the questions from the WOMAC into the KOOS, researchers are able to obtain WOMAC scores directly from the KOOS, reducing the number of questionnaires administered to patients.

### 1.5.3 Imaging

Visual inspection of the joint via second-look arthroscopy or magnetic resonance imaging (MRI) allows for direct visualization and quantification of cartilage loss in addition to other structural abnormalities such as bone lesions, ligament tears and joint effusion.<sup>112,113</sup> These imaging methods are also sensitive in detecting early joint degeneration compared to conventional radiography.<sup>112</sup>

### 1.5.4 Dissociation Between Outcomes

Pain is the most common symptom reported by individuals with knee OA and may act as a protective mechanism to favourably alter loads across the knee.<sup>114</sup> A reduction in pain achieved through pain medication produces an adverse increase in knee loading.<sup>115-117</sup> However, previous studies demonstrate a low to moderate association between pain and objective measures of knee loads, including dynamic knee alignment measures, such as the knee adduction moment.<sup>52,54,57,118,119</sup>

When evaluating the relationship between pain and objective outcomes, previous studies compared pain over time between individuals using specific patient-reported outcome measures.<sup>52,53,56-58,60,116</sup> However, pain is heavily influenced by a number of extraneous factors that differ between individuals. These factors include previous pain encounters,<sup>120</sup> expectations surrounding the effectiveness of analgesics,<sup>121</sup> coping strategies<sup>122</sup> and genetic predisposition.<sup>123</sup> Thus, investigations utilizing pain as an outcome should consider a within-subjects design that minimizes the effect of confounding factors. Establishing the relationship between pain and external knee moments provides the ability to predict the progression of symptoms based on objective measures of gait.

## 1.6 Study Rationale

With an aging population and greater participation in physical activity, interventions designed to address known risk factors for knee OA are required. Both patient-reported outcomes, especially pain, and more objective measures of patient performance, including gait biomechanics, are critical to consider in the evaluation of such interventions. Although there is rationale for performing combined HTO and ACL reconstruction with the intent of improving pain and gait biomechanics, there is a paucity of research investigating the combined procedure. Thus, the overall aim of this thesis was to clarify the relationship between pain and gait biomechanics (external knee moments) in order to investigate the long-term effects of combined medial opening-wedge HTO and ACL reconstruction in individuals with concomitant medial compartment knee OA, varus malalignment and ACL deficiency. The specific objectives and hypotheses for each study are summarized below.

## 1.7 Thesis Overview

The overall purpose of this thesis was to examine the association between pain and selected external knee moments during walking, and the long-term (5 years) effects of combined HTO and ACL reconstruction on those outcomes. The thesis consists of three studies. All studies were completed in the Wolf Orthopaedics Biomechanics Laboratory, Fowler Kennedy Sport Medicine Clinic, Western University.

**Chapter 2 (Study 1):** Evaluation of the cross-sectional association between pain and external knee moments among patients with medial tibiofemoral OA suggests a low relationship of questionable clinical importance. However, evaluation of this relationship within individuals (between limbs) offers the ability to control for extraneous factors that may influence pain perception. Thus, the objective of this study was to examine the relationship between pain and selected external knee moments in all three planes when controlling for extraneous factors by comparing limbs within individuals. Results from this study provided further rationale for evaluating objective and subjective outcomes within individuals with concomitant medial knee OA and ACL deficiency.

**Chapter 3 (Study 2):** Concomitant HTO and ACL reconstruction aims to permanently alter knee biomechanics in multiple planes to favourably redistribute loads across the knee. However, research evaluating the long-term biomechanical effects is greatly limited. Thus, the objective of this study was to examine the long-term effects of combined medial opening-wedge HTO and ACL reconstruction on peak external knee moments and angles in all three planes during walking. Changes in radiographic and patient-reported outcomes were also investigated.

**Chapter 4 (Study 3):** It is difficult to ascertain whether the specific effects of combined HTO and ACL reconstruction can be attributed to the osteotomy or the ligament reconstruction. Therefore, it is unclear whether ACL reconstruction offers additional benefits beyond medial opening-wedge HTO. Thus, the objective of this study was to compare the peak external knee adduction and flexion moments between two groups of patients with concomitant ACL deficiency, varus malalignment and medial compartment knee OA who received either combined HTO and ACL reconstruction or HTO alone.

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## Chapter 2

### 2 Associations Between Knee Loading and Pain After Walking in Patients with Knee Osteoarthritis: Within-Patient Between-Limb Analyses

#### 2.1 Summary

As knee pain is influenced by various factors that differ among patients with knee OA, its association with dynamic knee joint loading may be influenced by between-person confounding. The objective of the present study was to investigate the association between knee pain and external knee moments during walking, while controlling for extraneous factors by comparing limbs within patients with medial knee OA. 265 patients with medial compartment tibiofemoral OA and discordant changes in knee pain between limbs after walking were identified from a gait registry of patients with knee OA. All patients had rated their pain in each knee on an 11-point numeric rating scale before and after a six-minute walk and then completed three-dimensional gait analysis. For each limb, the change in pain was recorded as an increase ( $\geq 1$  points) or not ( $\leq 0$  points). Among paired limbs, the associations between an increase in pain and selected external moments about the knee during walking were evaluated using conditional logistic regression before and after adjusting for Kellgren and Lawrence grade of radiographic severity. An increase in pain was significantly associated with the peak knee adduction moment (OR=2.43, 95%CI=1.77, 3.33), adduction impulse (OR=6.62, 95%CI=3.46, 12.7), peak knee flexion moment (OR=0.46, 95%CI=0.36, 0.60) and peak knee internal rotation moment (OR=7.89, 95%CI=3.41, 18.2). Associations remained significant ( $p=0.05$ ) after adjusting for Kellgren and Lawrence grade. When between-person confounding is lessened among patients with medial knee OA, there are significant associations between knee pain and external knee moments during walking in all three planes that vary in magnitude and direction.

## 2.2 Introduction

Pain is the most common complaint in individuals with symptomatic knee osteoarthritis (OA), leading to mobility impairments, functional limitations, decreased quality of life and increased use of medical services.<sup>1-3</sup> Knee OA pain is commonly worsened by activities that load the knee and relieved by rest.<sup>2</sup> Various biomechanical measures derived from three-dimensional quantitative gait analysis are frequently used to represent dynamic knee joint loads, yet the reported relationships between knee pain and gait biomechanics are generally quite low, questioning their clinical relevance.<sup>4-12</sup> Specifically, cross-sectional studies investigating the external knee adduction moment during walking report only weak-to-moderate associations with pain, with correlation coefficients ranging from 0.0 to 0.6.<sup>4-12</sup>

Importantly, when investigating the relationship between knee pain and gait biomechanics, cross-sectional studies make comparisons between individuals.<sup>4,5,8-10,12,13</sup> Consequently, extraneous factors that may influence pain perception differ among individuals and may alter the overall relationship between pain and gait biomechanics. The fact that extraneous factors influence pain perception is well-accepted in OA research and helps explain the relatively low associations often reported between pain and other measures relevant to OA, such as performance-based measures of function<sup>6,14,15</sup> and structural measures of joint degeneration.<sup>16</sup>

Pain encompasses multiple experiences unique to each individual, including previous pain encounters,<sup>2,17</sup> expectations surrounding the effectiveness of analgesics,<sup>2,18</sup> coping strategies<sup>2</sup> and genetic predisposition.<sup>19</sup> As the interplay between extraneous factors and pain is exclusive to each individual, within-subject designs are appealing when studying pain relationships. The use of naturally matched pairs, where one limb within an individual is compared to the opposite limb, may help control for the influence of extraneous factors when studying knee OA pain.<sup>20</sup> For example, Neogi et al. (2009)<sup>20</sup> showed a strong association between radiographic features of OA and pain levels when evaluating paired knees discordant in pain severity and frequency.<sup>20</sup> We are unaware of similar research designs used in the study of gait biomechanics and knee pain.

The relationship between pain and the external knee adduction moment during walking is most commonly studied because it is widely accepted as a valid proxy for mediolateral



distribution of dynamic loads across the knee<sup>21,22</sup> and a risk factor for structural disease progression.<sup>23,24</sup> However, the external knee moments in the sagittal plane (e.g. peak knee flexion moment) and the transverse plane (e.g. peak knee internal rotation moment) may also influence the development and progression of medial knee OA and be related to knee pain.<sup>25,26</sup> Therefore, a thorough investigation of the relationship between pain and knee moments in all three planes of motion may provide a greater ability to predict symptoms of OA and identify patients who may benefit from interventions that target knee biomechanics. Thus, the objective of the present study was to investigate the association between knee pain and external knee moments during walking, while controlling for extraneous factors by comparing limbs within patients with medial knee OA.

## 2.3 Methods

### 2.3.1 Participants

Participants were from an ongoing registry of gait, imaging and patient-reported outcomes for patients with knee OA. Patients had been referred to a tertiary care clinic and then subsequently, to the biomechanics laboratory, due to ongoing knee pain. All patients had a diagnosis of knee OA based on the criteria described by Altman & Gold (2007).<sup>27</sup> Radiographic Kellgren and Lawrence (K/L) severity ratings<sup>28</sup> and mechanical axis angles<sup>29,30</sup> were completed for both knees. For the present study, only patients with neutral or varus alignment (mechanical axis angle  $\leq 0$  degrees) and pain located primarily in the medial tibiofemoral compartment were included. All participants provided informed consent, including the use of their data for future unknown research questions. The gait registry was approved by the institution's Research Ethics Board for Health Sciences Research Involving Human Subjects.

**Table 2.1** Patient demographics and clinical characteristics for both limbs in patients with discordant changes in knee pain (N=265).

|  | Mean (SD)  |
|--|------------|
| Sex, M/F                                       | 196/69     |
| Age, yr  | 47 (9)     |
| BMI, kg/m <sup>2</sup>                         | 30 (5)     |
| <i>Increased Pain Knee</i> MAA, degrees        | -7.0 (4.5) |
| <i>Not Increased Pain Knee</i> MAA, degrees    | -4.1 (3.7) |
| <i>Increased Pain Knee</i> K/L Grade, N(%)     |            |
| 0  | 4 (1.5)    |
| 1  | 44 (17)    |
| 2  | 42 (16)    |
| 3  | 100 (38)   |
| 4  | 75 (28)    |
| <i>Not Increased Pain Knee</i> K/L Grade, N(%) |            |
| 0  | 84 (32)    |
| 1  | 86 (32)    |
| 2  | 31 (12)    |
| 3  | 48 (18)    |
| 4  | 16 (6.0)   |

BMI, body mass index.

MAA, mechanical axis angle.

K/L, Kellgren-Lawrence grade of OA severity.

**Table 2.2** Patient demographics and clinical characteristics for both limbs in patients with no discordant changes in knee pain (N=311).

|  | Mean (SD)  |
|--|------------|
| Sex, M/F                                 | 226/85     |
| Age, yr                                  | 47 (10)    |
| BMI, kg/m <sup>2</sup>                   | 30 (5)     |
| <i>Surgical Knee</i> MAA, degrees        | -7.2 (4.0) |
| <i>Non-Surgical Knee</i> MAA, degrees    | -4.8 (3.9) |
| <i>Surgical Knee</i> K/L Grade, N(%)     |            |
| 0  | 3 (1.0)    |
| 1  | 36 (12)    |
| 2  | 106 (34)   |
| 3  | 112 (36)   |
| 4  | 54 (17)    |
| <i>Non-Surgical Knee</i> K/L Grade, N(%) |            |
| 0  | 80 (26)    |
| 1  | 93 (30)    |
| 2  | 75 (24)    |
| 3  | 42 (14)    |
| 4  | 21 (6.8)   |

BMI, body mass index.

MAA, mechanical axis angle.

K/L, Kellgren-Lawrence grade of OA severity.

### 2.3.2 Pain Assessment

We asked the participants to rate the level of pain in each knee using an 11-point numeric rating scale. The scale ranged from 0 to 10 with 0 representing no pain and 10 representing the worst pain possible. Patients rated pain in each knee immediately before and after completing a 6-minute walk. A stopwatch was used to record the time while the patient walked around an 80 foot track while wearing their own shoes. Patients were instructed to walk as far as possible without running and were informed that breaks were allowed if necessary.<sup>31,32</sup> At approximately 5 minutes of walking, patients were informed they had almost completed the test. Otherwise, no further encouragement was provided.

### 2.3.3 Gait Analysis

Patients completed bilateral gait analysis using an eight-camera motion capture system (Motion Analysis Corporation, Santa Rosa, CA) synchronized with a floor-mounted force platform (Advanced Mechanical Technology Inc., Watertown, MA). Passive-reflective markers were placed on bony landmarks using a 22-marker, modified Helen Hayes marker set. During a static trial on the force platform, additional markers were placed over the medial knee joint line and medial malleolus to determine knee and ankle joint centers. Before gait testing, these four extra markers were removed. Marker (60 Hz) and forceplate (1200 Hz) data were collected while patients walked barefoot across a 10m walkway at their typical walking speed. At least five trials for each extremity were collected. Inverse dynamics was used to calculate external knee moments from the camera and force plate data and were expressed relative to the tibial anatomical frame of reference.<sup>33,34</sup> The same methods and version of software were used to analyze gait data for all participants (Orthotrak 6.0, Motion Analysis Corporation). Knee angles and moments were averaged over five trials and normalized to 100% stance. The knee adduction, flexion and internal rotation moments were evaluated as these variables have previously been associated with disease progression and load distribution<sup>21-26</sup> and can be measured reliably.<sup>35-37</sup> The greatest magnitudes for each external knee moment in either a positive or negative direction were identified as the peaks for each gait cycle waveform. Moments were normalized to bodyweight and height (BW×Ht). To simplify interpretation of the results, each external knee moment was

expressed as a positive value. We also calculated the knee adduction impulse ( $BW \times Ht \times s$ ) by integrating the knee adduction moment waveform with respect to time.

### 2.3.4 Statistical Analysis

The change in pain for both knees was calculated by subtracting the pain rating completed before, from the pain rating completed after, the 6-minute walk. Knees with an increase in pain (i.e. change score  $\geq 1$ ) were classified as "increased" whereas knees with either a decrease or no change in pain (i.e. change score  $\leq 0$ ) were classified as "not increased". Participants with one knee classified as "increased" and the other "not increased" were identified as discordant pairs and included in the analysis. Participants with both knees classified the same (i.e. both "increased" knees or both "not increased" knees) were excluded from the analysis.

We examined the relationship between the change in pain after walking (dependent variable) with the first peak knee adduction moment, adduction impulse, peak knee flexion and peak knee internal rotation moment (independent variables) using four separate conditional logistic regression models. Gait variables were analysed as continuous variables. For each model, a test for an interaction with K/L grade of OA severity was performed, and where the interaction was non-significant, each moment was evaluated adjusting for K/L grade of OA severity.

## 2.4 Results

There were 576 patients (1152 knees) in the gait data registry. Of these, 265 patients were identified as having discordant changes in pain after walking. Patient demographics and clinical characteristics for these 265 patients are presented in *Table 2.1*. Additionally, patient demographics and clinical characteristics for the excluded 311 patients with no discordant changes in pain are presented in *Table 2.2*. Gait waveforms showing the external knee moments in all three planes for both limbs are displayed in *Figure 2.1*. The average gait speed ( $\pm$ SD) was 1.0 (0.19) for both the "increased pain" knee and the "not increased pain" knee. These gait speeds were similar to previously reported gait speeds for both younger and older individuals with medial knee OA,<sup>38</sup> although slower than the standardized gait speeds used in the evaluation of pain and its corresponding effects on knee loads.<sup>39,40</sup>

There was no evidence of an interaction between K/L grade of OA severity and any of the models ( $p=0.15$ ,  $p=0.53$ ,  $p=0.31$  and  $p=0.13$  for the adduction moment and impulse, flexion moment and internal rotation moment, respectively). Unadjusted and adjusted odds ratios (OR) are shown in *Table 2.3*.

In the frontal plane, there was a statistically significant, positive association between the peak knee adduction moment and pain after walking ( $p<0.001$ , OR (95%CI) of 2.43 (1.77, 3.33)). Similarly, there was a statistically significant, positive association between the adduction impulse and pain after walking ( $p<0.001$ , OR (95%CI) of 6.62 (3.46, 12.7)). After adjusting for K/L grade of OA severity, the associations remained statistically significant ( $p=0.012$ , OR (95%CI) of 1.67 (1.12, 2.48) and  $p=0.011$ , OR (95%CI) of 2.83 (1.26, 6.35) for the adduction moment and adduction impulse, respectively).

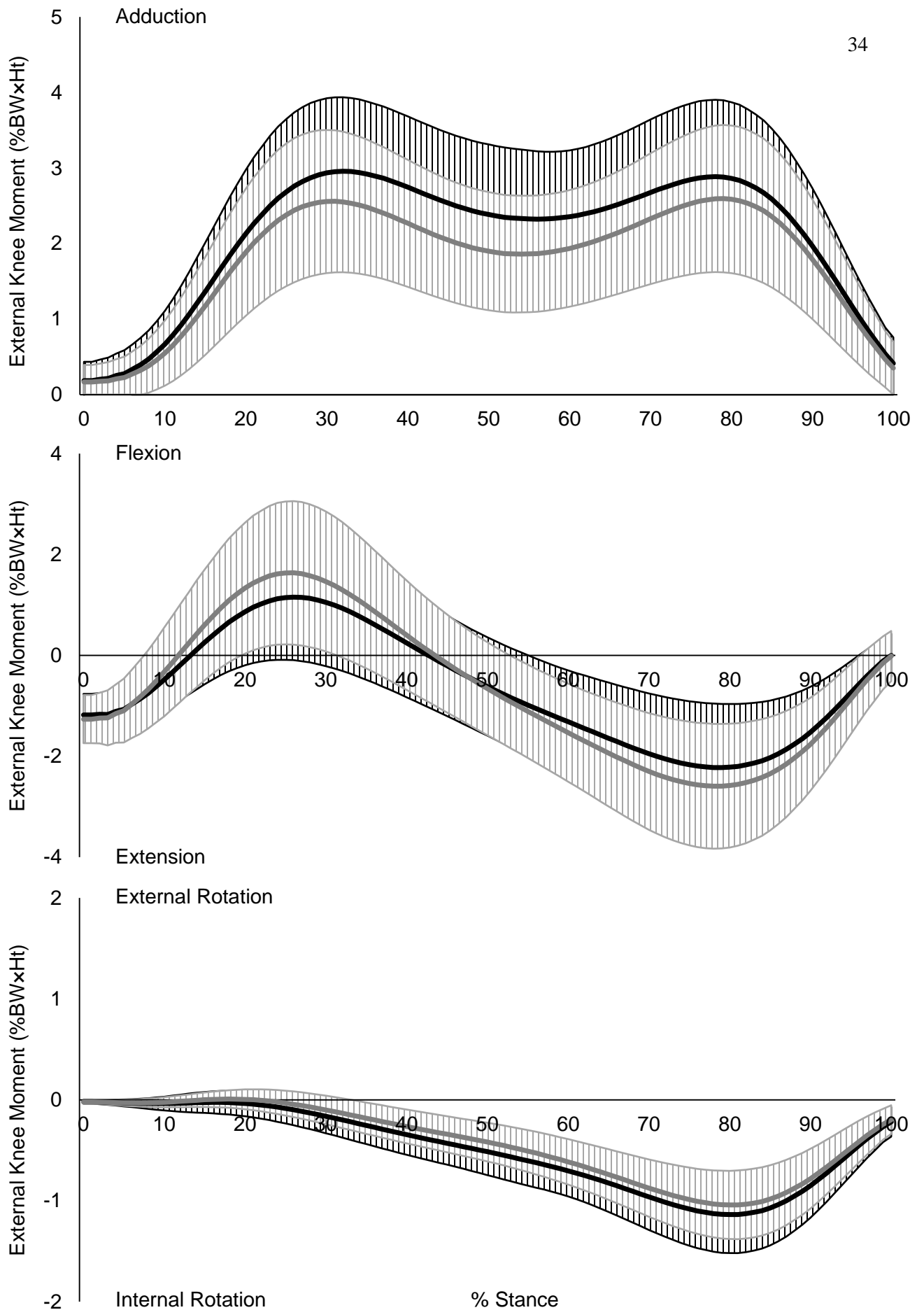
In the sagittal plane, there was a statistically significant, negative association between the peak knee flexion moment and pain after walking ( $p<0.001$ , OR (95%CI) of 0.46 (0.36, 0.60)). After adjusting for K/L grade of OA severity, the association remained statistically significant ( $p=0.006$ , OR (95%CI) of 0.66 (0.49, 0.89)).

In the transverse plane, there was a statistically significant, positive association between the peak knee internal rotation moment and pain after walking ( $p<0.001$ , OR (95%CI) of 7.89 (3.41, 18.2)). After adjusting for K/L grade of OA severity, the association approached statistical significance ( $p=0.05$ , OR (95%CI) of 3.02 (0.99, 9.19)).

**Table 2.3** Association of each gait variable with increased knee pain after the 6-minute walk (N=265).

|                         | Unadjusted        |         | Adjusted <sup>γ</sup> |         |
|-------------------------|-------------------|---------|-----------------------|---------|
|                         | OR (95% CI)       | P Value | OR (95% CI)           | P Value |
| <b>Frontal Plane</b>    |                   |         |                       |         |
| Adduction               | 2.43 (1.77, 3.33) | <0.001  | 1.67 (1.12, 2.48)     | 0.01    |
| Impulse                 | 6.62 (3.46, 12.7) | <0.001  | 2.83 (1.26, 6.35)     | 0.01    |
| <b>Sagittal Plane</b>   |                   |         |                       |         |
| Flexion                 | 0.46 (0.36, 0.60) | <0.001  | 0.66 (0.49, 0.89)     | 0.01    |
| <b>Transverse Plane</b> |                   |         |                       |         |
| Internal Rotation       | 7.89 (3.41, 18.2) | <0.001  | 3.02 (0.99, 9.19)     | 0.05    |

<sup>γ</sup> Adjusted for K/L grade of OA severity.



**Figure 2.1.** Ensemble averages (N=265) for the external knee moments in the frontal (top), sagittal (middle) and transverse (bottom) planes for the “increased pain” knee (black) and “not increased pain” knee (grey). Shaded areas represent  $\pm$ SD.

## 2.5 Discussion

The present results illustrate a moderate-to-strong association<sup>41</sup> between external knee moments, in all three planes of motion, and an increase in knee pain after 6 minutes of walking. For both the knee adduction and internal rotation moments, greater values were associated with greater odds of experiencing an increase in pain after walking. In contrast, a greater knee flexion moment was associated with decreased odds of an increase in pain (*Table 2.3*). Additionally, there were no significant interactions with radiographic severity and the associations remained significant after controlling for K/L grade, suggesting the findings are applicable across different stages of disease.

The present results also suggest that for every 1% BW×Ht×s increase in the knee adduction impulse during walking, there is a 6.6 times greater odds of experiencing an increase in pain (*Table 2.3*). The OR corresponds to the odds associated with a 1% BW×Ht increase in the knee moment (or 1% BW×Ht×s for the knee adduction impulse) which is a relatively large portion of a typical knee moment. Therefore, to help interpret the present findings, it may be helpful to also describe the odds associated with a 0.5% BW×Ht increase. For every 0.5% BW×Ht×s increase in the knee adduction impulse during walking, there is a 2.6 times greater odds of experiencing an increase in pain.

Although the present moderate-to-strong associations between pain and external knee moments may seem to contrast previous studies evaluating this relationship, differences in study designs must be emphasized.<sup>6,7,9,11</sup> Most importantly, our study used a within-subjects design which mitigated the influence of factors that affect knee pain perception, such as personal factors, pain medication and other factors.<sup>2,17-19</sup> Notably, the within-patient design also controls for biomechanical variables such as walking speed, footwear and the loading stimulus (walking time and distance). In addition to differences in study design, previous studies typically assessed pain during activities experienced over time (e.g. previous week), often evaluated as part of patient-reported outcome measures such as the Knee Osteoarthritis Outcome Score or the Western Ontario and McMaster Universities Arthritis Index. Alternatively, we specifically assessed whether knee pain increased following a 6-minute bout of walking observed within the lab. This evaluation of pain also differs from previous studies where pain was induced via saline injections<sup>40</sup> or relieved through pain medication.<sup>39</sup>



The moderate-to-strong positive associations between increased knee pain with walking and the adduction moment, especially the adduction impulse, are consistent with previous studies showing the adduction moment can distinguish well between radiographic disease severities<sup>42</sup> and is associated with radiographic<sup>24</sup> and MRI measures of medial compartment OA progression.<sup>23,43,44</sup> The strong association observed for the knee internal rotation moment is also consistent with previous results suggesting a greater internal rotation moment is associated with greater disease severity.<sup>25</sup> Notably, the OR for the association between the internal rotation moment and increased pain was greatly reduced after controlling for radiographic disease severity and may suggest that changes in symptoms are more dependent on disease severity rather than transverse plane moments.

The relationship between pain and the peak knee flexion moment was negative, so that greater peak knee flexion moments were associated with lower odds of experiencing an increase in knee pain after walking. Although the external knee adduction moment represents the distribution of mediolateral loads across the knee, the external knee moments in the sagittal plane may represent other aspects of loading. There is some evidence to suggest that the flexion moment may reflect net flexor-extensor muscle activity.<sup>45</sup> Individuals with knee OA demonstrate greater muscle cocontraction,<sup>46</sup> reduced sagittal plane knee moments<sup>47,48,49</sup> and sagittal plane knee motion<sup>49</sup> compared to healthy controls. Greater muscle cocontraction may be used to reduce knee symptoms by limiting sagittal plane knee motion.<sup>46</sup> Although muscle activation was not directly measured in the current study, the present association between greater knee flexion moments and no increase in pain (or conversely, lower knee flexion moments and an increase in pain) may suggest that patients are increasing muscle activity to limit sagittal plane knee motion.<sup>49</sup> However, without corresponding measures of muscle activation, we can only speculate about the significance of the association between pain and the sagittal plane knee moments.

It should also be noted that a greater knee flexion moment may be associated with increased risk of disease progression,<sup>26</sup> although evidence to support this relationship is variable.<sup>43</sup> Pain may also act as a protective mechanism to favourably redistribute loads across the knee.<sup>40</sup> Thus, the clinical significance of the present association between a greater knee flexion moment and no increase in pain is difficult to ascertain. However, such an association

suggests that without an increase in pain to act as a warning signal to reduce the knee flexion moment and redistribute loads across the knee, disease progression may be accelerated. Importantly, greater muscle cocontraction is also associated with greater structural disease progression.<sup>50</sup> Therefore, reductions in pain that may be achieved through greater muscle activation in an attempt to control sagittal plane knee motion, could also conceivably contribute to disease progression.

Previous longitudinal studies reporting a relationship between external knee moments and future structural progression of knee OA<sup>23,24,43</sup> are often cited as rationale for the development and use of biomechanical interventions that target knee moments. Alternatively, a cross-sectional study reporting weak associations between pain and knee moments questioned the clinical benefit of such interventions, especially in individuals with mild radiographic severity.<sup>12</sup> The present results suggest that when between-person confounding is lessened, the associations between external knee moments and knee pain can be quite substantial. Although high level evidence demonstrating that alterations in external knee moments during gait can reduce pain in knee OA remains elusive, the present results suggest that a lack of association with pain should not deter the development and use of biomechanical interventions.

Our study has several strengths. In contrast to other studies that evaluate the relationship between biomechanics and symptoms in patients with knee OA, our study was able to reduce the influence of extraneous factors by comparing limbs within individuals. Particularly for pain, extraneous factors can greatly alter the perception of pain<sup>2,17-19</sup> and these factors often differ between individuals. Thus, by using the contralateral limb as a control, the influence of these extraneous factors becomes negligible, allowing us the opportunity to ascertain the relationship between knee moments and pain. Additionally, our sample size of 265 patients was larger than samples from similar cross-sectional studies.<sup>4-6,8,9,12,13</sup> Limitations of our study also need to be acknowledged. The ability to accurately and reliably measure transverse plane biomechanics is less compared to the frontal and sagittal planes.<sup>51,52</sup> Therefore, results for the internal rotation moment should be interpreted cautiously. The lack of statistical significance for the adjusted association between the internal rotation moment and an increase in pain, may be due to decreased repeatability of transverse plane

biomechanics. Future studies should examine the relationship between knee pain and knee biomechanics in the context of different pain models that may help to clarify why some patients experienced a decrease in pain after walking.

In conclusion, results of our study illustrate that the external knee moments in all three planes, and the adduction impulse, are associated with an increase in pain when the influence of extraneous factors is reduced by comparing, within individuals, limbs discordant in reported pain levels. Furthermore, this relationship is evident after controlling for radiographic disease severity.

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## Chapter 3

### 3 Five-year Changes in Gait Biomechanics After Concomitant High Tibial Osteotomy and ACL Reconstruction in Patients with Medial Knee Osteoarthritis

#### 3.1 Summary

Concomitant high tibial osteotomy (HTO) and ACL reconstruction is a combined surgical procedure intended to improve kinematics and kinetics in the unstable, ACL-deficient knee with varus malalignment and medial compartment knee osteoarthritis (OA). The objective of this study was to investigate 5-year changes in gait biomechanics, radiographic and patient reported outcomes bilaterally after unilateral, concomitant medial opening-wedge HTO and ACL reconstruction. 33 patients ( $39 \pm 9$  years) with varus malalignment (mechanical axis angle =  $-5.9 \pm 2.9^\circ$ ), medial compartment knee OA and ACL deficiency completed three-dimensional gait analysis preoperatively, 2 and 5 years postoperatively. Primary outcomes were the peak external knee adduction (first peak) and flexion moments. Secondary outcomes were the peak external knee extension and transverse plane moments, peak knee angles in all three planes, radiographic static knee alignment measures (mechanical axis angle and posterior tibial slope) and Knee Injury and Osteoarthritis Outcome Scores (KOOS). There was a substantial decrease in the knee adduction moment in the surgical limb [ $-1.49\% \text{BW} \times \text{Ht}$  (95% CI:  $-1.75$  to  $-1.22$ )] and a slight increase in the non-surgical limb [ $0.16\% \text{BW} \times \text{Ht}$  (95% CI:  $0.03$  to  $0.30$ )] from preoperative to 5 years postoperative. There was also a decrease in the knee flexion moment for both the surgical [ $-0.67\% \text{BW} \times \text{Ht}$  (95% CI:  $-1.19$  to  $-0.15$ )] and non-surgical limbs [ $-1.06\% \text{BW} \times \text{Ht}$  (95% CI:  $-1.49$  to  $-0.64$ )]. Secondary outcomes suggested substantial improvements were maintained at 5 years, although smaller declines were observed in several measures and in both limbs from 2 to 5 years. Changes in the peak external moments about the knee in all three planes during walking are observed 5 years after concomitant medial opening-wedge HTO and ACL reconstruction. These findings are consistent with an intended, sustained shift in the mediolateral distribution of knee loads.

## 3.2 Introduction

Despite current conservative and surgical treatments for anterior cruciate ligament (ACL) tears, post-traumatic tibiofemoral osteoarthritis (OA) is common following ACL injury.<sup>1,2</sup> In addition to factors associated with the initial ACL injury, such as meniscus tears and subchondral bone bruises,<sup>1</sup> persistent changes in various measures of ambulatory biomechanics are suggested to contribute to subsequent knee OA and several studies question the ability of ACL reconstruction to restore normal ambulatory biomechanics.<sup>1,3-7</sup> Both the peak external knee adduction and flexion moments are important risk factors for the development and progression of knee OA.<sup>8,9,10</sup> Specifically, previous studies suggest changes in knee moments and angles during walking contribute to the progression of knee OA following ACL reconstruction.<sup>4,5,11,12</sup> A decrease in the knee flexion moment following ACL injury is frequently observed<sup>12-14</sup> and an increase in the external knee adduction moment has also been reported.<sup>15</sup> Furthermore, different methods of *in vivo* modeling of the ACL deficient knee suggest an interaction between abnormal knee motion and a shift in load bearing from areas of conditioned cartilage to areas infrequently loaded.<sup>3,16,17</sup>

Varus malalignment is also a strong risk factor for tibiofemoral OA, primarily affecting the medial compartment, due to its effects on the distribution of load across the knee.<sup>3,18</sup> Thus, when ACL deficiency and varus malalignment coexist, the combination of disproportionate loading across an unstable knee may accelerate the degenerative process and is consistent with studies suggesting that higher external knee adduction and flexion moments during walking are risk factors for knee OA.<sup>8-10</sup>

Medial opening-wedge high tibial osteotomy (HTO) aims to correct varus malalignment of the lower limb, thereby decreasing the external knee adduction moment and attenuating the degenerative cycle.<sup>19</sup> Although a valgus-producing HTO creates a large change in frontal plane knee alignment, the procedure may also alter biomechanics in the sagittal and perhaps transverse planes, either inadvertently, or in a planned fashion. Specifically, the posterior tibial slope can be manipulated to decrease excessive anterior tibial translation by altering the relative geometry of the tibial plateau.<sup>20-22</sup>

Although concomitant HTO and ACL reconstruction aims to provide permanent changes in knee biomechanics that may be evident through altered joint moments and angles in multiple planes, there is limited research on the combined procedure,<sup>23-25</sup> and we are unaware of previous studies investigating the 5-year changes in gait biomechanics. Thus, the primary objective of the present study was to investigate the 5-year effects of concomitant medial opening-wedge HTO and ACL reconstruction on external knee moments and angles during walking. Secondary objectives were to explore changes in various radiographic and patient reported outcomes. We hypothesized that concomitant HTO and ACL reconstruction would produce changes in the 3D knee kinematics and kinetics indicative of favourable changes in load distribution across the knee.

### 3.3 Methods

#### 3.3.1 Study Design

The study was approved by the institution's Research Ethics Board for Health Sciences Research Involving Human Subjects and all patients provided informed written consent. Patients were prospectively evaluated using three-dimensional gait analysis, radiographs and patient reported outcomes before, two and a minimum of five years ( $68 \pm 11$  months) after concomitant medial opening-wedge HTO and primary ACL reconstruction.

**Table 3.1** Patient baseline demographics and clinical characteristics.<sup>a</sup>

|   | Mean $\pm$ SD (Range)           |
|---|---------------------------------|
| Sex, M(%)                                   | 28 (84.8)                       |
| Age, yr                                     | 39.6 $\pm$ 9.0 (21 to 58)       |
| Height, m                                   | 1.74 $\pm$ 0.08 (1.57 to 1.89)  |
| Mass, kg                                    | 86.4 $\pm$ 19.0 (54 to 143)     |
| Body Mass Index, kg/m <sup>2</sup>          | 28.3 $\pm$ 5.3 (21 to 45)       |
| Mechanical Axis Angle, degrees <sup>b</sup> | -5.90 $\pm$ 2.87 (-12.0 to 1.2) |
| Kellgren-Lawrence Grade, n(%) <sup>c</sup>  |                                 |
| 0   | 0                               |
| 1   | 8 (25.8)                        |
| 2   | 15 (48.4)                       |
| 3   | 8 (25.8)                        |
| 4   | 0                               |

<sup>a</sup>Results are reported as mean  $\pm$  SD (range) unless otherwise indicated.

<sup>b</sup>Negative mechanical axis angle values correspond to varus alignment.

<sup>c</sup>Preoperative radiographs for 2 patients were unavailable.

### 3.3.2 Participants

33 patients were enrolled in the study. Demographic and clinical characteristics are presented in *Table 3.1*. Indications for surgery included chronic ACL insufficiency (>1 year) with medial compartment OA (Kellgren-Lawrence (K/L)<sup>26</sup> Grade II-III) and varus malalignment confirmed on standing double limb hip-to-ankle radiographs. Patients aged  $\geq 60$  years or those with end-stage degenerative changes (K/L Grade IV) in two or more compartments were excluded as they were considered better candidates for total knee arthroplasty. Other exclusion criteria included inflammatory or infectious arthritis of the knee, symptomatic OA of the lateral compartment, end-stage patellofemoral compartment OA, previous HTO, multiligamentous instability and major neurological deficits affecting gait.

### 3.3.3 Surgery and Rehabilitation

During the same operative procedure, the HTO was completed prior to the ACL reconstruction. Planning of the desired correction and completion of the osteotomy were performed according to techniques previously described.<sup>27</sup> The weight-bearing line was moved laterally to a position no greater than 62.5% of the medial-to-lateral width of the tibial plateau. For corrections greater than 7.5 mm, bone allograft or autograft was used to fill the osteotomy gap. Fixation was achieved using a non-locking (Puddu) plate and confirmed by fluoroscopy. A/P sloped wedge Puddu plates were used in all cases to minimize the tendency to increase the posterior tibial slope (PTS). The plate was placed posteriorly on the tibia to avoid an inadvertent increase in the PTS and to minimize interference with placement of the tibial tunnel for the ACL reconstruction.

Immediately following the HTO procedure a four-bundle ACL graft was then constructed using semitendinosus and gracilis tendons, harvested through the osteotomy incision. All femoral tunnels were drilled within the femoral foot-print of the ACL using an anteromedial portal technique. An Endobutton<sup>TM</sup> was used for femoral fixation. For tibial fixation, multiple staples with or without interference screws were used to achieve graft fixation while the knee was extended and with the graft under tension. Postoperatively, the limb was supported in a range of motion brace and patients were toe-touch weight bearing for 6 weeks. Patients started a supervised physiotherapy program within two weeks of surgery to improve

range of motion, strength and function. Protected weight bearing progressed with radiographic and clinical signs of healing and full weight bearing was achieved by 12 weeks. Once the osteotomy was healed, the postoperative ACL rehabilitation program was implemented, focusing on improvements in proprioception, strength and progression to functional and strenuous activities within twelve months following surgery. A clinical exam was performed on all patients pre and postoperatively and indicated all patients returned to full range of motion. Two patients experienced an undisplaced lateral cortical breach. In both cases, the osteotomies healed without additional treatment and did not affect postoperative rehabilitation. One surgeon (RG) performed all of the surgeries and patient examinations.

### 3.3.4 Gait Analysis

Bilateral gait analysis was completed using an eight-camera motion capture system (Motion Analysis Corporation, Santa Rosa, CA) synchronized with a single, floor-mounted force platform (Advanced Mechanical Technology Inc., Watertown, MA). Passive-reflective markers were placed on patients using a 22-marker, modified Helen Hayes marker set.<sup>28,29</sup> Additional markers were placed bilaterally over the medial knee joint line and medial malleolus during a static trial on the force platform. This trial was necessary to determine knee and ankle joint centres (midpoint between medial and lateral knee and ankle markers, respectively). The four extra markers were removed before gait testing. Hip joint centres were defined by applying percentage offsets (32% lateral, 22% posterior and 34% inferior) relative to the anterior superior iliac spine (ASIS).

Patients were instructed to walk barefoot across a 10m walkway at their typical, self-selected speed while marker (60 Hz) and force plate (1200 Hz) data were sampled from at least five trials from each extremity. External knee moments were expressed relative to the tibial anatomical frame of reference and were calculated from the kinematic and kinetic data using inverse dynamics.<sup>30,31</sup> The same methods and version of software were used to analyze gait data for all time points (Orthotrak 6.6.1, Motion Analysis Corporation). Knee angles and moments in all three orthogonal planes were averaged over five trials for each limb and normalized to 100% stance. Moments were normalized to body weight and height (%BW×Ht). The greatest magnitudes for knee angles and moments in a positive or negative direction were identified as the peaks from each gait cycle waveform.

Given their importance to progression of knee OA,<sup>8-10</sup> our primary outcome measures were the peak external knee adduction (first peak) and flexion moments. Our secondary outcomes included the peak knee extension, internal rotation and external rotation moments and the peak knee adduction, flexion, extension, internal rotation and external rotation angles.

### 3.3.5 Radiographic Analysis

Radiographs were measured by two readers who were trained by an orthopaedic surgeon. We have previously evaluated the reliability of using our digital software to measure standing hip-to-ankle anterior-posterior (AP) and lateral digital radiographs with ICCs (2,1) > 0.81.<sup>32,33</sup>

The mechanical axis angle (MAA), posterior tibial slope (PTS) and patellar height (Blackburne-Peel and Insall-Salvati and Caton-Deschamps ratios) were evaluated preoperatively and 5 years postoperatively. The MAA was measured according to previously described techniques.<sup>33,34</sup> A negative angle indicated varus alignment. Severity of OA preoperatively was also evaluated using the K/L grading scale criteria for both the medial and lateral tibiofemoral compartments for both knees and is presented with the demographic and clinical characteristics in *Table 3.1*.<sup>26</sup>

Standing lateral radiographs were used to determine the PTS angle and patellar height. The digital X-ray software used the posterior tibial cortex as the vertical reference for the posterior tibial slope. Thus, the PTS angle was identified as the angle formed between a line perpendicular to the posterior cortex of the tibia and a line tangent to the surface of the medial tibial plateau.<sup>35</sup> A positive angle indicated a tibial plateau directed backward and inferiorly. Measurement of the Blackburne-Peel, Insall-Salvati and Caton-Deschamps ratios were performed according to previously described techniques.<sup>36,37,38</sup> All radiographic measurements from the digitized images were determined within 0.5 mm using custom software.<sup>33</sup>

### 3.3.6 Patient Reported Outcomes

Patients completed the Knee Injury and Osteoarthritis Outcome Score (KOOS).<sup>39</sup> The KOOS is a knee-specific questionnaire containing 42 items, with five response options per item and five separately reported domains, including pain (9 items), other symptoms (7 items), function in daily living (17 items), function in sports/recreation (5 items) and knee-related quality of life (4 items). Domain scores represent the average of all items in the domain, standardized to a score between 0 (worst) and 100 (best). The KOOS has appropriate reliability and responsiveness in patients with knee OA and patients with ACL deficiency.<sup>39</sup>

### 3.3.7 Statistical Analysis

The 95% confidence intervals (CI) around mean changes and standardized response means between preoperative and 5-year postoperative data were calculated for all primary and secondary outcomes. Comparisons between limbs over time were completed via a two (limb: surgical, non-surgical) by three (time: pre, post 24 months, and  $\geq 60$  months) repeated measures ANOVA with both time and limb treated as within-subject factors. Scheffe post hoc tests were completed following significant main effects and interactions. Statistical analyses were performed using Statistica (StatSoft Inc., Version 7.1, [www.statsoft.com](http://www.statsoft.com)). To explore the association between changes in radiographic alignment measures and gait biomechanics, Pearson correlation coefficients were also completed. In the event of significant changes, we also planned sequential linear regression analyses to determine the effects of changes in previously suggested covariates [gait speed (m/s), trunk lean ( $^{\circ}$ ) and toe-out angle ( $^{\circ}$ )] on the change in the peak external knee moments. Additionally, a sensitivity analysis was also completed, whereby the ANOVA was repeated while replacing the first peak knee adduction moment with the second peak and impulse. Statistical significance was set at  $p < 0.05$ .

## 3.4 Results

### 3.4.1 Primary Outcomes

Gait data across all time points and changes between preoperative and 5 year postoperative values are presented in *Tables 3.2* and *3.3*. There was a significant time by limb interaction

( $p < 0.001$ ) for the peak knee adduction moment, indicating changes over time differed between the surgical and non-surgical limbs. In the surgical limb, there was a significant decrease in the peak knee adduction moment from preoperative to 2 years postoperative ( $p < 0.001$ ) without a statistically significant change from 2 years to 5 years postoperatively (*Table 3.2, Figure 3.1*). In the non-surgical limb, the small increase in the peak knee adduction moment from preoperative to 5 years postoperative was statistically significant (*Table 3.2, Figure 3.1*). There was also a significant time by limb interaction ( $p = 0.012$ ) for the peak knee flexion moment, indicating changes over time differed between the surgical and non-surgical limbs. In the surgical limb, there was a significant decrease in the peak knee flexion moment from 2 years postoperative to 5 years postoperative ( $p = 0.013$ ) (*Table 3.2, Figure 3.1*). Likewise, there was a significant decrease in the peak knee flexion moment in the non-surgical limb from preoperative to 2 years postoperative ( $p < 0.001$ ) and a substantial reduction from baseline was maintained at the 5-year postoperative assessment ( $p < 0.001$ ); although there was no statistically significant change between 2 and 5 years postoperatively (*Table 3.2, Figure 3.1*). At preoperative evaluation, the peak knee flexion moment was lower in the surgical limb compared to the non-surgical limb ( $p = 0.019$ ); however, there was no statistically significant difference between limbs 2 years or 5 years postoperatively. Gait waveforms (ensemble averages) are presented in *Figure 3.2 to 3.4*.

### 3.4.2 Secondary Outcomes

Data for all other variables are presented in *Tables 3.2 to 3.5*. There was a significant time by limb interaction ( $p < 0.001$ ) for the peak knee extension moment with an increase in both the surgical ( $p = 0.013$ ) and non-surgical ( $p < 0.001$ ) limbs from preoperative to 5 years postoperative (*Table 3.2*). There was also a significant time by limb interaction ( $p < 0.001$ ) for the peak knee internal rotation moment with a decrease in the surgical limb from preoperative to 2 years postoperative ( $p < 0.001$ ) (*Table 3.2*). This reduction was maintained at the 5-year postoperative assessment with no change in the non-surgical limb (*Table 3.2*). Similarly, there was also a significant time by limb interaction ( $p = 0.001$ ) for the peak knee external rotation moment; however, there was only a small increase in the surgical limb from preoperative to 2 years postoperative ( $p = 0.008$ ) with no statistically significant change in either limb at the 5-year postoperative assessment (*Table 3.2*).



There was a significant time by limb interaction ( $p < 0.001$ ) for the peak knee varus angle with a decrease in the surgical limb from preoperative to 2 years postoperative ( $p < 0.001$ ) (*Table 3.3*). This reduction was maintained at the 5-year postoperative assessment ( $p < 0.001$ ) with no significant change in the non-surgical limb (*Table 3.3*). There was a significant time effect ( $p < 0.001$ ) for the peak knee flexion angle with a decrease in both the surgical and non-surgical limbs ( $p < 0.001$ ) from preoperative to 5 years postoperative (*Table 3.3*). There was also a significant time by limb interaction ( $p = 0.009$ ) for the peak knee extension angle with an increase at the 5-year postoperative assessment for both the surgical and non-surgical limbs ( $p < 0.001$ ) (*Table 3.3*). There was a significant time effect ( $p = 0.043$ ) and limb effect ( $p = 0.001$ ) for the peak internal rotation angle with the surgical limb less than the non-surgical limb and a decrease in the surgical limb from preoperative to 5 years postoperative ( $p = 0.029$ ) (*Table 3.3*). There was also a significant limb effect ( $p = 0.004$ ) for the peak knee external rotation angle with the surgical limb greater than the non-surgical limb. The mean increase in each of the KOOS domains from preoperative to 5 years postoperative was statistically significant and greater than suggested minimal clinically important differences<sup>39</sup> (*Table 3.5*).

Lastly, the regression analysis indicated that changes in gait speed, trunk lean and toe-out angle did not explain a significant amount of the variance in the observed changes in the peak external knee moments from preoperative to 5 years postoperative. Likewise, results obtained from the repeated measures ANOVA using the second peak of the external knee adduction moment and impulse as the dependent variable were consistent with the results obtained from the analysis using the first peak of the external knee adduction moment as the dependent variable.

**Table 3.2** Peak external knee moments (%BW×Ht).

|                          | Pre<br>Mean (SD) | 2-Year Post<br>Mean (SD) | 5-Year Post<br>Mean (SD) | Pre – 5-Year Post<br>Mean Change (95% CI) | Standardized<br>Response Mean |
|--------------------------|------------------|--------------------------|--------------------------|---|-------------------------------|
| <b>Surgical Knee</b>     |                  |                          |                          |   |                               |
| Adduction                | 2.94 (0.67)      | 1.39 (0.60)              | 1.46 (0.60)              | -1.49 (-1.75 to -1.22)                    | 1.97                          |
| Flexion                  | 1.97 (1.41)      | 1.89 (1.02)              | 1.30 (1.06)              | -0.67 (-1.19 to -0.15)                    | 0.45                          |
| Extension                | -2.51 (1.27)     | -2.64 (1.06)             | -2.96 (1.07)             | 0.45 (0.04 to 0.86)                       | 0.39                          |
| Internal Rotation        | -1.23 (0.31)     | -0.71 (0.23)             | -0.71 (0.25)             | -0.52 (-0.41 to -0.63)                    | 1.72                          |
| External Rotation        | 0.05 (0.06)      | 0.08 (0.07)              | 0.06 (0.06)              | 0.01 (-0.01 to 0.03)                      | 0.18                          |
| <b>Non-Surgical Knee</b> |                  |                          |                          |   |                               |
| Adduction                | 2.46 (0.84)      | 2.53 (0.78)              | 2.62 (0.79)              | 0.16 (0.03 to 0.30)                       | 0.75                          |
| Flexion                  | 2.54 (1.29)      | 1.82 (1.14)              | 1.48 (1.03)              | -1.06 (-1.49 to -0.64)                    | 0.89                          |
| Extension                | -2.46 (1.19)     | -3.39 (1.02)             | -3.44 (0.98)             | 0.98 (0.63 to 1.34)                       | 0.98                          |
| Internal Rotation        | -1.01 (0.31)     | -1.08 (0.29)             | -1.12 (0.25)             | 0.11 (0.05 to 0.17)                       | 0.63                          |
| External Rotation        | 0.08 (0.07)      | 0.06 (0.07)              | 0.06 (0.07)              | -0.01 (-0.04 to 0.01)                     | 0.20                          |

Note: Confidence intervals are not corrected for multiple comparisons.

**Table 3.3** Peak knee angles (°).

|                          | Pre<br>Mean (SD) | 2-Year Post<br>Mean (SD) | 5-Year Post<br>Mean (SD) | Pre – 5-Year Post<br>Mean Change (95% CI) | Standardized<br>Response Mean |
|--------------------------|------------------|--------------------------|--------------------------|---|-------------------------------|
| <b>Surgical Knee</b>     |                  |                          |                          |   |                               |
| Adduction                | -5.23 (4.69)     | 1.79 (4.70)              | 2.56 (4.44)              | -7.79 (-10.0 to -5.57)                    | 1.24                          |
| Flexion                  | 17.0 (6.76)      | 17.7 (5.63)              | 13.2 (5.41)              | -3.80 (-6.58 to -1.02)                    | 0.48                          |
| Extension                | 2.51 (5.50)      | 4.05 (5.73)              | 0.36 (5.87)              | 2.14 (-0.50 to 4.78)                      | 0.29                          |
| Internal Rotation        | -1.69 (10.9)     | -6.20 (13.5)             | -8.76 (9.42)             | -7.07 (-11.5 to -2.63)                    | 0.56                          |
| External Rotation        | -9.63 (11.4)     | -14.4 (12.3)             | -15.5 (10.3)             | 5.88 (1.03 to 10.7)                       | 0.43                          |
| <b>Non-Surgical Knee</b> |                  |                          |                          |   |                               |
| Adduction                | -1.85 (4.72)     | -1.57 (4.70)             | -2.01 (4.38)             | 0.17 (-1.27 to 1.60)                      | 0.04                          |
| Flexion                  | 18.1 (7.46)      | 16.7 (7.71)              | 13.6 (6.73)              | -4.43 (-7.20 to -1.66)                    | 0.57                          |
| Extension                | 0.70 (6.08)      | -0.69 (6.06)             | -2.81 (6.44)             | 3.50 (1.01 to 6.00)                       | 0.50                          |
| Internal Rotation        | 0.18 (10.1)      | -0.39 (13.0)             | -2.82 (11.0)             | -2.99 (-7.03 to 1.05)                     | 0.26                          |
| External Rotation        | -9.44 (9.34)     | -8.62 (13.4)             | 9.59 (11.4)              | 0.15 (-3.87 to 4.18)                      | 0.01                          |

Note: Confidence intervals are not corrected for multiple comparisons.

**Table 3.4** Radiographic outcomes.

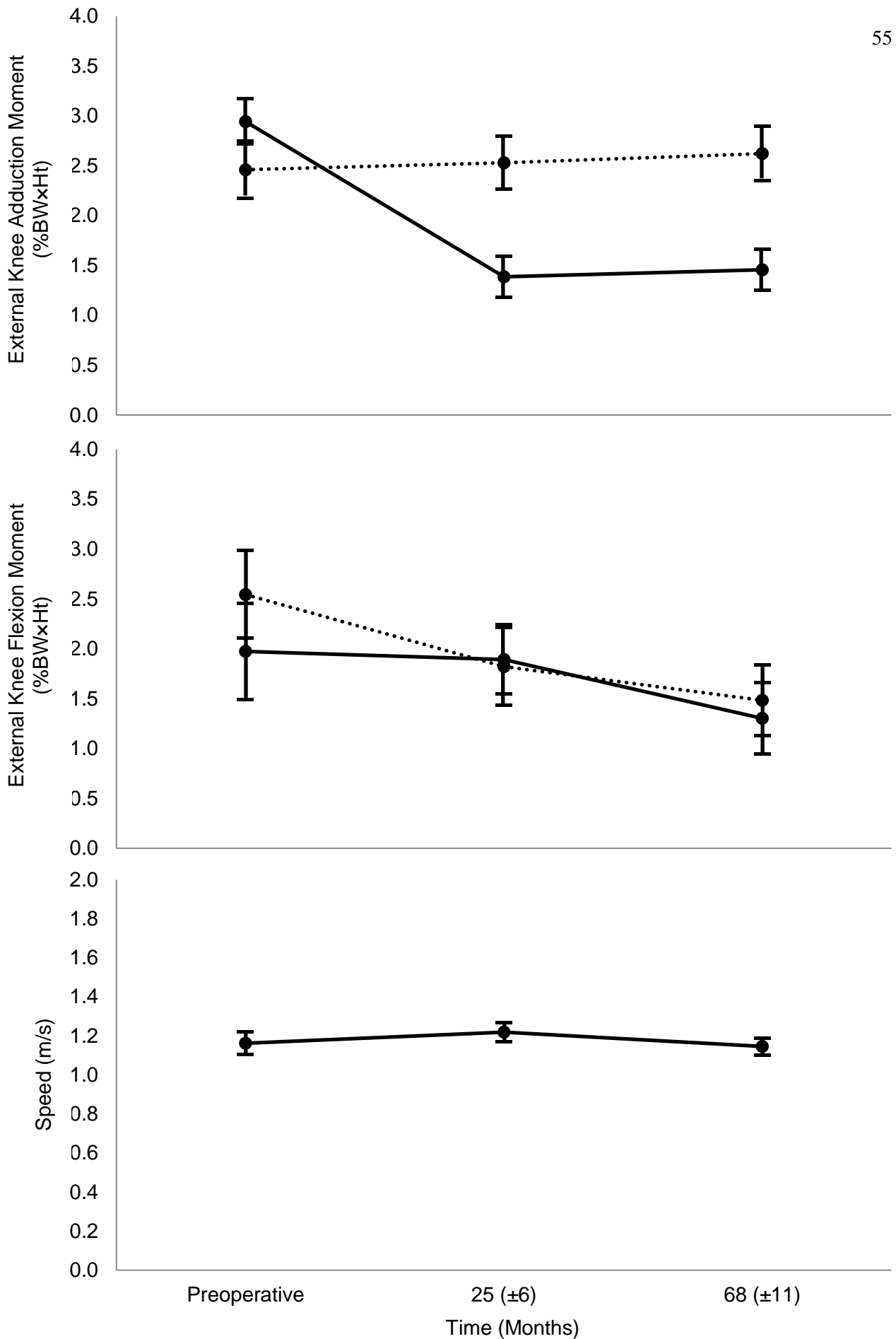
|                            | <b>Pre<br/>Mean (SD)</b> | <b>2-Year Post<br/>Mean (SD)</b> | <b>5-Year Post<br/>Mean (SD)</b> | <b>Pre – 5-Year Post<br/>Mean Change (95% CI)</b> | <b>Standardized<br/>Response Mean</b> |
|----------------------------|--------------------------|----------------------------------|----------------------------------|---|---------------------------------------|
| MAA Surgical Limb (°)      | -5.90 (2.87)             | 1.35 (1.95)                      | 1.69 (2.37)                      | -7.58 (-8.98 to -6.19)                            | 1.90                                  |
| MAA Non-Surgical Limb (°)  | -3.01 (3.15)             | -2.77 (2.81)                     | -3.37 (3.13)                     | 0.26 (-0.55 to 1.06)                              | 0.13                                  |
| Posterior Tibial Slope (°) | 5.17 (3.47)              | 6.22 (5.04)                      | 6.19 (5.08)                      | 0.99 (-0.81 to 2.80)                              | 0.23                                  |
| Insall-Salvati Ratio       | 1.07 (0.17)              | 0.96 (0.18)                      | 0.86 (0.20)                      | -0.20 (-0.27 to -0.14)                            | 1.25                                  |
| Caton-Deschamps Ratio      | 0.96 (0.20)              | 0.93 (0.17)                      | 1.00 (0.21)                      | 0.03 (-0.09 to 0.14)                              | 0.09                                  |
| Blackburne-Peel Ratio      | 0.84 (0.16)              | 0.82 (0.18)                      | 0.86 (0.18)                      | 0.01 (-0.08 to 0.11)                              | 0.05                                  |

Note: Confidence intervals are not corrected for multiple comparisons.

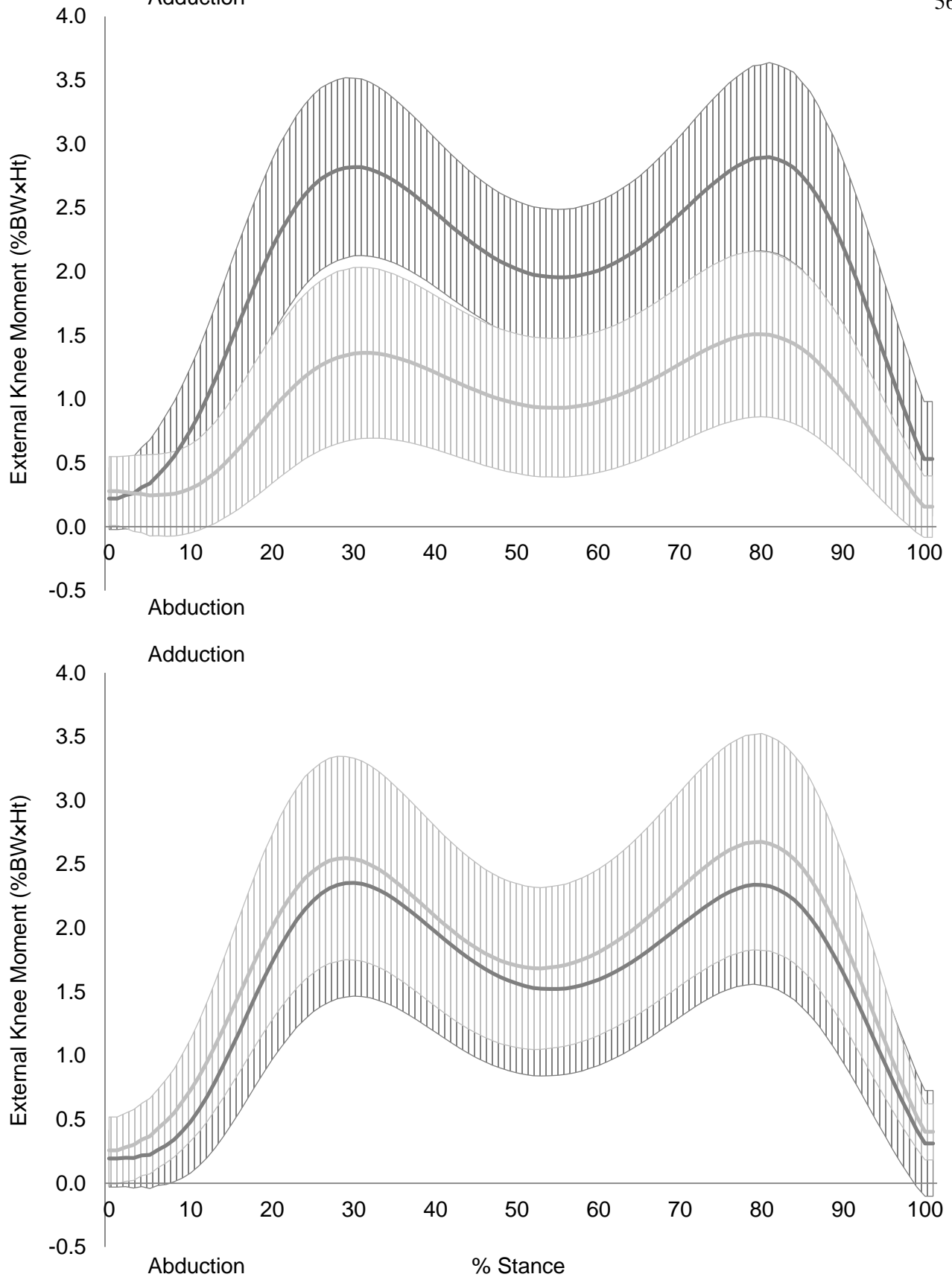
**Table 3.5** Knee Osteoarthritis Outcome Score.

|                               | <b>Pre<br/>Mean (SD)</b> | <b>2-Year Post<br/>Mean (SD)</b> | <b>5-Year Post<br/>Mean (SD)</b> | <b>Pre – 5-Year Post<br/>Mean Change (95% CI)</b> | <b>Standardized<br/>Response Mean</b> |
|-------------------------------|--------------------------|----------------------------------|----------------------------------|---|---------------------------------------|
| Pain                          | 64.9 (18.4)              | 86.9 (12.3)                      | 80.7 (16.1)                      | 15.8 (6.81 to 24.9)                               | 0.66                                  |
| Other Symptoms                | 61.5 (15.6)              | 75.7 (17.5)                      | 70.4 (19.3)                      | 8.81 (0.77 to 16.8)                               | 0.41                                  |
| Function in Daily Living      | 74.2 (19.9)              | 92.5 (9.88)                      | 87.1 (16.5)                      | 12.9 (3.82 to 22.0)                               | 0.53                                  |
| Function in Sports/Recreation | 36.3 (25.7)              | 69.0 (26.0)                      | 55.7 (28.3)                      | 19.3 (5.74 to 32.9)                               | 0.53                                  |
| Knee-Related Quality of Life  | 20.8 (17.1)              | 59.3 (24.6)                      | 55.2 (25.7)                      | 34.4 (23.6 to 45.1)                               | 1.20                                  |

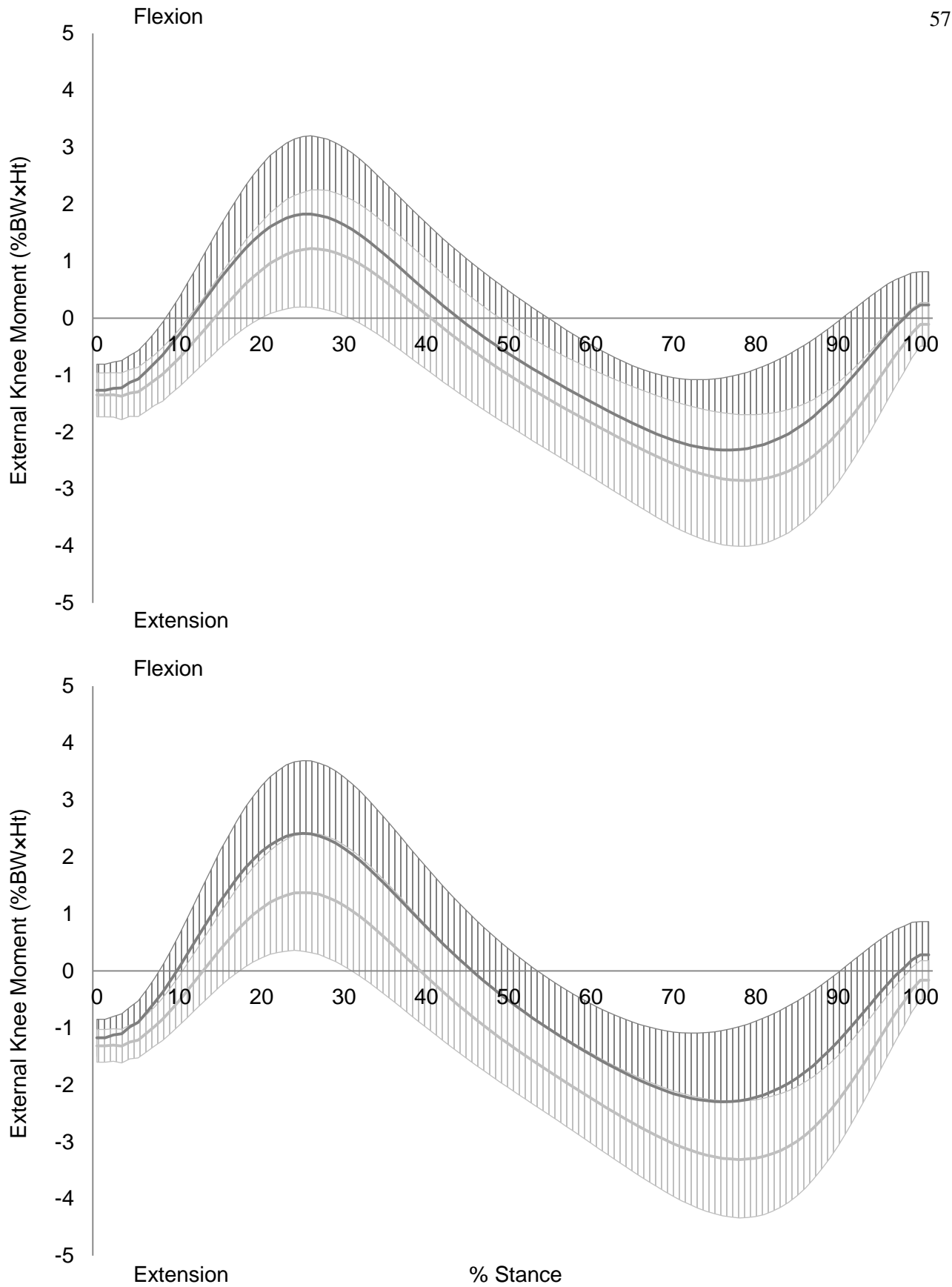
Note: Confidence intervals are not corrected for multiple comparisons.



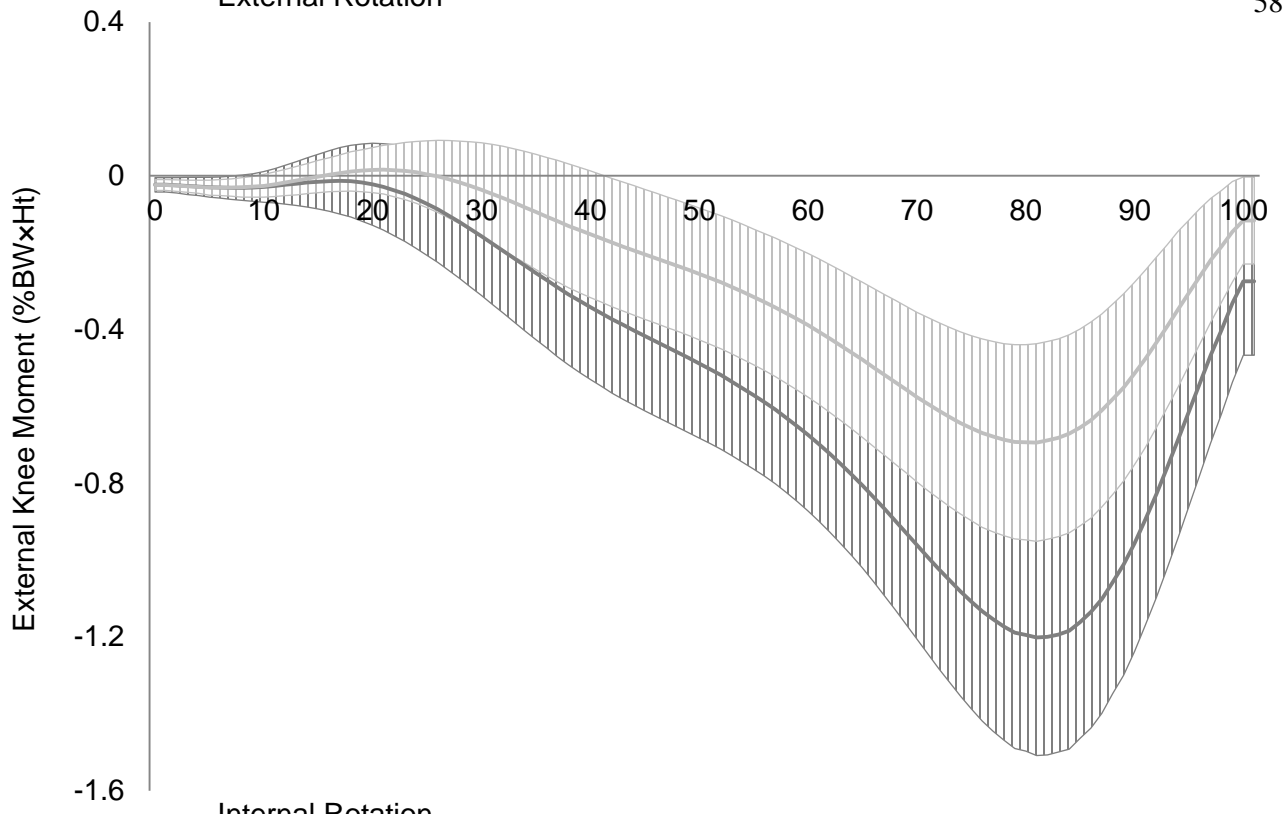
**Figure 3.1** Mean (95%CI) (N=33) for external knee adduction (top) and flexion (middle) moments for the surgical (solid) and non-surgical (dotted) limbs and for gait speed (bottom) at preoperative, 2 years and 5 years postoperative.



**Figure 3.2** Ensemble averages (N=33) for the external knee adduction moment for the surgical (top) and non-surgical (bottom) limbs. Dark grey lines represent preoperative data and light grey lines represent 5-year postoperative data. Shaded areas represent  $\pm$ SD.

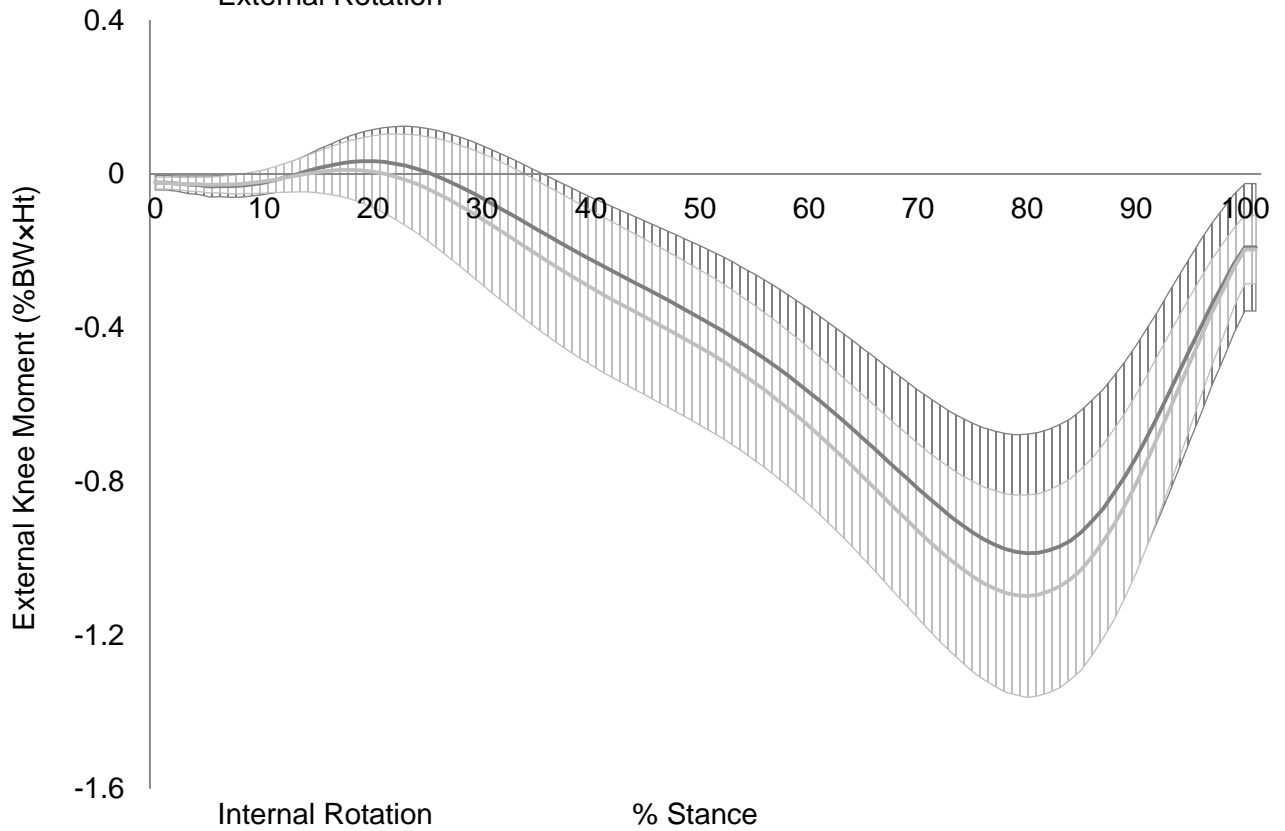


**Figure 3.3** Ensemble averages (N=33) for the external knee flexion moment for the surgical (top) and non-surgical (bottom) limbs. Dark grey lines represent preoperative data and light grey lines represent 5-year postoperative data. Shaded areas represent  $\pm$ SD.



Internal Rotation

External Rotation



**Figure 3.4** Ensemble averages (N=33) for the external knee internal rotation moment for the surgical (top) and non-surgical (bottom) limbs. Dark grey lines represent preoperative data and light grey lines represent 5-year postoperative data. Shaded areas represent  $\pm$ SD.

### 3.5 Discussion

The present findings demonstrate that concomitant medial opening-wedge HTO and ACL reconstruction substantially alters ambulatory knee biomechanics. Furthermore, the results suggest that both the surgical and non-surgical knees experience changes in all three orthogonal planes, albeit in different ways. By examining knee moments and angles in the three planes for both limbs, we can gain insight into the mechanisms underlying the observed changes. Overall, a large decrease in the knee adduction moment and a large increase in the KOOS remain at 5 years postoperative and are encouraging, particularly for individuals with ACL rupture, post-traumatic knee OA, varus alignment and low KOOS scores at baseline. However, although not statistically significant, the small decreases from 2 to 5 years in the peak knee flexion moments (bilaterally), gait speed and KOOS domains suggest that initial gains are declining over time (*Table 3.5, Figure 3.1*).

For the surgical limb, reductions in the peak knee adduction moment coincide with reductions in the peak knee varus angle, consistent with an expected decrease in varus alignment achieved through HTO. The lack of similar results in the non-surgical limb lends further support to surgical alterations in knee alignment as the primary contributor to the observed changes in frontal plane gait biomechanics. Likewise, for the transverse plane, coincident reductions in the peak knee internal rotation moment and angle in the surgical limb also suggest that surgical changes in lower limb alignment are the likely cause for the observed changes in the transverse plane. As expected, the correlation between the decrease in the peak knee adduction moment and the decrease in static varus alignment, quantified by the MAA, is relatively large ( $r=0.68$ ). Importantly, the correlation between changes in the peak knee internal rotation moment and MAA is also relatively large ( $r=0.73$ ).

In contrast to the frontal and transverse planes, the decrease in the peak knee flexion moment and increase in the peak knee extension moment observed in both limbs suggest that changes in knee alignment are not directly responsible for the observed changes in sagittal plane gait biomechanics. This suggestion is further supported by relatively low correlations between the changes in peak knee flexion and extension moments and the changes in MAA ( $r = 0.13$  and  $0.17$ , respectively) as well as the changes in PTS ( $r = 0.16$  and  $0.04$ , respectively).



Given that the external knee adduction moment is a validated proxy for mediolateral distribution of load across the knee,<sup>40,41</sup> while the external knee flexion moment represents net flexor-extensor muscle contraction,<sup>42</sup> the present findings are consistent with a lateral shift in the distribution of load across the knee, without a corresponding increase in total load. Previous studies show no change or decreased co-contraction after HTO.<sup>23,43</sup> Although limitations in making inferences about joint loading based on external measures are acknowledged, in total, these findings suggest that concomitant medial opening-wedge HTO and ACL reconstruction does indeed decrease load on the diseased medial compartment of the surgical knee, possibly by shifting load in both the frontal and transverse planes. It is unclear from the present study, however, if the ACL reconstruction contributes to these observed changes in load distribution, or if these changes are achieved solely by the HTO.

The size of the reduction in knee frontal plane gait biomechanics is also notable. The standardized response means for the change in both the peak knee adduction moment (1.97) and angle (1.24) are above the threshold value suggested for a large effect ( $>0.8$ )<sup>44</sup> and substantially larger than the effect sizes reported for conservative interventions for medial knee OA, such as valgus knee braces and lateral foot orthoses.<sup>45</sup> This magnitude of change is consistent with previous studies evaluating HTO alone.<sup>46,47,43</sup> The small increase in the external knee adduction moment in the non-surgical limb (*Table 3.2*) is consistent with recent reports of frontal plane knee moments in the contralateral limb after HTO.<sup>47,48</sup> However, the standardized response mean for the small increase in the knee adduction moment (0.42) was below the threshold for a moderate effect ( $<0.5$ ).<sup>44</sup> Furthermore, there was no associated increase in walking speed, peak varus angle or static varus malalignment in the non-surgical limb. Therefore, it is difficult to ascertain the cause for this small increase in the knee adduction moment and whether such an increase is clinically important for the risk of disease in the non-surgical limb. Although it is plausible that surgical procedures may affect disease progression of the contralateral limb, a substantial risk for medial knee OA already exists in the contralateral limb of these patients.<sup>48,49</sup> Therefore, the effect of surgery on the contralateral limb requires further research.

It is worth noting that the changes in the sagittal plane peak knee moments were accompanied by similar changes in the peak knee angles without a decrease in joint

excursions (*Tables 3.2 and 3.3*). Although their meaning is presently unclear, these changes are somewhat different than gait patterns indicating knee joint stiffness that can develop with ACL deficiency and OA.<sup>50,51</sup> Similar results bilaterally for the sagittal plane, together with negligible changes in the PTS, suggest surgical alterations in lower limb alignment are not responsible for the changes in the sagittal plane. The observed changes in the sagittal plane do suggest that the presumed redistribution of mediolateral tibiofemoral loading occurred without increasing total knee loads or compromising knee stability. Importantly, however, reductions in the knee flexion moment may suggest deterioration in function over time, similar to previous results following closing-wedge HTO.<sup>52</sup>

Similar to the results in the frontal plane for the surgical limb, unilateral changes in the peak internal rotation moment coincided with changes in the peak internal rotation angle (*Tables 3.2 and 3.3*). It is difficult to ascertain how these changes might alter the distribution of load across the knee and whether they are favourable or not. Knees demonstrating greater internal rotation moments have been associated with greater OA severity,<sup>53</sup> potentially indicating greater loads on cartilage that is less accustomed to transfer load.<sup>11,16,54</sup> Thus, the reduction observed presently in both the internal rotation moment and angle in knees with medial OA could indicate a realignment of femoral and tibial cartilage contact points. Interestingly, the medial opening-wedge HTO procedure creates an anteromedial gap across the proximal tibia and has a tendency to cause slight external rotation of the distal tibia relative to the proximal tibia. Therefore, during postoperative gait analysis, the marker located on the distal tibia may be externally rotated (less internally rotated) relative to the marker located on the knee. This external rotation of the distal tibia relative to the proximal tibia may be characterized as a decrease in the peak knee internal rotation angle without an actual alteration in the location of femoral and tibial cartilage contact points. Importantly a post-hoc analysis of hip kinematics suggested no change in hip rotation angles. Although the present findings suggest concomitant medial opening-wedge HTO and ACL reconstruction alters knee transverse plane moments and perhaps knee rotation angles, these results should be interpreted cautiously. We suggest that the ability of surgical procedures to intentionally alter transverse plane knee biomechanics for the purpose of redistributing loads to less diseased locations in patients with primarily unicompartmental knee OA is an important topic for future research.

Importantly, medial knee pain was the primary reason for referral to this clinic. The majority of patients were middle-aged with chronic ACL injuries. Differences in this patient population and that typically described in the ACL reconstruction literature (i.e. young adults with acute ACL ruptures) must be recognized and results generalized accordingly.

Limitations in the present study must be acknowledged. Although validated and clinically important,<sup>55</sup> external moments about the knee during gait are surrogate measures rather than direct measures of actual force on the knee. The present design makes it difficult to determine whether the changes observed, whole or in part, are due to the HTO, the ACL reconstruction or the passage of time in middle-aged patients with the present disease characteristics. Although bilateral comparisons over time enable considerable insight, future comparisons including greater sample sizes and other therapies are required. The use of one surgeon who was not blinded to postoperative clinical exams also limits generalizability of these findings.

In summary, substantial changes in gait biomechanics consistent with an intended, sustained shift in the mediolateral distribution of load across the knee, and large improvements in patient-reported outcomes, are observed 5 years after concomitant medial opening-wedge HTO and ACL reconstruction. These results are encouraging, particularly for individuals with chronic ACL deficiency, post-traumatic knee OA, varus alignment and low KOOS scores at baseline. Longer term follow-up and comparisons with other treatment strategies are both warranted and required to better evaluate the clinical impact of this seemingly biomechanically efficacious procedure.

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## Chapter 4

### 4 Gait Biomechanics After Combined HTO/ACL Reconstruction Versus HTO Alone: A Matched Cohort Study

#### 4.1 Summary

The purpose of the present study was to compare bilateral external knee moments during gait in patients with concomitant medial compartment knee OA, varus malalignment and anterior cruciate ligament (ACL) deficiency who underwent either medial opening-wedge high tibial osteotomy alone (HTO-Alone) or simultaneous HTO and ACL reconstruction (HTO-ACLR). 52 patients (26 matched pairs) completed three-dimensional gait analysis preoperatively and at a minimum 5 years postoperatively. Patients were matched for preoperative age, sex, body mass index and osteotomy plate size. Primary outcomes selected *a priori* were the peak knee adduction (KAM) and knee flexion (KFM) moments during stance. Moments were compared using mixed model repeated measures ANOVAs. The total and subscale scores (pain, stiffness, physical function) of the Western Ontario and McMaster Universities Arthritis Index were also evaluated. For the KAM, there was a significant time by limb interaction. For both surgical groups, there were similar reductions in the peak KAM 5 years postoperatively in the surgical limb only [-1.34%BW×Ht (-1.71, -0.96) and -1.72%BW×Ht (-1.99, -1.44) for HTO-Alone and HTO-ACLR, respectively]. For the peak KFM, there was a significant time by group by limb interaction. There was a decrease in the peak KFM 5 years postoperatively in the HTO-Alone group [-0.88 %BW×Ht (-1.45, -0.31)] but not in the HTO-ACLR group [0.03 %BW×Ht (-0.43, 0.48)]. The mean difference (95%CI) in the peak KFM change scores between groups for the surgical limb was -0.91 %BW×Ht (-1.61, -0.20). These results suggest that individuals with medial knee OA, varus malalignment and ACL deficiency who undergo simultaneous medial opening-wedge HTO and ACL reconstruction may not experience the same long-term (5-year) changes in sagittal plane knee biomechanics observed in patients undergoing HTO alone.

## 4.2 Introduction

Altered gait biomechanics may adversely affect knee loading and contribute to degenerative joint changes. The external knee flexion moment (KFM) and knee adduction moment (KAM) during walking are thought to be particularly important to the progression of knee osteoarthritis (OA) because of their associations with the magnitude and distribution of dynamic loads across the tibiofemoral joint.<sup>1-5</sup> A larger KAM<sup>6-11</sup> and less commonly, a larger KFM,<sup>8,9</sup> are associated with the progression of medial tibiofemoral OA.

The development of OA after anterior cruciate ligament (ACL) injury remains a common problem<sup>12,13</sup> and the risk appears higher for individuals with concomitant varus malalignment.<sup>14</sup> Individuals who sustain an ACL injury also exhibit altered moments about the knee in the sagittal and frontal planes. Most notably, a reduction in the peak KFM is often observed in individuals with ACL deficiency<sup>15,16</sup> and after ACL reconstruction<sup>17-19</sup> including 5 years after ACL reconstruction in individuals with medial knee OA.<sup>20</sup> Individuals with ACL deficiency may also exhibit a greater KAM.<sup>21</sup> Thus, for patients with ACL injury and medial knee OA, altered gait biomechanics in the sagittal and frontal planes that deviate from a normal gait pattern, may be appropriate targets of interventions.

Medial opening-wedge high tibial osteotomy (HTO) is a surgical procedure designed to correct lower limb malalignment, redistribute dynamic loading in the frontal plane and lessen loads on the medial compartment.<sup>22</sup> HTO may also alter the orientation of the tibial plateau in the sagittal plane and thereby indirectly affect anteroposterior stability of the knee, especially in patients who are ACL deficient.<sup>23-25</sup> Alternatively, ACL reconstruction is a surgical procedure that directly addresses sagittal plane instability by reconstructing the ligament with autograft or allograft tissue. Therefore, ACL reconstruction is sometimes performed as an adjuvant treatment to HTO with the aim of better altering knee joint biomechanics in the frontal and sagittal planes.

Despite the proposed biomechanical effects of ACL reconstruction for individuals with ACL deficiency and medial knee OA undergoing HTO, there are few studies investigating the effects of the combined procedure.<sup>26-29</sup> Previous results suggest substantial improvements in knee kinematics and kinetics following the combined procedure;<sup>27</sup> however, it remains

unclear whether the ACL reconstruction offers any benefits above those offered by HTO alone. Thus, the purpose of the present study was to compare bilateral external knee moments during gait in patients with concomitant medial compartment knee OA, varus malalignment and ACL-deficiency who underwent either medial opening-wedge HTO alone (HTO-Alone) or simultaneous HTO and ACL reconstruction (HTO-ACLR). We hypothesized that although both groups would experience similar changes in the external KAM, they would experience significantly different changes in the external KFM.

## 4.3 Methods

### 4.3.1 Study Design

In this retrospective matched cohort study (level III evidence), patients were prospectively evaluated using three-dimensional (3D) gait analysis before and at a minimum 5 years (67.6 months  $\pm$ 14.6) after undergoing either HTO-Alone or HTO-ACLR. Patients in each group were matched retrospectively based on sex, age, body mass index (BMI) and osteotomy plate size. Given the importance of the frontal and sagittal plane moments previously reported, we selected *a priori* the first peak KAM and the peak KFM as the outcomes of primary interest. We also assessed patient reported outcomes. The study was approved by the institution's Research Ethics Board for Health Sciences Research Involving Human Subjects. All patients provided informed written consent.

### 4.3.2 Participants

Data from fifty-two patients were included in this study. To be included, patients had to have had persistent medial compartment pain with activity, knee instability, mechanical varus alignment and medial compartment knee OA,<sup>30</sup> with greatest severity in the medial compartment of the tibiofemoral joint, and had to have sustained a previous ACL rupture. The mechanical axis angle (MAA) was measured following previously described techniques.<sup>31-33</sup> Varus alignment was indicated by a negative angle. Radiographic measurements from the digitized images were determined using custom software.<sup>32</sup> There were twenty-six patients included in the HTO-ACLR group and another twenty-six patients included in the HTO-Alone group. Patient demographics and clinical characteristics for each group are presented in *Table 4.1*.

**Table 4.1** Baseline demographics and clinical characteristics.

|                          | <b>HTO-Alone<br/>Mean (SD)</b> | <b>HTO-ACLR<br/>Mean (SD)</b> |
|--------------------------|--------------------------------|-------------------------------|
| Sex, M(%)                | 21 (80.8)                      | 21 (80.8)                     |
| Age, yr                  | 43.7 (8.4)                     | 41.6 (8.7)                    |
| Height, m                | 1.75 (0.1)                     | 1.75 (0.1)                    |
| Mass, kg                 | 89.5 (14.9)                    | 87.1 (16.0)                   |
| BMI, kg/m <sup>2</sup>   | 29.0 (3.7)                     | 28.3 (3.8)                    |
| MAA, °                   | -4.6 (3.7)                     | -3.9 (2.4)                    |
| Osteotomy Plate Size, mm | 11.1 (3.4)                     | 10.3 (2.8)                    |
| K/L Grade, N(%)          |                                |                               |
| 0                        | 0                              | 0                             |
| 1                        | 5 (19.2)                       | 5 (19.2)                      |
| 2                        | 2 (7.69)                       | 6 (23.1)                      |
| 3                        | 13 (50.0)                      | 15 (57.7)                     |
| 4                        | 5 (19.2)                       | 0                             |

BMI, body mass index.

MAA, mechanical axis angle.

K/L, Kellgren-Lawrence grades of OA severity.

### 4.3.3 Surgery and Rehabilitation

For individuals in the HTO-ACLR group, the HTO was completed prior to the ACL reconstruction within the same operative procedure. The osteotomy was completed according to techniques previously described.<sup>34</sup> The weight-bearing line was moved laterally no greater than 62.5% of the medial-to-lateral tibial plateau width. A/P sloped wedge Puddu (non-locking) plates were used to achieve fixation and were placed posteriorly on the tibia to minimize an inadvertent increase in the posterior tibial slope (PTS) and reduce interference with the tibial tunnel required for the ACL reconstruction. Fixation was confirmed intraoperatively by fluoroscopy.

Semitendinosus or gracilis tendons were harvested through the osteotomy incision to create a four-bundle ACL graft. An anteromedial portal technique was used to drill the femoral tunnels within the femoral footprint of the ACL. Tibial graft fixation was achieved using multiple staples with or without interference screws while the graft was under tension. An Endobutton<sup>TM</sup> was used for femoral fixation. Patients were toe-touch weight bearing for 6 weeks postoperatively with the knee supported in a range of motion brace. Within two weeks of surgery, patients started a physiotherapy program to improve function, strength and range

of motion. Progressive weight bearing was allowed provided there were radiographic and clinical signs of healing, with full weightbearing achieved by 12 weeks. For patients in the HTO-ACLR group, a postoperative ACL rehabilitation program was started once osteotomy healing was complete to improve proprioception and strength with progression to functional activities within twelve months postoperatively. A clinical exam performed pre and postoperatively indicated return to full range of motion for all patients.

#### 4.3.4 Gait Analysis

Bilateral gait analysis was completed using an eight-camera motion capture system (Motion Analysis Corporation, Santa Rosa, CA) synchronized with a single, floor-mounted force platform (Advanced Mechanical Technology Inc., Watertown, MA). Passive-reflective markers were placed on patients using a 22-marker, modified Helen Hayes marker set. Additional markers were also placed over the medial knee joint line and medial malleolus during a static trial on the force platform to determine knee and ankle joint centers. These four extra markers were removed before gait testing.

Patients walked barefoot across a 10 m walkway at their typical walking speed while marker (60 Hz) and forceplate (1200 Hz) data were collected from a minimum of five trials for each extremity. External knee moments were calculated from the marker and force plate data using inverse dynamics and were expressed relative to the tibial anatomical frame of reference.<sup>35,36</sup> The same methods and version of software were used to analyze gait data for all time points (Orthotrak 6.0, Motion Analysis Corporation). Knee moments were averaged over five trials and normalized to 100% stance. The greatest magnitude in a positive or negative direction was identified as the peak for each gait cycle waveform. In the frontal plane, the first peak during the initial 50% of stance was identified as the first peak KAM. In the sagittal plane, the first peak during stance was identified as the peak KFM. Moments were normalized to bodyweight and height (%BW×Ht). Previous studies suggest external moments about the knee are reliable and sensitive to change after HTO.<sup>37,38</sup>

#### 4.3.5 Patient Reported Outcomes

Patients completed the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) preoperatively and postoperatively. The WOMAC is a validated tool to evaluate

knee OA and consists of a 24-item questionnaire with 5 response options per item. There are three separate domains including pain (5 items), stiffness (2 items) and physical function (17 items) and the scores within each domain are summed. We rescaled the scores so that a higher number indicated a better outcome.

#### 4.3.6 Statistical Analysis

We first plotted the ensemble average gait waveforms and the means and 95% confidence intervals (95%CI) for the peak KAM and KFM for both limbs before and after surgery for both groups. For the KAM, KFM and WOMAC scores, we also calculated the surgical limb preoperative-to-postoperative mean change scores with 95% CIs and then the between-group mean difference in change scores with 95% CIs. Peak KAM and peak KFM were compared separately using a two (time: pre, post 60 months) by two (group: HTO-Alone, HTO-ACLR) by two (limb: surgical, non-surgical) repeated measures ANOVA. Both time and limb were treated as within-subject factors and group was treated as a between-subjects factor.

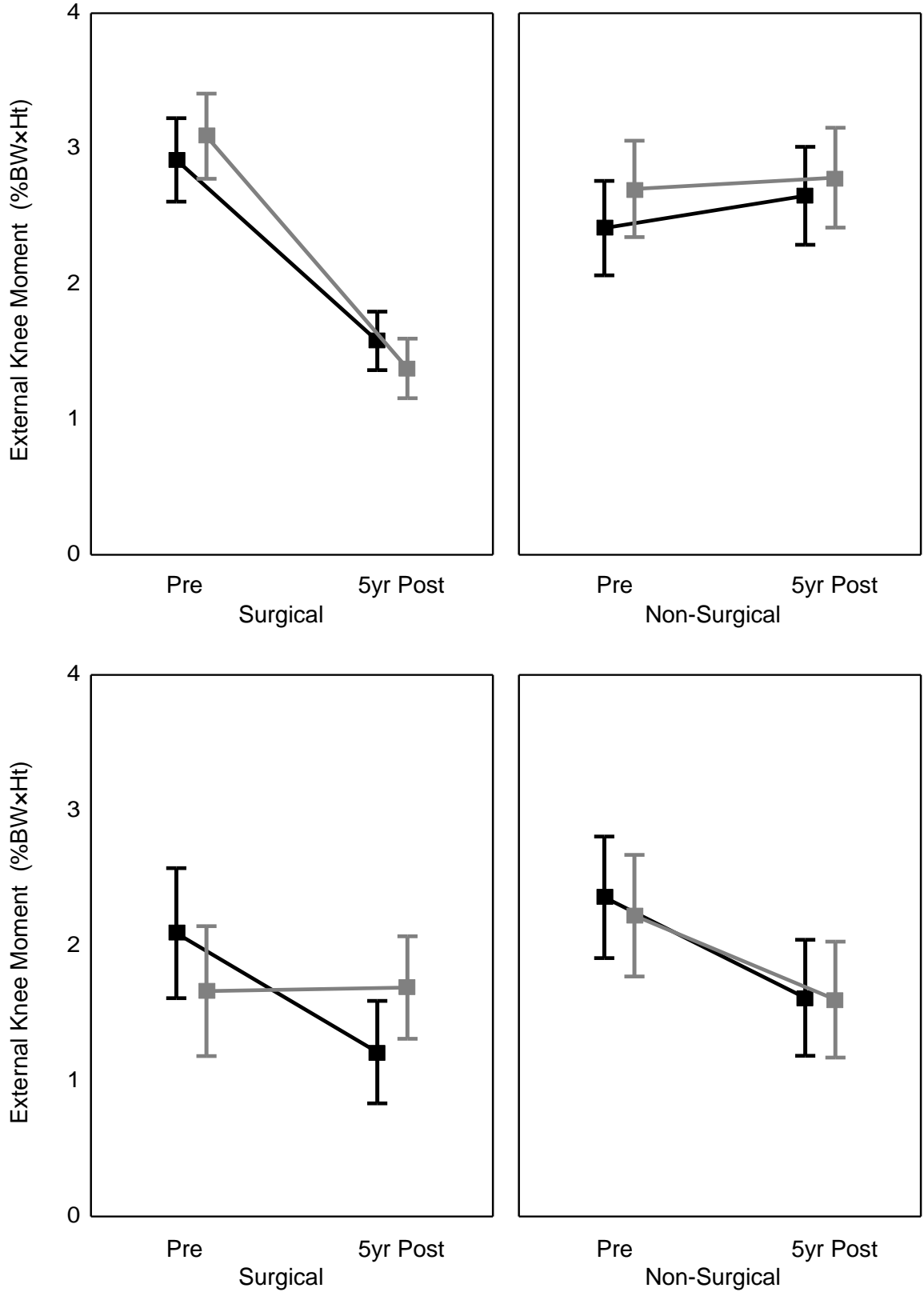
Significant interactions were further analyzed using Scheffe post-hoc test. Shapiro-Wilk's Test and Levene's Test were used to determine whether normal distribution and equality of variance assumptions were satisfied, respectively. Lastly, 5-year postoperative WOMAC scores were compared between groups while controlling for baseline values. Statistical significance was set at  $p < 0.05$ . Statistical analyses were completed using SPSS 24 (SPSS Inc., Chicago, IL) and Statistica (StatSoft Inc., Version 7.1, [www.statsoft.com](http://www.statsoft.com)).

## 4.4 Results

Ensemble average gait waveforms along with the means and 95%CI for the KAM and KFM are presented in *Figures 4.1 to 4.3*. ANOVA suggested a significant time by limb interaction ( $p < 0.001$ ) for the KAM, indicating changes over time differed between limbs. Across groups, there was a decrease in the KAM in the surgical limb from preoperative to postoperative ( $p < 0.001$ ) with no change in the non-surgical limb ( $p = 0.42$ ). For the KAM, the mean change (95%CI) from preoperative to postoperative for the surgical limb for the HTO-Alone and HTO-ACLR groups was  $-1.34 \% BW \times Ht$  ( $-1.71, -0.96$ ) and  $-1.72 \% BW \times Ht$  ( $-1.99, -1.44$ ), respectively. The mean difference (95%CI) in change scores between groups for the surgical limb was  $0.38 \% BW \times Ht$  ( $-0.08, 0.84$ ).

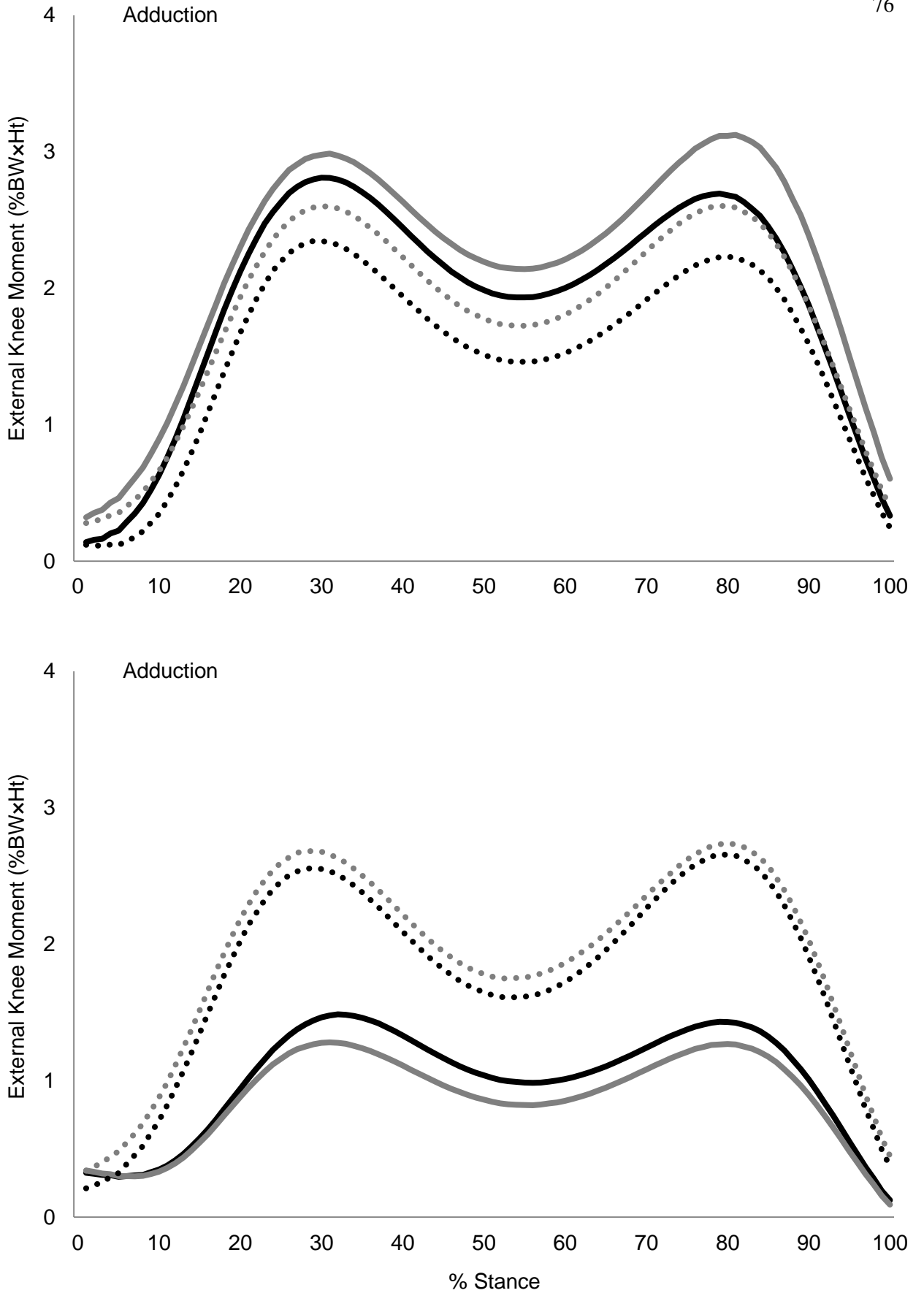
ANOVA suggested a significant time by limb by group interaction ( $p=0.02$ ) for the KFM, indicating changes over time differed between groups and limbs. For the HTO-Alone group, there was a decrease in the KFM from preoperative to postoperative for both the surgical ( $p=0.001$ ) and non-surgical ( $p=0.01$ ) limbs. However, for the HTO-ACLR group, there was no change in the KFM from preoperative to postoperative for either limb ( $p>0.05$ ). For the KFM, the mean change (95%CI) from preoperative to postoperative for the surgical limb for the HTO-Alone and HTO-ACLR groups was  $-0.88 \%BW \times Ht$  ( $-1.45, -0.31$ ) and  $0.03 \%BW \times Ht$  ( $-0.43, 0.48$ ), respectively. The mean difference (95%CI) in change scores between groups for the surgical limb was  $-0.91 \%BW \times Ht$  ( $-1.61, -0.20$ ).

For the HTO-Alone group, the mean change (95%CI) from preoperative to postoperative for the total WOMAC and WOMAC subscales (pain, stiffness, physical function) was  $9.75$  ( $1.66, 17.8$ ),  $13.2$  ( $3.67, 22.7$ ),  $2.00$  ( $-8.50, 12.5$ ) and  $9.65$  ( $1.24, 18.1$ ), respectively. For the HTO-ACLR group, the mean change (95%CI) from preoperative to postoperative for the total WOMAC and WOMAC subscales (pain, stiffness, physical function) was  $17.0$  ( $11.7, 22.2$ ),  $16.4$  ( $11.2, 21.6$ ),  $18.0$  ( $9.18, 26.8$ ) and  $17.0$  ( $11.2, 22.8$ ), respectively. The mean difference (95%CI) in change scores between groups for the total WOMAC and WOMAC subscales (pain, stiffness, physical function) was  $7.20$  ( $-2.20, 16.6$ ),  $3.20$  ( $-7.40, 13.8$ ),  $16.0$  ( $2.64, 29.4$ ) and  $7.35$  ( $-2.61, 17.3$ ), respectively. ANCOVA suggested there was no difference between groups in postoperative total WOMAC ( $p=0.12$ ) or WOMAC subscales ( $p=0.28$ ,  $p=0.18$ ,  $p=0.13$  for pain, stiffness and physical function, respectively) while controlling for baseline values.

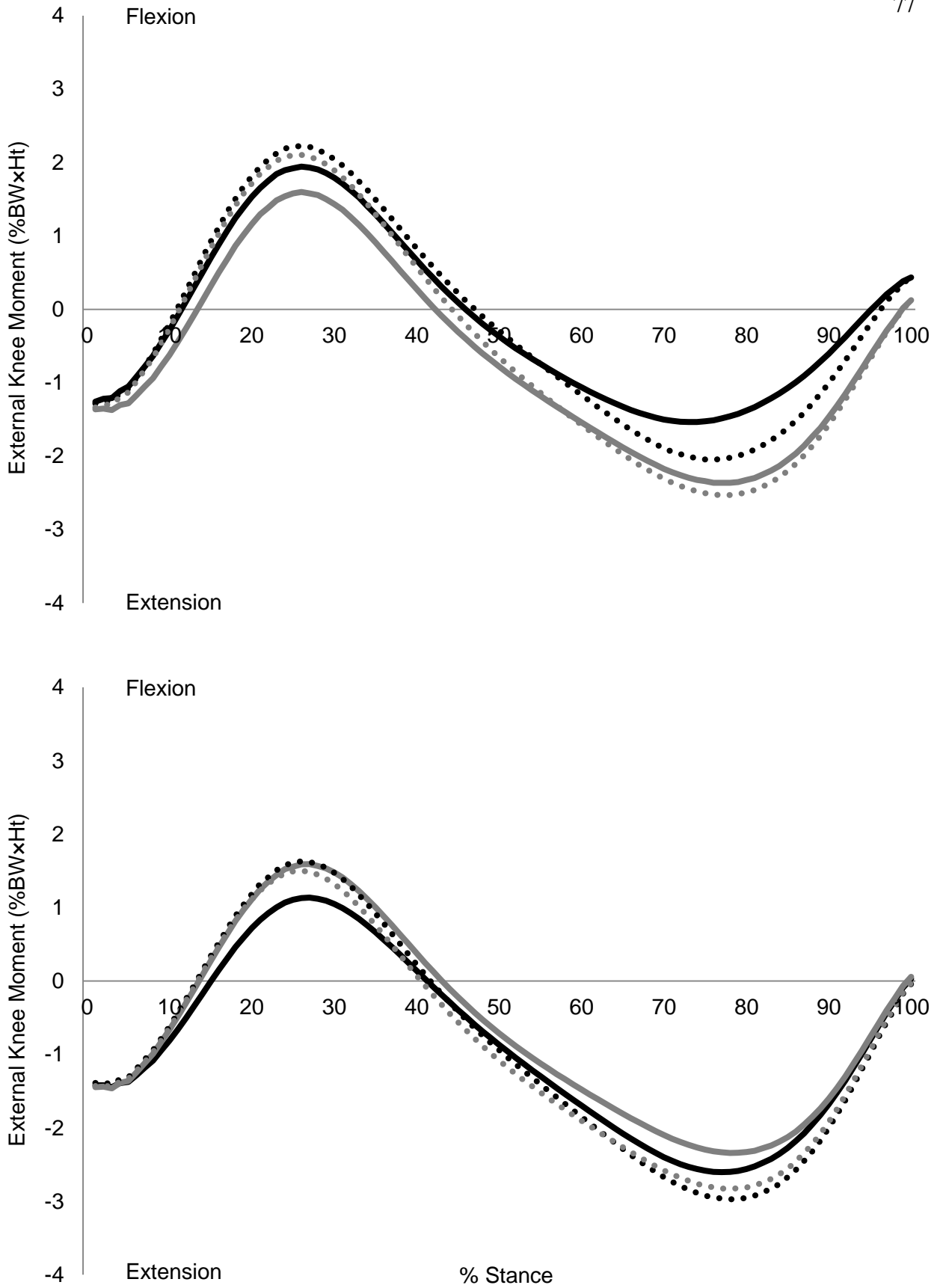


**Figure 4.1** Preoperative and 5-year postoperative values (mean  $\pm$ 95%CI) for the peak external knee adduction (top) and flexion (bottom) moments for the surgical and non-surgical limbs for the HTO-Alone (black) and HTO-ACLR (grey) groups.





**Figure 4.2** Preoperative (top panel) and 5-year postoperative (bottom panel) ensemble averages for the frontal plane external knee moments for the surgical (solid) and non-surgical (dotted) limbs for the HTO-Alone (black) and HTO-ACLR (grey) groups.



**Figure 4.3** Preoperative (top panel) and 5-year postoperative (bottom panel) ensemble averages for the sagittal plane external knee moments for the surgical (solid) and non-surgical (dotted) limbs for the HTO-Alone (black) and HTO-ACLR (grey) groups.

## 4.5 Discussion

This is the first study comparing gait biomechanics in patients with medial knee OA, varus malalignment and ACL deficiency who undergo either HTO alone or combined HTO and ACL reconstruction. Results are generally consistent with our hypotheses. As expected, patients who underwent medial opening-wedge HTO had large reductions in the KAM in the surgical limb, regardless of whether ACL reconstruction was performed. However, changes observed in the KFM differed significantly between the surgical groups. Patients who underwent the combined procedure experienced minimal change in the KFM over 5 years while patients who underwent HTO alone experienced a decrease.

Previous authors investigating gait in individuals with ACL injury and reconstruction have reported a decrease in the peak external KFM.<sup>15,17,18</sup> This gait pattern is believed to represent a compensatory gait strategy (i.e. quadriceps avoidance gait) wherein, quadriceps activation is reduced in an attempt to attenuate anterior translation of the tibia.<sup>15</sup> Thus, the presently observed decrease in the KFM in only the HTO-Alone group may suggest that patients with ACL deficiency who forego ACL reconstruction develop similar sagittal-plane biomechanics previously reported in ACL deficient individuals attempting to decrease anterior tibial translation. This would be consistent with the goal of the combined surgery where it may preserve more normal sagittal plane biomechanics.

Interestingly, for individuals with medial knee OA, a larger KFM may contribute to increased joint loading and future disease progression.<sup>8</sup> Additionally, increases in the KFM may negate decreases in medial compartment loading attempted through altering load distribution in the frontal plane.<sup>5</sup> Thus, the lack of an increase in the KFM in both groups should also be noted as a potentially favourable outcome. However, previous research also indicates reduced KFM in individuals with severe OA relative to healthy controls<sup>39</sup> and an association with poorer function in healthy older adults.<sup>40</sup> Therefore, the overall goal for OA interventions may be to normalize sagittal plane gait biomechanics rather than significantly decreasing the KFM, although the association between observed changes in the KFM and longer term outcomes after HTO alone requires further research.

Similar to previous studies evaluating the effects of medial opening-wedge HTO,<sup>37,41,42</sup> there was a large decrease in the KAM (standardized response mean (SRM)=1.44 and 2.54 for HTO-Alone and HTO-ACLR, respectively) and moderate to large improvements in the total WOMAC (SRM=0.50 and 1.33 for HTO-Alone and HTO-ACLR, respectively). Although the change scores for the total WOMAC and WOMAC subscales were consistently larger for the HTO-ACLR group, there were no significant differences postoperatively between groups after controlling for baseline values. The overall similarity in frontal plane biomechanics between groups may suggest HTO alone is largely responsible for the observed improvements in patient-reported outcomes. However, only the HTO-Alone group experienced a reduction in the KFM (SRM=0.63) while the HTO-ACLR group experienced minimal change in the KFM (SRM=0.02). This disparity between groups suggests patients who underwent the combined procedure may not experience the same changes in the sagittal plane as patients who underwent HTO alone. Additionally, the reduction observed in the sagittal plane was moderate compared to the reduction observed in the frontal plane. This more modest reduction further suggests that changes in bony alignment may not be solely responsible for the changes observed in the sagittal plane and the addition of ligament reconstruction to medial opening-wedge HTO may limit changes in sagittal plane knee moments over 5 years.

The external knee adduction moment is commonly described as a proxy for mediolateral distribution of loading across the knee during walking.<sup>2,38,43,44</sup> Our findings suggest that individuals with concomitant varus malalignment and ACL deficiency, who undergo medial opening-wedge HTO, will experience a favourable shift in load distribution and a potential reduction in the progression of medial knee OA, regardless of ACL reconstruction. For the HTO-Alone group, changes in the frontal and sagittal plane gait biomechanics were comparable to the long-term (>5 years) changes observed following combined HTO and ACL reconstruction in a similar group of individuals.<sup>27</sup>

There are limitations in our study. Most importantly, our two groups were matched retrospectively. Although our matches were based on factors most likely to affect our primary outcomes, patients were not randomized to surgical group and there may have been other factors unaccounted for that influenced our results. Specifically, factors related to

activity levels and symptoms other than pain, such as instability, may have differed between groups. Thus, for one reason or another, the surgeon selected specific patients to receive the combined procedure over HTO alone. Although not known, patients may have demonstrated specific clinical findings that influenced surgical preference and such clinical findings may or may not be related to postoperative outcomes. Additionally, patients in each group would have received different rehabilitation protocols. Patients within the HTO-ACLR group would have received rehabilitation focusing on both the HTO and ACL reconstruction while rehabilitation for patients within the HTO-Alone group would have only addressed the HTO. Although the early stages of rehabilitation for these two surgical procedures often have comparable goals and are overall quite similar, rehabilitation required to address a combined procedure is inherently longer than the rehabilitation required to address a single procedure. Thus, the between-group differences observed in the present study may have been influenced by specific rehabilitation protocols that can affect many factors related to external knee moments, such as lower extremity muscle strength. Finally, the patient reported outcome measures used in the present study focused primarily on the symptoms associated with OA. However, our patients presented with both OA and ACL deficiency. Thus, patient reported outcomes specific to ACL injury such as the Anterior Cruciate Quality of Life Questionnaire, may have provided further insight into potential differences in outcomes between the combined procedure and HTO alone.

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## Chapter 5

### 5 Thesis Summary and General Discussion

The purpose of this chapter is to summarize the main findings of the thesis, relate the findings between different studies and discuss their implications. In doing so, I have combined and compared data from the different studies to better illustrate important concepts. The strengths and limitations of the overall thesis are reviewed in addition to future directions for the biomechanical evaluation of combined medial opening-wedge HTO and ACL reconstruction.

#### 5.1 Thesis Overview

This thesis had two objectives. The first objective was to evaluate pain during functional loading while controlling for extraneous factors by comparing changes between limbs within patients with medial tibiofemoral OA. The second objective was to evaluate the long-term biomechanical effects of combined HTO and ACL reconstruction in individuals with varus malalignment, medial tibiofemoral OA and ACL deficiency. To reduce the influence of extraneous factors and further clarify the effects of surgery, changes in gait biomechanics and patient reported outcomes were compared between limbs within patients. Medial opening-wedge HTO is a surgical procedure designed to slow the progression of medial knee OA by redistributing load across the knee through the correction of varus malalignment. Although medial opening-wedge HTO produces a large change in frontal plane knee alignment, biomechanics in the sagittal or transverse planes can also be altered. Importantly, these alterations in static alignment, with or without ACL reconstruction, may (theoretically) reduce OA progression by facilitating a favourable redistribution of loads across the knee following ACL injury, and warrants future research.

**Chapter 2 (Study 1):** This cross-sectional study examined the relationship between changes in knee pain and external knee moments while controlling for extraneous factors through comparison of limbs within individuals. Establishing the relationship between subjective and objective measures of disease is necessary to accurately interpret the effects of disease-modifying interventions. Patients rated their knee pain on an 11-point numeric rating scale before and after a six-minute walk and then completed 3D gait analysis. For each limb, the change in pain was recorded as either an "increase" or "no change" in pain. Among paired limbs with discordant changes in knee pain, the external knee moments during walking were compared. A greater knee adduction moment, adduction impulse and internal rotation moment were associated with greater odds of an increase in pain after walking. In contrast, a lower knee flexion moment was associated with greater odds of an increase in pain after walking. These associations remained significant after adjusting for K/L grade of OA severity. Thus, when controlling for extraneous factors by comparing outcomes between limbs within individuals, pain after walking was significantly related to the external knee moments in all three planes.

**Chapter 3 (Study 2):** This prospective cohort study evaluated the long-term changes in external knee moments and angles in all three orthogonal planes following combined medial opening wedge HTO and ACL reconstruction. Changes in knee biomechanics in the surgical limb were also compared to changes in the nonsurgical limb. Patients completed 3D gait analysis, radiographic knee alignment measures (MAA, PTS) and patient reported measures (KOOS) preoperatively, two years postoperatively and at a minimum five years postoperatively. There were significant reductions in the knee adduction, flexion and internal rotation moments in the surgical limb from preoperative to five years postoperative. There was also a significant increase in the knee extension moment from preoperative to five years postoperative. Although reductions in the frontal and transverse plane knee moments only occurred in the surgical limb, the changes in the sagittal plane knee moments occurred in both the surgical and nonsurgical limb. These bilateral changes in sagittal plane knee moments suggests surgical alterations in knee alignment are likely not responsible for the postoperative changes. Additionally, the standardized response means for the knee adduction and internal rotation moments (1.97 and 1.72, respectively) indicates large effect sizes that were substantially greater than the standardized response means for the knee flexion and

extension moments (0.45 and 0.39, respectively), further suggesting that surgical alterations in knee alignment were only responsible for the changes in the frontal and transverse planes. Overall, these findings are consistent with a positive shift in the mediolateral distribution of loads across the knee. The change in the knee flexion moment observed over time in both knees is consistent with recent evidence suggesting a decrease in the knee flexion moment with age, and perhaps OA progression, providing incentive for future research.

**Chapter 4 (Study 3):** This retrospective matched cohort study compared changes in the external knee adduction and flexion moments in individuals with medial knee OA, varus malalignment and ACL deficiency who received either combined HTO and ACL reconstruction (HTO-ACLR) or HTO alone (HTO-Alone). The WOMAC total and the three WOMAC subscales were also evaluated. Patients were matched based on sex, age and BMI and were assessed preoperatively and at a minimum five years postoperatively. Both groups experienced a significant reduction in the knee adduction moment in the surgical limb. For the HTO-Alone group, there was a significant decrease in the knee flexion moment in both limbs from preoperative to postoperative. However, for the HTO-ACLR group, there was no change in the knee flexion moment in either limb. These results indicate that patients with medial knee OA and ACL deficiency who undergo combined HTO and ACL reconstruction may not experience the same changes in sagittal plane knee moments as patients who receive HTO alone.

## 5.2 The Relationship Between Subjective and Objective Measures of Medial Knee Osteoarthritis

Findings from Chapter 2 emphasized the importance of comparing changes within individuals to accurately evaluate the effectiveness of different interventions. Utilizing such a design highlighted the strong association between an increase in pain and objective measures of knee biomechanics. Importantly, this relationship may facilitate the identification of individuals who would benefit from different interventions based on a number of biomechanical and radiographic characteristics. Clarifying this relationship between patient reported outcomes and changes in knee biomechanics contributes to the methods used in the next two studies to evaluate individuals with concomitant ACL injury and medial knee OA.

Findings from Chapters 3 and 4 identify the long-term effects of surgical interventions for individuals with concomitant ACL injury and medial knee OA. The association between different outcomes identified in Chapter 2 suggests the observed changes in knee biomechanics 5 years after surgery are likely associated with changes in pain and function. Thus, patient reported measures may be used to predict whether patients are likely to experience favourable changes in knee biomechanics following surgery and whether additional treatments may be required. To determine whether the association between subjective and objective measures observed in Chapter 2 also exists in individuals with combined ACL injury and medial knee OA, the analysis completed in Chapter 2 was also repeated with the cohort of eligible patients from Chapters 3 and 4. The patients who would eventually undergo ACL reconstruction in addition to medial opening-wedge HTO were analysed separately from individuals who would only receive medial opening-wedge HTO. The results indicated that the association between the external knee moments and an increase in pain were similar to the associations obtained in Chapter 2. Notably, the magnitude of the odds ratios appeared to be greater for individuals who would eventually receive only the osteotomy in lieu of the combined procedure. However, after controlling for radiographic disease severity, the associations were no longer significant.

### **5.3 The Role of Medial Opening-Wedge HTO in Mitigating Disease Progression in Patients with Medial Knee OA, Varus Malalignment and ACL Deficiency**

Findings from this thesis suggest that medial opening-wedge HTO is an effective therapy for individuals with concomitant medial knee OA, varus malalignment and ACL injury. The postoperative alterations in external knee moments provide insight into the magnitude and distribution of loads across the knee that may be conducive to mitigating disease progression. This distribution of loads across the knee is influenced by a combination of factors, including static malalignment and muscle activation.

Depending on the knee pathology, specific changes in external knee moments and muscle activation may indicate either an improvement or deterioration in disease progression. It has been suggested that for individuals with medial knee OA and varus malalignment, a decrease in both the adduction and flexion moments indicates a reduction in medial contact force<sup>1</sup> that

may be favourable to reducing disease progression. However, for individuals with ACL injuries, a decrease in the external knee flexion moment may also indicate reduce quadriceps activation.<sup>2,3</sup> Thus, the significance of changes in external knee moments experienced by individuals with medial knee OA is in direct contrast to individuals with ACL injuries. However, findings from this thesis were obtained from individuals with concomitant medial knee OA and ACL deficiency. The observed alterations in external knee moments may be indicative of favourable changes in load distribution across the knee. More specifically, the decrease in the knee adduction moment without an increase in the knee flexion moment would suggest an overall decrease in load across the knee in addition to a redistribution of loads. Whether such changes are driven more by the OA aspects of the disease or the residual effects of the ACL injury remains unknown. Identifying which pathology is driving the changes will determine the most appropriate treatment intervention.

#### 5.4 Pain After Walking: Correlation with Changes in Patient Reported Outcomes

Pain is the most frequently reported symptom in patients with OA.<sup>4</sup> There are several patient-reported measures of pain available and each measure may quantify different aspects of pain. The 6-minute walk test is a valid proxy of functional capacity and demonstrates excellent test-retest reliability<sup>5,6</sup> and responsiveness<sup>5</sup> in patients with tibiofemoral OA. Patients tested in the present thesis rated their pain on an 11-point numeric rating scale before and after six minutes of walking. Therefore, the pain reported reflects the immediate response to six minutes of walking. In contrast, pain measures obtained from the subscales of the KOOS and WOMAC reflect pain levels experienced over the past week during various forms of physical activity, rated on a 5-point Likert scale. Patients with tibiofemoral OA often experience symptoms after a period of activity. However, a specific duration of physical activity is not defined in the KOOS or WOMAC. Thus, reported pain immediately following the 6-minute walk test and the pain subscales of the KOOS and WOMAC may be measuring different aspects of pain and provide different information related to tibiofemoral OA.

To determine whether the change in pain following the 6-minute walk and pain obtained from the KOOS and WOMAC describe the same construct, the associations between each measure were quantified using Pearson Correlation Coefficients (*Table 5.1*) in patients from

Chapter 2. Statistically significant negative correlations were obtained for each KOOS and WOMAC score, indicating a decrease in pain after the 6-minute walk was associated with an increase (i.e. improvement) in the KOOS and WOMAC scores. However, although these correlations were significant, the magnitude of the correlations were very low. Thus, changes in pain following the 6-minute walk and measures of pain obtained from the KOOS and WOMAC are not strongly correlated, suggesting these measures assess substantially different constructs related to pain. Such findings also support the use of multiple measures of pain, especially those measures that evoke pain in a meaningful and functional manner, when evaluating chronic, progressive diseases such as OA.

**Table 5.1** Pearson Correlation Coefficients (R) between the change in pain after the 6-minute walk test and patient reported outcome measures (subdomains of the KOOS) in the surgical limb of patients with medial knee OA and varus malalignment prior to medial opening-wedge HTO (N=559).

| <b>Knee Injury and Osteoarthritis Outcome Score (KOOS)</b>               | <b>Change In Pain</b> |
|--|-----------------------|
| Pain   | -0.189 (p<0.001)      |
| Symptoms   | -0.115 (p=0.007)      |
| Activities of Daily Living   | -0.174 (p<0.001)      |
| Sports and Recreation  | -0.175 (p<0.001)      |
| Quality of Life  | -0.128 (p=0.002)      |
| <b>Western Ontario and McMaster Universities Arthritis Index (WOMAC)</b> | <b>Change In Pain</b> |
| Pain   | -0.163 (p<0.001)      |
| Stiffness  | -0.121 (p=0.004)      |
| Function   | -0.174 (p<0.001)      |
| Total  | -0.174 (p<0.001)      |

Bilateral changes in pain after the 6-minute walk provided an estimate of pain in response to functional loading. Importantly, however, to further describe the relationship between pain and functional loading, associations were obtained from discordant pairs, illustrating the potential advantages of comparing outcomes between limbs within individuals.

## 5.5 Comparison of Changes in Pain After the Six Minute Walk in HTO-Alone Versus HTO-ALCR

Evaluation of reported pain levels before and after the 6-minute walk in the cohort of patients from Chapter 4 provided insight into the utility of the 6-minute walk as a functional outcome measure in patients with medial knee OA, varus malalignment and ACL deficiency. The number of patients in each group who experienced a decrease in pain (<0), no change in pain (0), an increase in pain by one point (1) and an increase in pain greater than one point (>1), for both limbs, preoperatively and postoperatively, are provided in *Table 5.2*. Overall, both groups tended to have an equal distribution of change scores.

**Table 5.2** Change in knee pain after the 6-minute walk in the surgical and non-surgical limbs, preoperatively and postoperatively, for the HTO-Alone (N=17) and HTO-ALCR (N=21) groups. The number and percentage of patients with each change score is reported.

|                          |    | HTO-Alone<br>N(%) | HTO-ALCR<br>N(%) |
|--------------------------|----|-------------------|------------------|
| <b>Preoperative</b>      |    |                   |                  |
| <b>Surgical Limb</b>     | <0 | 1 (5.90)          | 0                |
|                          | 0  | 7(41.2)           | 11(52.4)         |
|                          | 1  | 6(35.3)           | 4(19.0)          |
|                          | >1 | 3(17.7)           | 6(28.6)          |
| <b>Non-Surgical Limb</b> | <0 | 1 (5.90)          | 0                |
|                          | 0  | 11(64.7)          | 17(81.0)         |
|                          | 1  | 3(17.6)           | 3(14.3)          |
|                          | >1 | 2(11.8)           | 1(4.80)          |
| <b>Postoperative</b>     |    |                   |                  |
| <b>Surgical Limb</b>     | <0 | 1 (5.90)          | 0                |
|                          | 0  | 9(52.9)           | 16 (76.2)        |
|                          | 1  | 4(23.5)           | 2(9.50)          |
|                          | >1 | 3(17.7)           | 3(14.3)          |
| <b>Non-Surgical Limb</b> | <0 | 1 (5.90)          | 0                |
|                          | 0  | 10(58.8)          | 20 (95.2)        |
|                          | 1  | 4(23.5)           | 1 (4.80)         |
|                          | >1 | 2(11.8)           | 0                |

To further quantify the difference between groups, the difference in changes scores (95%CI) was calculated for each limb preoperatively and postoperatively (Table 5.3). In general, there



were no significant differences between groups ( $p>0.05$ ). However, the difference between groups in change scores approached statistical significance for the postoperative change in the non-surgical limb. These evaluations demonstrated a potential difference between groups based on a relatively simple measure of pain in response to functional loading and highlighted the importance of measuring outcomes in both the symptomatic and less symptomatic limb. In contrast, the findings described in Chapter 4 demonstrated minimal difference between groups in the WOMAC scores, lending further support for the use of different measures that assess different constructs related to pain.

**Table 5.3** Comparison of the change in knee pain after the 6-minute walk between HTO-Alone (N=17) and HTO-ACLR (N=21) for the surgical and non-surgical limbs both preoperatively and postoperatively.

| Time          | Limb         | Difference Between Groups (95% CI) |        |
|---------------|--------------|------------------------------------|--------|
| Preoperative  | Surgical     | 0.13 (-0.72, 0.98)                 | p=0.76 |
|               | Non-Surgical | 0.23 (-0.33, 0.80)                 | p=0.41 |
| Postoperative | Surgical     | 0.16 (-0.46, 0.78)                 | p=0.60 |
|               | Non-Surgical | 0.48 (-0.00, 0.97)                 | p=0.05 |

## 5.6 Limitations and Future Directions

An important limitation to consider for each study was the use of retrospective data. The evaluation of long-term effects following surgical interventions for chronic, degenerative diseases often necessitates multiple years of follow-up. As a result, the studies required the inclusion of some patients that had previously undergone surgery before I started my PhD. However, by comparing limbs within individuals and evaluating individuals over time, the influence of extraneous factors is mitigated. Additionally, all patients underwent surgery performed by the same surgeons with the majority of surgeries (~80%) performed by one surgeon. Thus, any changes in surgical techniques likely to influence outcomes were minimized.

A limitation specific to the study described in Chapter 4 was the comparison of patients not randomly allocated to groups. Although patients were matched based on multiple demographic factors, other factors potentially influencing the outcomes of interest may have

differed between groups. Thus, it is more difficult to ensure that the observed differences between groups are a result of the different surgical procedures.

Future directions should focus on well-controlled, randomized trials examining the effects of different surgical interventions on disease progression in patients with medial knee OA, varus alignment and ACL deficiency. Studies should also evaluate the effects of treatment on both the symptomatic and asymptomatic limbs. Additionally, studies should consider comparing the effects of interventions between limbs to reduce the influence of extraneous factors and gain greater insight into the treatment effects.

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# Appendix A

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| Author            | Kendal Marriott, Trevor B. Birmingham, Crystal O. Kean, et al   |
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# Appendix B

## Ethics Approval Form



**Western  
Research**

Research Ethics

Use of Human Participants - Ethics Approval Notice

**Principal Investigator:** Dr. Trevor Birmingham  
**File Number:** 1187  
**Review Level:** Delegated  
**Approved Local Adult Participants:** 900  
**Approved Local Minor Participants:** 0  
**Protocol Title:** Medial Opening Wedge High Tibial Osteotomy for the Treatment of Knee Osteoarthritis: Evaluation of Dynamic Joint Loads and Health-Related Quality of Life - 09812E  
**Department & Institution:** Health Sciences/Physical Therapy, Western University  
**Sponsor:** Canadian Institutes of Health Research

**Ethics Approval Date:** March 26, 2013 **Expiry Date:** April 30, 2017

**Documents Reviewed & Approved & Documents Received for Information:**

| Document Name                           | Comments | Version Date |
|---|----------|--------------|
| Revised Letter of Information & Consent |          |              |
| Revised Western University Protocol     |          |              |

This is to notify you that The University of Western Ontario Research Ethics Board for Health Sciences Research Involving Human Subjects (HSREB) which is organized and operates according to the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans and the Health Canada/ICH Good Clinical Practice Practices: Consolidated Guidelines; and the applicable laws and regulations of Ontario has reviewed and granted approval to the above referenced revision(s) or amendment(s) on the approval date noted above. The membership of this REB also complies with the membership requirements for REB's as defined in Division 5 of the Food and Drug Regulations.

The ethics approval for this study shall remain valid until the expiry date noted above assuming timely and acceptable responses to the HSREB's periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the University of Western Ontario Updated Approval Request Form.

Members of the HSREB who are named as investigators in research studies, or declare a conflict of interest, do not participate in discussion related to, nor vote on, such studies when they are presented to the HSREB.

The Chair of the HSREB is Dr. Joseph Gilbert. The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

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# KENDAL MARRIOTT

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## EDUCATION

| <u>DEGREE</u> | <u>INSTITUTION</u>            | <u>FACULTY</u>   | <u>DATE</u>  |
|---------------|-------------------------------|------------------|--------------|
| PhD           | University of Western Ontario | Physical Therapy | 2012-Present |
| MPT           | University of Western Ontario | Physical Therapy | 2014-2016    |
| BSc           | University of Western Ontario | Kinesiology      | 2008-2012    |

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## PEER REVIEWED JOURNAL ARTICLES

**Marriott K**, Birmingham TB, Kean CO, Hui C, Jenkyn TR, Giffin JR. (2015) Five-year changes in gait biomechanics after concomitant high tibial osteotomy and ACL reconstruction in patients with medial knee osteoarthritis. *The American Journal of Sports Medicine* 43(9): 2277-85.

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## PEER REVIEWED ABSTRACTS

**Marriott KA**, Birmingham TB, Moyer R, Leitch K, Pinto R, Primeau C, Giffin RJ. (2017) Association between high external knee adduction moment and increased pain during walking: Within-limb comparisons in patients with medial compartment knee OA. *Osteoarthritis and Cartilage*. In print.

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**Marriott KA**, Birmingham TB, Giffin RJ. (2015) Gait biomechanics after combined HTO/ACL reconstruction versus HTO alone: A matched cohort study. *Osteoarthritis and Cartilage* 23, A110.

**Marriott KA**, Birmingham TB, Giffin RJ, Jones IC. (2014) Gait biomechanics pre and post combined high tibial osteotomy and ACL reconstruction. *Osteoarthritis and Cartilage* 22, S112-S113.

**Marriott K**, Holmes S, Tay J, Heath M. (2012) Goal-directed grasping: Visual and haptic percepts of object size influence early but not late aperture shaping. *Journal of Vision* 12(9).

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## ORAL PRESENTATIONS

**Marriott K**. Gait biomechanics pre and post combined high tibial osteotomy and ACL reconstruction. *16th Research Colloquium in Rehabilitation, McGill University, Montreal, QC, 2014*

**Marriott K**. Gait biomechanics pre and post combined high tibial osteotomy and ACL reconstruction. *Health and Rehabilitation Sciences Research Forum, University of Western Ontario, London, ON, 2014*

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## POSTER PRESENTATIONS

**Marriott K**, Birmingham TB, Moyer R, Leitch K, Pinto R, Primeau C, Giffin JR. Association between high external knee adduction moment and increased pain during walking: Within-limb comparisons in patients with medial compartment knee OA. *Osteoarthritis Research Society International (OARSI), Las Vegas, NV, 2017*

**Marriott KA**, Birmingham TB, Jones IC, Giffin JR. Gait biomechanics after combined HTO/ACL reconstruction versus HTO alone: A matched cohort study. *Osteoarthritis Research Society International (OARSI), Seattle, WA, 2015*

**Marriott KA**, Birmingham TB, Jones IC, Giffin JR. Gait biomechanics pre and post combined HTO and ACL reconstruction. *Osteoarthritis Research Society International (OARSI), Paris, 2014*

**Marriott K**, Tay J, Holmes SA, Heath M. Goal-directed grasping: Haptic and visual percepts of object size influence early but not late aperture shaping. *Vision Sciences Society (VSS), Naples, FL, 2012*  
*Canadian Society for Psychomotor Learning and Sport Psychology (SCAPPS), Winnipeg, MB, 2011*

**Marriott K**, Mulla A, Heath M. A Re-Evaluation of Fitts (1954): Veridical target width and effector precision influence the scaling of reach trajectories. *Canadian Society for Psychomotor Learning and Sport Psychology (SCAPPS), Ottawa, ON, 2010*

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## FUNDING

2016-2017. Ontario Graduate Scholarship. Funds Awarded: \$15000/1 Year  
 2015-2016. Ontario Graduate Scholarship. Funds Awarded: \$15000/1 Year  
 2014-2015. Ontario Graduate Scholarship. Funds Awarded: \$15000/1 Year  
 2014-2015. FKSMC Internal Research Competition. Funds Awarded: \$2700/1 Year  
 2011-2012. Undergraduate Research Student Award-Natural Sciences and Engineering  
 Research Council of Canada (URSA-NSERC). Funds Awarded: \$6900/1 Year

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## ONGOING RESEARCH

**Marriott KA**, Birmingham TB, Pinto R, Primeau C, Bryant D, Degen R, Giffin JR. Gait biomechanics after combined HTO-ACL reconstruction versus HTO alone: A matched cohort study. Manuscript in preparation.

**Marriott KA**, Birmingham TB, Moyer RF, Leitch KM, Walton D, Giffin JR. Associations between knee loading and pain after walking in patients with knee osteoarthritis: Within-patient between-limb analyses. Manuscript in preparation.

**Marriott KA**, Birmingham TB, Leitch KM, Pinto R, Giffin JR. Known-groups validity and test-retest reliability of the total moment of the knee during gait in patients with medial knee OA. Manuscript in preparation.

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## RESEARCH HISTORY

|              |   |
|--------------|---|
| 2012-Present | Doctorate of Philosophy<br>Wolf Orthopaedic Biomechanics Laboratory, Western University<br><i>Thesis: Dynamic Loading and Pain: Effects of Limb Realignment and Ligament Reconstruction Surgeries</i> |
| Jan-Apr 2013 | Research Assistant<br>Exercise and Health Psychology Laboratory, Western University   |
| May-Aug 2011 | Research Assistant<br>Neurobehavioral Laboratory, Western University  |
| May-Aug 2010 | Research Assistant<br>Neurobehavioral Laboratory, Western University  |

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**TEACHING**

| <u>ROLE</u>        | <u>INSTITUTION</u>  | <u>COURSE</u>   | <u>DATE</u> |
|--------------------|---|---|-------------|
| Guest Lecturer     | University of Western Ontario<br>School of Physical Therapy     | PT9524<br>Physical Therapy in<br>Community Settings I | 2017        |
| Teaching Assistant | University of Western Ontario<br>School of Occupational Therapy | OT9680<br>Fieldwork: Towards<br>Reflection in Action  | 2013        |
| Teaching Assistant | University of Western Ontario<br>School of Occupational Therapy | OT9595<br>Evidence Informed<br>Practice               | 2013        |

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**CLINICAL EXPERIENCE**

| <u>POSITION</u> | <u>INSTITUTION</u>                                  | <u>FACULTY</u>  |
|-----------------|---|---|
| Physiotherapist | London Health Sciences Centre,<br>Victoria Hospital | Inpatient Ward  |
| PT Student      | Western University                                  | Fowler Kennedy Sport Medicine<br>Clinic, 3M Centre        |
| PT Student      | Western University                                  | Victoria Hospital, Critical Care &<br>Trauma Centre       |
| PT Student      | Western University                                  | Chatham Kent Health Alliance,<br>Inpatient Rehabilitation |
| PT Student      | Western University                                  | Victoria Hospital, Thoracic<br>Surgery                    |
| PT Student      | Western University                                  | Canadian Back Institute, Sarnia                           |

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**ACADEMIC HONOURS & AWARDS**

| <u>AWARD</u>                            | <u>INSTITUTION</u> | <u>DATE</u>  |
|---|--------------------|--------------|
| Faculty of Health Sciences Travel Award | Western University | 2014-Present |
| Graduate Research Scholarship           | Western University | 2012-Present |
| Deans Honour List                       | Western University | 2008-2016    |

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**CERTIFICATIONS & ASSOCIATIONS**

| <u>CERTIFICATION</u>                 | <u>INSTITUTION</u>  | <u>DATE</u>  |
|--------------------------------------|---|--------------|
| Physiotherapist (#17679)             | College of Physiotherapists of Ontario                                  | 2017-Present |
| Physiotherapist Member<br>(#2030815) | Canadian Physiotherapy Association<br>Ontario Physiotherapy Association | 2016-Present |
| Tracheal Suctioning<br>O2 Titration  | Breathing Easier, LHSC  | 2017-Present |
| GLA:D Good Living With OA            | GLA:D Canada  | 2015-Present |
| CPR & First Aid                      | The Red Cross   | 2014-Present |

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