2011

STAGED MEDIAL OPENING WEDGE HIGH TIBIAL OSTEOTOMY FOR BILATERAL VARUS GONARTHROSIS

Emily Louise Sischek

STAGED MEDIAL OPENING WEDGE HIGH TIBIAL OSTEOTOMY FOR BILATERAL VARUS GONARTHROSIS

(Spine title: Staged HTO for Bilateral Varus Gonarthrosis)

(Thesis format: Monograph)

by

Emily L. Sischek

Graduate Program in Health and Rehabilitation Sciences

A thesis submitted in partial fulfillment
of the requirements for the degree of
Master of Science

School of Graduate and Postdoctoral Studies
The University of Western Ontario
London, Ontario, Canada

THE UNIVERSITY OF WESTERN ONTARIO
School of Graduate and Postdoctoral Studies

CERTIFICATE OF EXAMINATION

Supervisor	Examiners
Dr. Trevor B. Birmingham	Dr. Dianne Bryant
Supervisory Committee	Dr. Bert Chesworth
Dr. J. Robert Giffin	Dr. Kevin Willits

The Thesis by

Emily Louise Sischek

entitled:

Staged Medial Opening Wedge High Tibial Osteotomy for Bilateral Varus Gonarthrosis

is accepted in partial fulfilment of the
requirements for the degree of
Master of Science

Date____________________________

____
Chair of the Thesis Examination Board

ABSTRACT

Background: Medial opening wedge high tibial osteotomy (HTO) aims to improve pain and function by correcting varus alignment and lessening aberrant medial compartment knee joint loads. Because varus gonarthrosis often affects both knees, staged bilateral HTO may be an appropriate treatment approach for such patients. However, we are unaware of any previous studies evaluating outcomes after these staged procedures.

Objectives: 1) To evaluate radiographic alignment, dynamic knee joint loading, performance-based and patient-reported outcomes after staged bilateral medial opening wedge HTO, and 2) To compare outcomes in patients undergoing the second surgery within, or beyond, 12 months of the first surgery.

Hypotheses: 1) Patients will experience statistically and clinically significant improvements in all measured outcomes; 2) Those patients undergoing the second surgery within 12 months of the first surgery will report greater improvements than those undergoing the second surgery beyond 12 months.

Study Design: Case Series; Level of evidence, 4

Methods: 37 patients with bilateral varus alignment (-8.36° ± 2.98°) and medial compartment osteoarthritis (OA) underwent staged bilateral medial opening wedge HTO. Patients underwent full-limb standing anteroposterior radiographs to determine frontal plane alignment (mechanical axis angle) and 3-dimensional gait analysis to estimate knee joint loading (external adduction moment about the knee). Patients also completed the six-minute walk test (6MWT), the Knee Injury and Osteoarthritis Outcomes Scores (KOOS), Lower Extremity Functional Scale (LEFS), and the Short Form Health Survey (SF-12). Both limbs were evaluated for all measures preoperatively and approximately 6, 12 and 24 months after each surgery.

Results: There were large improvements in outcomes. Mean changes (95%CI) were: mechanical axis angle 9.43° (8.37°, 10.39°); peak knee adduction moment -1.72 %BW*Ht (-2.06, -1.38 %BW*Ht); 6MWT 36.72 m (19.43, 54.01m); and KOOS Pain 25.60 (19.76, 31.44). There were no statistically significant differences in the improvements between those patients who had the second HTO within or beyond 12 months of the first HTO. Mean differences (95% CI) were: mechanical axis angle 0.43° (-1.72°, 2.58°); peak knee adduction moment -0.20 %BW*Ht (-0.89, 0.49 %BW*Ht); 6MWT 15. 07 m (-19.79, 49.93m); and KOOS Pain -3.01 (-14.55, 8.53).

Conclusions: Patients experience large, clinically important improvements in frontal plane alignment, dynamic knee joint loading, and patient-reported outcomes after staged bilateral medial opening wedge HTO. Current findings suggest no difference in outcomes for patients who undergo the second surgery within, or beyond, 12 months of the first surgery.

Key Terms: *knee; osteoarthritis; varus gonarthrosis; high tibial osteotomy; bilateral knee surgery; staged knee surgery*

Acknowledgements

I would like to recognize the contributions made by several individuals, both to the completion of my thesis and to my experiences during my time spent in the Wolf Orthopaedic Biomechanics Lab:

- ♢ Dr. Trevor Birmingham: Thank you for your time and commitment; you've helped me to make this project the absolute best it could be. Your guidance made all the difference for it to be a success.
- ♢ Mr. Ian Jones: Your expertise in the lab (especially when I struggled with the computers) and your humour in my moments of frustration were always appreciated. I would not have made it to this point without your help.
- ♢ WOBL People: Thank you for all of the laughs, advice, assistance and fantastic memories! The last two years would not have been the same without all of you.
- ♢ Dr. Bob Giffin: Thank you for your valuable input into the development and completion of this project.
- ♢ My family: Mom, Dad, Steph & Julie – Thank you for your unconditional love and support over the last two years. You have all been a huge part of me achieving my goals throughout this process.

Table of Contents

List of Tables

List of Figures

List of Appendices

List of Abbreviations

3D	Three-dimensional
6MWT	Six minute walk test
ADL	Activities of Daily Living
BMI	Body mass index
BW	Body weight
CI	Confidence interval
FU	Follow-up (assessment time point)
Ht	Height
HTO	High tibial osteotomy
KL	Kellgren-Lawrence (grade of OA severity)
KOOS	Knee Injury and Osteoarthritis Outcome Score
L1	First operative limb
L2	Second operative limb
LEFS	Lower Extremity Functional Scale
LLD	Leg length discrepancy
MCS	Mental Health Component Score (of the SF-12 survey)
OA	Osteoarthritis
PCS	Physical Function Component Score (of the SF-12 survey)
SD	Standard Deviation
SF-12	12-item Short Form Health Survey
TKA	Total knee arthroplasty
UKA	Unicompartmental knee arthroplasty

CHAPTER 1 – INTRODUCTION

1.01 Introduction

Osteoarthritis (OA) is a leading cause of physical disability, pain and healthcare use worldwide.[21] Knee OA is one of the most prevalent forms of OA,[71] and is more commonly present in the medial compartment of the tibiofemoral joint.[72] Approximately 16% of adults in developed countries have symptomatic knee OA.[120] Although there are numerous risk factors, varus alignment consistently emerges as a potent risk factor for disease progression in the medial compartment.[22,26,101] The importance of alignment to disease progression may help explain the renewed interest in corrective osteotomy procedures.[34,54,89]

Varus gonarthrosis refers to the combined presence of varus alignment and knee OA that is greater in severity in the medial compared to lateral compartment. Medial opening wedge high tibial osteotomy (HTO) is suggested to be an effective intervention for relatively young, active patients with varus gonarthrosis.[5,16] We have previously reported large improvements in patient-reported outcomes and three-dimensional (3D) gait kinetics in 126 patients two years after unilateral medial opening wedge HTO.[16] This finding is consistent with other reports demonstrating good short- and long-term clinical outcomes following this surgery.[84,86,91]

Importantly, knee OA is often bilateral. In fact, in patients with known radiographic knee OA (Kellgren-Lawrence grade [KL] ≥ 2) it is more common to have bilateral than unilateral involvement.[33,72] If bilateral symptomatic knee OA is accompanied by varus alignment, it may be appealing to perform HTO on both limbs. Because medial opening wedge HTO usually requires a period of non-weight-bearing postoperatively, bilateral HTO is frequently performed in a staged manner. Despite this, we are unaware of any studies evaluating outcomes after staged bilateral HTO.

In general, bilateral orthopaedic surgeries may be completed in a simultaneous, sequential or staged fashion.[73,113] Staged bilateral orthopaedic procedures are typically defined as two surgeries occurring under two separate anaesthetics, often months apart.[73] The optimal timing for staged lower extremity surgeries is presently unclear.[59,70,104,124] Patients who undergo staged bilateral total knee arthroplasty (TKA) usually receive the two surgeries within 12 months.[73] We have previously demonstrated that patient-reported outcomes continue to improve beyond the first 12 months after unilateral medial opening wedge HTO.[16] As a result, it may be beneficial to wait 12 months before performing the second surgery. Alternatively, most of the improvement is observed within that time period, and dynamic loading of the nonoperative limb may actually increase after the first surgery in patients with bilateral varus.[18] Therefore, performing the two surgeries within 12 months may enable the patient to achieve maximum overall benefit from the two surgeries.

1.02 Study Objectives and Hypotheses

The primary objective of this study was to evaluate radiographic alignment, dynamic knee joint loading, and performance-based and patient-reported outcome measures for patients undergoing staged bilateral medial opening wedge HTO. The secondary objective was to compare outcomes in patients who undergo the second surgery either within, or beyond, 12 months of the first surgery. We hypothesized that patients will experience statistically and clinically significant improvements in all outcomes by 24 months after the second surgery. We also hypothesized that patients undergoing the second surgery within 12 months of the first surgery will report greater improvements (at 24 months after the second surgery) than those undergoing the second surgery beyond 12 months of the first surgery.

CHAPTER 2 – REVIEW OF THE LITERATURE

2.01 Arthritis

Arthritis is a broad-based term used to encompass a group of common musculoskeletal disorders and diseases characterized by localized joint pain, articular cartilage degeneration, physical disabilities and decreased quality of life.[25,110,120] Arthritis can affect any of the bony joints of the body and has the potential to be debilitating for those individuals who are afflicted.[21,110] Currently, nearly 15.3% of the Canadian population (4.2 million people) self-reports having arthritis of at least one joint.[105] The prevalence of arthritis is expected to increase as the "baby boomer" population advances in age.[120] It is anticipated that 21% to 26% of the Canadian population will have arthritis by 2021.[11]

2.02 Osteoarthritis

Osteoarthritis (OA) is the most common form of arthritis[9,41,100] and women are affected more often than men.[110,120] The overall prevalence of OA increases with age. Statistics Canada reports that more than 1 in 10 Canadians over 15 years of age has been diagnosed with OA of at least one joint.[105] This number is expected to increase to almost 1 in 6 by the year 2031.[11,41] Osteoarthritis is also a leading cause of chronic disability, [25,41] especially in industrialized countries.[25] According to the World Health Organization, osteoarthritis is expected to become the fourth leading cause of global disability by 2020.[77]

Osteoarthritis is the degeneration of a synovial joint. It is generally characterized by progressive softening, fibrillation and consequent loss of articular cartilage. This is followed by the body's attempt to repair the cartilage, sclerosis of the subchondral bone and eventually the formation of osteophytes and subchondral cysts.[120] The initial onset and subsequent progression of OA can be influenced by both mechanical events and biological events. The impact of these events eventually leads to a destabilization of the coupling between the normal cellular processes of degeneration and resynthesis of articular cartilage. The imbalance created between cartilage degeneration and cartilage resynthesis favours the process of degeneration.[100] The imbalance can continue in an uncontrolled manner and may ultimately lead to complete focal cartilage degeneration and potential osteonecrotic changes to the underlying subchondral bone.

2.03 Knee Osteoarthritis

Of the weight-bearing joints, the knee is most commonly afflicted with OA.[71] Knee OA is classified as degeneration being present in either of the medial or lateral tibiofemoral compartments.[72] Diagnosis preferably includes both radiographic evidence of osteoarthritic degeneration and the presence of pain symptoms on most days.[3,38,65,120] Knee OA is one of the leading causes of physical disability worldwide,[41,51,120] with approximately 10% of adults being affected by a symptomatic knee at some point within their lifetime.[21,120] Knee OA accounts for more dependency and difficulty with walking, stair climbing, and other lower extremity tasks than any other disease.[38,51] Knee OA has been shown to affect people of various ethnic backgrounds and different geographic locations.[38] It is not a disorder that is isolated to a specific population.[120]

As is true with nearly all forms of OA, knee OA is a multifactorial disorder. It has primary and secondary forms that differ in their modalities of onset. Primary knee OA is considered to be idiopathic in nature; secondary knee OA is considered to be associated with a preceding event, such as a traumatic injury to the knee joint.[100] Knee OA is also a disease that varies in its methods of initiation and progression, as evidenced by the fact that many people with knee OA have mild degeneration that remains stable over a long period of time, while others have knee OA that progresses to end stages rapidly. Moreover, it is not a disorder that affects the entire joint uniformly. Prevalence of OA is greatest in the medial tibiofemoral compartment of the knee joint as compared to the other compartments of the knee.[72] Overall, there is still much uncertainty behind the etiology of knee OA.

Risk Factors for Knee OA

As the processes of OA initiation and progression differ, it is important to attempt to determine risk factors leading to both the onset and progression of knee OA. Risk factors can be considered to be local, as they directly affect the knee joint, or they can be systemic. Local risk factors are usually considered to have mechanical influences on the joint, thought to come into play primarily in determining the exposure of individual joints to injury and to excess loading conditions that lead to joint degeneration. Systemic risk factors are usually considered to have biochemical influences on the joint, and act by increasing the susceptibility of joints to injury by causing direct damage to joint tissues, or by impairing the process of repair in damaged joint tissue.[9,41] Some risk factors, such as obesity, are thought to potentially exhibit both biomechanical and biochemical effects.[44]

Incident knee OA is considered to be the transition of the knee joint from a classification of a healthy knee to that of OA being present. Radiographically it is considered to be the change from a Kellgren-Lawrence (KL) rating of 0 or 1 to that of ≥ 2.[30] Local risk factors for incident knee OA include varus alignment,[22,101] leg length discrepancy,[51] congenital and developmental deformities of the knee joint,[100] previous injury to the bony or soft tissue components of the knee joint,[30,100] occupational activity,[6,40,79,100] and recreational and sports participation.[100] Systemic risk factors that have been associated with incident knee OA include age,[41,100] gender,[41,74,100] genetic factors or predisposition,[41,100,125] overweight/obese body mass index (BMI ≥ 25), [30,33,41,74,100,108,115] and elevated bone mineral density.[24,41]

Progression of knee OA is considered to be an increase in the severity of degeneration present within the knee joint. This can be determined from radiographs based on joint space narrowing[3] or joint space narrowing in conjunction with the formation of osteophytes.[65] It is considered to be an increase of at least one unit on the KL scale, starting from a minimum rating of 2.[30] Local risk factors for knee OA progression include varus/valgus alignment,[22,26,36,99,101] varus thrust,[28] an elevated peak external knee adduction moment,[10,81] an elevated knee adduction moment impulse[13] and prior joint injury.[33] Systemic risk factors associated with knee OA progression include an overweight/obese BMI,[33] nutritional deficiencies[41] and decreased bone mineral density.[41]

Many risk factors for both incidence and progression of knee OA have been shown to pose significant risk while acting independently, and their effects are increased when they are acting in conjunction with one or more other risk factors. According to Cooper et al,[30] if an individual is obese (BMI of ≥30) they have an odds ratio of 2.60 (95% CI, 1.0 – 6.8) of knee OA progressing from KL rating of 1 to that of ≥ 2. When an individual has both a BMI ≥30 and varus alignment of the leg, their risk of knee OA progression increases to an odds ratio of 5.06 (95% CI, 1.71–14.94). It is in the best interest of an individual to actively modify, minimize or remove as many potential risk factors as possible in order to slow or stop the disease process, as symptoms and joint degeneration can progress rapidly without intervention.

2.04 Risk Factors for Medial Compartment Knee OA

Varus Limb Alignment

The precise role of limb alignment in the degenerative processes of medial knee OA is still unclear. However, varus alignment has been associated with a three- to four-fold increase in risk of medial tibiofemoral compartment OA progression.[10,22,26,99] The specificity of compartment effects is further evidenced by the association of varus alignment, medial cartilage loss and subsequent medial joint space narrowing. The loss of articular cartilage and subsequent joint space narrowing leads to a continuous cycle of increased degree of varus limb alignment, increased medial tibiofemoral compartment loading and further progression of OA and joint space loss (Figure. 2.1).

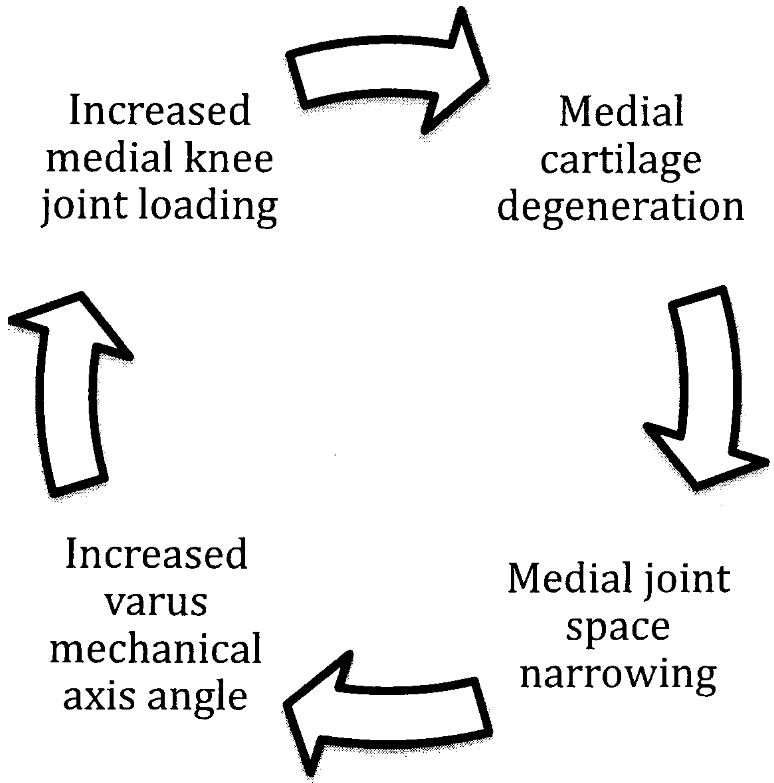

Figure 2.1 The "vicious cycle" of medial knee OA progression

Dynamic Joint Loads and the External Knee Adduction Moment

Synovial joints such as the knee require regular loading to maintain tissue function and health;[8] however, excessive loading in magnitude and/or frequency has the potential to exceed the tolerance level of tissues and contribute to the OA degenerative process.[40] It has been determined that abnormal gait biomechanics can influence both the incidence and progression of medial compartment knee OA.[12,13,28] One of the most widely used values in reporting joint loading in patients with medial knee OA is the external knee adduction moment. The knee adduction moment has previously been shown to be associated with medial compartment compressive loading in the knee.[12,56] As such, it is often used as a proxy for the magnitude of loading that the medial tibiofemoral compartment of the knee experiences during ambulation.[7] In patients with medial tibiofemoral compartment knee OA, the magnitude of the peak knee adduction moment has been shown to be greater than those without knee OA.[12,56] The external knee adduction moment is also suggested to be indicative of the severity of medial knee OA present.[83,98]

2.05 Risk Factor for Bilateral Knee OA: Obesity

Obesity is one of the most strongly associated risk factors for knee OA, and this is true regardless of how knee OA is defined (symptomatic or radiographic) and what compartment of the knee the degeneration is present.[33,38,39,74,75,108,115] Manninen et al[74] demonstrate a direct relationship between BMI and the development of OA over a 10-year time span (odds ratio 1.4, 95% CI = 1.2 - 1.5). Cooper et al[30] report that a BMI >25.4 carries an increased risk of incident OA of KL grade 1 (odds ratio 9.1, 95% CI = 2.6 – 32.2) and grade 2 (odds ratio 18.3, 95% CI = 5.1 – 65.1) and progression of OA (odds ratio 2.6, 95% CI = 1.0 – 6.8) over a 5 year time span.

The knee joint experiences loads 2-3 times greater than body weight during the stance phase of gait, so understandably even small increases in body weight will greatly impact the load the knee experiences. In the majority of the non-pathological population, it could be presumed that both knees would experience nearly identical load conditions during ambulation and therefore both knees would likely be at a similar risk for developing OA. Stürmer et al[108] demonstrate that of a population of patients undergoing TKA for knee OA ≥ KL grade 2, 85.9% were either overweight (BMI ≤ 25.0 = 45.0%) or obese (BMI ≤ 30.0 = 40.9%) and 87.4% had bilateral knee OA. When separated by weight classes, 86.1% of the overweight patients (adjusted O.R. 5.92, 95% CI = 2.0 – 17.5) and 93.3% of the obese patients (adjusted O.R. 8.13, 95% CI = 2.39 – 27.7) had bilateral knee OA, and a 5 unit increase in BMI resulted in an adjusted O.R. of 2.63 (95% CI = 1.37 -5.05) of having bilateral knee OA ≥ KL grade 2. Davis et al[33] report similar results of obesity being one of the strongest predictors of bilateral knee OA (O.R. 6.6, 95% CI = 4.71 – 9.18).

2.06 Management of Medial Compartment Knee Osteoarthritis

There is currently no known cure for OA, and no known absolute method of prevention. However, once the degeneration process has started, management of medial knee OA can occur by either moderating the symptoms the patient is experiencing or by attempting to slow or stop the progression of the disease.

Management modalities can be classified as non-surgical or surgical. Non-surgical modalities include pharmacotherapy, physiotherapy, activity management or modification, and the use of orthotics and braces. They may temporarily alter the joint characteristics or biomechanics but they tend to be geared towards symptom management. Non-surgical modalities do not permanently alter the joint anatomy itself and outcomes are not considered to be permanent. Surgical modalities for knee OA may include high tibial osteotomy (HTO), unicompartmental knee arthroplasty (UKA) and total knee arthroplasty (TKA). Surgical modalities physically alter the bony structure of the joint or limb in an attempt to permanently modify or remove risk factors for disease progression. The method of OA management chosen is based on a patient's characteristics, current physical capabilities and disabilities, current risk factors, the severity of symptoms and the current disease state of the affected joint.

More advanced cases of knee OA are often accompanied by pain and symptoms that are not adequately managed with the use of non-surgical modalities. Substantially decreased quality of life due to pain, mobility restrictions and degenerative changes in one or more compartments of the knee that have reached advanced or end stages of OA often lead to referral to an orthopaedic specialist. In these instances, surgical intervention may be deemed the most appropriate option. The patient's overall medical condition, diagnosed cause of knee OA (if there is one) and the extent and location of OA within the knee joint may point to the most appropriate surgical intervention. Surgical recommendations may be either to remove and replace the articular components of the joint, as in with a UKA or TKA, or to correct for some of the diagnosed risk factors while maintaining the natural articular components of the joint, as with a HTO. Both surgical procedures have been shown to aid in the management of knee OA for pain, mobility restrictions and quality of life. However, they differ in the extent of invasiveness to the patient, recovery time, and activity limitations following surgery.[93,104] They also differ in the potential surgical risks and unanticipated outcomes for the patient.[59,70,80,93,102,104,124] Therefore, careful selection of who is deemed an appropriate surgical candidate for UKA, TKA or HTO is taken in order to maximize the likelihood of surgical success.

2.07 Impact of Timing for Clinical Intervention

The manner in which certain risk factors may affect a knee joint can depend on which stage of the OA degenerative process that joint is currently in.[100] This knowledge might be used to determine the most effective methods and time points for intervention to occur for both a specific individual, as well as for the general public. In terms of public health strategies and initiatives, it has been suggested that preventing the progression of OA from a mild to moderate/severe state is more cost effective to the individual and to the health care system than attempting to prevent incident cases.[30]

2.08 Clinical Measures of Medial Knee OA Patients

Radiographic Measures

Radiographs provide a simple method of monitoring knee OA progression and tracking certain risk factors associated with both initiation and progression of knee OA. Two measures that are commonly used in patients with medial knee OA are the mechanical axis angle and grading of the severity of OA present within the joint. Double-limb standing hip-to-ankle digital radiographs are useful, especially if preoperative planning is necessary.

Mechanical Axis Angle

Lower limb alignment can be considered neutral, varus (bowlegged) or valgus (knock-kneed). Limb alignment is commonly quantified using the mechanical axis angle.[23,82,103] The mechanical axis angle is an angle created by the mechanical axis of the femur and the mechanical axis of the tibia. Visually, it is the included angle created from a line joining the hip centre to the centre of the knee, and a line from the ankle centre to the centre of the knee. Varus alignment is considered to be a risk factor for progression of medial tibiofemoral knee OA, and is also associated with the external knee adduction moment.

Figure 2.2 Mechanical axis angle of a varus aligned limb. The mechanical axis angle is the included angle created by a line joining the centre of the hip to the centre of the knee, and the centre of the knee to the centre of the ankle.

Grading of Knee OA

Monitoring medial knee OA with the use of a radiographic grading scale can assist clinicians to determine if the extent and/or severity of OA present within the joint is worsening. This can then assist in selecting treatment options. The KL grading system[65] is based on the presence of joint space narrowing, osteophyte formation and abnormalities in the articular surfaces, and is frequently used in clinical research.

Analysis of Gait Biomechanics

Gait analysis is a non-invasive method for determining the kinetics and kinematics of the load-bearing joints of the body, providing an accurate depiction of what the limb experiences during ambulation. Three-dimensional gait analysis has become an important tool for quantifying normal and pathological walking patterns. It has also been suggested to be useful for selecting treatment options and evaluating their results.[91] Gait biomechanics of patients with knee OA have been widely reported. [10,13,16,19,34,48,92]

Dynamic Joint Loading

The external knee adduction moment is a proxy for the load on the medial compartment of the knee during walking. The adduction moment is in the frontal plane and acts to adduct the shank about the knee joint. This results in compression of the medial tibiofemoral compartment. The knee adduction moment is created by the projection of the ground reaction force (GRF) medial to the centre of rotation of the knee joint (Figure 2.2). The external knee adduction moment is largely influenced by the magnitude of the GRF and the perpendicular distance from the knee joint centre to the line of action of the GRF vector (the frontal plane lever arm). The adduction moment curve for a typical adult displays a "double hump" shape (Figure 2.3) similar to that of a typical GRF curve (Figure 2.4). The peak adduction moment often occurs early in the stance phase of gait, corresponding to the loading response of the stance limb when the GRF is the highest. This demonstrates the direct effect that the magnitude of the GRF has on the adduction moment.

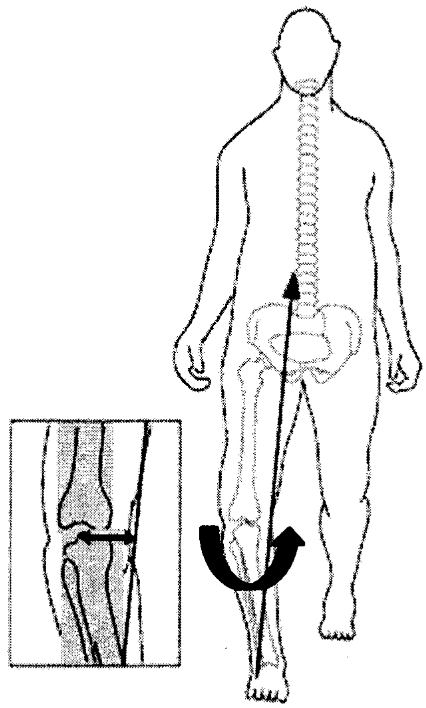

Figure 2.3 Illustration of the GRF acting a distance medial to the centre of the knee joint, and the external knee adduction moment creating a turning force about the knee joint.

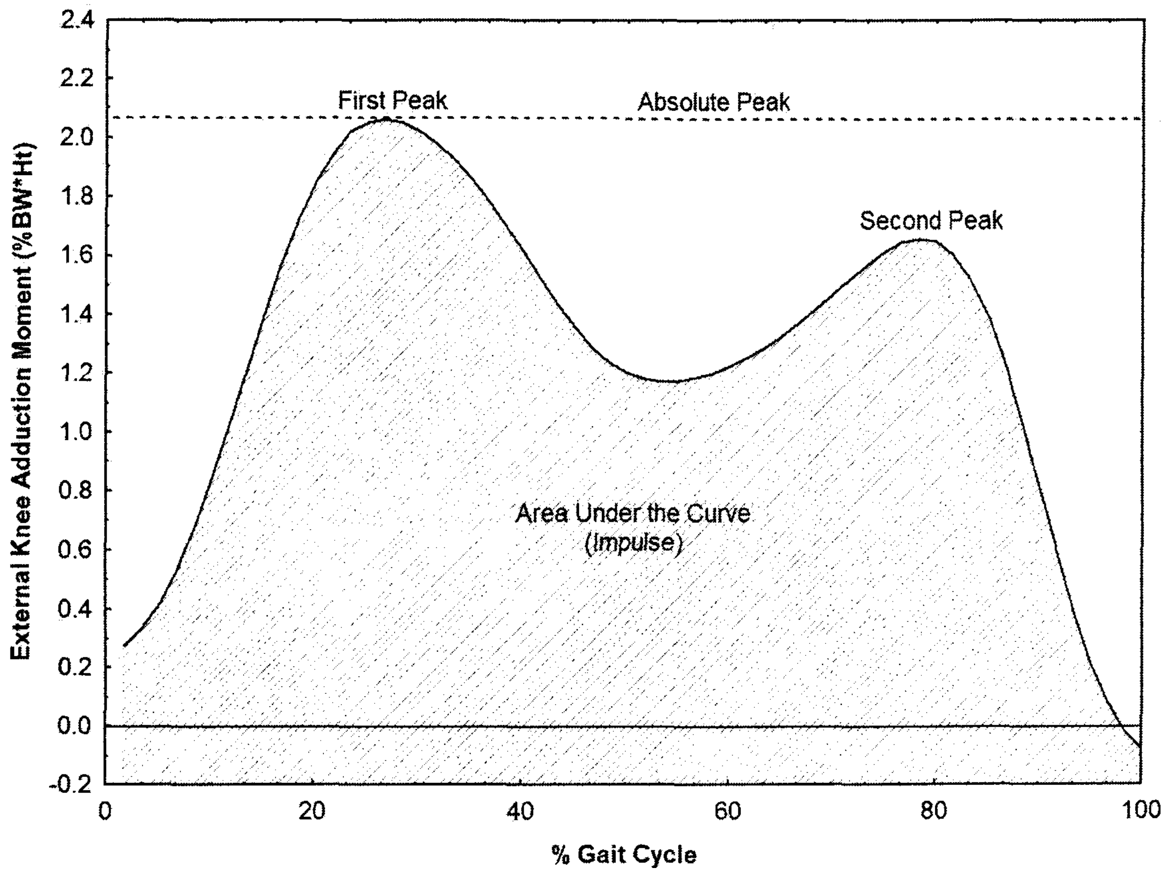

Figure 2.4 Illustration of a typical "double hump" curve of the external knee adduction moment during the gait cycle

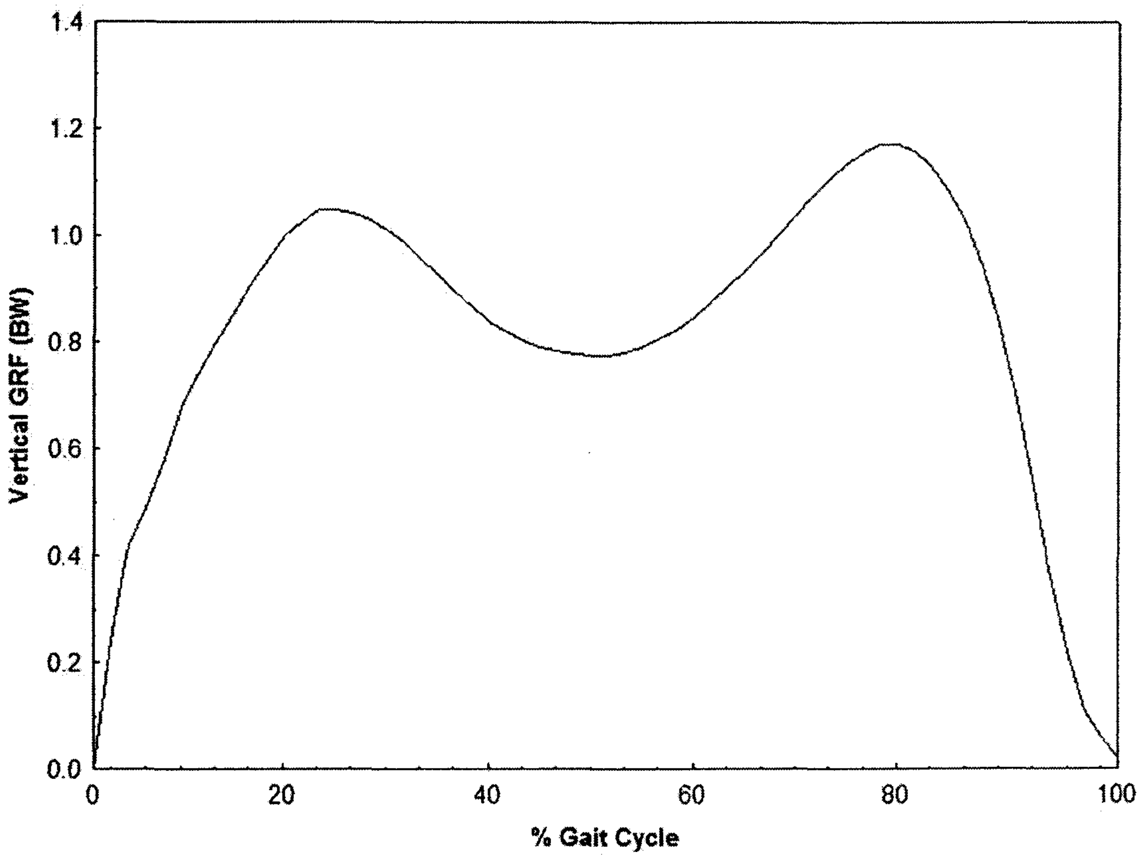

Figure 2.5 Illustration of a typical "double hump" curve of the vertical ground reaction force (GRF) during the gait cycle

Gait Adaptation Techniques

Certain gait adaptations have been shown to affect the magnitude of the peak external knee adduction moment, and therefore are also considered to be of clinical importance. Gait adaptation techniques that decrease the magnitude of the peak external knee adduction moment are suggested to be adopted by patients who have medial knee OA in order to moderate their pain and symptoms.[8] Those that are seen commonly include decreasing gait speed,[48] shortening stride length,[49,117] increasing the toe-out angle[27,60,117] and increasing the lateral trunk lean over the stance limb.[8,19,55] Of particular biomechanical interest are the effects of increasing the toe-out angle and the lateral trunk lean. Increases in toe-out angle are thought to create a lateral transfer of the centre of pressure, especially in late stance. This is thought to decrease the magnitude of the frontal plane lever and thereby results in a decreased knee adduction moment.[60] Lateral trunk lean over the stance limb shifts the centre of mass of the body laterally; this in turn results in a lateral shift of the projection of the GRF vector. This too decreases the frontal plane lever arm and results in a decreased peak knee adduction moment.[55]

Performance-based Measures

Performance-based measures allow a clinician to assess a patient's abilities to successfully complete tasks associated with activities of daily living (ADL). Many individuals with knee OA struggle with ADL related to lower extremity function, such as walking or rising out of a chair. As walking is one of the most common ADL, it is considered to be an essential functional capability. Measures of ADL can be used in patients with knee OA to monitor their function during the progression of disease, and to determine if an intervention has had the desired outcome (increased functional capabilities relating to ADL).

6 Minute Walk Test

The 6 minute walk test (6MWT) is a measure of the maximal distance an individual can cover in a 6 minute time span. It is considered to be safer, easier, better tolerated by a variety of patient types and more reflective of ADL as compared to other walk tests.[37,106] Depending on the severity of OA present, patients with knee OA often have some degree of difficulty with ambulation over both short and long distances and tend to walk at a slower pace than individuals not affected by knee OA.[61] The 6MWT can reflect this functional shortfall, as well as any gains or losses made due to intervention as it is a valid and reliable measure when utilized over multiple assessments.[87]

Patient-Reported Measures

Self-report questionnaires can be used to gain a more thorough indication of a patient's opinion of their own health. Questionnaires can be targeted to address patients' perceptions of themselves as a whole, of a general region of their body, or of a specific body part affected by a particular condition. For patients with knee OA, the 12-item Short-Form Health Survey (SF-12), Lower Extremity Functional Scale (LEFS) and Knee Injury and Osteoarthritis Outcome Score (KOOS) have shown to provide clinically relevant insight into the individual, body region[15] and specific joint[96] respectively. It is of a general consensus that both generic measures, such as the SF-12, and specific measures, such as the LEFS and KOOS, should be used in assessment of knee OA as they provide different scopes of information.[25,90]

2.09 Surgical Management of Medial Knee OA: High Tibial Osteotomy

High tibial osteotomy is a surgical procedure intended to improve symptoms and potentially slow or stop the progression of unicompartmental knee OA. [5,53] Importantly, HTO does not remove or replace any of the articular components of the knee joint. High tibial osteotomy is based on the premise that corrections are made to both orientation of the knee joint articular surfaces and the lower limb alignment in the frontal plane.[43] Ideally, the postoperative limb is corrected into slight valgus alignment. This is done in order to decrease the magnitude of load in the arthritic medial compartment of the knee joint and create a less imbalanced load distribution within the knee joint.[2] The end result is achieved by altering the bony structure of the proximal tibia and how the proximal tibial articular surfaces interact with the distal femoral articular surfaces. There are generally three main types of HTO used to treat medial tibiofemoral compartment OA: the dome osteotomy, lateral closing wedge HTO and medial opening wedge HTO.

The first report of HTO described its purpose in management of unicompartmental osteoarthritis in both valgus and varus knees. Achieved via surgically correcting the limb to "proper neutral alignment", Jackson and Waugh[58] proposed that the imbalanced forces and loads that were acting on the knee joint and leading to unicompartmental OA would be corrected, and further progression within the damaged compartment could be minimized. This has proven to be at least partially true in the management of medial compartment knee OA in the varus knee, as high tibial osteotomy can be effective in the correction of alignment of a varus knee and improving pain and disability.[5,32,57,84,86] Naudie et al.[84] demonstrated survivorship (where failure or endpoint was deemed as the patient undergoing TKA) of 73% at 5 years, 51% at 10 years and 30% at 20 years following 106 valgus-producing (lateral closing wedge) high tibial osteotomies. This is similar to other reports where satisfactory outcomes were achieved in approximately 80% of patients at 5 years and 60% of patients at 10 years following valgus-producing high tibial osteotomies.[1,14,32,46,53,57,86]

The prevalence of HTO for medial compartment knee OA has varied considerably since its inception.[69,122] This variance has been influenced by several factors within the surgical community. Advancements in surgical methods and hardware used for performing HTO, as well as more stringent criteria for patient selection, have allowed for more predictable outcomes following surgery.[107] Methods and technologies that can be used to define surgical success (such as those that can quantitatively measure biomechanical factors of gait of medial knee OA patients) have become more advanced and have proven to be reliable.[17,64] There have also been advancements in methods and hardware for other surgical procedures, specifically TKA, that are used to effectively manage knee OA. The likelihood of HTO being performed is also heavily dependent upon surgeon preferences and skill sets.[122]

Preoperative planning for HTO

Patient Selection

Proper patient selection is suggested to be crucial for the success of any of method of HTO.[4,14,20,57,84] Table 2.1 provides a thorough overview of factors previously suggested to be considered in decision making regarding treatment options for medial compartment knee OA. Ideal patients are suggested to be young, active and healthy – generally, less than 65 years of age, normal weight, with higher activity levels than those of normal ADL and few to no other medical diagnoses.[5,31,50,84] Naudie et al. reported that with patients younger than 50 years and 120° of knee flexion that survivorship of the HTO can approach 95% at 5 years, 80% at 10 years and 60% at 15 year postoperative time points.[84] Patients who are older than 65 years of age or who are not physically active are suggested to be better suited for TKA.[31]

Table 2.1 Factors suggested to be considered in the decision making of operative treatment for unicompartmental osteoarthritis of the knee

Preoperative condition of the patient	Understanding and cooperation of the patient Expectations of the patient Rheumatological status (should be negative) History of infection Age of the patient (chronological and physiological) Necessity for bilateral procedures
Preoperative condition of the joint	Severity of the osteoarthrosis Status of the other compartments of the knee Ligamentous integrity Degree of varus or valgus angulation Presence or absence of osseous defects Range of motion of the knee Tibial morphology Adductor moment
Surgical considerations	Ease of the operative procedure (perceived) Potential intraoperative complications Duration of the operative procedure (by the particular surgeon performing it) Loss of blood Cost
Postoperative condition considerations	Activities permitted by the procedure Potential postoperative complications Durability of the operative result (perceived) Cosmetic appearance Need for immobilization Time of hospitalization Ease of revision or conversion to a total knee replacement

Chart adapted from Grelsamer, 1995[50]

Preoperative Assessments

All methods of HTO require somewhat similar methods of preoperative planning. A thorough patient history must be taken, including any prior lower limb injuries and surgeries that may have affected the limb's stability or alignment, health conditions that might contraindicate a surgical intervention and the level of acceptance of the patient to follow post-surgical requirements necessary to allow the bone to properly heal. A physical examination of the patient to identify any accompanying deficiencies, such as ligament laxity or injury, provides additional information. It is recommended to acquire double-limb, weight-bearing, hip-to-ankle anteroposterior (AP) radiographs,[23,31,50] with accompanying lateral and skyline view radiographs.[43] The AP radiograph is utilized to measure the mechanical axis angle and mechanical axis deviation as well as to grade the level of arthritic degeneration. The proposed degree of surgical correction can also be calculated from the AP radiograph. Lateral and skyline view radiographs are useful for confirmation of preoperative diagnosis of OA, as well as determination of disease stage in each of the three articular compartments.[50]

Three-dimensional gait analysis using a motion analysis system with synchronized force plate is beneficial in the diagnosis of biomechanical factors that may be contributing to a patient's knee OA progression, and therefore is recommended by some authors.[47-50] Biomechanical risk factors are dynamic and therefore cannot be determined from radiographs. These may include such risk factors as an increased or abnormal external knee adduction moment, or the presence of a varus thrust during the stance phase. A preoperative gait analysis also provides baseline measures that a patient can be compared against as they progress postoperatively.

Knee arthroscopy may also be performed to verify that OA is present primarily in the medial tibiofemoral compartment and to carefully assess the status of the lateral compartment. Transferring load from the damaged medial compartment to an equally damaged lateral compartment would not be beneficial to the patient. Arthroscopy allows for a thorough visual inspection of the joint by the surgeon to determine existing issues or injuries that might also need to be corrected.[31] Arthroscopy undertaken during the same anaesthetic administration as that of the anticipated HTO also provides the opportunity for assessment of the knee's current condition, and a more informed decision about whether proceeding with the HTO will be in the best interest of the affected joint and the patient as a whole.[47]

2.10 Surgical Methods of HTO

Dome Osteotomy

Sundaram et al[109] have previously described the surgical methodology of a dome osteotomy. Dome osteotomy is undertaken with curved osteotomes used in an AP direction to create a complete separation of the tibia into two segments. This results in a curved dome-like surface to the distal segment of the tibia with a corresponding arced surface to the proximal segment. Rotation of the distal tibial segment in the frontal plane relative to the proximal segment along the domed surface of the bone cut produces the realignment. The realigned tibial segments are secured in place with surgical staples, and occasionally external fixation, in order to ensure sufficient contact of the tibial segments along the bony seam.[109]

Lateral Closing Wedge HTO

Amendola[4] gives a thorough review of several different HTO techniques, including the lateral closing wedge HTO. Lateral closing wedge HTO involves the removal of a predetermined sized wedge of bone from the lateral aspect of the tibia following two bone saw incisions into the tibia. The medial tibial cortex is left intact and acts as an osseous hinge point to close the wedge space. This achieves the intended realignment of the limb. Hardware fixation, in the form of a plate and bone screws, keeps the two bony surfaces in proximity to allow for bone healing. Fibular resection, fibular osteotomy or fibular ligament release usually must accompany a lateral closing wedge HTO in order to to accommodate for the newly shortened tibia. [45,50]

Medial Opening Wedge HTO

Medial opening wedge HTO techniques have previously been described by Fowler[43] and Amendola[4]. Medial opening wedge HTO uses a progressive series of both rigid and flexible osteotomes to create an opened wedge space on the medial aspect of the tibia while striving to maintain an intact lateral tibial cortex. The lateral cortex acts as a hinge point. The wedge is opened until the predetermined degree of correction has been achieved. Bone segments are held in place with hardware fixation in the form of either locking or non-locking plates and bone screws. The wedge space is usually packed with bone graft or a synthetic substitute to facilitate bone growth and healing. [43,45,97]

2.11 Benefits of Medial Opening Wedge HTO

Achieving Surgical Correction

Medial opening wedge HTO has especially benefitted from advancements in surgical methodology and has grown in popularity compared to other methods of HTO.[80] Medial opening wedge HTO can achieve bi-planar correction simultaneously in the frontal and sagittal planes more easily and accurately than the lateral closing wedge HTO and dome osteotomy. This allows for correction not only of limb alignment, but also joint reorientation if necessary. The ability to achieve correction gradually via the use of osteotomes to open the wedge can result in necessary "fine-tuning" adjustments in both planes. Similarly, small corrections of less than 5° are more easily achieved with medial opening wedge than lateral closing wedge HTO.[43] A similar result is difficult to repeat with the lateral closing wedge or dome osteotomy. Lateral closing wedge HTO requires two cuts of the bone that would achieve both the intended size wedge for removal and appropriate opposition of the two bone faces to facilitate healing.[20] Dome osteotomy does not allow for much correction in the sagittal plane as the two bone segments can truly only articulate in the frontal plane along the corresponding domed and arced surface.[20]

Surgical Complications of Lateral Closing Wedge and Dome Osteotomy

All forms of HTO share certain risks of surgical complication (Table 2.2). However, there are adverse outcomes that are associated with the lateral closing wedge or dome osteotomy that are not found with medial opening wedge HTO. Both of these methods of HTO can shorten the lateral aspect of the tibia[20] resulting in the fibula is now longer than what the tibia can accommodate. This creates additional strain in the ligamentous components holding the fibula in place, and there is the potential for disarticulation of the fibula at both its proximal and distal joints. An accommodation must be made to compensate for the mismatch in bone lengths. Therefore, it is often deemed necessary to release the fibular ligament, perform a fibular osteotomy or resect the middle third of the fibula.[4] All of these options induce more surgical stress on the limb, pose an additional risk to the surrounding soft tissue structures and can potentially create instability of the tibiofibular joints.

The dome osteotomy is suggested to be more difficult to properly execute in comparison to other HTO techniques. The correct osteotome curvature must be chosen in order to allow the distal tibial segment to rotate far enough to achieve proper correction. Too severe of an arc will prevent the distal segment from rotating far enough, while too shallow of an arc may not make enough of a correction. Furthermore, with complete separation of the tibia into two distinct segments in an AP direction there is a risk for unintentional violation of components of the posterior compartment of the leg, especially the popliteal artery. Violations of any of the neurovascular components of the posterior compartment of the knee have great potential to hinder recovery and pose additional postoperative risks. Similarly to the lateral closing wedge HTO, the fibula must be sectioned to allow for adequate rotation of the tibial components and to accommodate a change in lateral tibial length.[109]

Table 2.2 - Complications associated with high tibial osteotomy

Type of Complication	Percentage	References
Delayed union	6.6 – 8.5	Warden, 2005; Naudie, 1999
Nonunion	1.6 – 5.7	Warden, 2005; Naudie, 1999
Intraarticular fracture	1.9 – 4.3	Naudie, 1999; Miller, 2009
Infection	2.3 – 54.5	Spahn, 2003
Superficial	9.4*	Naudie, 1999
Deep	0.9	Naudie, 1999
Osseous hinge fracture		
Intraoperative	4.3	Miller, 2009
Postoperative	4.3	
Loss of angular correction	1.7 – 15.2	W-Dahl, 2005; Miller, 2009
Instability	0.9	Naudie, 1999
Deep vein thrombosis	1.3 – 9.8	Naudie,1999; Spahn, 2003; Spahn, 2005; Miller, 2009; W-Dahl, 2005;
Peroneal nerve palsy [a]	2.0 – 16.0	Naudie, 1999; Spahn, 2003
Compartment syndrome [b]		
Avascular necrosis		Spahn, 2003; Howell, 1997
Vascular injury	0.4	Spahn, 2003; Georgoulis, 1999
Symptomatic hardware	4.3	Miller, 2009

Chart adapted from Naudie 1999; Spahn, 2003; Miller, 2009

* author notes this value was abnormally high

[a] only likely with lateral closing wedge HTO

[b] exact frequencies not available in literature, but are described in case reports

2.12 Surgical Management of Bilateral Medial Knee OA

Bilateral medial compartment knee OA where surgical interventions are indicated requires several considerations. A decision regarding the timing of surgical intervention on each limb must be addressed in terms of the urgency of surgical correction, the recovery times necessitated for the surgeries being considered, the patient's comorbidities, as well as the potential risks and unintentional effects of completing bilateral surgeries simultaneously or in a staged manner.[70,85,91,123] As there is minimal literature on bilateral HTO or UKA, a review of the bilateral TKA literature may be useful.

Bilateral Total Knee Arthroplasty

Bilateral TKA is more commonly necessary for elderly patients as a result of advanced stages of knee OA and severe degeneration of the knee joints. Due to the relatively quick turn-around from surgery to patient partial weight bearing (1 to 7 days) and commencement of rehabilitation, bilateral TKA can occur in a simultaneous (one anaesthetic administration with two orthopaedic teams operating), sequential (one anaesthetic administration with one orthopaedic team operating), staggered (one hospitalization, with a time lapse of 2 to 7 days between two surgeries) or staged manner (two hospitalizations, with a time lapse of generally greater than 6 weeks between two surgeries).[85,93] The majority of orthopaedic surgeons in Ontario perform bilateral TKA in a staged manner, with a 3, 6 or 12 month interval between surgeries.[73]

The main advantage of simultaneous and sequential bilateral TKA surgery is that they tend to be viewed as "money-saving" procedures, [93] as patients are only administered one anaesthetic and are only hospitalized once. Patients also tend to be hospitalized for a shorter cumulative number of days, [124] but there is still debate if simultaneous bilateral TKA surgery results in fewer cumulative intensive care or cardiac intensive care days.[70,93] The decreased cost has the potential to influence decisions of surgeons and patients, especially in countries that do not have subsidized healthcare.[93] However, once the consideration for rehabilitation costs is factored in, the cost difference between simultaneous and staged bilateral TKA becomes much smaller.[70]

Careful consideration must be taken in the choosing of patients to undergo simultaneous or staggered bilateral TKA due to the increased physiological demands placed on the body during simultaneous and sequential surgeries.[85,124] The single anaesthetic must be administered for a longer period of time and the total amount of intraoperative blood loss can potentially be 17 times greater than unilateral TKA.[70] Anecdotally, there is the potential for a higher risk of infection because there are multiple operative sites with which the body must cope; however, the literature surrounding this issue is conflicting.[70,85,124] Patients who are elderly, or who have pre-existing cardiac conditions are strongly recommended to not undergo simultaneous bilateral TKA. Cardiovascular and pulmonary complications can be more than three times greater for simultaneous TKA in comparison to unilateral TKA,[70] but again this is not always the case. Yoon et al[124] demonstrated comparable complication rates between simultaneous and staged bilateral TKA patients. Decisions must be made on a case-by-case basis in terms of what will be best for the individual.

Staged bilateral TKA has a lower mortality rate compared to simultaneous bilateral TKA, as there is less overall trauma induced on the body per surgery.[85] However, there are complications and outcomes that can occur as a result of staged bilateral TKA, especially in the case of individuals who are naturally varus-aligned. The initial TKA both replaces the joint and, if done properly, straightens the limb – of which both outcomes can create a surgically induced leg length discrepancy (LLD).[114] If the time lapse between staged TKA goes beyond the period of non-weight bearing, then the LLD may negatively alter the individual's gait biomechanics for both the post-operative knee and the contralateral pre-operative knee.[63,78,119] Understandably, most patients do not achieve maximum benefit in functional gains and symptom resolution until after the second TKA has been performed.[104]

Bilateral High Tibial Osteotomy

Few studies on bilateral HTO exist. Takeuchi et al[111] evaluated a small sample of patients (N=10) that had undergone simultaneous bilateral HTO with the use of rigid, locking plates (TomoFix) to facilitate early weight-bearing. The authors reported good outcomes with the American Knee Society Knee Score and Function Score, as well as acceptable valgus corrections determined from weight-bearing anteroposterior radiographs. They based functional outcome of the patients on the ability to sit "comfortably in Japanese style". Follow-up was variable (range 6 – 39 months). Other authors do report performing more HTOs procedures than the total number of participants in the study, suggesting that the bilateral procedure was indeed performed.[14,32,53,57,68,76,86,97,117] However, those subgroups of patients were not evaluated. As a whole, the evidence for bilateral HTO is very limited and weak, and there are no published studies evaluating the staged bilateral procedure. Information on changes in radiographic, gait, performance-based and patient-reported outcomes after staged bilateral HTO are required.

CHAPTER 3 – METHODS

3.01 Study Design

We conducted a case series (objective 1) with subgroup analyses (objective 2) to evaluate staged bilateral medial opening wedge HTO. The study was conducted at the Fowler Kennedy Sport Medicine Clinic and Wolf Orthopaedic Biomechanics Laboratory. All participants were patients of four orthopaedic surgeons at this tertiary care centre that specializes in adult orthopaedic sport medicine. From April 2003 through June 2011, we assessed radiographic measures of alignment and 3D gait characteristics for both lower limbs, performance-based outcomes and patient-reported outcomes preoperatively and approximately, 6, 12, and 24 months postoperatively. The study was approved by the Research Ethics Board for Health Sciences Research Involving Human Subjects at the University of Western Ontario (London, Ontario, Canada). All participants provided informed consent.

3.02 Participants

Eligible patients were those undergoing medial opening wedge HTO on both lower limbs within 24 months and meeting the following inclusion and exclusion criteria. Inclusion criteria included baseline evidence of OA (radiographic or confirmed with arthroscopy) in the medial compartment of the tibiofemoral joint of both knees, and greater degeneration in the medial compared to lateral compartments of the tibiofemoral joints with concomitant bilateral varus alignment. Exclusion criteria included having undergone a previous HTO, undergoing other lower limb surgery (except for concomitant arthroscopic procedures or hardware removal following HTO) during the 2-year postoperative period, inflammatory or infectious arthritis of the knee, multi-ligamentous instability, major neurological deficit that would affect gait, pregnancy, inability to speak or read English, or a psychiatric condition that could limit informed consent.

3.03 Intervention

Operative Procedure

The HTO was performed using a medial opening wedge technique similar to the method previously described by Fowler et al.[43] Fixation was achieved with a 4-hole non-locking plate (Arthrex Opening Wedge Osteotomy System; Arthrex, Naples, FL). The desired correction for the osteotomy was calculated preoperatively according to the method described by Dugdale et al[35], which recommends moving the weight-bearing line to no greater than 62.5% of the width of the tibial plateau, measuring from the medial border. Preoperative templating was also dependent on the degree of correction required to achieve neutral alignment and the status of the articular cartilage in the lateral tibiofemoral compartment. A guide pin was inserted under fluoroscopy and the osteotomy was performed with a combination of both flexible and rigid osteotomes. Following opening of the osteotomy site to the desired width, limb alignment was confirmed with fluoroscopy. Posterior tibial slope was assessed and adjustments were made, if necessary, by distracting the osteotomy more anteriorly or posteriorly. The plate was fixed proximally and distally with cancellous and cortical bone screws, fixation was confirmed by fluoroscopy and finally bone filler (cancellous allograft bone) was used in osteotomies greater than 7.5mm.

Postoperative Management

Following completion of the HTO, patients were placed in a hinged knee brace. Crutch use was mandated for at least 6 weeks with only feather-touch weight bearing. With radiographic and clinical evidence of surgical site healing, partial weight bearing was permitted at 6 weeks and full weight bearing at 12 weeks. Patients started exercising in the brace approximately 3 weeks postoperatively until healing of the osteotomy site had occurred. Exercises were assigned to limit swelling, joint contracture and muscle atrophy from disuse. Active and passive range of motion exercises were completed for both the knee and hip. Strengthening exercises for knee extension/flexion and hip extension were initially isometric. Non weight-bearing concentric exercises using weights or Thera-Band (Hygienic Corporation, Akron, OH) started at approximately 8 weeks postoperatively and progressed until weight-bearing was allowed. Weight bearing exercises focused on balance and proprioceptive control and were implemented approximately 12 weeks after surgery and progressed until patients demonstrated normal gait patterns determined at the physiotherapist's discretion. All patients followed the same general postoperative guidelines unless modification was deemed necessary.

3.04 Patient Assessment Schedule

Follow-up assessments for the first (L1) and second (L2) limbs were defined a priori. Baseline (preoperative L1) assessments occurred before the L1 surgery as close to the surgical date as feasible. Follow-ups for L1 alone occurred at 6 and perhaps 12 months postoperatively, depending on when the L2 surgery was performed. The L2 preoperative assessments coincided with a L1 postoperative assessment. Follow-ups then occurred 6, 12 and 24 months after the L2 surgery and continued on an annual basis.

3.05 Outcome Measures

Radiographic Measurements

Double limb full weight-bearing hip to ankle digital radiographs were assessed using custom computerized software. Radiographs were taken in an anteroposterior direction with the patient's feet straight ahead to control for foot rotation and to allow for accurate measurements in the frontal plane. Mechanical axis angle and Kellgren-Lawrence ratings for the medial and lateral tibiofemoral compartments were assessed for both limbs.

The mechanical axis angle was defined as the angle formed by lines connecting the centre of the hip to the centre of the knee, and the centre of the knee to the centre of the ankle. The centre of the hip was defined to be the centre of a circular template placed over the femoral head. The centre of the knee was defined as the midpoint of the tibial spines, extrapolated inferiorly to the intercondylar eminence. The centre of the ankle was defined as the midpoint of the width of the tibia and fibula at the level of the tibial plafond. Positive mechanical axis angle values indicated valgus alignment and negative values indicated varus alignment. Measures of joint degeneration were made using the Kellgren-Lawrence rating scale for both the medial and lateral tibiofemoral compartments. All radiographic measurements were completed by one investigator.

Gait Analysis

Patients underwent gait analyses using an eight-camera 3-dimensional optical motion capture system (Motion Analysis Corporation, Santa Rosa, USA) that was synchronized with a single floor-mounted force plate (Advanced Mechanical Technology Inc., Watertown, USA). A modified Helen Hayes marker configuration was used, with twenty-two passive reflective markers attached to the patient over significant boney landmarks.[61] Four additional makers were placed bilaterally over the medial knee joint line and medial malleolus for an initial static, standing trial with the patient stationary on the force plate and all markers visible to determine the patient's body mass, the marker orientations and relative joint centres for the hips, knees and ankles. The four extra markers were removed prior to gait testing.

Patients were instructed to walk over an 8-meter runway at their natural, self-selected pace. Patients walked barefoot so as to negate the potential confounding effects of different types of footwear. Each patient performed two practice trials to become accustomed to the testing and to allow the investigator to modify the starting position on the walkway, if necessary, so that one foot would strike the floor-mounted force plate with each pass. Five walking trials were collected for each limb, having an adequate force plate strike from one foot. Kinematic data (sampled at 60 Hz) and kinetic data (sampled at 1200 Hz) were collected during the middle of several strides to avoid the acceleration and deceleration phases at the start and end, respectively, of each trial. Gait data were processed using commercial software (Motion Analysis Corporation, Santa Rosa, USA) and custom post processing programs.

Gait characteristics that are suggested to affect knee joint loading in patients with knee OA were calculated and then averaged across the five collected trials for each lower limb of the patient. The external knee adduction moment was normalized to body weight and height and summarized in the following ways: first peak (maximum value in the first half of stance), second peak (maximum value in the second half of stance) and the absolute peak (higher of first or second peak). Gait speed was defined as the average speed of the tested limb between successive footsteps. Toe-out angle was defined as the angle created between the midline of the foot (a line from the centre of the ankle to the head of the second metatarsal) and the straight-forward line movement of the body. Lateral trunk lean over the stance limb was defined as the angle created from the vertical by a line drawn between the midpoints of the acromion processes and the midpoints of the anterior superior iliac spines.

Performance-based Measures

Patients completed the six minute walk test (6MWT). The test was completed on a level, 24.4 meter (80 foot) track inside the laboratory that had 1.2 meter (4 foot) increments marked on the ground. Patients were instructed to walk at a self-selected pace for six minutes, and were given verbal cues for how much time remained during the test. Walking aids, such as canes, were allowed if necessary. Timing commenced with a verbal cue and stopped at the 6 minute mark. Distance traveled was calculated to the nearest foot and converted to meters. The 6MWT has shown to be a reliable measure of physical function in patients with knee OA.[66] A change of 54 meters in distance walked during the test is suggested to be clinically meaningful.[66]

Patient Reported Measures

We used the 12-item Short Form Health Survey (SF-12), Knee Injury and Osteoarthritis Outcome Score (KOOS) and Lower Extremity Functional Scale (LEFS) to assess patient-reported outcomes.

The SF-12 is a generic and multipurpose questionnaire used to assess an individual's physical function and mental health. It does not target a specific age or disease group, and has shown to be reliable and valid across an array of age groups and clinical populations. We used the SF-12 health survey to assess the patient's overall physical function, mental health, and wellbeing. SF-12 scores were calculated for both the physical function component summary score (PCS) and the mental health component summary score (MCS). Scores were standardized to a 0 to 100 range scale, with scores of 0 being the lowest possible level of health and 100 being the best possible level of health.

The KOOS is a 42-item knee-specific questionnaire to determine how a patient perceives their knee and their general health. The KOOS is comprised of five different subscales: Symptoms (7 items), Pain (9 items), Function during Activities of Daily Living (17 items), Function during Sports and Recreational Activities (5 items) and Quality of Life in relation to the knee (4 items). Each item is scored on a 5-point Likert scale, and each point on the scale is assigned a value of 0 to 4 with 0 being the worst and 4 being the best possible answer. A normalized score out of 100 is calculated for each subscale, with higher scores indicating greater knee function and health. A change of ten points on a KOOS subscale is suggested to be clinically meaningful.[96] The KOOS has been shown to be valid and reliable for individuals with knee OA and ligamentous injuries, and is responsive to changes following knee surgery.[94] It is considered an appropriate tool for following individuals through the course of injury and rehabilitation outcomes[95,96,118].

The LEFS is a 20-item questionnaire used to assess overall function of the lower extremity. Each item is scored on a 5-point Likert scale ranging from extreme difficulty to no difficulty. Each point on the scale is assigned a value of 0 – 4 with 0 corresponding to extreme difficulty and 4 to no difficulty. A total score for the questionnaire out of 80 is calculated. Higher scores indicate higher functional capabilities. A change of nine points on the LEFS is suggested to be clinically meaningful.[15] The LEFS has shown to be valid, reliable and responsive to change in patients who have sought out medical treatment for a lower limb issue.

3.06 Statistical Analysis

For our primary objective, we first calculated means and standard deviations for all variables that were measured at baseline and the final assessment for both limbs. We also calculated mean changes with 95% confidence intervals (95%CI) between baseline and final assessments and completed paired t-tests. If data were missing for the L2 24 month postoperative assessment, data from the next annual assessment were used. For the outcomes of most interest, we plotted all data at the interim assessment time points (seven time points in total). These outcomes were determined a priori and included mechanical axis angle, peak knee adduction moment, 6MWT, KOOS Pain and the SF-12 PCS. Any missing data for these interim points were imputed using the linear trend at each point (SPSS, Chicago, IL). For our secondary objective, we repeated the above analyses for each subgroup. We also calculated mean differences in the improvements between subgroups with 95% CIs and compared them using independent t-tests.

CHAPTER 4 – RESULTS

4.01 Study Demographics

37 patients were considered to be eligible and were included in the study. Patient flow through the study is illustrated in Figure 1. Baseline demographic and clinical characteristics are provided in Table 4.1. Patients were primarily male, relatively young, had a BMI classifying them as overweight, had substantial bilateral varus alignment and advanced bilateral arthritic degeneration isolated mainly to the medial tibiofemoral compartments. One patient had a small area of advanced arthritic degeneration in one lateral tibiofemoral compartment, but the surgeon deemed it to still be in the best interest of the patient to proceed with the HTO.

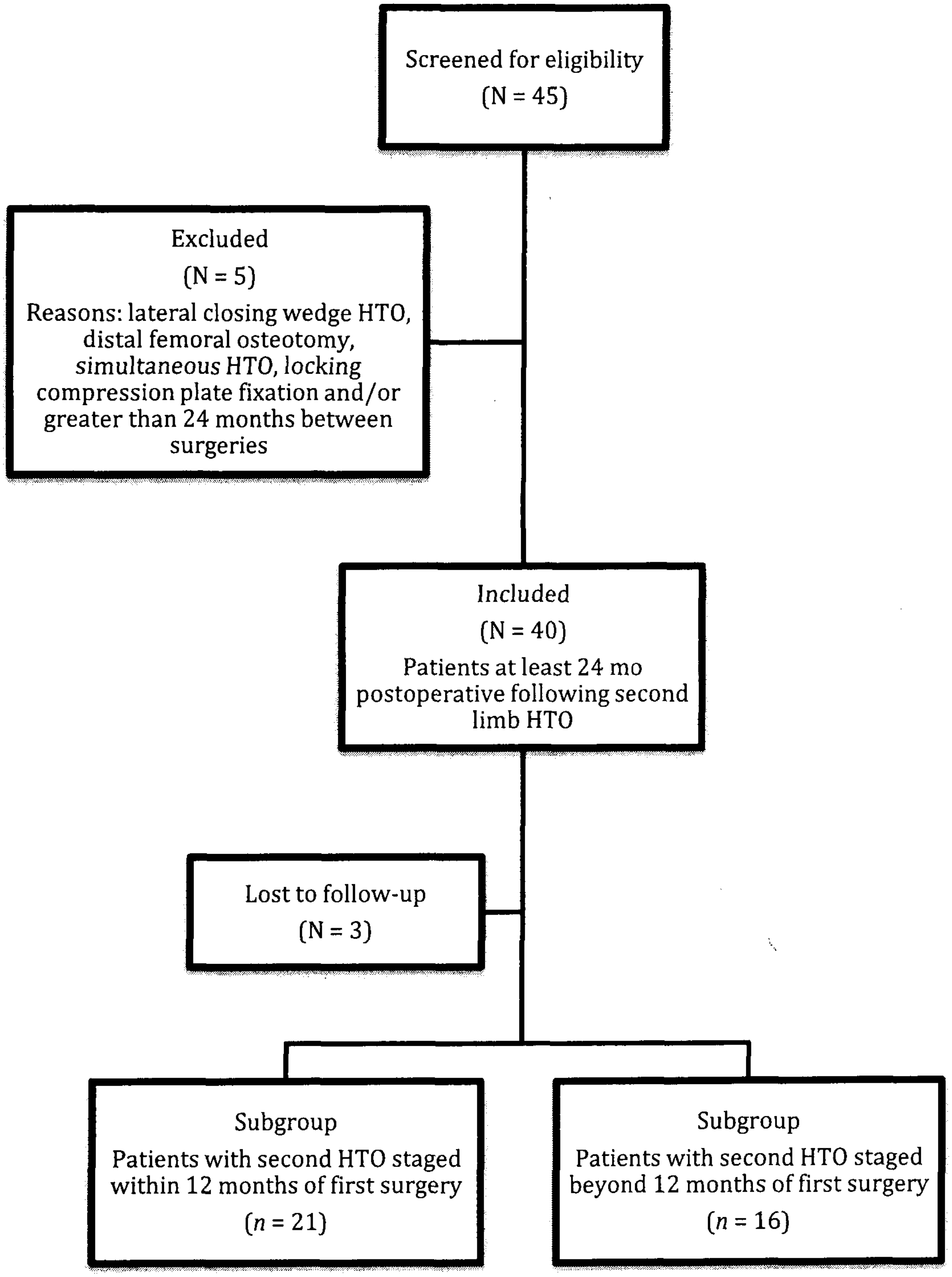

Figure 4.1 Patient flow through study

Table 4.1 Baseline demographic and clinical characteristics (N = 37)*

Characteristic	Value
Sex, no. (%)	
Male	29 (78.4)
Female	8 (21.6)
Age, years	49.3 ± 7.7
Height, meters	1.77 ± 0.09
Weight, kg	93.60 ± 17.17
BMI, kg/m^2	29.7 ± 4.4
Time between surgeries, months	14.7 ± 8.2
Mechanical axis angle [a], degrees	
Limb 1 (L1)	-8.95 ± 3.58
Limb 2 (L2)	-7.84 ± 2.96
Medial compartment OA grade [b], no. (%)	
L1:	
0	0 (0)
1	2 (5.4)
2	2 (5.4)
3	5 (13.5)
4	28 (75.7)
L2:	
0	0 (0)
1	2 (5.4)
2	3 (8.1)
3	23 (62.2)
4	9 (24.3)
Lateral compartment OA grade [b], no. (%)	
L1:	
0	13 (35.1)
1	14 (37.8)
2	9 (24.3)
3	1 (2.7)
L2:	
0	2 (5.4)
1	22 (59.5)
2	13 (35.1)
3	0 (0)

Note: Limb 1 is the first limb to receive HTO, Limb 2 is the second limb to receive HTO
* Values reported as means with standard deviations unless otherwise noted.
[a] Negative values indicate varus alignment
[b] Kellgren-Lawrence scale grade of OA severity

4.02 Concomitant Surgical Procedures

Cancellous bone allograft was used in both limbs for all patients. Knee arthroscopy was undertaken for the majority of patients: 33 (89.2%) and 34 (91.9%) for L1 and L2, respectively. Arthroscopy revealed medial meniscal tears in 31 (83.8%) of both L1 and L2, as well as compromised anterior cruciate ligaments (fraying, partial or total discontinuity) for 5 (13.5%) L1 and 3 (8.1%) L2. Concomitant surgeries included anterior cruciate ligament reconstruction for one limb and tibial tuberosity osteotomy for 11 (29.7%) of L1 and 9 (24.3%) of L2.

4.03 Intraoperative and Postoperative Complications

No major intraoperative complications were noted. Six limbs had evidence of lateral cortex violations intraoperatively. An additional screw or staple was used in three of these cases. No patients experienced neurovascular injuries, compartment syndrome, deep vein thrombosis, or pulmonary embolism during surgery or follow-up; two patients had hematomas. Twelve patients had delayed union of the bone at 6 weeks following surgery, successfully treated conservatively with an extended period of non-weight bearing. Three patients had aseptic non-union, also treated successfully with extended non-weight bearing. Eleven patients elected to have their hardware removed (total of 16 limbs).

4.04 Postoperative Follow-up

All patients attended Baseline (preoperative L1), Follow-up 1 (6 months postop L1) or Follow-up 3 (preoperative L2) assessments and had a final assessment at least two years after the L2 surgery. Assessment dates measured from the date of surgery for L1 were: Baseline (preoperative L1), -1.2 ± 1.5 months; Follow-up 1 (L1 6 months postoperative), 5.9 ± 4.9 months; Follow-up 2 (preoperative L2), 11.9 ± 6.4 months; Follow-up 3 (L2 6 months postoperative), 21.0 ± 9.0 months; Follow-up 4 (L2 12 months postoperative) , 27.4 ± 8.5 months; Follow-up 5 (L2 24 months postoperative), 40.8 ± 9.3 months; Last Follow-up, 47.2 ± 16.4 months).

4.05 Outcome Measures

Objective 1

Tables 4.2 and 4.3 summarize the overall changes in radiographic alignment, gait measures, performance-based and patient-reported outcomes. Note that all mean changes were statistically significant, with 95% CIs excluding the value zero, with the exception of the SF-12 MCS. Also, the 95% CIs were all quite narrow and even their lower ends suggested large, clinically important improvements.

Table 4.2 Gait and radiographic measures (N=37)

Outcome Measure	Limb 1			Limb 2		
	Baseline Mean ± SD	Last assessment Mean ± SD	Mean Change (95% CI)	Baseline Mean ± SD	Last assessment Mean ± SD	Mean Change (95% CI)
Radiographic						
Mechanical axis angle, degrees	-8.95 ± 3.58	0.79 ± 2.75	9.74 (8.35, 11.13)‡	-7.84 ± 2.96	1.65 ± 2.62	9.49 (8.33, 10.65)‡
Gait						
Knee adduction moment						
First peak, %BW×Ht	3.24 ± 0.91	1.70 ± 0.74	-1.54 (-1.90, -1.18)‡	3.19 ± 1.15	1.41 ± 0.67	-1.78 (-2.18, -1.37)‡
Second peak, %BW×Ht	3.12 ± 0.96	1.54 ± 0.77	-1.58 (-1.98, -1.19)‡	2.87 ± 0.93	1.33 ± 0.84	- 1.54 (-1.91, -1.17)‡
Absolute peak, %BW×Ht	3.40 ± 0.99	1.78 ± 0.69	-1.62 (-1.99, -1.25)‡	3.33 ± 1.02	1.51 ± 0.72	-1.81 (-2.21, -1.42)‡
Angular impulse, %BW×Ht×secs	1.63 ± 0.50	0.79 ± 0.36	-0.84 (-1.02, -0.67)‡	1.59 ± 0.55	0.68 ± 0.46	-0.91 (-1.09, -0.73)‡
Speed, meters/second	1.08 ± 0.20	1.17 ± 0.17	0.09 (0.05, 0.12)‡	1.08 ± 0.20	1.17 ± 0.17	0.09 (0.05, 0.12)‡
Toe-out angle, degrees	11.27 ± 5.58	12.46 ± 5.57	1.19 (0.05, 2.43)*	12.71 ± 5.00	14.10 ± 4.97	1.40 (0.07, 2.73)*
Lateral trunk lean, degrees	3.30 ± 2.92	1.53 ± 1.97	-1.77 (-2.88, -0.66)‡	3.42 ± 2.83	1.61 ± 1.69	-1.80 (-2.84, -0.77)‡

‡ $P \leq 0.001$; * $P \leq 0.05$

The changes in mechanical axis angle, peak knee adduction moment, 6MWT, KOOS domain scores and SF-12 component scores over all of the assessments are plotted in Figures 4.2 – 4.6. The mechanical axis angle data (Figure 4.2) shows large changes from substantial varus to mild valgus. The figure also shows that the surgical correction was maintained by both limbs through follow-up to at least 24 months after the second surgery. Interestingly, at baseline the mechanical axis angle of L1 was more varus than that of L2.

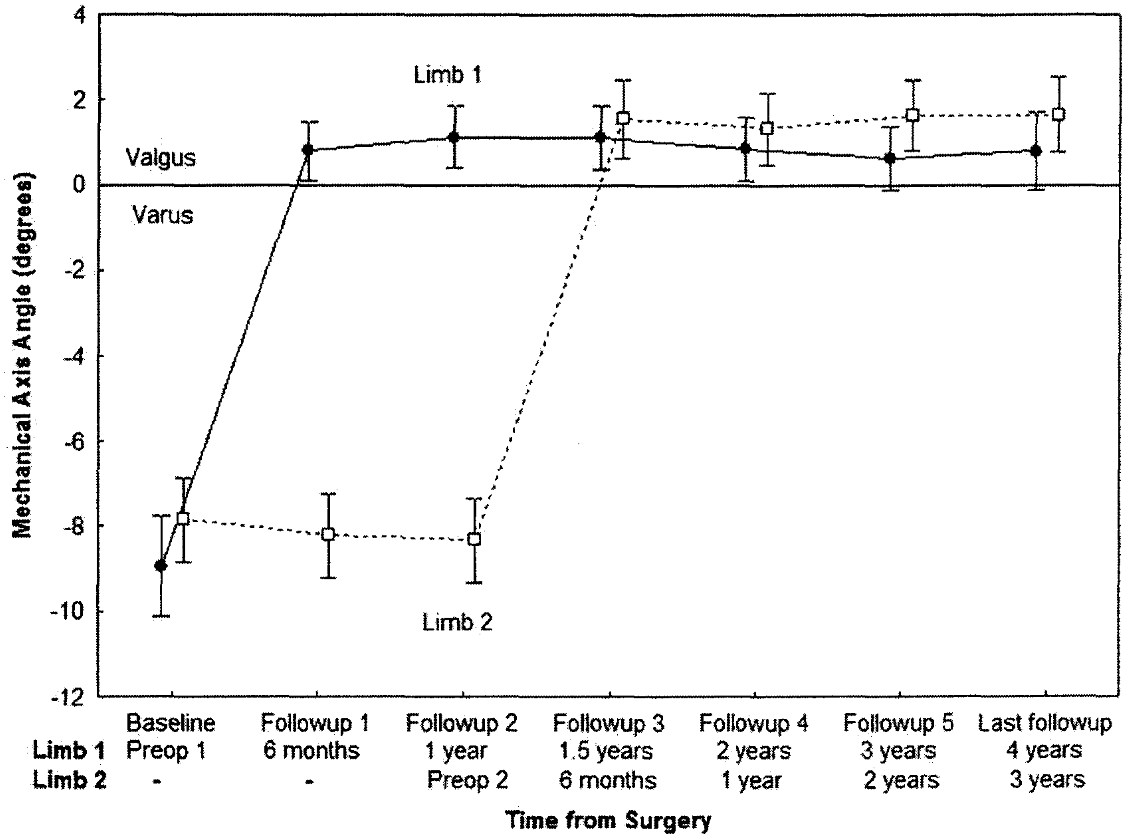

Figure 4.2 Mean mechanical axis angles (degrees) ± 95% confidence intervals for all assessment. Both limbs were assessed at all time points. Negative values indicate varus alignment.

Peak knee adduction moment data are plotted in Figure 4.3. Similar to the mechanical axis angle, there were large changes in both limbs after each surgery. Although the plot shows very small increases in knee adduction moments after their 6-month follow-ups, changes were not significant.

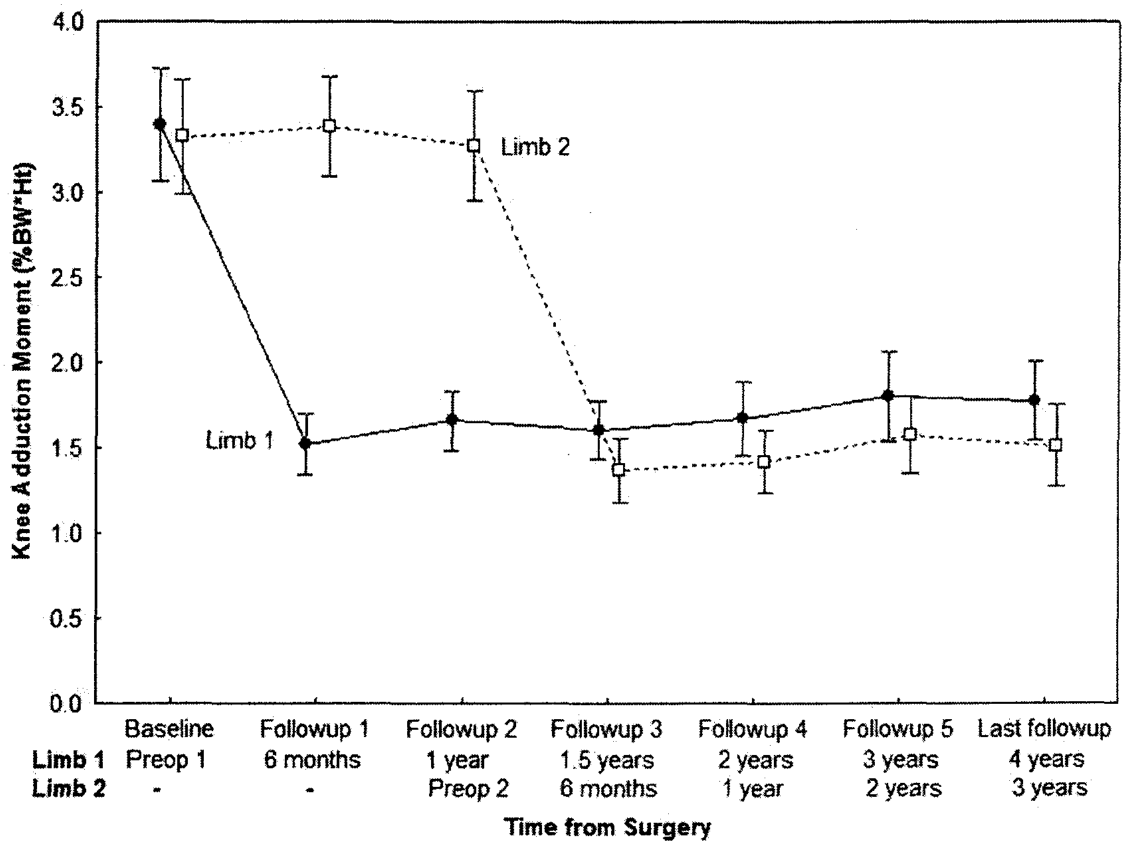

Figure 4.3 Mean external knee adduction moment (%BW * Ht) ± 95% confidence intervals for all assessments. Both limbs were assessed at all time points.

Data for the 6MWT are plotted in Figure 4.4. Distance walked increased substantially from baseline to Follow-up 4, then plateaued. This overall increase was lower than the conservatively estimated minimal clinically important difference of 54 meters,[66] although the upper end of the 95%CI does include this value.

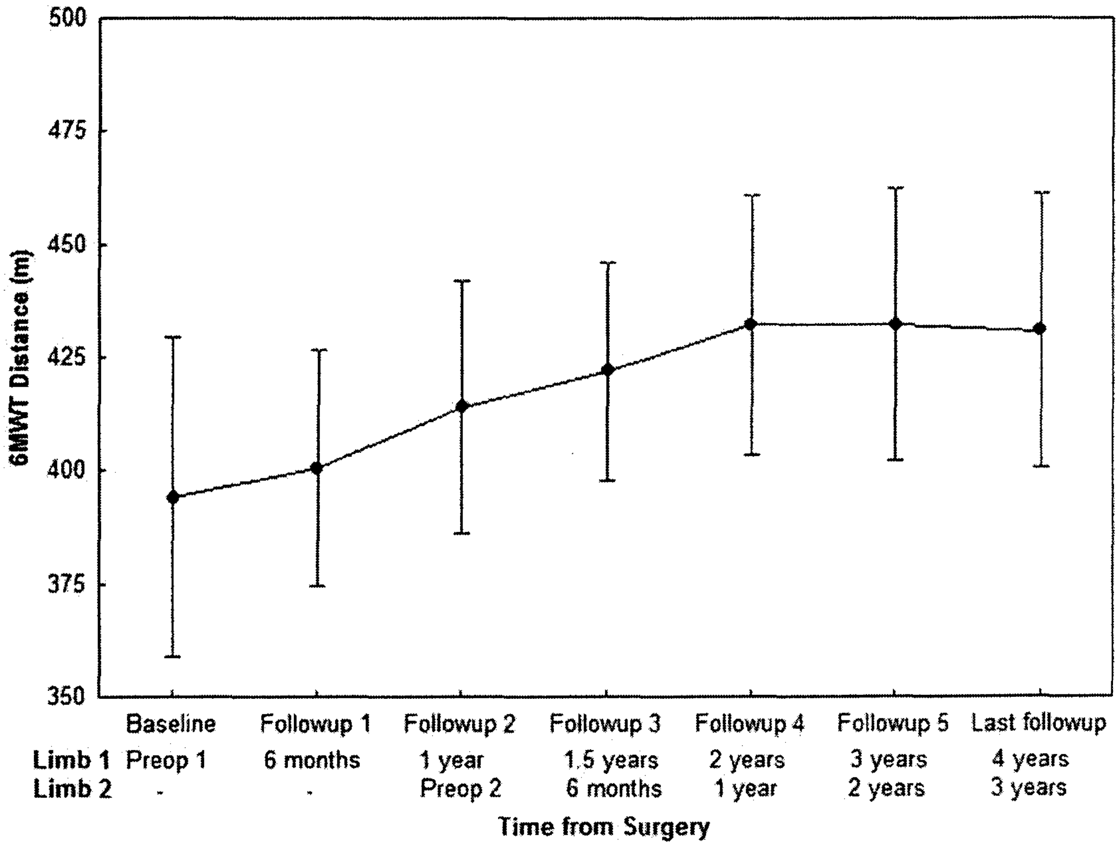

Figure 4.4 Mean 6MWT distance (m) ± 95% confidence intervals for all assessments.

Scores for the KOOS domains are plotted in Figure 4.5. All domain scores increased by values greater than the suggested minimal clinically important change of 10 points by the first follow-up. Smaller improvements continued up until the final follow-up, with notable decreases in the Sport & Recreation and Symptoms domains from Follow-up 2 to Follow-up 3 (i.e. preoperative L2 to 6-month postoperative L2).

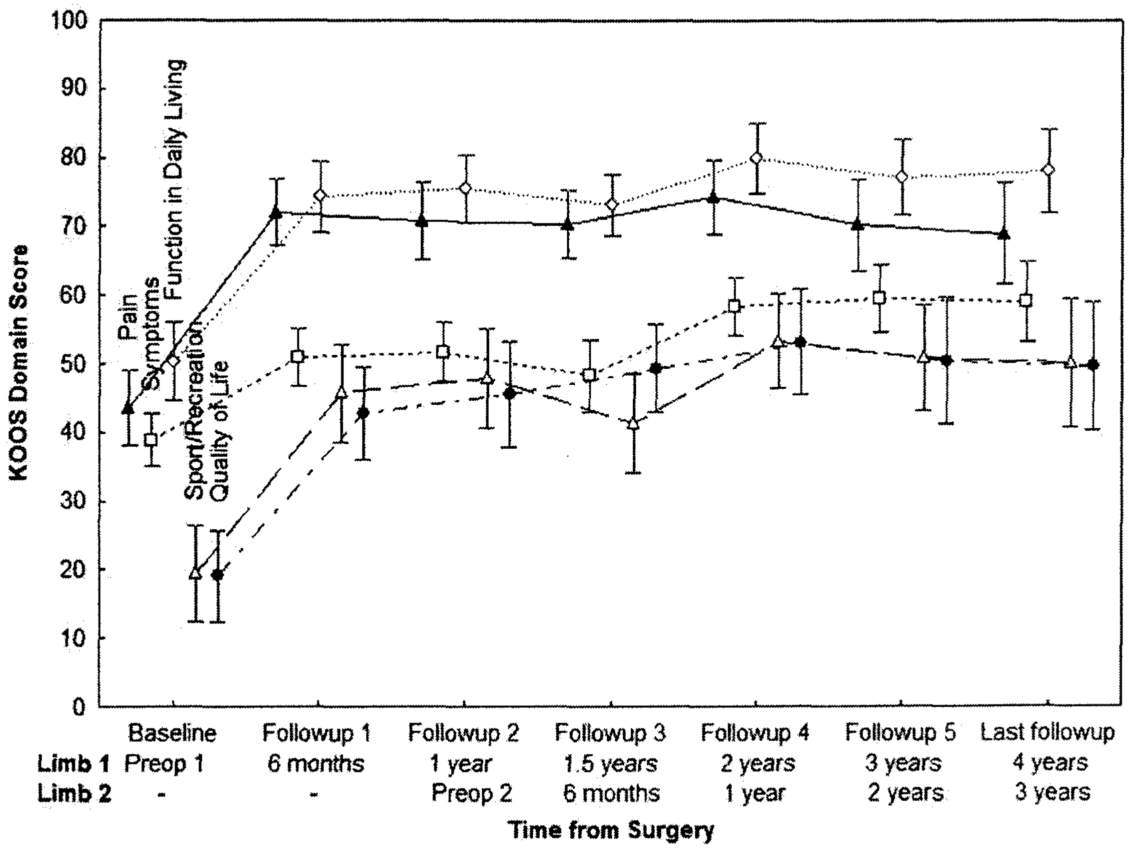

Figure 4.5 Mean Knee Injury and Osteoarthritis Outcome Score (KOOS) domain scores ± 95% confidence interval for all assessments.

Scores for the PCS and MCS of the SF-12 are presented in Figure 4.6. The PCS increased steadily from baseline to the final follow-up assessment, while the MCS did not.

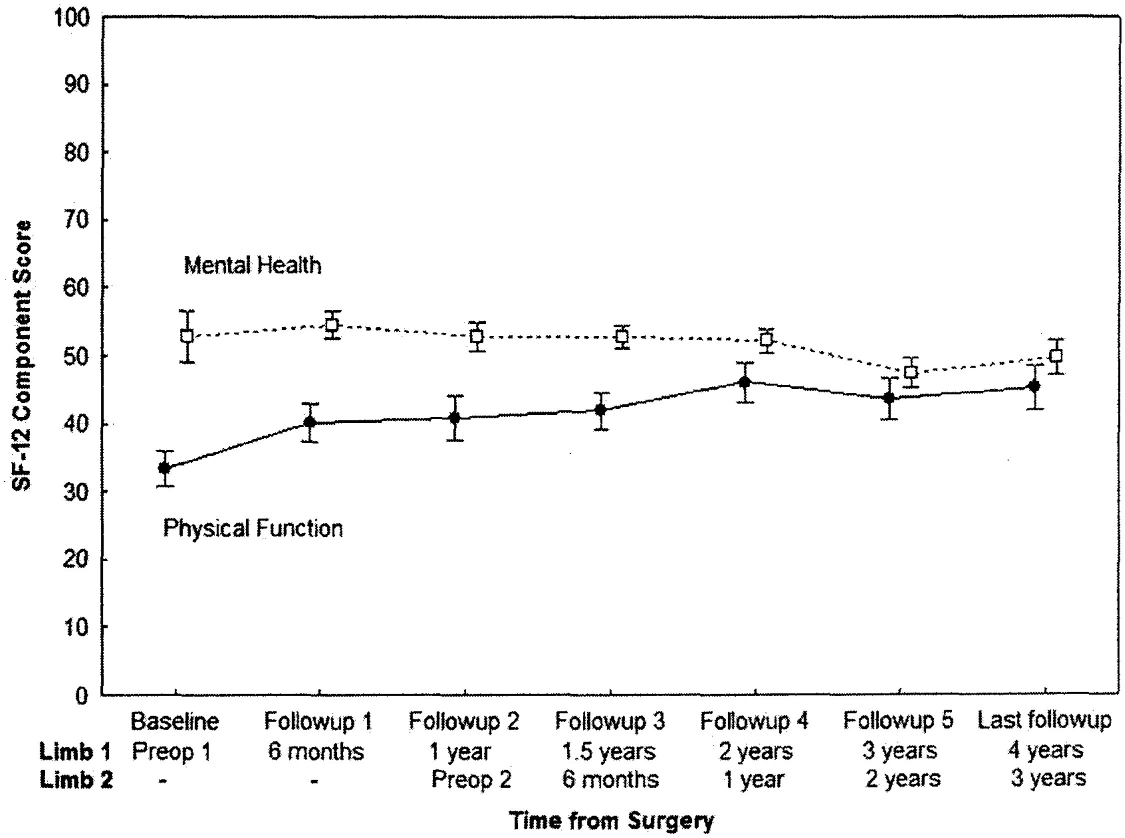

Figure 4.6 Short Form-12 (SF-12) PCS and MCS ± 95% confidence intervals for all assessments.

Objective 2

All subgroup data are presented in Appendix II. Subgroup baseline demographics and characteristics are presented in Appendix II Table 1. Overall the two subgroups were very similar. Appendix II Tables 2 and 3 summarize the overall changes in radiographic alignment, gait measures, performance-based and patient-reported outcomes for both subgroups. Appendix II Table 2(continued) and Table 3 (continued) summarize the mean differences in improvements between the subgroups. With the exception of the L2 lateral trunk lean, the mean differences between subgroups were not significant.

The changes in mechanical axis angle, peak knee adduction moment, 6MWT, KOOS domain scores and SF-12 component scores over all of the assessments for both subgroups are plotted in Appendix II Figures 1-5. Although the overall patterns of improvements were similar for both subgroups, there were some notable differences worth future investigation. Specifically, patients in the "Beyond 12 months" subgroup had differences in mechanical axis angles between limbs at baseline [mean difference between limbs -2.07° (95%CI -3.49°, -0.65°)]. This subgroup also exhibited a slightly steeper (though still small) increase in the peak knee adduction moment of both limbs in follow-ups after 6-months. This subgroup also experienced a decrease in all KOOS domains, with the exception of Quality of Life, at Follow-up 3 (i.e. the L2 6-month postoperative assessment) before continuing to increase.

CHAPTER 5 - DISCUSSION

This study has provided some of the first clinically relevant data focused solely on the population of individuals who undergo staged bilateral medial opening wedge HTO. We hypothesized that patients with bilateral varus gonarthrosis would exhibit large, clinically important improvements in both limbs for relevant radiographic measures, dynamic gait parameters, performance-based and patient-reported outcomes. Our findings strongly support this hypothesis. Effect sizes for mechanical axis angle (L1: 2.71; L2: 3.18), peak knee adduction moment (L1: 1.63; L2: 1.78), all KOOS domains (1.43-1.82,), LEFS (1.53) and SF-12 physical function component score (1.52) were all well above Cohen's threshold for a large effect size of 0.80.[29] Mean changes and the lower 95% CIs at the last follow-up assessment for the peak knee adduction moment, all KOOS domain scores and LEFS score exceed the suggested minimum clinically important differences. Overall, the biomechanical and patient-reported gains observed nearly 4 years following the first surgery and nearly 3 years following the second surgery strengthen the argument that surgical correction of both lower limbs to neutral alignment has the potential to greatly benefit this patient population.

Although the present sample was similar to individuals who undergo unilateral HTO in most descriptive and anthropomorphic measures (gender distribution, height, weight, BMI and age), it did differ in some baseline characteristics. We have previously reported that the operative limb of patients undergoing unilateral medial opening wedge HTO had a mechanical axis angle of -

7.5° ± 4° with advanced degeneration (KL grade ≥3) in 72% of medial compartments and 10% of lateral compartments.[16] In the present study, the mechanical axis angle of L1 and L2 were 19% and 5% greater, respectively, than those of the unilateral patients. Advanced degeneration (KL ≥ grade 3) was present in 89% of L1 and 87% of L2 medial compartments and only 3% of L1 and 0% of L2 lateral compartments.

We observed several changes in gait that support the underlying biomechanical principle for HTO. The patients in the current study exhibited preoperative knee adduction moments in both L1 and L2 that were greater in magnitude than those of comparable patients undergoing unilateral HTO.[16] Importantly, both limbs experienced large decreases of the knee adduction moment postoperatively, despite increases in gait speed and decreases in lateral trunk lean toward the stance limb, all of which would normally act to increase loading on the medial compartment of the knee. Interestingly, an increase in toe-out angle, a characteristic that would serve to decrease the knee adduction moment, was also observed bilaterally postoperatively. It is not clear whether this occurred following a modification in gait pattern by the patient, or was an anatomical change in external rotation of the tibia itself brought about by the osteotomy.

After surgery, the mechanical axis angle was quite stable over all follow-ups (i.e. the angle of correction was maintained). Alternatively, the knee adduction moment of both limbs appeared to steadily increase (although by a small amount) beyond 6 months. This finding was similar to our previous study and deserves further investigation.

All KOOS domain scores, with the exception of Quality of Life, decreased slightly at the 6 months postoperative assessment following the second surgery, before continuing to increase. Although none of these decreases were statistically significant they do reflect the short-term detrimental effects of undergoing a second surgery.

We also hypothesized that patients who undergo their second HTO within 12 months of the first HTO will report better final outcomes than those who undergo their second HTO beyond 12 months of the first surgery. This hypothesis was not supported. There were, however, some interesting findings during the preoperative and interim assessments worth further exploration. Patients who had the second surgery within 12 months had similar varus alignment between limbs at baseline, but had slightly greater peak knee adduction moments in L1. Conversely, patients who had the second surgery beyond 12 months had slightly greater varus alignment in L1, but similar peak knee adduction moments. Toe-out angle and trunk lean were both slightly higher in L2 compared to L1 in patients who underwent surgeries within 12 months, which may have contributed to their marginally lower knee adduction moment in L2. However, the opposite is not true of patients who had the second surgery beyond 12 months. Those patients had a higher toe-out angle, but less trunk lean in L2 compared to L1. Further investigation is required to determine what factors may be causing the inconsistencies between these subgroups.

Interestingly, following surgery, patients who had their second surgery beyond 12 months from the first experienced a significant increase in peak knee adduction moment from 6 months postoperatively to final assessment in both limbs (mean increase: L1 0.35 [95%CI 0.04, 0.66] %BW*Ht, p=0.028; L2 0.34 [95%CI 0.09, 0.59] %BW*Ht, p=0.011). Despite this postoperative increase, even these patients maintained peak knee adduction moments in both limbs that were still approximately one half of the preoperative values.

Patients who had their second surgery beyond 12 months of the first experienced a significant decrease in the KOOS Sport and Recreation domain scores at 6 months after the L2 surgery (mean difference -13.12 [95%CI -21.87, -4.38]. As these patients had a longer period between surgeries, they made further gains in their rehabilitation after the L1 surgery. Therefore, the imposed activity restrictions following the second surgery likely impacted these patients more. This is supported by the fact that patients who had their second surgery within 12 months of the first, experienced only a slight plateau in the KOOS domains and the SF-12 PCS after the second surgery. While both patient groups ultimately reached very similar improvements by the final assessment, those individuals who had the second surgery sooner, reached the maximum improvements sooner, and lessened the set-backs in patient-reported outcomes observed 6 months after the first surgery.

The inclusion and exclusion criteria for this study were slightly different than some previous reports on HTO. Patients included in this study were of a wide range in age and had bilateral varus gonarthrosis with the greatest radiographic severity and symptoms isolated to the medial compartment of the knees. We did not exclude individuals who also had evidence of lateral compartment disease as long as the medial compartment was more severe. Our patients were typically young individuals with substantial varus alignment who were not considered to be candidates for arthroplasty. High tibial osteotomy is not typically considered to be a treatment option for patients with bicompartmental tibiofemoral OA; however, as previously noted, one patient (age 65 years) did have a small area of OA of KL grade 3 severity in their L1 lateral compartment and underwent the procedure. This patient had substantial preoperative varus alignment in LI (-15.4°) and was not corrected all the way to neutral alignment (-4.6°). Despite this, the patient has experienced a decrease in peak knee adduction moment of approximately 0.6% BW*Ht and had substantial improvements in all KOOS domains, including an improvement in the KOOS Pain score of 50 points at his final assessment nearly 6.5 years after the first surgery.

The strengths of this study include its prospective design and the range of validated outcome measures relevant to HTO. Limitations of this study include a relatively a small sample size, particularly for the subgroups. This study was conducted without a control group or randomization, and it is unclear why the time between surgeries was what it was. However, Kooistra et al[67] remind us of the important role that case series study designs have in research, as they most accurately reflect clinical practice.

CHAPTER 6 – CONCLUSION

The present study indicates that patients with bilateral symptomatic varus gonarthrosis who undergo staged bilateral medial opening wedge HTO have large improvements in radiographic, dynamic gait, performance-based and patient-reported outcome measures by 2 years after their second surgery. Maximum benefits are achieved following the second surgery and outcome measures continue to improve up to 24 months after the second surgery. Although longer term follow-up continues, the present results suggest substantial improvements remain at 4 years after the first surgery and 3 years after the second surgery.

Patients who undergo staged bilateral medial opening wedge HTO experience large improvements by 2 years after the second surgery, regardless of the amount of time the surgeries are staged apart. Although the current findings suggest no statistically significant differences between subgroups in final outcomes, further research evaluating the potential for decreased time between surgeries to result in quicker improvements without setbacks in recovery is warranted.

References

1. Aglietti P, Buzzi R, Vena LM, Baldini A, Mondaini A. High tibial valgus osteotomy for medial gonarthrosis: a 10- to 21-year study. J Knee Surg. 2003;16(1):21-6.

2. Agneskirchner JD, Hurschler C, Wrann CD, Lobenhoffer P. The effects of valgus medial opening wedge high tibial osteotomy on articular cartilage pressure of the knee: a biomechanical study. Arthroscopy. 2007;23(8):852-61.

3. Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K et al. Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and therapeutic criteria committee of the American Rheumatism Association. Arthritis Rheum. 1986;29(8):1039-49.

4. Amendola A. Unicompartmental osteoarthritis in the active patient: the role of high tibial osteotomy. Arthroscopy. 2003;19 Suppl 1:109-16.

5. Amendola A, Bonasia DE. Results of high tibial osteotomy: review of the literature. Int Orthop. 2010;34(2):155-60.

6. Anderson JJ, Felson DT. Factors associated with osteoarthritis of the knee in the first National Health and Nutrition Examination Survey (HANES I). Evidence for an association with overweight, race, and physical demands of work. Am J Epidemiol. 1988;128(1):179-89.

7. Andriacchi TP. Dynamics of knee malalignment. Orthop Clin North Am. 1994;25(3):395-403.

8. Andriacchi TP, Mündermann A. The role of ambulatory mechanics in the initiation and progression of knee osteoarthritis. Curr Opin Rheumatol. 2006;18(5):514-8.

9. Arden N, Nevitt MC. Osteoarthritis: epidemiology. Best Pract Res Clin Rheumatol. 2006;20(1):3-25.

10. Astephen JL, Deluzio KJ, Caldwell GE, Dunbar MJ. Biomechanical changes at the hip, knee, and ankle joints during gait are associated with knee osteoarthritis severity. J Orthop Res. 2008;26(3):332-41.

11. Badley EM. Arthritis in Canada: what do we know and what should we know? J Rheumatol Suppl. 2005;72:39-41.

12. Baliunas AJ, Hurwitz DE, Ryals AB, Karrar A, Case JP, Block JA et al. Increased knee joint loads during walking are present in subjects with knee osteoarthritis. Osteoarthritis Cartilage. 2002;10(7):573-9.

13. Bennell KL, Bowles KA, Wang Y, Cicuttini F, Davies-Tuck M, Hinman RS. Higher dynamic medial knee load predicts greater cartilage loss over 12 months in medial knee osteoarthritis. Ann Rheum Dis. 2011;

14. Berman AT, Bosacco SJ, Kirshner S, Avolio A. Factors influencing long-term results in high tibial osteotomy. Clin Orthop Relat Res. 1991;(272):192-8.

15. Binkley J, Stratford P, Lott S, Riddle D. The Lower Extremity Functional Scale (LEFS): scale development, measurement properties, and clinical application. North American Orthopaedic Rehabilitation Research Network. Phys Ther. 1999;79(4):371-83.

16. Birmingham TB, Giffin JR, Chesworth BM, Bryant DM, Litchfield RB, Willits K et al. Medial opening wedge high tibial osteotomy: a prospective cohort study of gait, radiographic, and patient-reported outcomes. Arthritis Rheum. 2009;61(5):648-57.

17. Birmingham TB, Hunt MA, Jones IC, Jenkyn TR, Giffin JR. Test-retest reliability of the peak knee adduction moment during walking in patients with medial compartment knee osteoarthritis. Arthritis Rheum. 2007;57(6):1012-7.

18. Boulougouris A, Birmingham TB, Moyer RF, Jones IC, Giffin J. Increased dynamic knee joint load on the non-operative limb after high tibial osteotomy. Osteoarthritis Cartilage. 2011;19(Suppl. 1):S17

19. Briem K, Snyder-Mackler L. Proximal gait adaptations in medial knee OA. J Orthop Res. 2009;27(1):78-83.

20. Brinkman JM, Lobenhoffer P, Agneskirchner JD, Staubli AE, Wymenga AB, van Heerwaarden RJ. Osteotomies around the knee: patient selection, stability of fixation and bone healing in high tibial osteotomies. J Bone Joint Surg Br. 2008;90(12):1548-57.

21. Brooks PM. The burden of musculoskeletal disease--a global perspective. Clin Rheumatol. 2006;25(6):778-81.

22. Brouwer GM, Tol AWV, Bergink AP, Belo JN, Bernsen RMD, Reijman M et al. Association between valgus and varus alignment and the development and progression of radiographic osteoarthritis of the knee. Arthritis Rheum. 2007;56(4):1204-11.

23. Brown G, Amendola A. Radiographic evaluation and preoperative planning for high tibial osteotomies. Operative Techniques in Sports Medicine. 2000;8(1):2.

24. Burger H, van Daele PL, Odding E, Valkenburg HA, Hofman A, Grobbee DE et al. Association of radiographically evident osteoarthritis with higher bone mineral

density and increased bone loss with age. The Rotterdam Study. Arthritis Rheum. 1996;39(1):81-6.

25. Carr AJ. Beyond disability: measuring the social and personal consequences of osteoarthritis. Osteoarthritis Cartilage. 1999;7(2):230-8.

26. Cerejo R, Dunlop DD, Cahue S, Channin D, Song J, Sharma L. The influence of alignment on risk of knee osteoarthritis progression according to baseline stage of disease. Arthritis Rheum. 2002;46(10):2632-6.

27. Chang A, Hurwitz D, Dunlop D, Song J, Cahue S, Hayes K et al. The relationship between toe-out angle during gait and progression of medial tibiofemoral osteoarthritis. Ann Rheum Dis. 2007;66(10):1271-5.

28. Chang A, Hayes K, Dunlop D, Hurwitz D, Song J, Cahue S et al. Thrust during ambulation and the progression of knee osteoarthritis. Arthritis Rheum. 2004;50(12):3897-903.

29. Cohen J. Statistical power analysis for the behavioural sciences. 2 ed. Hillside (NJ): 1988.

30. Cooper C, Snow S, McAlindon T, Kellingray S, Stuart B, Coggon D et al. Risk factors for the incidence and progression of radiographic knee osteoarthritis. Arthritis Rheum. 2000;43(5):995-1000.

31. Coventry MB. Upper tibial osteotomy for osteoarthritis. J Bone Joint Surg Am. 1985;67(7):1136-40.

32. Coventry MB, Ilstrup DM, Wallrichs SL. Proximal tibial osteotomy. A critical long-term study of eighty-seven cases. J Bone Joint Surg Am. 1993;75(2):196-201.

33. Davis MA, Ettinger WH, Neuhaus JM, Cho SA, Hauck WW. The association of knee injury and obesity with unilateral and bilateral osteoarthritis of the knee. Am J Epidemiol. 1989;130(2):278-88.

34. DeMeo PJ, Johnson EM, Chiang PP, Flamm AM, Miller MC. Midterm follow-up of opening-wedge high tibial osteotomy. Am J Sports Med. 2010;38(10):2077-84.

35. Dugdale TW, Noyes FR, Styer D. Preoperative planning for high tibial osteotomy. The effect of lateral tibiofemoral separation and tibiofemoral length. Clin Orthop Relat Res. 1992;(274):248-64.

36. Eckstein F, Le Graverand MPH, Charles HC, Hunter DJ, Kraus VB, Sunyer T et al. Clinical, radiographic, molecular and MRI-based predictors of cartilage loss in knee osteoarthritis. Ann Rheum Dis. 2011;70(7):1223-30.

37. Enright PL. The six-minute walk test. Respir Care. 2003;48(8):783-5.

38. Felson D, Zhang Y. An update on the epidemiology of knee and hip osteoarthritis with a view to prevention. Arthritis Rheum. 1998;41(8):1343-55.

39. Felson DT, Anderson JJ, Naimark A, Walker AM, Meenan RF. Obesity and knee osteoarthritis. The Framingham study. Ann Intern Med. 1988;109(1):18-24.

40. Felson DT, Hannan MT, Naimark A, Berkeley J, Gordon G, Wilson PW et al. Occupational physical demands, knee bending, and knee osteoarthritis: results from the Framingham study. J Rheumatol. 1991;18(10):1587-92.

41. Felson DT, Lawrence RC, Dieppe PA, Hirsch R, Helmick CG, Jordan JM et al. Osteoarthritis: new insights. Part 1: the disease and its risk factors. Ann Intern Med. 2000;133(8):635-46.

42. Foroughi N, Smith R, Vanwanseele B. The association of external knee adduction moment with biomechanical variables in osteoarthritis: a systematic review. Knee. 2009;16(5):303-9.

43. Fowler P, Tan J, Brown G. Medial opening wedge high tibial osteotomy: how I do it. Operative Techniques in Sports Medicine. 2000;8(1):32.

44. Gandhi R, Dhotar H, Tsvetkov D, Mahomed NN. The relation between body mass index and waist-hip ratio in knee osteoarthritis. Can J Surg. 2010;53(3):151-4.

45. Gardiner A, Gutierrez Sevilla GR, Steiner ME, Richmond JC. Osteotomies about the knee for tibiofemoral malalignment in the athletic patient. Am J Sports Med. 2010;38(5):1038-47.

46. Giagounidis EM, Sell S. High tibial osteotomy: factors influencing the duration of satisfactory function. Arch Orthop Trauma Surg. 1999;119(7-8):445-9.

47. Giffin JR, Shannon FJ. The role of high tibial osteotomy in the unstable knee. Sports Med Arthrosc Rev. 2008;115(1):23-31

48. Goh JC, Bose K, Khoo BC. Gait analysis study on patients with varus osteoarthrosis of the knee. Clin Orthop Relat Res. 1993;(294):223-31.

49. Gök H, Ergin S, Yavuzer G. Kinetic and kinematic characteristics of gait in patients with medial knee arthrosis. Acta Orthop. 2002;73(6):647-52.

50. Grelsamer RP. Unicompartmental osteoarthrosis of the knee. J Bone Joint Surg Am. 1995;77(2):278-92.

51. Guccione AA. Arthritis and the process of disablement. Phys Ther. 1994;74(5):408-14.

52. Harvey WF, Yang M, Cooke TDV, Segal NA, Lane N, Lewis CE et al. Association of leg-length inequality with knee osteoarthritis: a cohort study. Ann Intern Med. 2010;152(5):287-95.

53. Hernigou P, Medevielle D, Debeyre J, Goutallier D. Proximal tibial osteotomy for osteoarthritis with varus deformity. a ten to thirteen-year follow-up study. J Bone Joint Surg Am. 1987;69(3):332-54.

54. Hinterwimmer S, Beitzel K, Paul J, Kirchhoff C, Sauerschnig M, von Eisenhart-Rothe R et al. Control of posterior tibial slope and patellar height in open-wedge valgus high tibial osteotomy. Am J Sports Med. 2011;39(4):851-6.

55. Hunt MA, Birmingham TB, Bryant D, Jones I, Giffin JR, Jenkyn TR et al. Lateral trunk lean explains variation in dynamic knee joint load in patients with medial compartment knee osteoarthritis. Osteoarthritis Cartilage. 2008;16(5):591-9.

56. Hurwitz DE, Ryals AB, Case JP, Block JA, Andriacchi TP. The knee adduction moment during gait in subjects with knee osteoarthritis is more closely correlated with static alignment than radiographic disease severity, toe out angle and pain. J Orthop Res. 2002;20(1):101-7.

57. Insall JN, Joseph DM, Msika C. High tibial osteotomy for varus gonarthrosis. A long-term follow-up study. J Bone Joint Surg Am. 1984;66(7):1040-8.

58. Jackson JP, Waugh W. Tibial osteotomy for osteoarthritis of the knee. Proc R Soc Med. 1960;53(10):888.

59. Jankiewicz JJ, Sculco TP, Ranawat CS, Behr C, Tarrentino S. One-stage versus 2-stage bilateral total knee arthroplasty. Clin Orthop Relat Res. 1994;(309):94-101.

60. Jenkyn TR, Hunt MA, Jones IC, Giffin JR, Birmingham TB. Toe-out gait in patients with knee osteoarthritis partially transforms external knee adduction moment into flexion moment during early stance phase of gait: a tri-planar kinetic mechanism. J Biomech. 2008;41(2):276-83.

61. Kadaba MP, Ramakrishnan HK, Wootten ME. Measurement of lower extremity kinematics during level walking. J Orthop Res. 1990;8(3):383-92.

62. Kaufman KR, Hughes C, Morrey BF, Morrey M, An KN. Gait characteristics of patients with knee osteoarthritis. J Biomech. 2001;34(7):907-15.

63. Kaufman KR, Miller LS, Sutherland DH. Gait asymmetry in patients with limb-length inequality. J Pediatr Orthop. 1996;16(2):144-50.

64. Kawakami H, Sugano N, Yonenobu K, Yoshikawa H, Ochi T, Hattori A et al. Gait analysis system for assessment of dynamic loading axis of the knee. Gait Posture. 2005;21(1):125-30.

65. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. Ann Rheum Dis. 1957;16(4):494-502.

66. Kennedy DM, Stratford PW, Wessel J, Gollish JD, Penney D. Assessing stability and change of four performance measures: a longitudinal study evaluating outcome following total hip and knee arthroplasty. BMC Musculoskelet Disord. 2005;6:3.

67. Kooistra B, Dijkman B, Einhorn TA, Bhandari M. How to design a good case series. J Bone Joint Surg. 2009;91(Supplement 3):21-6.

68. Koshino T, Murase T, Saito T. Medial opening-wedge high tibial osteotomy with use of porous hydroxyapatite to treat medial compartment osteoarthritis of the knee. J Bone Joint Surg. 2003;85(1):78.

69. Krackow KA. Proximal tibial osteotomy: where did you go? J Arthroplasty. 2004;19(4 Suppl 1):5-8.

70. Lane GJ, Hozack WJ, Shah S, Rothman RH, Booth RE, Eng K et al. Simultaneous bilateral versus unilateral total knee arthroplasty. Outcomes analysis. Clin Orthop Relat Res. 1997;(345):106-12.

71. Lawrence RC, Helmick CG, Arnett FC, Deyo RA, Felson DT, Giannini EH et al. Estimates of the prevalence of arthritis and selected musculoskeletal disorders in the United States. Arthritis Rheum. 1998;41(5):778-99.

72. Ledingham J, Regan M, Jones A, Doherty M. Radiographic patterns and associations of osteoarthritis of the knee in patients referred to hospital. Ann Rheum Dis. 1993;52(7):520-6.

73. Leitch K, Dalgorf D, Borkhoff C, Kreder H. Bilateral total knee arthroplasty--staged or simultaneous? Ontario's orthopedic surgeons reply. Can J Surg. 2005;48(4):273-6.

74. Manninen P, Riihimäki H, Heliövaara M, Mäkelä P. Overweight, gender and knee osteoarthritis. Int J Obes Relat Metab Disord. 1996;20(6):595-7.

75. Marks R. Obesity profiles with knee osteoarthritis: correlation with pain, disability, disease progression. Obesity (Silver Spring). 2007;15(7):1867-74.

76. Masrouha KZ, Sraj S, Lakkis S, Saghieh S. High tibial osteotomy in young adults with constitutional tibia vara. Knee Surg Sports Traumatol Arthrosc. 2011;19(1):89-93.

77. Mathers C, Fat DM, Organization WH, Boerma JT. WHO report global burden of disease (2006). The global burden of disease. 2008. p. 146.

78. McCaw ST, Bates BT. Biomechanical implications of mild leg length inequality. Br J Sports Med. 1991;25(1):10-3.

79. McWilliams DF, Leeb BF, Muthuri SG, Doherty M, Zhang W. Occupational risk factors for osteoarthritis of the knee: a meta-analysis. Osteoarthritis Cartilage. 2011;19(7):829-39.

80. Miller BS, Downie B, McDonough EB, Wojtys EM. Complications after medial opening wedge high tibial osteotomy. Arthroscopy. 2009;25(6):639-46.

81. Miyazaki T, Wada M, Kawahara H, Sato M, Baba H, Shimada S. Dynamic load at baseline can predict radiographic disease progression in medial compartment knee osteoarthritis. Ann Rheum Dis. 2002;61(7):617-22.

82. Moreland JR, Bassett LW, Hanker GJ. Radiographic analysis of the axial alignment of the lower extremity. J Bone Joint Surg Am. 1987;69(5):745-9.

83. Mündermann A, Dyrby CO, Andriacchi TP. Secondary gait changes in patients with medial compartment knee osteoarthritis: increased load at the ankle, knee, and hip during walking. Arthritis Rheum. 2005;52(9):2835-44.

84. Naudie D, Bourne RB, Rorabeck CH, Bourne TJ. The Insall award. Survivorship of the high tibial valgus osteotomy: a 10- to -22-year followup study. Clin Orthop Relat Res. 1999;(367):18-27.

85. Noble J, Goodall J, Noble D. Simultaneous bilateral total knee replacement: a persistent controversy. Knee. 2009;16(6):420-6.

86. Papachristou G, Plessas S, Sourlas J, Levidiotis C, Chronopoulos E, Papachristou C. Deterioration of long-term results following high tibial osteotomy in patients under 60 years of age. Int Orthop. 2006;30(5):403-8.

87. Parent E, Moffet H. Comparative responsiveness of locomotor tests and questionnaires used to follow early recovery after total knee arthroplasty. Arch Phys Med Rehabil. 2002;83(1):70-80.

88. Park MS, Kim SJ, Chung CY, Choi IH, Lee SH, Lee KM. Statistical consideration for bilateral cases in orthopaedic research. J Bone Joint Surg Am. 2010;92(8):1732-7.

89. Parker DA, Beatty KT, Giuffre B, Scholes CJ, Coolican MRJ. Articular cartilage changes in patients with osteoarthritis after osteotomy. Am J Sports Med. 2011;39(5):1039-45.

90. Pollard B, Johnston M. The assessment of disability associated with osteoarthritis. Curr Opin Rheumatol. 2006;18(5):531-6.

91. Prodromos C, Andriacchi T, Galante J. A relationship between gait and clinical changes following high tibial osteotomy. J Bone Joint Surg Am. 1985;67(8):1188-94.

92. Ramsey DK, Snyder-Mackler L, Lewek M, Newcomb W, Rudolph KS. Effect of anatomic realignment on muscle function during gait in patients with medial compartment knee osteoarthritis. Arthritis Rheum. 2007;57(3):389-97.

93. Ritter M, Mamlin LA, Melfi CA, Katz BP, Freund DA, Arthur DS. Outcome implications for the timing of bilateral total knee arthroplasties. Clin Orthop Relat Res. 1997;(345):99-105.

94. Roos E, Toksvig-Larsen S. Knee Injury and Osteoarthritis Outcome Score (KOOS)--validation and comparison to the WOMAC in total knee replacement. Health Qual Life Outcomes. 2003;1(1):17.

95. Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynnon BD. Knee Injury and Osteoarthritis Outcome Score (KOOS)--development of a self-administered outcome measure. J Orthop Sports Phys Ther. 1998;28(2):88-96.

96. Roos EM, Lohmander LS. The Knee Injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis. Health Qual Life Outcomes. 2003;1:64.

97. Santic V, Tudor A, Sestan B, Legovic D, Sirola L, Rakovac I. Bone allograft provides bone healing in the medial opening high tibial osteotomy. Int Orthop. 2010;34(2):225-9.

98. Sharma L, Hurwitz DE, Thonar EJ, Sum JA, Lenz ME, Dunlop DD et al. Knee adduction moment, serum hyaluronan level, and disease severity in medial tibiofemoral osteoarthritis. Arthritis Rheum. 1998;41(7):1233-40.

99. Sharma L, Song J, Felson DT, Cahue S, Shamiyeh E, Dunlop DD. The role of knee alignment in disease progression and functional decline in knee osteoarthritis. JAMA. 2001;286(2):188-95.

100. Sharma L, Kapoor D, Issa S. Epidemiology of osteoarthritis: an update. Curr Opin Rheumatol. 2006;18(2):147-56.

101. Sharma L, Song J, Dunlop D, Felson D, Lewis CE, Segal N et al. Varus and valgus alignment and incident and progressive knee osteoarthritis. Ann Rheum Dis. 2010;69(11):1940-5.

102. Spahn G. Complications in high tibial (medial opening wedge) osteotomy. Arch Orthop Trauma Surg. 2004;124(10):649-53.

103. Specogna A, Birmingham T, DaSilva J, Milner J, Kerr J, Hunt M et al. Reliability of lower limb frontal plane alignment measurements using plain radiographs and digitized images. J Knee Surg. 2004;17(4):203-10.

104. Stanley D, Stockley I, Getty CJ. Simultaneous or staged bilateral total knee replacements in rheumatoid arthritis. a prospective study. J Bone Joint Surg Br. 1990;72(5):772-4.

105. Statistics Canada. Health Trends. Statistics Canada Catalogue No. 82-213-XWE. Ottawa: 2010.

106. Steffen T, Hacker T, Mollinger L. Age- and gender-related test performance in community-dwelling elderly people: six-minute walk test, Berg balance scale, timed up & go test, and gait speeds. Phys Ther. 2002;82(2):128-37.

107. Stoffel K, Stachowiak G, Kuster M. Open wedge high tibial osteotomy: biomechanical investigation of the modified Arthrex osteotomy plate (Puddu plate) and the Tomofix plate. Clin Biomech (Bristol. 2004;19(9):944-50.

108. Stürmer T, Günther KP, Brenner H. Obesity, overweight and patterns of osteoarthritis: the Ulm osteoarthritis study. J Clin Epidemiol. 2000;53(3):307-13.

109. Sundaram NA, Hallett JP, Sullivan MF. Dome osteotomy of the tibia for osteoarthritis of the knee. J Bone Joint Surg Br. 1986;68(5):782-6.

110. Symmons D, Mathers C, Pfleger B. Global burden of osteoarthritis in the year 2000. Geneva: WHO. 2006;

111. Takeuchi R, Aratake M, Bito H, Saito I, Kumagai K, Ishikawa H et al. Simultaneous bilateral opening-wedge high tibial osteotomy with early full weight-bearing exercise. Knee Surg Sports Traumatol Arthrosc. 2008;16(11):1030-7.

112. Tanamas S, Hanna FS, Cicuttini FM, Wluka AE, Berry P, Urquhart DM. Does knee malalignment increase the risk of development and progression of knee

osteoarthritis? A systematic review. Arthritis Rheum. 2009;61(4):459-67.

113. Taylor BC, Dimitris C, Mowbray JG, Gaines ST, Steensen RN. Perioperative safety of two-team simultaneous bilateral total knee arthroplasty in the obese patient. Journal of Orthopaedic Surgery and Research. 2010;5:38.

114. Vaidya SV, Patel MR, Panghate AN, Rathod PA. Total knee arthroplasty: limb length discrepancy and functional outcome. Indian journal of orthopaedics. 2010;44(3):300-7.

115. Visscher TL, Seidell JC. The public health impact of obesity. Annu Rev Public Health. 2001;22:355-75.

116. Wada M, Imura S, Nagatani K, Baba H, Shimada S, Sasaki S. Relationship between gait and clinical results after high tibial osteotomy. Clin Orth Rel Res. 1998;354:180-8.

117. Wang JW, Kuo KN, Andriacchi TP, Galante JO. The influence of walking mechanics and time on the results of proximal tibial osteotomy. J Bone Joint Surg Am. 1990;72(6):905-9.

118. W-Dahl A, Toksvig-Larsen S, Roos EM. A 2-year prospective study of patient-relevant outcomes in patients operated on for knee osteoarthritis with tibial osteotomy. BMC Musculoskelet Disord. 2005;6:18.

119. White SC, Gilchrist LA, Wilk BE. Asymmetric limb loading with true or simulated leg-length differences. Clin Orthop Relat Res. 2004;(421):287-92.

120. Woolf A, Pfleger B. Burden of major musculoskeletal conditions. Bull World Health Organ. 2003;81(9):646-56.

121. Wright J, Crockett H, Slawski D, Madsen M, Windsor R. High tibial osteotomy. J Am Acad Orthop Surg. 2005;13(4):279-89.

122. Wright J, Heck D, Hawker G, Dittus R, Freund D, Joyce D et al. Rates of tibial osteotomies in Canada and the United States. Clin Orthop Relat Res. 1995;(319):266-75.

123. Wu CC, Lin CP, Yeh YC, Cheng YJ, Sun WZ, Hou SM. Does different time interval between staggered bilateral total knee arthroplasty affect perioperative outcome? A retrospective study. J Arthroplasty. 2008;23(4):539-42.

124. Yoon HS, Han CD, Yang IH. Comparison of simultaneous bilateral and staged bilateral total knee arthroplasty in terms of perioperative complications. J Arthroplasty. 2010;25(2):179-85.

125. Zhai G, Ding C, Stankovich J, Cicuttini F, Jones G. The genetic contribution to longitudinal changes in knee structure and muscle strength: a sibpair study. Arthritis Rheum. 2005;52(9):2830-4.

APPENDIX I - Ethics

- ◇ Ethics Approval Form
- ◇ Letter of Information
- ◇ Consent Form

Western

Office of Research Ethics

The University of Western Ontario
Room 4180 Support Services Building, London, ON, Canada N6A 5C1
Telephone: (519) 661-3036 Fax: (519) 850-2466 Email: ethics@uwo.ca
Website: www.uwo.ca/research/ethics

Use of Human Subjects - Ethics Approval Notice

Principal Investigator: Dr. T.B. Birmingham
Review Number: **09812E** **Revision Number: 3**
Review Date: May 15, 2008 **Review Level:** Expedited
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
Department and Institution: Physical Therapy, University of Western Ontario
Sponsor: CANADIAN INSTITUTES OF HEALTH RESEARCH
Ethics Approval Date: May 15, 2008 **Expiry Date:** April 30, 2012
Documents Reviewed and Approved: *Revised co-investigator, study methods, number of study participants.* Letter of Information and Consent.
Documents Received for Information:

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 UWO Updated Approval Request Form.

During the course of the research, no deviations from, or changes to, the protocol or consent form may be initiated without prior written approval from the HSREB except when necessary to eliminate immediate hazards to the subject or when the change(s) involve only logistical or administrative aspects of the study (e.g. change of monitor, telephone number). Expedited review of minor change(s) in ongoing studies will be considered. Subjects must receive a copy of the signed information/consent documentation.

Investigators must promptly also report to the HSREB:

a) changes increasing the risk to the participant(s) and/or affecting significantly the conduct of the study;
b) all adverse and unexpected experiences or events that are both serious and unexpected;
c) new information that may adversely affect the safety of the subjects or the conduct of the study.

If these changes/adverse events require a change to the information/consent documentation, and/or recruitment advertisement, the newly revised information/consent documentation, and/or advertisement, must be submitted to this office for approval.

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.

[redacted]

Chair of HSREB: Dr. Joseph Gilbert

Ethics Officer to Contact for Further Information			
☐ Janice Sutherland (jsutherl@uwo.ca)	☐ Elizabeth Wambolt (ewambolt@uwo.ca)	☑ Grace Kelly (grace.kelly@uwo.ca)	☐ Denise Grafton (dgrafton@uwo.ca)

This is an official document. Please retain the original in your files.

cc: ORE File
LHRI

Wolf Orthopaedic Biomechanics Laboratory

3M Centre, The University of Western Ontario, London, Ontario, N6A 3K7

Information Letter

Title of Study: Medial Opening Wedge High Tibial Osteotomy for the Treatment of Knee Osteoarthritis: Evaluation of Dynamic Joint Loads and Health-Related Quality of Life

Investigators: Dr. T. Birmingham, Dr. P. Fowler, Dr. R. Giffin, Dr. R Litchfield, Dr. B. Chesworth, Dr. T. Jenkyn, Mr. Ian Jones, Dr. D. Bryant

The purpose of this letter is to provide you with the information you require to make an informed decision about participating in this research.

You are being invited to participate in a research study looking at whether certain characteristics of walking affect the results of knee realignment surgery, termed high tibial osteotomy. We are asking you to take part because you will be undergoing this type of surgery for the treatment of your knee osteoarthritis.

If you agree to participate in the study, you will be asked to undergo a walking test (also called a gait analysis) before your knee surgery and at several different times after your surgery. These tests will be scheduled at 6, 12, and 24 months, 5 years, 8 years and 10 years after surgery to coincide with your follow-up visits with your orthopaedic surgeon at the Fowler Kennedy Sport Medicine Clinic. Information from the walking tests will be combined with information recorded from your chart, including x-rays and questionnaires. Walking tests will take place in the Fowler Kennedy Sport Medicine Clinic, in the Wolf Orthopaedic Biomechanics Lab. Each walking test will require approximately 60 minutes of your time.

The biomechanics lab is equipped with special cameras mounted on the walls, and a force plate embedded in the centre of the floor. You will be asked to walk a distance of approximately 8 meters at a self-selected pace across the force plate, as the cameras follow several reflective markers placed on your skin over your feet, knees, hips, arms and shoulders. These markers will be fastened to your skin using double-sided tape. Although markers are removed easily, they may cause some pulling if stuck to hair, and we may shave some areas with a plastic disposable razor to limit discomfort. To assist in the placement of markers, you will be asked to wear shorts (or tights) and a T-shirt or tank top. We will ask you to walk for approximately 10-20 minutes continuously on the flat tile floor of the lab. You will be encouraged to take rest breaks if needed.

There are no known risks or benefits to your participation in this study. Participation in this study is voluntary. You may refuse to participate, refuse to answer any questions or withdraw from the study at any time with no effect on your future care.

Ian Jones from the Wolf Orthopaedic Biomechanics Lab will be coordinating this study. If you have any questions about the study procedures, you can contact Ian Jones at (XXX) XXX-XXXX ext. XXXXX. Any information that you provide will be kept in a locked cabinet in the Wolf

Orthopaedic Biomechanics Lab and will be destroyed after completion of the study. All information will be kept confidential. If the results of the study are published, your name will not be used and no information that discloses your identity will be released or published.

If you have any questions about the conduct of this study or your rights as a research subject you may contact The Director, Office of Research Ethics, The University of Western Ontario, Phone (519) 661-3036.

This letter is yours to keep.

Thank you.

Trevor Birmingham

Consent Form

Title of Study: Medial Opening Wedge High Tibial Osteotomy for the Treatment of Knee Osteoarthritis: Evaluation of Dynamic Joint Loads and Health-Related Quality of Life

I have read the Letter of Information, have had the nature of the study explained to me and I agree to participate. All questions have been answered to my satisfaction.

________________________________ Date:______________________

Signature of Participant

________________________________ Date:______________________

Signature of Person Obtaining Consent

APPENDIX II – Subgroup Analysis

- ◇ Demographics
- ◇ Radiographic Data
- ◇ Gait Data
- ◇ Performance-based Data
- ◇ Patient Self-report Data
- ◇ Mean Mechanical Axis Angle Graphs
- ◇ Mean External Knee Adduction Moment Graphs
- ◇ Mean KOOS Domain Score Graphs
- ◇ Mean SF-12 Component Score Graphs

Table 1 - Baseline demographic and clinical characteristics of patient subgroups.

Characteristic	Value Within 12 mo (N=21)	 Beyond 12 mo (N=16)
Sex, no. (%)		
Male	18 (85.7)	11 (68.8)
Female	3 (14.3)	5 (31.2)
Age, years	49.0 (9.4)	49.8 (4.8)
Height, meters	1.78 (0.09)	1.77 (0.10)
Weight, kg	93.38 (14.75)	93.87 (20.43)
BMI, kg/m^2	29.58 (3.93)	29.72 (5.00)
Time between surgeries, months	9.9 (2.2)	21.2 (8.9)
Mechanical axis angle [a], degrees		
Limb 1	-8.77 (3.90)	-9.18 (3.21)
Limb2	-8.40 (3.51)	-7.11 (1.89)
Medial compartment OA grade [b], no. (%)		
Limb 1		
0	0 (0)	0 (0)
1	1 (4.8)	1 (6.3)
2	1 (4.8)	1 (6.3)
3	4 (19.0)	1 (6.3)
4	15 (71.4)	13 (81.3)
Limb 2		
0	0 (0)	0 (0)
1	1 (4.8)	1 (6.3)
2	1 (4.8)	2 (12.5)
3	14 (66.6)	9 (56.3)
4	5 (23.8)	4 (25.0)
Lateral compartment OA grade [b], no. (%)		
Limb 1		
0	8 (38.1)	5 (31.3)
1	7 (33.3)	7 (43.8)
2	5 (23.8)	4 (25.0)
3	1 (4.8)	0 (0)
Limb 2		
0	0 (0)	2 (12.5)
1	13 (61.9)	9 (56.3)
2	8 (38.1)	5 (31.3)
3	0 (0)	0 (0)

Note: Limb 1 is the first limb to receive MOWHTO, Limb 2 is the second limb to receive MOWHTO
* *Values reported as means with standard deviations unless otherwise noted.*
[a] Negative values are indicative of varus alignment
[b] Kellgren-Lawrence scale grade of OA severity

Table 2 - Gait and radiographic measures for the "Within 12 months" subgroup

Within 12 months (*n*=21)	**Limb 1**			**Limb 2**		
Outcome Meausre	**Baseline Mean ± SD**	**Last assessment Mean ± SD**	**Mean Change (95% CI)**	**Baseline Mean ± SD**	**Last assessment Mean ± SD**	**Mean Change (95%CI)**
Radiographic						
Mechanical axis angle, degrees	-8.77 ± 3.90	0.18 ± 3.15	8.94 (7.08, 10.81)‡	-8.40 ± 3.51	2.07 ± 2.74	10.35 (8.73, 11.87)‡
Gait						
Knee adduction moment						
First peak, %BW×Ht	3.30 ±1.00	1.64 ± 0.84	-1.66 (-2.19,-1.13) ‡	3.02 ± 1.19	1.31 ± 0.74	-1.71 (-2.28, -1.15) ‡
Second peak, %BW×Ht	3.20 ± 0.99	1.36 ± 0.83	-1.83 (-2.37, -1.29) ‡	2.72 ± 0.93	1.14 ± 0.91	-1.58 (-2.09,-1.08) ‡
Absolute peak, %BW×Ht	3.50 ± 1.04	1.78± 0.81	-1.71 (-2.24, -1.19)‡	3.30 ± 1.11	1.39 ± 0.78	-1.91 (-2.47, -1.34)‡
Angular impulse, %BW×Ht×secs	1.63 ± 0.53	0.77 ± 0.40	-0.86 (-1.08, -0.64) ‡	1.53 ± 0.56	0.63 ± 0.54	-0.90 (-1.13, -0.67) ‡
Speed, meters/second	1.12 ± 0.24	1.19 ± 0.20	0.07 (0.02, 0.13)*	1.12 ± 0.24	1.19 ± 0.13	0.07 (0.02, 0.12)*
Toe-out angle, degrees	11.64 ± 5.35	12.12 ± 5.42	0.48 (-1.32, 2.29)	12.47 ± 5.44	13.64 ± 5.61	1.16 (-0.94, 3.26)
Lateral trunk lean, degrees	2.60 ± 2.63	1.59 ± 1.94	-1.00 (-2.25, 0.23)*	3.76 ± 2.61	1.01 ± 1.69	-2.74 (-4.10, -1.39) ‡

‡ $P \leq 0.001$; * $P \leq 0.05$

Table 2 - Gait and radiographic measures for the "Beyond 12 months" subgroup

Beyond 12 months (*n*=16) Outcome Measures	Limb 1			Limb 2		
	Baseline Mean ± SD	**Last assessment Mean ± SD**	**Mean Change (95% CI)**	**Baseline Mean ± SD**	**Last assessment Mean ± SD**	**Mean Change (95%CI)**
Radiographic						
Mechanical axis angle, degrees	-9.18 ± 3.21	1.14 ± 2.24	10.32 (8.09, 12.55) ‡	-7.11 ± 1.89	1.10 ± 2.42	8.21 (6.60, 9.83)‡
Gait						
Knee adduction moment						
First peak, %BW×Ht	3.15 ± 0.81	1.77 ± 0.61	-1.38 (-1.89, 0.86) ‡	3.40 ± 1.11	1.54 ± 0.57	-1.86 (-2.52,-1.20) ‡
Second peak, %BW×Ht	3.03 ± 0.95	1.77 ± 0.62	-1.26 (-1.86, -0.66) ‡	3.06 ± 0.93	1.59 ± 0.67	-1.47 (2.09,-0.86) ‡
Absolute peak, %BW×Ht	3.27 ± 0.94	1.77 ± 0.51	-1.50 (-2.08, -0.91)‡	3.37 ± 0.91	1.67 ± 0.62	-1.72 (-2.30, -1.14)‡
Angular impulse, %BW×Ht×secs	1.62 ± 0.47	0.80 ± 0.43	-0.82 (-1.13, -0.52)‡	1.67 ± 0.55	0.75 ± 0.34	-0.92 (-1.25, -0.60)‡
Speed, meters/second	1.04 ± 0.14	1.14 ± 0.13	0.11 (0.06, 0.16)‡	1.04 ± 0.13	1.15 ± 0.13	0.11 (0.06, 0.16)‡
Toe-out angle, degrees	10.78 ± 6.01	12.90 ± 5.90	2.12 (0.37, 3.87)*	13.01 ± 4.52	14.72 ± 4.06	1.71 (0.05, 3.37)*
Lateral trunk lean, degrees	4.22 ± 3.10	1.46 ± 2.07	-2.76 (-4.81, -0.71)*	2.97 ± 3.13	2.40 ± 1.38	-0.57 (-2.11, 0.97)

‡ $P \leq 0.001$; * $P \leq 0.05$

Table 2 (cont'd) - Mean differences between subgroups for radiographic and dynamic gait outcome measures

Outcome Measures	Limb 1		Limb 2	
	Mean Difference (95%CI)	**Significance**	**Mean Difference (95%CI)**	**Significance**
Radiographic				
Mechanical axis angle, degrees	-1.38 (-4.16, 1.41)	0.323	2.09 (-0.12, 4.30)	0.630
Gait				
Knee adduction moment				
First peak, %BW×Ht	-0.28 (-1.02,0.45)	0.437	-0.58 (-1.36, 0.21)	0.146
Second peak, %BW×Ht	0.14 (-0.69, 0.98)	0.728	-0.11 (-0.87, 0.65)	0.777
Absolute peak, %BW×Ht	-0.22 (-0.69, 0.98)	0.563	-0.19 (-0.98, 0.61)	0.637
Angular impulse, %BW×Ht×secs	-0.04 (-0.39,0.31)	0.838	0.02 (-0.35, 0.40)	0.899
Speed, meters/second	-0.04 (-0.11, 0.04)	0.323	-0.04 (-0.11, 0.03)	0.264
Toe-out angle, degrees	-1.64 (-4.13,0.84)	0.189	-0.55 (-3.27, 2.17)	0.686
Lateral trunk lean, degrees	1.75 (-0.44, 3.95)	0.113	-2.17 (-4.15, -0.19)	0.03

Table 3 - Performance-based and patient-reported outcome measures split by patient subgroups

Outcome Measures	Within 12 months (*n*=21)			Beyond 12 months (*n*=16)		
	Baseline Mean ± SD	Last assessment Mean ± SD	Mean Change (95% CI)	Baseline Mean ± SD	Last assessment Mean ± SD	Mean Change (95%CI)
Performance-based **						
6MWT, meters	421.84 (92.46)	441.35 (108.51)	47.55 (38.61)	417.17 (136.75)	431.51 (86.26)	32.72 (68.12)
Patient-reported						
SF-12 Physical Function (range 0-100)	35.06 ± 8.62	47.83 ± 9.01	12.80 (7.78, 17.82)‡	30.99 ± 5.87	42.07 ± 9.88	11.09 (6.10, 16.07)‡
SF-12 Mental Health (range 0 - 100)	55.21 ± 7.61	49.60 ± 6.56	-5.55 (-9.04, -2.06)‡	49.83 ± 14.35	50.01 ± 9.78	0.18 (-6.64, 7.00)
KOOS (range (0 - 100)						
Pain	46.08 ± 16.03	70.21 ± 25.49	24.28 (15.43, 33.12)‡	40.28 ± 16.26	67.36 ± 17.26	27.08 (19.08, 35.09)‡
Other Symptoms	40.60 ± 12.69	60.75 ± 16.98	20.34 (11.20, 29.47)‡	36.61 ± 9.27	56.92 ± 18.09	20.31 (10.42, 30.21)‡
Function in Activities of Daily Living	52.68 ± 16.16	78.90 ± 21.20	26.41 (17.63, 35.20)‡	47.24 ± 18.11	76.93 ± 14.23	29.69 (20.41, 38.96)‡
Function in Sport & Recreation	24.05 ± 24.32	54.45 ± 28.58	30.71 (16.86, 44.56)‡	13.44 ± 13.99	44.69 ± 27.96	31.25 (17.65, 44.85)‡
Quality of Life	22.59 ± 22.14	53.71 ± 31.43	31.27 (16.19, 46.35)‡	14.45 ± 16.09	44.53 ± 22.35	30.08 (18.59, 41.56)‡
LEFS	37.75 ± 14.43	55.85 ± 19.61	18.10 (9.39, 27.81)‡	34.56 ± 9.85	53.88 ± 15.70	19.31 (12.05, 26.57)‡

‡ $P \leq 0.001$; * $P \leq 0.05$

** N=30; there were no performance-based measures for 7 patients; scores reported as medians with interquartile ranges because data were not normally distributed

Table 3 (cont'd) – Mean differences between subgroups for performance-based and patient-reported outcomes.

Outcome Measure	Mean Difference (95% CI)	Significance
Performance-based **		
6MWT, meters	N/A	0.279
Patient-reported		
SF-12 Physical Function (range 0-100)	1.71 (-5.26, 8.68)	0.621
SF-12 Mental Health (range 0 - 100)	-5.73 (-12.59, 1.13)	0.100
KOOS (range (0 - 100)		
Pain	-2.81 (-14.71, 9.10)	0.636
Other Symptoms	0.26 (-13.06, 13.12)	0.997
Function in Activities of Daily Living	-3.27 (-15.75, 9.20)	0.597
Function in Sport & Recreation	-0.54 (-19.69, 18.60)	0.954
Quality of Life	1.19 (-18.17, 20.56)	0.901
LEFS (range 0-80)	-1.02 (-12.95, 10.92)	0.864

‡ $P \leq 0.001$; * $P \leq 0.05$

* *6MWT had non-normal distribution, significance level determined with Mann-Whitney U test

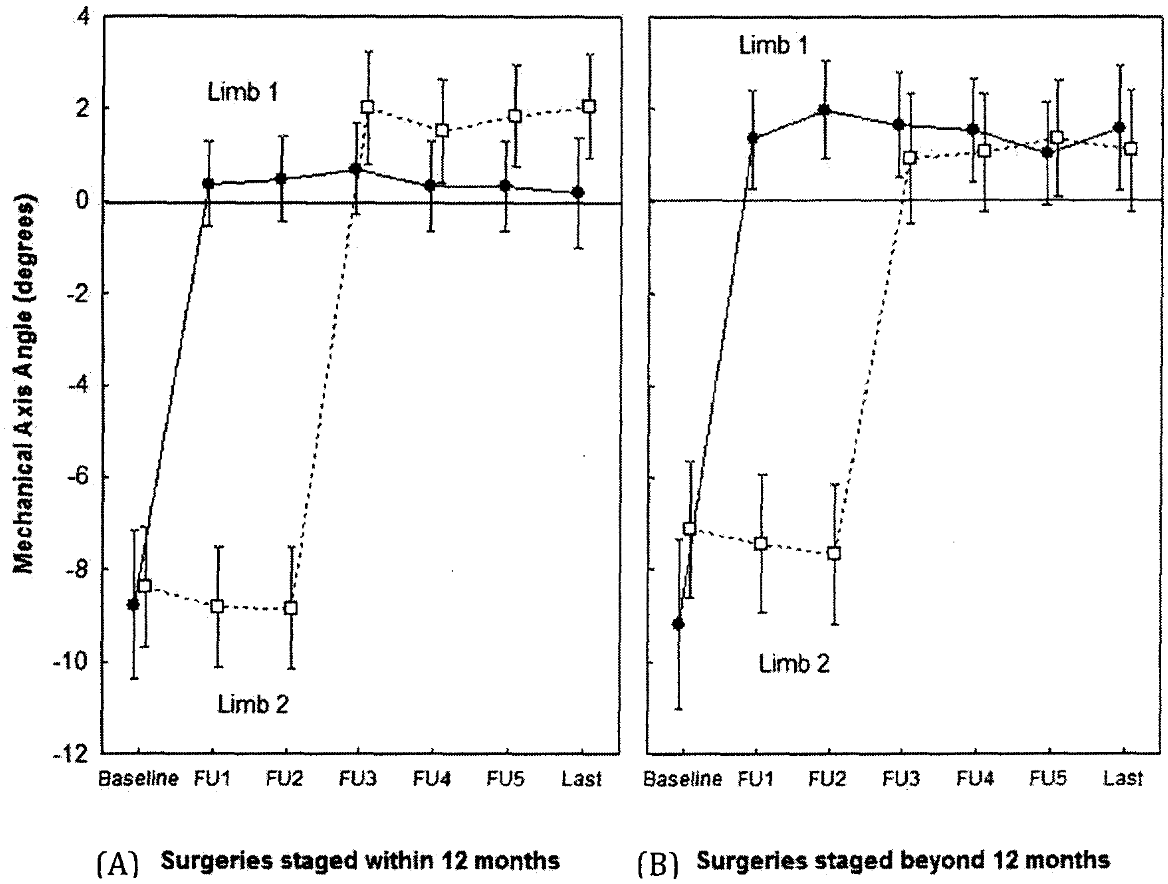

Figure 1. Mean mechanical axis angle (degrees) ± 95% CI for all assessments for patients who underwent the second HTO (A) within, or (B) beyond, 12 months of the first HTO. Both limbs were assessed at all time points. Negative values indicate varus alignment.

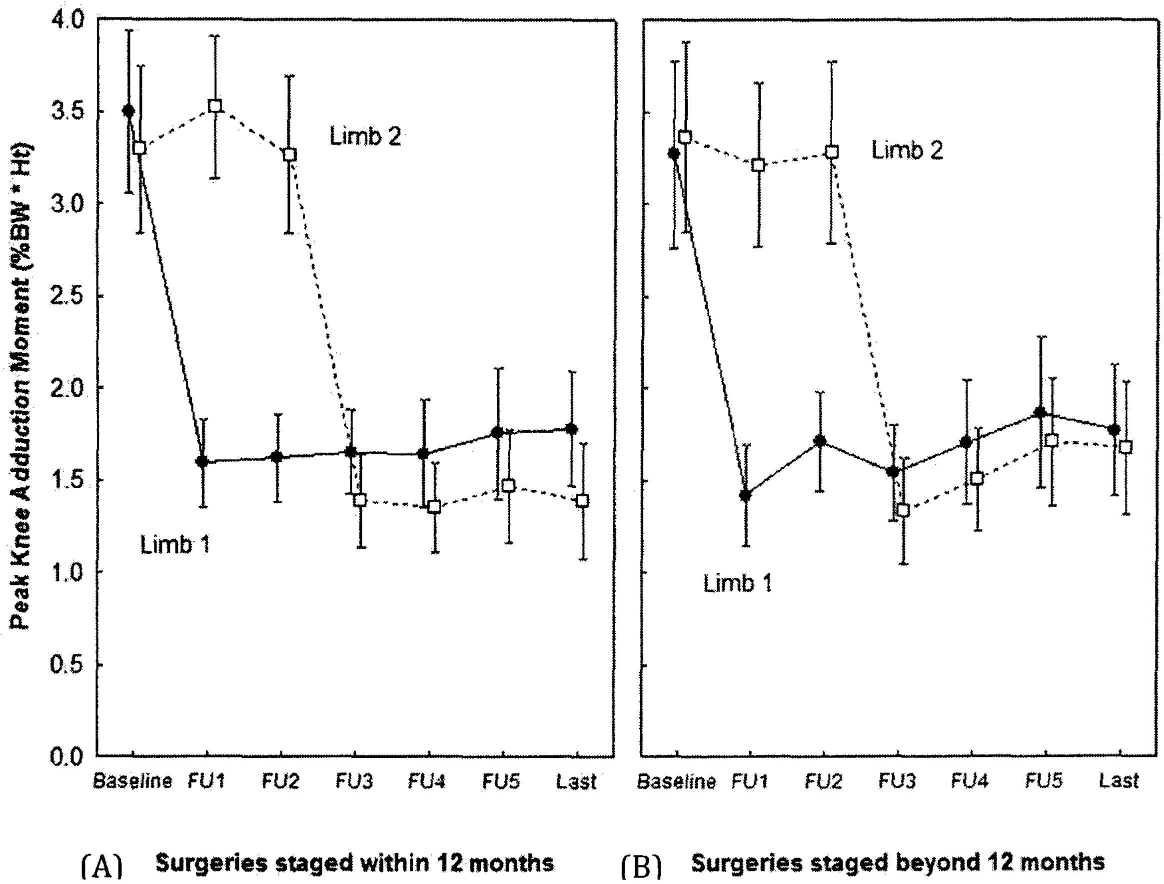

Figure 2. Mean peak knee adduction moment (%BW * Ht) ± 95% CI for all assessments for patients who underwent the second HTO (A) within, or (B) beyond, 12 months of the first HTO. Both limbs were assessed at all time points.

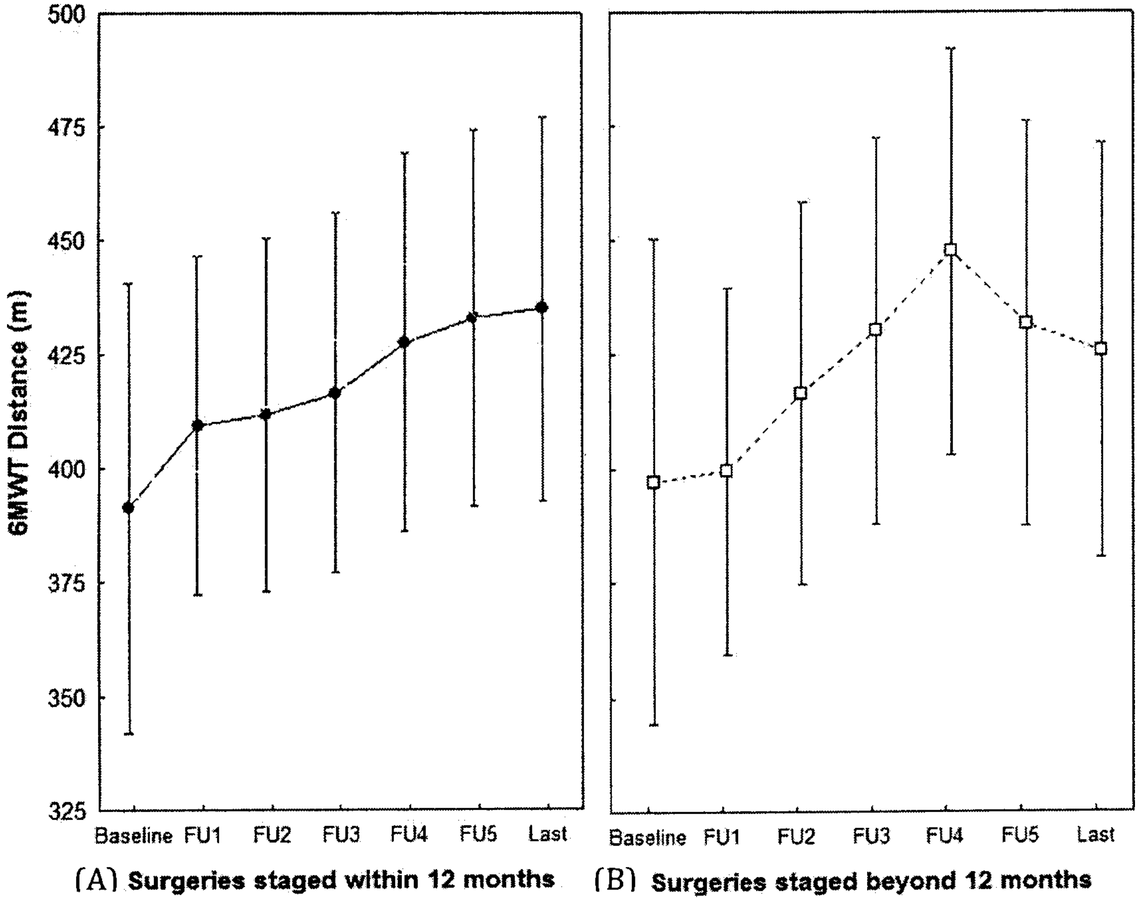

Figure 3. Mean six minute walk test (m) ± 95% CI for all assessments for patients who underwent the second HTO (A) within, or (B) beyond, 12 months of the first HTO.

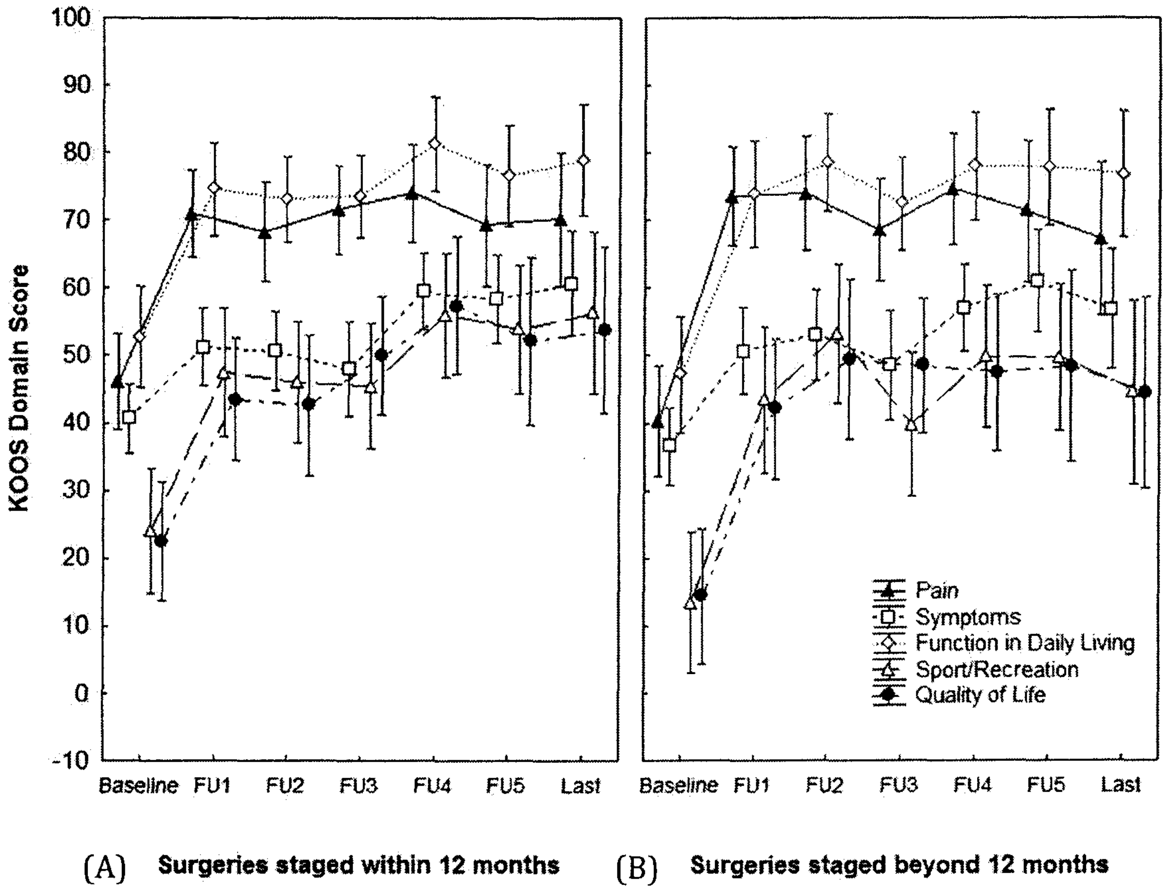

Figure 4. Mean KOOS domain scores ± 95% CI for all assessments for patients who underwent the second HTO (A) within, or (B) beyond, 12 months of the first HTO.

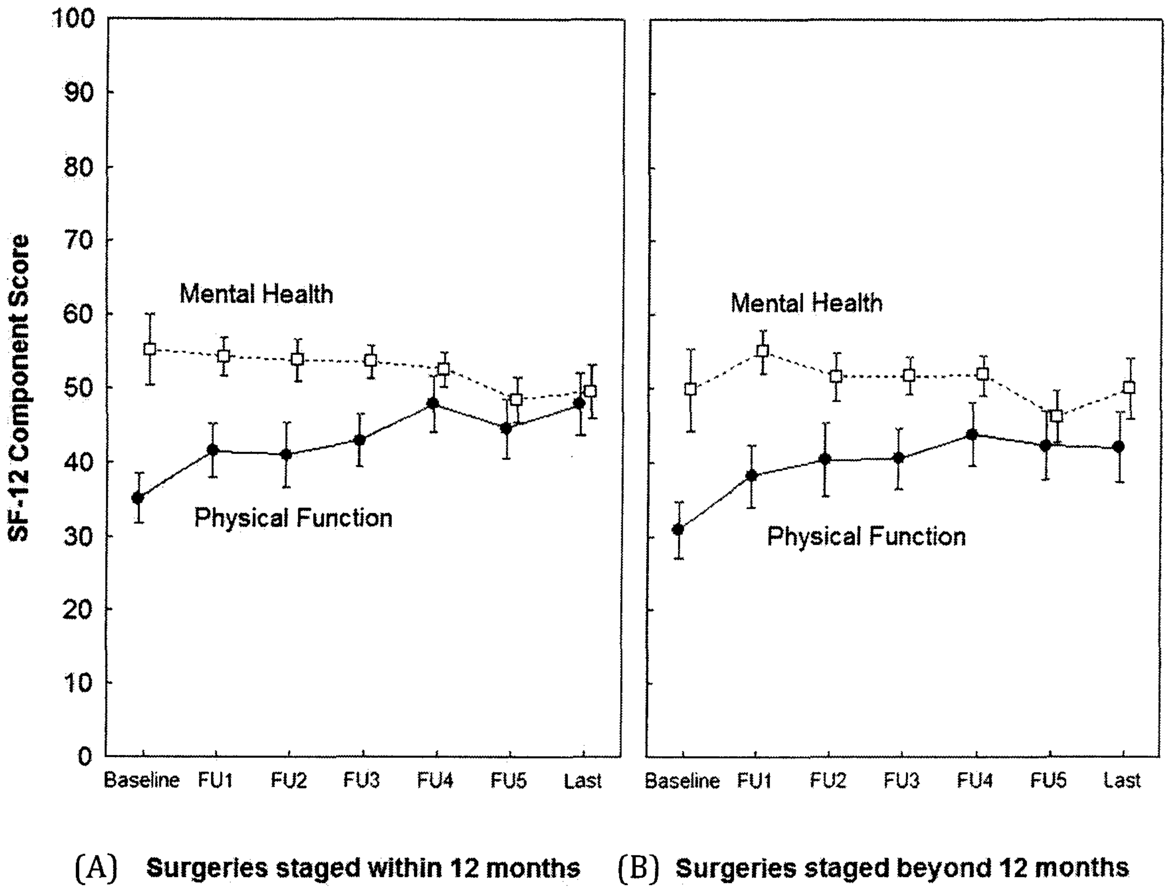

Figure 5. Mean SF-12 PCS and MCS ± 95% CI for all assessments for patients who underwent the second HTO (A) within, or (B) beyond, 12 months of the first HTO