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Biomechanical Evaluations of Bilateral and Unilateral TKR Patients During Level Walking and Stair Negotiation

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Biomechanical Evaluations of Bilateral and Unilateral TKR Patients During Level Walking and
Stair Negotiation

A Dissertation Presented for the
Doctor of Philosophy
Degree
The University of Tennessee, Knoxville

Derek Scott Yocum

August 2019

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Dedication

This dissertation is dedicated to my wife Maggie, my daughter Isabella, my family, and the friends I've gained throughout this process. I would not be where I am today if my wife wasn't constantly pushing me to give my best and supporting me through all the difficulties that come with this path. My daughter has inspired me to remember to have fun along the way and to put this process into the proper perspective. Further, my family and friends have continued to show support throughout this process, and their support has helped to provide the drive to finish.

Acknowledgement

There are many people who deserve acknowledgement for helping me throughout this process. I would like to thank those in which inspired me to pursue this doctoral degree and provided useful insight along the way. While all of those in the lab have provide useful conversations and ideas, I would like to specifically thank Dr. Hunter Bennett and Dr. Kevin Valenzuela, who provided insight and made everyday life in the lab an amazing experience.

Further, this doctoral degree would not have been possible without my committee members: Drs. Songning Zhang, Joshua T. Weinhandl, Jeffrey Reinbolt, and Eugene Fitzhugh. All committee members played a vital role in my development as a researcher and teacher. A special thank you to my advisor Dr. Zhang, who has been pivotal in my growth from when I first arrived at Tennessee, with little to no biomechanics experience, to now finishing my doctoral degree and becoming a biomechanist. Through my five years at Tennessee, he would always be open for my, numerous, questions, clarifications, and numerous revisions of all my writings. Thank you for your continued support and guidance throughout my time at Tennessee.

Abstract

Many total knee replacement (TKR) patients will need to have a contralateral knee replacement. Biomechanical differences between 1st and 2nd replaced limbs of bilateral TKR have not been examined during level walking or stair negotiation. Further, it is unknown if hip and ankle biomechanics of bilateral patients are altered, compared to the replaced and non-replaced limbs of unilateral patients during level walking and stair negotiation. Study one and two compared hip, knee, and ankle biomechanics of the 1st and 2nd replaced limbs of bilateral patients and both replaced and non-replaced limbs of unilateral patients during level walking and stair negotiation, respectively. Study three compared knee joint waveforms of the 1st replaced limbs of bilateral patients, replaced limbs of unilateral patients, and selected limbs of asymptomatic controls during level walking.

Study one found that 2nd replaced limbs exhibited lower peak loading-response knee extension moment (KEM) than the first replaced limbs. Bilateral patients exhibited lower loading-response KEM, knee abduction moments (KAbM), and dorsiflexion moments, compared to unilateral patients. Bilateral patients also exhibited lower push-off peak hip flexion moments and vertical ground reaction force (GRF).

Study two found during ascent, bilateral patients exhibited decreased peak loading-response KEM and push-off plantarflexion moments. Unilateral replaced limbs KEM was lower than non-replaced. During descent, bilateral patients descended significantly slower, had lower peak loading-response vertical GRF and KEM, and push-off KEM. Bilateral patients had higher peak loading-response hip extension and push-off plantarflexion moments, and increased knee adduction range of motion (ROM).

Study three found TKR patients exhibited more flexed and abducted knees throughout stance, decreased sagittal knee ROM, increased early-stance adduction ROM, decreased loading-response knee extension and push-off knee flexion moments, decreased loading-response and push-off KAbM, increased KAbM at midstance, increased midstance vertical GRF, as well as decreased loading-response and push-off vertical GRF. Additionally, bilateral patients exhibited reduced sagittal knee ROM, increased adduction ROM, decreased sagittal knee moments throughout stance, decreased KAbM throughout stance, an earlier loading-response peak vertical GRF, and a decreased push-off vertical GRF, compared to unilateral patients.

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Chapter I

Introduction

Background

Osteoarthritis (OA) is a debilitating joint disease that involves the degradation of joint articular cartilage and surrounding tissues. Aside from cartilage damage, there is remodeling of bone, formation of osteophytes, increased joint laxity, weakened muscles, and joint inflammation (181). OA is often described by the level of severity of the condition, and can be identified radiographically using a Kellgren-Lawrence grade (KL) ranging from zero (none) to four (severe) (150). Patients with severe knee OA (KL grades 3 and 4) have radiographic evidence of multiple/large osteophytes, joint space narrowing, sclerosis, and bony deformities (100, 150, 171). The 8.6 million people estimated to have severe knee OA in the United States are likely to receive a recommendation for total knee replacement (TKR) (80, 115, 181, 266).

The purpose of a TKR is to alleviate daily pain, improve knee joint range of motion (ROM), improve joint alignment, and reduce daily activity limitations (45, 330, 357). In 2010, the prevalence of people living with knee replacement was 1.52% (4.7 million), with over 700,000 TKR surgeries performed in the U.S. that year (70, 195). This number is expected to grow by 673% to 3.5 million TKR surgeries per year by 2030 (161). Due to the high number of individuals with TKRs, and the expected growth in surgeries performed, it is important to understand how these surgeries effect the functional capacity of TKR patients.

Functional capacities are often determined using surveys given to the patients. Two commonly used surveys used to score the functional capacity of TKR patients are the Knee Injury and Osteoarthritis Outcome Score (KOOS) and the Knee Society Scoring System. The KOOS uses five separate sections, each with multiple questions, to score a patient. This self-

administered survey asks questions regarding the level of pain during common daily activities, how strong knee symptoms related to knee OA are throughout the day, the level of difficulty in performing common activities of daily living, difficulty in performing recreational activities, and overall knee-related quality of life (267). To evaluate individual patient outcomes, the Knee Society Knee Scoring System (KSS) uses objective (alignment, stability, ROM, and pain) and subjective (satisfaction, expectations, functional capacity, an awareness of the replacement) data from TKR patients both pre- and post-op (284).

Using these scoring systems to evaluate functional capacity and quality of life, reports indicate that pain is decreased, and knee flexion ROM during level walking is increased following TKR surgery (47, 123, 157). Despite these findings, compared to healthy controls, TKR patients tend to exhibit a quadriceps avoidance gait (209). This avoidance leads to lower ROM and knee flexion, and well as decreased peak knee flexion moments during gait, compared to asymptomatic controls (190, 321).

Stair negotiation is a common activity that many people perform on a regular basis. However, this activity may be more difficult for patients who have undergone TKR. Many previous studies have examined the capacity of TKR patients to perform this task (27, 30, 32, 56, 95, 104, 142, 151, 190, 192, 197, 198, 230, 244, 251, 277, 305, 306, 337). TKR patients tend to have lower knee flexion ROM through stance phase of stair ascent (27, 32, 56, 95, 306) and stair descent (32, 337), compared to asymptomatic controls. Further, TKR patients tend to have reduced internal peak knee extension moments (KEM) during stair ascent (27, 56, 95, 197, 245) and descent (197, 337). This avoidance of the quadriceps may make stair negotiation increasingly difficult for TKR patients. Further, TKR may produce asymmetries between replaced and non-replaced limbs. This asymmetrical loading on the non-replaced limb may act to

hasten the progression of OA in that limb, potentially leading to a need for a second knee replacement (211).

Metcalfe et al. (205) and Milner (211) found that at 12 and 28 months, respectively, non-replaced limbs of TKR patients had significantly higher loading-response peak knee abduction moment (KAbM) during level walking, compared to the replaced limb and asymptomatic controls. Additionally, Alnahdi et al. (8) stipulated that even though peak KAbM was similar between the non-replaced limbs of their unilateral TKR patients and asymptomatic controls, the slower gait speed of TKR patients may increase the number of times the knee is loaded, potentially furthering the progression of OA in the non-replaced knee.

Estimations on the risk for contralateral TKR show that between 37% and 46% of all unilateral TKR patients will have the contralateral knee replaced (203, 279, 291). Research shows that bilateral TKR patients exhibit similar pain and functional capacity scores as unilateral TKR patients (132). During level walking, Ro et al. (262) found that bilateral TKR patients walked significantly slower, generated a significantly lower peak KEMs, and had significantly less knee ROM than healthy controls. This is a similar finding to unilateral TKR patients. Only one study has examined differences between unilateral and bilateral TKR patients (197). This study examined only the sagittal plane and found that during stair negotiation, there were no differences between the maximum knee flexion angle and peak knee flexion moments during both stair ascent and descent. To date, no study has thoroughly examined biomechanical differences between the limbs of unilateral and bilateral TKR patients during level walking or stair negotiation.

Most biomechanical research uses discrete events and related values to analyze group differences of the effects of some intervention. These events are typically determined to be of

importance prior to the collection of the data. These values typically include discrete parameters such as local peaks. The data collected and computed, however, is most commonly represented as a waveform, describing the motion of a joint throughout the gait cycle. When analyzing biomechanical data by extracting discrete parameters, information regarding waveform characteristics through the entire movement phase may be lost (76). In order to perform a robust analysis of the entire waveform of biomechanical data, researchers can use statistical techniques that capture the entire waveform, rather than individual points. One of these techniques is principal component analysis (PCA).

PCA, a multivariate statistical technique, identifies variations in waveform patterns and what gait characteristics are influencing these variations. This analysis technique has been used previously in knee OA (41, 50, 77-79, 97, 110, 121, 144, 155, 159, 180, 254-256, 263, 264, 273) and unilateral TKR (12, 15, 78, 120, 122, 194, 204, 205, 262, 318) research. These studies have found that knee OA patients exhibit lower knee flexion angles throughout stance phase, decreased internal KEM magnitude during early stance, and increased KAbM throughout stance (77). Following surgery, unilateral TKR patients tend to exhibit decreased KAbM throughout stance, increases knee flexion angles throughout stance, and increased KEM, compared to pre-operation levels, during level walking (120). One study examined changes in the knee flexion angle of bilateral TKR patients before and after surgery. This study found that the patients had higher knee flexion angles and greater ROM throughout stance after TKR surgery, however, bilateral patients exhibited lower ROM than controls (262).

During stair negotiation, Trinler et al. (318) found no differences in knee flexion angles, KEMs, or knee power generation between TKR patients and asymptomatic controls. This is a

surprising result as most previous studies using discrete variables tend to find significant group differences among these variables.

The aforementioned studies each generated PCA models for individual variables and therefore all results were independent of the others. However, other researchers have found that a more robust analysis of biomechanical data would be to combine the waveforms of the variables of interest (39, 158, 221). The variance within the variables of interest of a single PC identifies correlated changes, while other PCs remain uncorrelated (39). To date, no study has used this multivariate approach to study the biomechanical waveforms of TKR patients.

Statement of the Problem

To our knowledge, no studies have examined how the presence of bilateral TKR affects gait biomechanics during level walking and stair negotiation. Additionally, no studies have examined differences in knee biomechanics between first and second knee replacements. This may be beneficial as advancements in TKR designs and degradation of older TKRs may generate differences between these limbs. Investigation into the differences in knee joint mechanics between first and second replacements may provide clinicians information critical to improving the rehabilitation protocol of bilateral TKR patients. Further, many TKR studies exclude bilateral TKR patients as potential participants due to concerns of variation due to multiple implants. This generates an issue with patient recruitment as approximately 40% of unilateral TKR patients will need a second replacement (203, 279, 291). If bilateral TKR patients are found to have statistically similar joint mechanics as unilateral TKR patients, this exclusion criteria could be potentially eliminated in future TKR research. Finally, no studies have implemented a multivariate PCA on the biomechanical waveforms of bilateral TKR patients with comparisons

to unilateral patients and asymptomatic controls during level walking. Therefore, the purposes of the proposed studies are:

Study One: The primary purpose of this study was to examine differences in knee biomechanics of 1st and 2nd replaced limbs of bilateral patients during level walking; and compare differences in knee biomechanics of 1st and 2nd replaced limbs of bilateral patients, with replaced and non-replaced limbs of unilateral patients. The secondary purpose was to examine hip and ankle kinematics and kinetics of these patients.

Study Two: The primary purpose of this study was to examine differences in knee biomechanics of 1st and 2nd replaced limbs of bilateral patients during stair negotiation; and compare differences in knee biomechanics of 1st and 2nd replaced limbs of bilateral patients, with replaced and non-replaced limbs of unilateral patients. The secondary purpose was to examine hip and ankle kinematics and kinetics of these patients.

Study Three: The purpose of this study was to examine knee joint biomechanical differences in level walking between bilateral patients, unilateral patients, and asymptomatic controls, using multivariate PCA.

Research Hypotheses

Study One

1. It was hypothesized that bilateral TKR patients would have similar knee extension and abduction moments and ROM between the 1st and 2nd replaced limbs.
2. It was hypothesized that bilateral TKR patients would exhibit similar knee extension and abduction moments and ROM compared to the replaced limb of unilateral TKR patients, but decreased KEMs and ROM compared to the non-replaced limb of unilateral TKR patients.

3. It was hypothesized that both bilateral limbs and the replaced limb of unilateral patients would have similar hip and ankle sagittal plane moments, indicating similar compensations following TKR, but different moments than the non-replaced limb of unilateral patients.

Study Two

1. It was hypothesized that peak KEM, KAbM, and knee extension and abduction ROM would not be statistically different between 1st and 2nd replaced limbs of bilateral patients.
2. It was further hypothesized that 1st and 2nd replaced limbs of bilateral patients would have similar peak KEM and KAbM as replaced limbs, but lower KEM and KAbM compared to non-replaced limbs of unilateral patients.
3. It was hypothesized that hip and ankle kinetics and kinematics would be similar between 1st and 2nd replaced limbs of bilateral patients and replaced limbs of unilateral patients, but hip extension moments would be higher compared to non-replaced limbs of unilateral patients.

Study Three

1. It was hypothesized that bilateral and unilateral patients would have similar PC-scores, indicating no differences in the waveforms.
2. It was hypothesized that the PC-scores of bilateral and unilateral patients would differ significantly different from those of asymptomatic controls, indicating significant differences in the waveforms.

Delimitations

The exclusion criteria for bilateral TKR patients were:

- Diagnosed osteoarthritis at the ankle or hip joint as reported by the patient.
- Any additional lower extremity joint replacement.
- Any lower extremity joint arthroscopic surgery or intra-articular injection within past 3 months.
- Systemic inflammatory arthritis (rheumatoid arthritis, psoriatic arthritis) as reported by the patient.
- BMI greater than 40.
- Neurologic disease (e.g. Parkinson's disease, stroke patients) as reported by the patient.
- Any additional major lower extremity injuries/surgeries except for the replaced knees.
- Inability to walk without a walking aid.
- Any visual conditions affecting gait or balance.
- Women who are pregnant or nursing.
- Simultaneous Bilateral TKR

The inclusion criteria for bilateral TKR patients included:

- Men and women between the ages of 50 and 75.
- Total knee replacement in two knees.
- At least 12-months from the second TKR.
- No more than 10-years from the first TKR.
- Cruciate retaining TKR.

Limitations

- A laboratory setting was used for all tests.
- Increased body fat reduced the accuracy of skin marker placement on boney landmarks.
- Reflective markers placed on the shoe may not accurately capture foot movement.
- Due to the time required to set-up the staircase, level walking was always performed last, limiting the randomization within the study.

Chapter II

Literature Review

Introduction

The purpose of the first study was to examine differences in knee joint biomechanics in both limbs of bilateral TKR patients and replaced and non-replaced limbs of unilateral TKR patients during level walking. The purpose of study two analyze differences in knee joint biomechanics in both limbs of bilateral TKR patients and replaced and non-replaced limbs of unilateral TKR patients during stair negotiation. The purpose of study three was to examine knee joint biomechanical differences between both limbs of bilateral TKR patients and the replaced limb of unilateral TKR patients during level walking using principal component analysis.

The purpose of this chapter is to summarize: 1) epidemiology of knee OA, unilateral TKR, and bilateral TKR in the US, 2) gait biomechanics of end-stage knee OA patients during level walking , 3) gait biomechanics of unilateral TKR patients during level walking, ramp walking, and stair negotiation, 4) gait biomechanics of bilateral TKR patients, and 5) principal component analyses of knee OA and TKR patients.

Epidemiology of Knee OA

Osteoarthritis is highly prevalent in the United States with 27 million adults clinically diagnosed with the disease (166). One of the most common forms of OA is knee OA. Knee OA is a leading cause of disability in the United States and worldwide. Along with hip OA, Knee OA is ranked as the 11th highest contributor to global disability as of 2010, with 3.8% of all people being estimated to have the condition (66, 72). In the United States, it is estimated that over 15 million people have symptomatic knee OA, with 8.6 million people having K/L grade 3 or 4 (severe symptomatic knee OA, with women having higher prevalence of knee OA than men (80,

181, 266). This estimate (2011-2012) is much higher than previous population estimates (9.3 million, 2005) (166). A dramatic rise in knee OA prevalence from prehistoric and pre-industrial (8% and 6%, respectively) to post-industrial (i.e. after 1900, 16%) eras suggests that there may be environmental/modifiable risk factors associated with knee OA (327).

In addition to the physical burden of OA, the financial burden is substantial (185). Overall, osteoarthritis was the second most expensive condition in 2013 at \$16.52 billion billed to payers (i.e. Medicaid and private insurance) (315). The average direct cost per OA patient has been reported to range from \$1,400 to over \$21,000 (185, 343). Due to the increasing prevalence of knee OA and the physical and economic burden of the disease, understanding the risk factors associated with the development of knee OA is key to understand how this disease develops. There have been many risk factors that have been suggested for the development of knee OA, these risk factors include both modifiable (overweight/obesity, activity level, reduced lower limb strength, malalignment) and non-modifiable (age, sex, genetics/ethnicity, previous joint injury) (31, 143). In the next two sections, the non-modifiable and modifiable risk factors for OA development will be discussed.

Non-Modifiable Risk Factor: Age-Gender Relationship

Age is one the best predictors of OA development (7, 100, 143, 181, 219, 227, 231, 326). In general, incidence rates of knee OA rise steeply from age 50-70, followed by a small decline in the final years of life (246). A large cohort study of over 3.2 million participants observed an incidence rate of 6.5 per 1,000 person-years. However, this rate was much higher for females (8.3) than males (4.6) (246). A multiple linear regression by Calce et al. (51) demonstrates that, while controlling for body mass, height, and torsional rigidity (i.e. the ability of the bone to resist twisting forces), age had a significant relationship with OA, explaining 25-56% of the variance

in OA severity. While there is clear evidence on the effect of aging on the incidence of OA, there are currently no reports on how the risk of the development of knee OA increases per year of life. A multiple linear regression of age on knee OA development, when controlling for sex, body mass, and previous knee injury would provide useful information in describing the epidemiology of knee OA.

Non-Modifiable Risk Factor: Genetics and Ethnicity

Of all non-modifiable risk factors, genetics may be the strongest determinant of OA risk. Various studies have reported a 30-65% risk of OA development that is genetically determined (60, 90, 143, 234, 303, 326). Warner et al. (329) reviewed genetic susceptibility of OA development and found that there have been 21 identified loci that have shown increased OA predisposition. Two studies have found specific genes (67, 346) and chromosomes (153) that promote OA development.

The effect of race on the development of OA is often disputed. Some studies reported that African-Americans may be at increased risk of OA development, especially in the hip and knee (7, 326, 358). However, Deshpande et al. (80) demonstrated that there is a higher percentage of non-Hispanic white individuals (7.5%) than non-Hispanic black individuals (6.9%) and Hispanic individuals (4.4%) with knee OA. This resulted in an estimation of 139 million non-Hispanic white individuals and 23 million non-Hispanic black individuals with knee OA in the United States (80).

Non-Modifiable Risk Factor: Previous Knee Injury

Knee joint injury is a strong predictor for the onset of knee OA. Unlike the previously discussed risk factors, the presence of a knee injury is the only non-modifiable risk factor that is preventable, as it happens at some point during life and does not occur in every person. The most

prominent knee injuries associated with the future development on knee OA are ACL injuries, meniscal tears, and articular cartilage damage (7, 143, 219, 259, 297, 302, 326, 358). This type of osteoarthritis is typically defined as post-traumatic OA (PTOA), which accounts for approximately 12% of the overall burden of the disease (260). A review on the epidemiology of PTOA by Thomas et al. (312) shows that there are conflicting reports on the prevalence of knee PTOA following isolated ACL injury (13% - 39%), as well as when ACL injury is combined with a meniscal tear (21% - 100%). It is suggested that this wide range of estimates is due to poor methodological approaches (223).

ACL injuries are very common in the United States with approximately 250,000 occurring each year, along with 175,000 ACL reconstruction surgeries (116, 117, 312). Unfortunately, the act of reconstructing ACL may increase the likelihood of knee PTOA development (186). The review by Luc et al. (186) found that patients with ACL reconstruction had a significantly higher (7%) risk to develop knee OA, compared to those patients who did not undergo reconstruction. This study additionally found that these rates were increased when a meniscectomy was performed.

Studies on meniscal injuries and surgeries demonstrate the importance of the meniscus as a protective mechanism against knee joint degradation. While the Osteoarthritis Initiative has demonstrated that there is not a significant effect of meniscal injury on knee OA development within two years, those that did develop knee OA were significantly likely to have had meniscal injuries (16). Long-term follow up studies in patients with meniscal injuries and surgeries show that the risk of OA development in the long term is greatly increased (88, 237). Further, when comparing meniscus repairs to partial and complete meniscectomies, evidence shows that 40.2% fewer patients receiving a repair developed radiographic changes than those with a

meniscectomy. Additionally, 39% fewer patients developed PTOA following partial meniscectomy, compared to complete, and had an odds ratio of 3.6 of developing knee PTOA following complete meniscectomy (9, 87, 88, 201, 307, 312).

The studies discussed above show that when knee injuries occur, there is a substantial risk of knee OA development. Therefore, to reduce the risk of OA development, it is important to reduce the occurrence of knee injury. The prevention of knee injury is a crucial first step in primary prevention of knee OA. Prevention programs focus on both neuromuscular and strength training to improve the joint stabilizing capacity of muscles crossing the knee joint and to improve movement patterns to reduce loading experienced by knee ligaments (220). A report by Palmieri-Smith et al. (233) recommends educating both those at risk for PTOA and athletic trainers on the importance of maintaining a healthy body weight, appropriate physical activity levels, and self-managements strategies is crucial in prevention and management of PTOA. A systematic review containing 10 studies and approximately 27,000 participants demonstrated that neuromuscular and educational interventions may reduce ACL injury risks by up to 50% (109). While most research in injury prevention, especially in the knee, pertains to preventing injuries in athletes. Despite this, it would be beneficial for those not actively participating in sports to undergo a pre-habilitation program focused on strengthening muscles in the lower extremity and improving their capacity to move safely during daily life.

Modifiable Risk Factor: Reduced Lower Limb Strength

Despite evidence that improving lower extremity muscle strength may provide a preventative contribution to reducing knee joint injuries, especially when combined with neuromuscular training (220), there is conflicting evidence on the ability of strength training on the prevention of knee OA development. A recent report of 161 Osteoarthritis Initiative

participants concluded that reduced knee extensor and knee flexor strength may increase the risk of incident radiographic knee OA in women, but not in men, with odds ratios of 1.47 and 1.41, respectively (73). Lower quadriceps muscle strength is also associated with increased knee pain after a five-year follow-up in women, but not in men, with a risk ratio of 1.28 (112). This is comparable to the finding by Segal et al. (286) who determined that increased quadriceps strength may protect against incident symptomatic knee OA, but not radiographic knee OA. A meta-analysis of five cohort studies, including over 5,700 participants, determined that the odds ratio for developing symptomatic knee OA due to knee extensor weakness was 1.65, indicating a significant impact of muscle weakness on knee OA (127, 148, 224, 225, 287, 299).

In contrast, Kemnitz et al. (152) found that loss of muscle strength encourages progression of knee OA but had no influence on the development of the disease. Further, Turkiewicz et al. (319) found that for every 47 Nm increase in knee extensor strength, men had an increased hazard ratio of 1.12 for knee OA development.

To date, there is no research into the efficacy of strength training to reduce incident knee OA. Many studies have focused on strength training knee OA patients in prevention of further knee joint deterioration and improve knee joint stability (43). This systematic review by Brosseau et al. (43) demonstrates that strength training exercise that is either isotonic, isokinetic, or isometric is capable of reducing knee pain and improving quality of life in knee OA patients.

Modifiable Risk Factor: Knee Joint Alignment

When the knee is not aligned neutrally, the joint forces become unevenly distributed, which can lead to increased joint deterioration (10, 99, 143, 293). In neutrally aligned knees, a majority of the load experienced within the knee joint masses through the medial compartment. This is due to the femoral head being medial to the ankle joint center, where the force passes

through (10). Increasing varus and valgus alignment causes the force distribution to shift medially and laterally, respectively (46, 129). Since it is suggested that all OA may be caused by increased localized forces within a joint, and that anatomical abnormalities, such as malalignment, cause changes in the force distribution at the knee, it is a logical progression that knee malalignment may lead to the development of knee OA (99).

Data from the Multicenter Osteoarthritis Study (MOST) cohort study reveals that varus knee malalignment increased incident medial cartilage damage odds ratio compared to neutral (OR 2.32) and non-varus (OR 3.53) aligned knees. Further, valgus alignment exhibited greater odds ratios for lateral cartilage damage compared to neutral (OR 0.97) and non-valgus (OR 1.49) aligned knees (293). This same cohort group was studied for the incidence of knee OA development. It was found that varus alignment was significantly associated with knee OA development (OR 1.49), while valgus alignment was not significantly related to knee OA development. However, varus (OR 3.59) and valgus (OR 4.85) malalignment was significantly associated with knee OA progression in the medial and lateral compartments, respectively (294).

In contrast to these findings, a study using the cohort from the Framingham OA Study found that knee malalignment does not predict the development of knee OA, but only influences the progression of the disease. However, an additional cohort study by Brouwer et al. (44) found valgus and varus aligned knees had odds ratios of 1.54 and 2.06, respectively, of developing knee OA.

Two recent studies on the risk of incident knee OA due to a varus thrust during gait have provided interesting evidence on the effect of excessive varus motion of the knee during gait. These studies were both conducted on the MOST cohort. These studies, which were conducted by the same group of researchers, found that this excessive frontal plane motion increases the

incidence and worsening of bone marrow lesions within the knee joint (340). However, despite this increased degradation of the bones of the knee, there was no significant increase in the development of knee OA (292). Despite the lack of association between varus thrust and onset of knee OA, there was a significant relationship with the progression of knee OA.

Currently, there are no recommendations for correcting knee malalignment in patients who do not already have knee OA. All research into correcting knee alignment has been performed on patients with knee OA and total knee replacement (TKR). There are two possible solutions for correcting knee malalignment in patients with knee OA. Those experiencing malalignment can either choose to pursue surgical intervention or more conservative approaches. Surgical interventions include high tibial osteotomy and chondral resurfacing, as well as total knee replacement (283). Prior to these surgical interventions, many patients may elect to pursue more conservative options for knee OA management. The two most common forms of knee OA management include knee braces and foot orthotics, which intend to unload or shift the loading away from the medial compartment, which is intended to reduce cartilage deterioration and pain. There have been many studies comparing the effectiveness of knee braces and foot orthoses on reducing knee joint loading (5, 83-85, 92-94, 114, 119, 140, 154, 162, 295). Recent reviews of literature on the effectiveness of knee bracing and foot orthotics conclude that using knee braces to hold the knee more naturally aligned is successful at reducing knee joint pain and external knee adduction moment, which is commonly associated with medial knee loading (17, 188, 240). There is conflicting evidence for the effectiveness of foot orthotics on reducing knee joint pain (17, 344).

Modifiable Risk Factor: Obesity

Chronic overloading of the knee joint due to increased body mass is a likely contributor to knee osteoarthritis development (99). The increasing prevalence of knee OA in recent decades has been strongly associated with the rise in the prevalence of obesity (327). Research on the impact of obesity on the development of knee OA confirms that there is a significant relationship between body mass index (BMI) and knee OA risk (31, 98, 100, 143, 181, 271, 272, 297, 326). A recent cohort study of over 1.7 million participants demonstrated that there is a dose-response relationship between BMI and knee OA risk. In normal weight participants, the incidence rate per 1,000 person-years was 3.7, overweight (BMI 25-<30 kg/m²) participants had an incidence rate of 8.0. This trend continues to dramatically rise in obese participants with grade I obese participants (BMI 30-34 kg/m²) exhibiting an incidence rate of 13.5, and grade II (BMI ≥ 35 kg/m²) participants having a 19.5 incidence rate (257). In addition, this study found that for every one-point increase in BMI, there was significant increases in hazard ratios for incident clinical diagnosis of knee OA for overweight (2.00), grade I obese (3.19), and grade II obese (4.72) participants. These findings are similar to those reported in a meta-analysis by Jiang et al. (141) and Zheng et al. (360) who report for each 5-point increase in BMI, there is a 35% increase in knee OA development.

The presence of a significant relationship between body mass and knee OA development provides a simple solution to modify this risk factor: weight loss. To date, there has been few studies demonstrating the efficacy of weight-loss intervention on reducing knee OA risk (74, 269, 270, 272). Each of these studies demonstrate that a minimum of 5% reduction in weight within the first year of a weight-loss program is needed to significantly reduce incident clinical knee OA by 14% and a 7% reduction in weight is needed to reduce radiographic knee OA

development by 10%. An older study from the Framingham cohort reveals that there is a small, but significant reduction (OR 0.46) in the risk of OA development when weight was lost (101).

The studies on weight loss as an intervention to reduce knee OA risk show that while there are small decreases in OA risk, they are much smaller than the increased risk of developing knee OA with increased BMI. Due to this, it may be crucial for knee OA prevention for increased focus on lifetime prevention of weight gain so that the damage has not already been done by excess weight.

Modifiable Risk Factor: Physical and Occupational Activity

Due to the association with increased loading at the knee joint with the development of knee OA, it is often hypothesized that increased physical activity and certain occupations may lead to increased likelihood of developing knee OA. Due to the capability of physical activity to help improve other modifiable risk factors (i.e. muscle strength and obesity), it is distressing to consider that this intervention may prove to increase the probability of developing the disease that it is intended to prevent.

There is strong evidence that an association between occupational activities and the development of knee OA. Reviews on occupational risk factors for OA conclude that strenuous physical workloads and knee joint stressors strongly influence the development of knee OA. These factors include deep knee bending (such as kneeling or squatting), heavy lifting, and stair climbing (53, 91, 232, 259, 324, 350). Despite the strong evidence for occupational activities and the development on knee OA, conflicting evidence continues to persist in this area.

Allen et al. (6) reported from a cohort of approximately 2,700 participants in the Johnson County Osteoarthritis Project that lifting greater than 10 pounds, crawling, and standing while performing heavy tasks increases the risk of symptomatic knee OA development (OR 1.4-2.1). In

contrast, Gholami et al. (111) showed no significant relationship between occupational tasks of squatting, climbing, kneeling, lifting, and carrying heavy weights and knee OA. Additionally, the review by Verbeek et al. (324) found that there is only a dose-response relationship in the increase in knee OA risk for kneeling (OR 1.26 per 5,000 hours), and no dose-response for lifetime lifting (OR 1.00 per 100,000 kg).

Fortunately, research into the effects of physical activity appear to show that there is minimal risk, if any, in the development of knee OA due to physical activity (169). A recent cohort study from the Osteoarthritis Initiative demonstrated that those who actively participated in moderate to vigorous activity were not at increased risk for incident radiographic (OR 1.52) or symptomatic (OR 1.17) knee OA, or joint space narrowing (OR 0.87), when compared to an inactive population (248). This finding is similar to a previous cohort study by Barbour et al. (20), who found that participants in the highest physical activity group (≥ 300 minutes/week) had non-significantly higher risks for developing knee radiographic (HR 1.62) and symptomatic (HR 1.42) OA. Each of these studies demonstrate a trend towards a potentially detrimental effect of long-term exposure to vigorous exercise. A meta-analysis by Alentorn-Geli et al. (3) found that competitive runners and sedentary individuals experienced a higher prevalence of knee OA (13.3% and 10.2%, respectively) compared to recreational runners (3.5%). This analysis reveals a potential protective effect of recreation running against knee OA development but increased exposure to the more vigorous competitive running may prove to negate this effect. A protective effect of running on knee OA prevention was also found in the meta-analysis by Timmins et al. (314).

Running is not the only sport with potentially detrimental effects. Another review by Driban et al. (82) reviewed the association between participation in sports and knee OA. This

study found that there was no difference in the prevalence in sport participants and controls (OR 1.1). However, significantly higher prevalence was found when considering specific sports. These sports include elite-level long-distance running (OR 3.3), soccer (OR 3.5), competitive weight lifting (OR 6.9), and wrestling (OR 3.8). Additional studies have demonstrated the risk for knee OA development is higher in soccer players (316)

Many of the studies included in these meta-analyses present a similar major limitation within their findings. As previously discussed, there is a significant effect of knee joint injury on the development of knee OA later in life, and many of the studies used in estimating the effect of physical activity and sport participation do not account for the covariate of previous joint injury, skewing the results. Few studies to date have examined the risk for knee OA development due to physical activity while controlling for the history of joint injury. Iosifidis et al. (138) examined clinical and radiographic OA in former elite male athletes that did not have any history of lower extremity injury. They found that there was a significantly higher prevalence for radiographic knee OA in the former athletes (36.6%), compared to the control group (23.9%). However, no difference in clinical knee OA was found between groups. Further, this study found that former soccer players had the highest prevalence of radiographic knee OA (37%) compared to athletes who competed in skiing (13%), volleyball (4%), martial arts (3%), track and field (2%), and basketball (3%) (138). Due to a lack of participants in individual sports, however, it was not possible to determine significant differences in the risk for OA development between activities. An additional study by Fernandes et al. (105) found that former soccer players had an adjusted risk ratio of 2.21 compared to controls, when adjusting for injury.

Despite the possibility of a moderately increased risk for OA development due to physical activity, it is recommended that all people maintain an active lifestyle to avoid the risks

associated with a sedentary lifestyle (i.e. obesity and muscle weakness). Further, the risk for OA development due to physical activity remain lower than those associated with joint injury and obesity (325). Future research on the impact of occupational or recreational physical activity on the development of knee OA should either exclude participants with previous knee joint injury or use statistical control to mitigate the effects of injury on the results.

Epidemiology of TKR

As previously discussed, the development of OA may be unavoidable to many people. To alleviate daily pain, improve knee joint range of motion (ROM), joint alignment, and reduce daily activity limitations, individuals with knee OA may elect for joint replacement surgery known as either total knee arthroplasty (TKA) or TKR (45, 330, 357). In 2010, the prevalence of people living with knee replacement was 1.52% (4.7 million), with over 700,000 TKR surgeries performed in the U.S. that year (70, 195). This number is expected to grow by 673% to 3.5 million per year by 2030 (161). Due to the high number of individuals with TKRs, and the expected growth in surgeries performed, it is important to understand how these surgeries effect the patients gait biomechanics.

To evaluate individual patient outcomes, the Knee Society Knee Scoring System uses objective (alignment, stability, ROM, and pain) and subjective (satisfaction, expectations, functional capacity, an awareness of the replacement) data from TKR patients both pre- and post-op (284). Pain is decreased, and ROM is increased following TKR surgery (47, 123, 157). This is likely the reason behind high satisfaction rates of TKR patients (102, 334). However, some patients may still report post-operative knee pain, as well as limitations to functional capacity (28, 222); such as reduced outcomes in clinical tests (timed up-and-go, six-minute walk, and sit-to-stand) compared to healthy control groups (34, 230). Overall, however, TKR

procedures greatly reduce pain (a reported 90-95% reduction in pain), have very low complication rates (1-2%), and continue to have high satisfaction rates years following surgery (54, 171).

As previously discussed, many TKR patients will need the contralateral knee replaced. Three studies have found that unilateral TKR patients have a 10-year risk of secondary TKA on the contralateral limb of 37.2% to 46% (203, 279, 291). The reason for this high risk for contralateral replacement may be due to altered knee joint loading in the non-operated limb. Milner and O'bryan (211) found that loading-response peak KAbM was significantly higher in the non-operated limb 28 months following surgery compared to the TKR limb and healthy controls. This is similar to findings by Metcalfe et al. (205), who found that abnormal loading of the contralateral limb was present 12 months following TKR. However, Debbi et al. (75) found that at six weeks following TKR, there was no differences in KAbM between the contralateral limb and healthy controls. Alnahdi et al. (8) also found similar KAbM between the contralateral limb and healthy controls at six months and one year following TKR. However, the authors stipulate that the decreased stride length and slower walking speed of TKR patients may lead to the knee being loaded more repetitively than healthy controls, and this may lead to faster joint deterioration.

Effects of Knee Osteoarthritis during Level Walking

In order to show deviations from the healthy population, patients with knee OA often have their gait biomechanics examined. These examinations often involve measures of spatio-temporal (cadence, stride length, step width, speed, single/double support time), kinematic (ROM, peak joint angles), and kinetic (ground reaction forces (GRF), joint moments) data. For

the purpose of this review, changes in knee joint kinematics and kinetics will be the primary focus.

Changes in Spatio-temporal Parameters

Measures of spatio-temporal parameters require the least amount of equipment and can be evaluated in both clinical and research environments (such as gait labs). These characteristics are key in beginning to understand the impact of this disease on the patients. Previous research has found that many of these parameters are affected in patients with severe knee OA (13, 63, 131, 135, 274, 311, 332, 352, 355).

Measuring gait speed is one of the simplest measurements of movement and can be performed clinically with a simple stop watch and recording the time it takes for a patient to walk a pre-defined distance. There patients with severe knee OA tend to walk significantly slower than healthy controls, however the actual speed of gait of severe knee OA patients varies between studies and typically falls between 0.84 m/s and 1.22 m/s (2, 13, 36, 52, 156, 190, 228, 278, 311, 352). This difference appears to only be present between severe knee OA patients and healthy controls, as research has often found that patients with less severe knee OA (243), and when all KL grades of knee OA are included (48, 124, 172), patients tend to have more similar walking speeds to healthy controls. In addition to a decrease in walking speed, knee OA patients tend to exhibit decreased stride length (0.75 to 1.18 m) (2, 13, 120, 160, 190, 311), and increased double (Healthy 0.26, knee OA 0.28-0.36) and single-limb support times (Healthy 0.39-0.67s, knee OA 0.41-0.85s) (13, 311), and stance phase percentage (Healthy 63%, knee OA 65%) (13, 311).

A kinematical analysis of gait is important in the understanding how the body is moving in space. For patients with knee OA, this type of analysis is critical in evaluation of the

deterioration of the patient's movement capacities and ability to perform common activities of daily living. When evaluating the motion of knee OA patients, both the sagittal and frontal planes should be considered; with some of the most important/clinically relevant measures being knee joint ROM, peak joint angles (flexion/abduction), and joint angles at heel contact (13, 19, 21, 49, 71, 77, 113, 156, 196, 207, 250, 323, 332, 351).

Sagittal Plane Kinematics

During over ground walking, patients with knee OA exhibit many kinematic differences from healthy participants (207, 323). These altered kinematics, like the spatio-temporal changes, tend to become more evident with increasing OA severity. The most commonly reported differences are decreased knee flexion ROM during both stance and swing phases, peak knee flexion, as well as knee flexion at heel strike (21, 156). Due to the tendency of knee OA patients to have a slower preferred walking speed, as previously discussed, when knee OA patients are required to walk at a faster pace, issues with knee ROM may be exacerbated. Two studies from Bejek et al. (21) and Ko et al. (156) found that as walking speed increased, OA patients experienced less knee flexion ROM than the healthy controls, signifying that they were unable to successively perform the motion properly because they are likely taking shorter steps and using less knee extension in order to keep up the required speed.

Many studies to date have confirmed that knee OA patients have significantly lower knee joint ROM (13, 19, 49, 71, 77, 113, 156, 196, 250, 332, 351). These studies show that healthy participants tend to walk on level ground with a knee flexion ROM between 56°(351) and 69°(13), while knee OA patients having ROM between 30° (351) and 59° (19). Moderate and severe OA patients have the smallest knee ROM ,from 30° (351) to 42° (250), compared to mild knee OA patients and healthy controls. Despite the large number of studies supporting decreased

ROM, not all studies have demonstrated this difference from healthy controls (310). The study by Tadano et al. (310) may have come to an opposing conclusion due to the wearable sensor system used, or due to the severity of the studied knees. In this study, there was one K/L grade I and II, 10 K/L grade III, and one K/L grade IV. Further, this study included patients with bilateral knee OA.

In addition to lower ROM, knee OA patients tend to also have lower peak knee flexion angles (13, 21, 49, 332); however, Balinus et al. (19) found that there was no differences between healthy controls (63°) and knee OA patients (59°). This again, is likely a difference in OA severity, as a study that investigated only patients which were diagnosed with severe knee OA (i.e. K/L grade IV) (13) found that there was a difference when only these types of patients were compared to healthy controls (healthy: 64° , severe knee OA: 45.9°). In addition to lower peak flexion, knee OA patients may also exhibit decreased peak knee extension (21, 49, 332) and knee flexion angle at heel strike (215, 351); however, these findings are less prevalent and have conflicting results (268, 310).

Frontal Plane Kinematics

Joint motion in the frontal plane is highly important to the study of knee osteoarthritis. This is because the development (31, 68) and progression (58) of medial compartment knee OA is strongly correlated with the internal KAbM (19, 31, 99, 136, 213, 359). The primary motions of interest in the frontal plane are abduction ROM, peak ab/adduction, and abduction at heel strike. The frontal plane motion of the knee is also important in determining the stability of the knee joint, as well as the length of the frontal plane moment arm and, therefore, KAbM.

Although many studies focus on sagittal plane motions and frontal plane moments, less studies provide information regarding frontal plane kinematics. Additionally, there are

conflicting results regarding this plane of motion, which may be due to the difficulty in accurately capturing the small motion that occurs in this plane. A more commonly reported characteristic of knee OA patients is the peak knee adduction angle. Peak knee adduction for healthy participants tends to range from 1.1° (48) to 5.3° (351). For knee OA patients, however, this peak angle appears to depend on not only the severity of OA (351), but the location of OA. Overall, patients with knee OA tend to have more adducted knees while walking over level ground (49, 57, 216); however, patients with medial knee OA appear to have more adducted knees with ranges from 5.6° (48, 49) to 12° (332), while lateral compartment knee OA tend to have more abducted knees with ranges from -2.3° to -6° (48, 332, 351). Weidow et al. (332) gives stronger evidence for this as they reported peak knee abduction angles in healthy controls (-3°), medial compartment knee OA patients (5°), and lateral knee OA patients (-11). These differences in peak frontal plane motion of the knee may be due to the varus alignment commonly reported in medial compartment knee OA patients (48).

Unlike peak knee adduction, frontal plane knee angle at heel contact and frontal knee ROM are reported less often, with more conflicting results. At contact, two studies found that healthy controls had an abduction angle of -0.83° (268) and -0.4° , while OA patients contacted with an adduction angle of 4.83° (268) and 5.7° (49). However, two studies found that severe OA patients were more abducted (-0.5° to -3.2°) than the healthy participants (1.7° to 0.6°) at heel strike (135, 351). Additionally, there are conflicting results on the differences between knee joint ab/adduction ROM. Zeng et al. (351) found that severe knee OA patients had significantly less abduction ROM (5.4°) compared to the healthy controls (9°), while Bytyqi et al. (49) found that knee OA patients had greater (non-significant) ROM.

In order to produce a more thorough examination of a gait profile of a participant, kinetics are typically also collected, calculated, and reported simultaneously with kinematics. This data is helpful to provide loading within joints, which is often reported and presented as joint moments. A joint moment is calculated via an inverse dynamics approach, and tends to cause rotation about the axis in the direction of the GRF vector. Joint moments are typically expressed as internal or external. These two moments are typically described as an inverse of each other; however, this can be deceptive, as the external moments are moments caused by external forces such as GRF, while internal moments are representative of the moments generated via internal muscle forces. While many studies in the OA literature report external moments, other studies tend to discuss internal moments. Additionally, moments may be reported as their default value (Nm) or normalized body mass (BM), giving resultant moments in units of Nm/kg, or by BM and height (Nm/kgm). Therefore, it is important that studies provide a description of the type of moment (internal versus external) and type of normalization being described in the study.

Changes in Sagittal Plane Knee Kinetics

An interesting study by Shafizadegan et al. (290) investigated the level of knee OA severity (using KL grades to define severity) on loading-response and push-off antero-posterior (AP1 and AP2) and loading-response and push-off vertical (VP1 and VP2) GRFs during level walking. AP1 was significantly lower in OA patients, but did not change with severity. However, AP2 was significantly lower in moderate (KL grade 3) and severe OA (KL grade 4) patients compared to mild (KL grade 2) OA patients; all OA patients had lower AP2 peak than healthy controls. Additionally, the VP2 was significantly lower in OA patients, but did not change with severity. Decreased push-off vertical GRF and impulse in knee OA patients (average KL grade

2.5) was also found by Wiik et al. (336). This study also found that this peak was highly asymmetrical when the healthy contralateral limb was considered. Peak external knee flexion moment (interchangeably: internal KEM) is an important characteristic in all biomechanical studies, and especially so in osteoarthritic studies. Recent work has established that the internal KEM is important in the progression of knee OA (62, 89, 317, 328). The importance of the internal KEM in the development and progression of knee OA is due to its influence on loading to the knee joint. Walter et al. (328) and Manal et al. (189) found that loading in the medial compartment is more accurately predicted by the inclusion of both the KAbM and internal KEM.

Zeni and Higginson (353) found that patients with knee OA have a tendency to rely less on the knee and more on the ankle when walking across level ground. By calculating the “total support moment” (summation of ankle, knee, and hip sagittal plane moments), they found that the OA group was unable to produce an equivalent total support moment at faster walking speeds, indicating an inability to perform the action as well as the controls participants. Individual joint contributions were lower in the knee for the OA group (32%) compared to the control group (51%); however, the knee OA group had significantly more ankle contribution (45%) than the healthy control group (25%). This decrease in peak knee external flexion (internal extension) moments during level walking has been previously established (13, 71, 77, 96, 113, 131, 164, 332). However, this difference may not always be present (19, 146, 280, 281). Reports of this variable indicate that patients with OA tend to have a peak flexion moment of 0.33 Nm/kg (13, 332), while healthy controls tend to have higher moments of approximately 0.55 Nm/kg (13, 332).

While this peak extension moment tends to happen during midstance, both healthy controls and knee OA patients tend to have internal KEMs at heel strike. Favre et al. (96) found

that severe knee OA patients also had a significantly lower peak internal knee flexion moments at heel strike (-1.8 %BW*Height) compared to healthy controls (-2.8 %BW*Height) and at terminal stance in OA patients (-1.5 %BW*Height) compared to healthy controls (-2.8 %BW*Height). It should be noted that these moments at heel strike are minimal and may not influence deterioration of the knee joint.

Peak internal KEMs may differ between severity of knee OA (13, 215). This may be due to gait modifications of patients with more severe knee OA. Previous studies have suggested that the peak knee flexion moment is inversely correlated with knee pain (89, 137, 282). Erhart-Hledik et al. (89) and Chehab et al. (61) independently found that the knee flexion moment is strongly associated with the deterioration of tibial cartilage, and that this primarily occurs in the early stages of knee OA. The primary driver for cartilage loss throughout early and late stage knee OA is the KAbM.

Changes in Frontal Plane Knee Kinetics

The KAbM has been undeniably the strongest focus of biomechanical studies on knee OA. There have been numerous reports on the moment's correlation with the development and progression of medial compartment knee OA (31, 68). This is because dynamic loading of the medial compartment (KAbM impulse) is strongly associated with the loss of cartilage in the knee joint (24, 147). Despite the evidence supporting this correlation, Kutzner et al. (163) has found that this correlation can vary widely between patients from very low ($R^2 = 0.09$) to very high ($R^2 = 0.90$), with an average moderate correlation of $R^2 = 0.56$. This correlation was stronger during earlier stance ($R^2 = 0.76$) than during late stance ($R^2 = 0.51$). This between-subject variability was also confirmed by Trepczynski et al. (317) during a variety of different movements including over ground walking, stair ascent and descent, and squatting. These studies confirm the

findings of Walter et al. (328) that decreased knee adduction moment may not guarantee a decreased medial compartment load, and the knee flexion moment should also be considered.

The general consensus for the relationship between peak KAbM and knee OA shows that patients with knee OA tend to have higher peak KAbM throughout the gait cycle, compared to healthy controls (13, 19, 48, 77, 113, 164, 215, 332). However, not all studies have found that OA patients exhibit higher peak KAbM (71, 135, 274). A lack of evidence may be due to the location of the OA in the knee joint. Butler et al. (48) and Weidow et al. (332) found that patients with medial compartment knee OA had significantly higher peak KAbM, ranging from -0.42 Nm/kg (48) to -0.70 Nm/kg (332), compared to healthy controls (-0.326 Nm/kg to -0.46 Nm/kg); healthy controls were significantly higher than KAbM of patients with lateral compartment knee OA (-0.193 Nm/kg to -0.17 Nm/kg).

In addition to the impact of location of the OA in the knee joint, the severity of the OA also effects the level of KAbM. Mundermann et al. (215) found that patients with severe knee OA had 11.4% higher loading-response KAbM than the healthy controls and 27.9% higher than patients with less severe knee OA. Additionally, patients with more severe knee OA had a 37.8% higher push-off response second peak KAbM than less severe OA patients. Increased peak KAbM compared to moderate knee OA patients was also confirmed by Astephen et al. (13). Loading-response and push-off peak KAbM have also been confirmed in patients with medial compartment knee OA K/L grade 2 or higher compared to healthy controls (281, 288).

Changes in EMG Activity with Knee OA

Electromyography (EMG) is an additional tool for analyzing human movement. EMG data is collected by either surface (most common) or imbedded electrodes. These electrodes measure the electrical activity within the neuromuscular pathway leading to the contraction of

the muscle. This is important because it enables us to develop an understanding of how muscles are being activated to produce a movement. Additionally, the force developed by these muscles (i.e. hamstrings, quadriceps, gastrocnemius) may influence the loading on the knee joint (183, 338, 339). Winby et al. (338) researched the impact of a generalized co-activation of the hamstrings and quadriceps (HQ), as well as specific co-activations (vastus medialis and medial hamstrings, VMMH) that may potentially increase the load in the medial compartment, as well as medial gastrocnemius and vastus medialis (VMMG). Additionally, specific co-activations for loading the lateral compartment were the vastus lateralis and lateral hamstrings (VLLH), as well as the vastus lateralis and lateral gastrocnemius (VLLG). This study found that HQ, VLLH, and VLLG were significantly correlated with the peak lateral knee joint contact force. However, no co-activations were significantly correlated with increased medial knee loading. The authors stated that due to the low correlations, additional variables, such as KAbM, should be used in conjunction with estimations of knee joint loading.

When reviewing studies involving EMG on knee OA patients, most studies focus on one (or more) of three areas in EMG: muscle co-contraction index (CCI), muscle amplitude, and muscle activity duration (208). Muscle co-contraction is a measurement of the simultaneous recruitment of synergistic muscles (298). The CCI estimates the relative recruitment of synergistic muscles as well as the magnitude of co-contraction, where lower and higher EMG indicates the less and more active EMG signals which were linear enveloped and MVIC normalized EMG (349). Muscle amplitude measurements refer to the peak height/magnitude of the EMG signal and is often reported as a percent of the maximum voluntary contraction (%MVIC), while muscle activity duration is a measurement of the duration of the onset to offset of the EMG activity.

Changes in CCI in Knee OA Patients

The CCI of the tibialis anterior (TA) and the medial (MG) or lateral (LG) gastrocnemius (TA:MG, TA:LG), while not commonly reported in knee OA literature, may be an important index that needs further investigation. Two studies found that knee OA patients had a significantly higher CCI between these muscles during gait, and that these values were between 9.0% (65) to 40% (128) higher than this CCI in the healthy controls. Altered muscle activation during gait may alter loading within the knee joint, potentially furthering progression of knee OA (128) .

The co-contraction of the lateral gastrocnemius and vastus lateralis (VL) is a commonly reported (LG:VL or VL:LG). When considering patients with moderate knee OA, three separate studies found that this CCI was not different than healthy controls (175, 176, 268). However, in patients with mild knee OA Schmitt and Rudolph (281) found that during the weight acceptance phase, patients had higher VL:LG CCI than healthy controls. Additionally, Hubley-Kozey et al. (134) found that patient with severe knee OA exhibited a 9.57 %MVIC higher VL:LG CCI than healthy controls, while patients with moderate knee OA did not exhibit this difference. This study theorized that the differences found in severe knee OA patients may be due to reduced strength of the hamstrings, quadriceps, and plantar flexors of these patients, while moderate knee OA patients did not have decreased muscle strength. This decreased strength may lead to an increase in EMG activity due to an increased need for muscle recruitment.

Another common CCI is between the vastus lateralis and bicep femoris (BF). When comparing general knee OA patients (any severity), the healthy controls had a CCI that was between 13 %MVIC (65) and 41 %MVIC (128). Several studied found that there was no difference in VL:BF CCI in patients with mild (281) and moderate (175, 176, 268) knee OA.

This CCI may be dependent on increased severity of knee OA. However, one study found that patients with severe knee OA had a significantly higher (23.5 %MVIC) VL:BF CCI than healthy controls, and 13.3% higher than patients with moderate knee OA (134).

A third CCI involving the vastus lateralis is with the semimembranosus (SM). A study by Zeni et al (356) compared this CCI in moderate and severe knee OA patients with healthy controls during walking at 1 m/s, preferred walking speed, and as fast as comfortable. At 1.0 m/s, both moderate and severe knee OA patients had a significantly higher VL:SM CCI (12.4 %MVIC and 11.5 %MVIC higher, respectively) than the healthy controls; the two knee OA groups were not different. At preferred walking speed and at fast walking speeds, the moderate knee OA patients continued to have a higher CCI than healthy controls, but severe OA patients were not different. This may be due to differences in the severe OA patients walking speed at the self-selected (1.05 m/s) and fast walking (1.4 m/s) compared to healthy controls (1.25 m/s and 1.75 m/s, respectively).

The semimembranosus is also involved in a CCI with the vastus medialis (VM:SM). Similar to other CCIs, there is conflicting evidence on the influence on knee OA on this CCI. Multiple reports have suggested that there is no difference between patients with moderate knee OA and healthy controls (134, 175, 176, 268). However, when comparing severe OA patients to healthy controls, Hubley-Kozey et al. (134) found that severe OA patients had a significantly higher (7.6 %MVIC) CCI.

The final CCI that is commonly used in knee OA literature is the vastus medialis and medial gastrocnemius (VM:MG). This CCI, like others, has conflicting reports. Two studies by Lewek et al. (175, 176) found that patients with moderate knee OA had significantly higher VM:ML CCI compared to healthy controls. However, three studies found that there were no

differences between either moderate (134, 268) or mild (281) knee OA patients and healthy controls. One of these studies (134) found that severe knee OA patients did have higher CCI.

Heiden et al. (124) examined CCIs that combined many muscles together. Their first CCI was lateral muscles to medial muscles (SM, VM, MG:BF, VL, LG) and found that patients with knee OA had greater CCI during loading and early stance phases, and that the lateral muscle activation was dominant. This increased lateral muscle activation may lead to increased KAbM (124). Additionally, this study found that knee extensor and flexor CCI also exhibited greater CCI during midstance, while the medial:lateral CCI was significantly less during midstance, compared to the rest of the stance phase.

Changes in EMG Amplitude in Knee OA Patients

In addition to CCI, many studies also report the amplitude of the EMG signal in %MVIC. There are many conflicting reports of EMG amplitudes in knee OA patients. The muscles of interest are the same as the muscles reported in CCI studies: MG/LG, BF, SM, VM/VL, , and rectus femoris (RF). Many of these studies also focus on how the EMG activity changes during different phases of the gait cycle. These phases include early stance (loading response) midstance, late stance (push-off), and swing.

Throughout stance, the mean EMG value for the RF tends to be significantly different in patients with knee OA than in healthy controls (14, 133). In patients with severe knee OA, the rectus femoris EMG amplitude tends to be lower in early and late state, but higher in mid-stance, compared to healthy controls (14). The presence of altered EMG patterns and magnitudes may be due to decreased muscle strength, therefore requiring increased muscle activation. Further, increased muscle activation during mid-stance may be a response to pain within the joint (14, 133, 175).

The VL has conflicting reports on differences between knee OA patients and healthy controls. Two studies found that there were no differences between these groups (14, 268). However, two other studies found that knee OA patients had a 47 % higher EMG amplitude, compared to controls, when averaged throughout stance phase (128, 281). This conflict of results may be indicative of differences in the disease severity. Zeni et al. (356) found that at 1 m/s, moderate knee OA patients had higher mean and peak VL activity, compared to healthy controls. However, no differences were found between severity groups, or at self-selected and fast walking speeds. This may be due to significantly slower walking speeds for the knee OA patients compared to the controls.

Similar to the VL, the VM has conflicting evidence for knee OA studies. EMG activity in the vastus medialis during level ground walking may not be different between groups during stance (14, 133, 268). However, two studies found that VM EMG amplitude is significantly lower during late stance and early swing at various walking speeds, compared to healthy controls (179). In contrast, during weight acceptance and midstance, the VM tends to exhibit higher activity in OA patients, compared to healthy controls (281).

There are fewer contrasting results regarding knee OA and biceps femoris activation. Despite disease severity, most studies confirm that the mean EMG activity of BF is higher in knee OA patients than healthy controls, and that this difference can be as high as 47% (14, 128, 133, 179, 281). However, one study did not find this difference (268).

Rudolph et al. (268) also found no differences in SM EMG amplitude between healthy controls and knee OA patients. However, like the VL, there is an influence of disease severity that may confound the results. The effects of severity on SM activation, however, is also conflicting. Astephen et al. (14) found that severe knee OA patients tended to exhibit higher

activation throughout the gait cycle compared to healthy controls. Zeni et al. (356) found that the SM had a significantly higher peak SM activation in moderate (35.6%) and severe (36.6%) knee OA patients, compared to controls (19.1%). However, at faster walking speeds, these differences disappeared.

When combining all of the aforementioned muscles together, Heiden et al. (124) found that patients with knee OA tend to exhibit higher net muscle activation during early stance (weight acceptance) periods than the healthy controls. Overall, the trend for knee OA patients is higher muscle activation during the loading phase, and lower muscle activation during the push-off phase, although muscle-by-muscle differences exist.

The amplitude of gastrocnemius EMG activity is one of the less commonly reported variables, in comparison to hamstring and quadriceps muscles. When averaged over the whole gait cycle, two studies found conflicting evidence for differences in mean MG amplitude, with reports of both higher (268) or lower (133) in moderate knee OA patients compared to healthy controls. This conflicting evidence may be due to changes in gastrocnemius activation from early to late stance. Patients with moderate knee OA had smaller changes in activation from early stance to late stance than healthy controls (275, 276). However, patients with severe knee OA had significant reductions in activation from early to late stance (276). These significant reduction in gastrocnemius activation for severe OA patients, but not moderate OA patients may be due to increased medial gastrocnemius activity during early stance and decreased activity during late stance, compared to the moderate OA patients (14). Due to increased activity in early stance, and decreased activity during late stance, when the EMG activity of the MG is averaged over stance phase, differences may not be evident.

Changes in EMG Duration and Onset/Offset Latency in Knee OA Patients

The length of duration of an active EMG signal is reported less often than CCI and amplitude. Similar to CCI and EMG amplitude, reports on EMG signal duration tends to include conflicting results. For the gastrocnemius, Hubly-Kozey et al. (133) and Rutherford et al. (275) found that there were no differences between moderate knee OA patients and healthy controls. Childs et al. (65) found that the MG was activated for 140 ms longer in OA patients than in healthy controls.

In addition to differences in MG duration of EMG activity, there are also differences reported for the time in which the EMG activity initiates. For severe knee OA patients, Astephen et al. (14) concluded that severe OA patients had active MG throughout most of the gait cycle, while the MG of moderate OA patients and healthy controls were not active until later in stance. This is in contrast to Rutherford et al. (276) who found that patients with severe knee OA had a significantly later activation of the gastrocnemius in stance than moderate OA and healthy controls.

For the quadriceps, two studies found that the vastus lateralis was activated for significantly longer (from late swing into early stance) in OA patients compared to healthy controls (65, 133). However, one study found that there was no differences (275). The biceps femoris and semimembranosus may also have prolonged activity compared to healthy controls (65, 133, 275).

Further, the quadriceps, hamstrings, and TA may begin activation earlier in swing phase, and remain active later in stance phase in knee OA patients. Similar to the previous discussion on the increased EMG amplitude in knee OA patients, this increase in the duration of muscle activation may be due to a decrease in muscular strength, as well as an attempt to increase the

stability of the knee joint due to increased joint laxity in knee OA patients. Further, decreased walking speeds and extended stance duration may contribute to the increased duration of EMG activity.

Effects of TKR on Biomechanical Variables during Level Walking

Knee OA reduces patients' quality of life and their ability to perform activities of daily living, many patients undergo TKR. Improved knee biomechanics is associated with improved quality of life of patients reporting good outcomes (218). The purpose of this review is to examine the biomechanical variables of patients during early recovery (before 12 months) from TKR. It is important to understand how well the TKR can return patients to healthy temporal-spatial, kinematic, and kinetic characteristics, and how quickly the patient can return to a quality of life that is equivalent to healthy controls.

Temporal-Spatial Variables

Gait speed is an indicator of mortality aging from 65-95, with significantly lower survival rates indicated for every 0.1 m/s decrease in gait speed (309), and, therefore, is a very important biomechanical characteristic to examine. Research suggests that deficits in function are common in the first months following surgery (8, 59, 167, 230, 342). A large study of 1765 TKR patients examined gait speed, at 4, 8, 12, and 16 weeks post-TKA, that was "as fast as comfortable." This study found that there was a large improvement in fast gait speed from 4 weeks (0.86 m/s) to 8 weeks (1.06 m/s), and these improvements continued through weeks 12 (1.14 m/s) and 16 (1.16 m/s) (247).

When comparing TKR patients to pre-TKR levels, the first two months following surgery yields conflicting evidence on gait speed. One study found that at as early as one month following TKR, patients had no significant difference in gait speed compared to pre-surgery

speed (59). Some patients may begin to see improvements as early as two months in their gait speed from pre-operation. Wegrzyn et al. (331) found that patients improved from a gait speed of 0.85 m/s to 0.97 m/s by the two-month follow up. However, the rate of improvement of gait speed may be patient specific, as Ouellet et al. (230) found a 0.2 m/s decrease in gait speed at two months, compared to pre-operation. Further evidence suggests that by three months post TKR, patients may match or surpass pre-operative speed (178, 345). By six months, patients tend to show significant improvement from pre-TKR speed (0.89 m/s) to 1.05 m/s, however, this is still slower than healthy controls (190). This trend continues at nine months following TKR, as patients see significant improvements in their walking speed from pre-operative measures (11, 320). Despite these improvements over time, many patients are still unable to walk at speeds similar to healthy controls (55).

Gait speed can easily be broken down into two components: stride length and stride frequency. Stride length is a measurement of the distance covered between ipsilateral heel contacts during gait, while stride frequency is the number of strides taken in one minute. Due to their relation to gait speed, it is expected that these variables may increase. However, there are conflicting reports of the progress of stride length following TKR. At one month after TKR, Chang et al. (59) found that the patients had a significant increase in stride length of 0.08 m. Similar to walking speed, Oulett et al. (230) found that patients had a 0.2 m decrease in stride length, while Wegrzyn et al. (331) found that patients significantly increased their stride length by 0.12 m. Two studies found no differences between pre- and post-operative stride lengths at three months (178, 345). At six months, Mandeville et al. (190) found that patients had a 0.11 m increase in stride length from pre-operative levels, but was still shorter than healthy controls.

This trend continues at nine months post-operation (11, 320), however patients still have significantly shorter stride lengths.

Stride frequency (or cadence), like speed and stride length, varies between studies and appears to be patient specific. At one month post-TKR, there was no difference in cadence compared to pre-surgery (59). . Two months following surgery, cadence was reduced in one study (85 steps/minute) compared to pre-surgery status (95 steps/minute) (230). However, another study showed a 4 step/min increase at two months (331). This may be due to the large difference in walking speed and cadence in the studies at both pre- (110 steps/min vs 31.8 steps/min) and post-surgery (85 steps/min vs 35.7 steps/min). Xu et al. (345) found no differences in cadence at three months following surgery. . At nine months post-operation, Apostolopoulos et al. (11) found that cadence increased from 99.3 steps/min to 110.5 steps/min.

These temporal-spatial disparities between healthy control participants and TKR patients demonstrates the need for improved TKR design, surgery, and rehabilitation techniques in order to provide the patients with an improved quality of life, and a return to normal function. While these patients may never be able to return to high impact movements, improving these variables may lead to improved quality of life and survivability. More advanced measurements, such as ground reaction force (GRF) may provide further insights to the influence of TKR on gait.

Ground Reaction Force

When an individual applies force onto the ground during gait, the ground exerts a reaction force (GRF) equal and opposite in nature. This GRF is a useful tool in measuring external loads (in Newtons) acting on the body. To compare these forces across different participants of different body weights, this variable is typically normalized to body weight (BW). Additionally, GRF is used to calculate the loading rate (N/s, BW/s), which described how

quickly this force is applied to the body. Peak vertical GRF (vGRF) and loading rate are reportedly similar between limbs of unilateral TKR patients from four to ninety-six months post-operation (211). Heterogeneous sampling in this study (different surgeons, different replacement types, and different times post-operation) may skew results.

Following TKR surgery, vGRF may increase compared to pre-operative levels (38). This increase in vGRF is not a surprising result, due to increased walking speed after surgery. As gait speed increases, there is a linear increase in vGRF (149). At three months post-operation, Yoshida et al. (348) found that TKR patients had significantly lower vGRF than healthy controls, and that this difference no longer existed by 12 months. Understanding the role of GRF in knee joint loading is essential to fully understand the impact of a TKR on gait biomechanics.

Nagura et al. (217) found that patients between one and four months can be divided into two groups: high KAbM and normal KAbM. They found that there was no difference in walking speed or vGRF between the groups. However, they did find that patients with significantly higher toe-out angle (6.4° higher) generated 2.2 %BW larger medio-lateral GRF.

Sagittal Plane Kinematics

The influence of TKR on the motion of the knee, such as maximum stance and swing phase knee flexion, and knee flexion range of motion (ROM), are important to develop an understanding of how successful the surgery was in restoring knee function. Passive ROM, a clinically important measurement, describes how much movement (flexion/extension) the knee can endure with the guidance of a clinician, and without muscular activation of the patient. This measurement allows for analyses of the patient's progression as the joint heals and physical therapy is pursued.

Pua et al. (247) examined how passive ROM changes over the first 16 weeks post-operation. This study found that at four weeks following surgery, patients could only pass through 105° of knee flexion. This passive ROM increased over the following weeks. At eight weeks, patients could be passively flexed 110°; by weeks 12 and 16, patients were able to be moved through 115° and 113° of knee flexion, respectively. At six months, there are differences in the passive ROM of TKR patients, compared to healthy controls. Benedetti et al. (23) found that patients still only had 104° of flexion ROM, while patients reported by Alnahdi et al (8) had a flexion ROM of 118° on average. Despite this increase in passive ROM during the first 6 months following TKR, patients do not reach healthy levels of ROM (134°) (8).

Another commonly reported change in knee motion following TKR is knee flexion ROM during gait. Knee flexion ROM in gait is often reported as either the amount of knee flexion from initial contact to loading-response peak knee flexion, or as the difference between maximum knee flexion and maximum knee extension during the gait cycle. Unless the phase of gait is noted, the following studies discuss the latter. At one month post-operation, Chang et al. (59) found that patients already exhibited greater flexion ROM (46.3°) compared to pre-operation (37.5°). At three months post-op, Bejek et al. (22) found that flexion ROM was higher than pre-operative values; however, at three months post-op TKR patients have significantly lower flexion ROM than healthy controls (167). However, at four (174) and six (228) months, two studies found that there was no difference from pre-TKR ROM. At nine months, however, Urwin et al. (320) found that TKR patients had increased flexion ROM (49.5°) compared to pre-TKR (41.9°). However, this total ROM was still significantly less than healthy controls (58°). Bonnefoy-Mazure et al. (33) found that the knee ROM was significantly improved at one year

post-operation (47.5°) compared to three months post-operation (42.2°) and pre-operation (44.2°).

Peak knee flexion angle during swing and stance are also commonly reported. Although no comparisons were available for prior to surgery, Wu et al. (342) found that patients had a peak knee flexion of 39.4° during swing phase, and 14.7° during midstance. This is similar to the 35° found at two months post-TKR by Ouellet et al. (230), which was significantly less than the peak knee flexion angle pre-TKR (44°) and healthy controls (47°). Peak swing phase knee flexion angle appears to increase by three months (22), however there are conflicting reports (178). Also at three months, Xu et al. (345) found significant increases in stance phase peak knee flexion (21.1°), compared to pre-TKR (11.5). Two studies found no differences in peak knee flexion at four months (174) or six months (190). At nine months, swing phase peak flexion angle was significantly higher (64.0°) than pre-TKR (54.8°), as was similar to healthy controls (64.2°) (320).

It is expected that these changes in knee motion are undertaken by TKR patients in a quadriceps avoidance pattern (i.e. avoidance of knee flexion) to reduce the load experienced on the knee (209). This avoidance gait may be associated with a kinesiophobia due to a pain-related fear of the movement task (106). While this gait pattern (decreased ROM and/or peak knee angles) may be acceptable for the patients so that they can accomplish a simple gait task, such as walking, more dynamic and challenging tasks may prove difficult. If a patient avoids quadricep usage, and they become weak, this will become a problem when trying to use stairs, perform a deep knee bend (squat), and will reduce knee stability.

Sagittal Plane Kinetics

Peak external KEM, which produces knee extension and resists knee flexion, is reported as being smaller in TKR patients (167). These differences have been reported as reductions of 0.16 Nm/kg (230) and 2.2 %BW*height (23). The loading-response peak internal KEM has been reported as 0.09 Nm/kg (301) and 1.9 %BW*height (191) higher in healthy controls, compared to TKR patients, during level walking.

Similar to kinematic variables, changes in sagittal plane knee moments vary with time post-TKR, with the largest differences occurring within the first few months after surgery. At two months post-operation, TKR patients exhibited a peak internal KEM of 0.18 Nm/kg (pre-TKR: 0.22 Nm/kg), while healthy controls were producing moments of 0.34 Nm/kg (230). Additionally, Ouellet et al. (230) also found that the internal KEM was significantly smaller at two months (0.13 Nm/kg) compared to pre-TKR (0.33 Nm/Kg) and healthy controls (0.44 Nm/kg). At three months, conflicting reports suggest that changes in extension and flexion moment may be patient specific. Lee et al. (167) found that patients had similar peak internal KEMs compared to healthy controls, but smaller peak internal knee flexion moments. A lack of difference between internal KEM may be due to similar increases in this moment found by Xu et al. (345) from pre-TKR to three months post-operation. However, like Ouellet et al. (230), Vahtrik et al. (321) found a non-significant decrease in the knee flexion moment at three months. By four months, Levinger et al. (174) began seeing a trend towards increased peak internal KEM. Two studies found that by six months post-TKR, patients exhibited increased internal KEMs, however, these were still smaller than healthy controls (190, 321). One study found no change from pre-TKR at six months (341). By nine months post-TKR, Urwin et al. (320) found that patients had a 0.21 Nm/kg increase in peak internal KEM and was equivalent to the healthy

controls. Twelve months after surgery, differences in peak internal knee flexion moments between pre- and post-operation were gone during mid-stance, and there was a 0.93 %BW*height increase during the loading-response (173). However, another study found that the loading-response peak external KEM was decreased by 0.9 %BW*height (191). This reduction in peak external KEM provides further evidence of a quadriceps avoidance pattern, especially early in recovery. Patients that used this pattern to avoid knee pain prior to surgery may continue with this gait modification post-surgery unless a conscious effort is made by the patient to avoid this atypical gait. The use of physical therapy for gait retaining may benefit these patients (173).

Frontal Plane Kinematics

Improvements in the frontal plane kinematics are apparent after TKR, as no differences are reported in peak knee adduction between TKR patients (4.1°) and healthy controls (3.9°) (193, 199). The ability of TKR to return knee adduction angle to healthy level may not be apparent immediately following surgery. At 14 days following surgery, Wu et al. (342) found that the operated limb was still more adducted (5.55°) compared to the non-operated limb (0.08°) during midstance. When comparing adduction angle at two, three, six, and nine months, there is a consistently reported significant decrease (1, 228, 320, 331, 345). One study shows that by six weeks post-operation, TKR patients early-stance peak knee adduction angle has reduced to 1.2°, which was a decrease from pre-operation peak adduction (4.2°) (75). In addition to reductions in peak knee adduction angle, some studies report significant increases in peak knee abduction angle (11, 190, 192, 320, 331). However, not all studies report this change (1, 345).

The ability to return to a healthy level of peak adduction, and being able to do so within a time as short as two months, shows that TKR surgeries successfully realign the knee joint in the frontal plane (228). It is a positive sign that the static alignment provided during surgery enable

improvements during dynamics movements. Correlations between static alignment and dynamic movement at the knee have been recently studied. Bennett et al. found that changes in static alignment (i.e. coronal mechanical angle) causes differences in peak frontal plane knee angles and moments (25). Specifically, those participants with a varus static alignment had more adducted knees during gait, as well as increased peak KAbM. Riviere et al. (261) found the coronal mechanical angle (angle formed by the hip, knee, and ankle centers with the vertex being at the knee joint center) was moderately positively correlated ($r=0.318, p=0.001$) with peak dynamic varus (adduction angle) during stance phase and mean KAbM ($r=0.31, p=0.02$), and inversely correlated with the peak KAbM ($r=-0.352, p<0.01$). Corrections in alignment have improved limb discrepancy for the peak adduction angle.

Frontal Plane Kinetics

As previously discussed, the KAbM is a surrogate for medial knee loading. The waveform of this moment is typically bimodal, with peaks corresponding to loading-response and push-off during stance. Often, the loading-response KAbM is larger (i.e. more negative) than the push-off peak. Reduction in the loading of the medial compartment of the knee is a critical to improving the longevity of the TKR, and overall success of the surgery in returning the patients to a healthy gait.

Conflicting evidence exists on the effects of TKR on frontal-plane knee kinetics. One study found that there was no difference between the KAbM of TKR patients (0.39 Nm/kg) and healthy controls (0.46 Nm/kg) (301). However, Benedetti et al. (23) found that both loading-response and push-off peaks were significantly reduced by 1.4 %BW*height and 1.0 %BW*height, respectively, compared to healthy controls. When comparing with non-operated limbs of patients, the peak internal KAbM was 0.7 Nm/kg (8), 0.67 %BW*height (75), and 0.012

Nm/fat free mass*height (211) lower in the operated limb. No differences were found, however, between the operated limb of TKR patients and healthy controls (8, 211). While it is a positive sign that TKR patients experience similar KAbM to healthy controls, it is worrisome that there is a discrepancy with the contralateral limb. This asymmetry may lead to changes in loading patterns of the non-replaced limb, altered loading patterns may increase deterioration within the non-replaced knee joint, leading to a TKR on the second knee.

Similar to frontal plane knee kinematics, TKR is able to quickly effect KAbM following surgery. Wegrzyn et al. (331) found that TKR patients had significantly lower KAbM at two months post-TKR (0.32 Nm/kg) compared to pre-TKR (0.41 Nm/kg). At three months, patients continue to show decreased KAbM (1, 345). Six months following TKR, Orishimo et al. (228) found that there was an 84% reduction in KAbM. Unfortunately, this patient group increased in KAbM by twelve months (3.0 %BW*height) compared to six months (2.7 %BW*height) and was no longer significantly different than pre-surgery levels (3.2 %BW*height). Two other studies also found decreases in KAbM (192, 341), as well as KAbM impulse (341), which has been previously described as being critical in the loss of cartilage in the knee joint (24, 147). At nine months following TKR, patients continued to show decreased KAbM (11, 320). Some studies also showed a trend towards a significant decrease in KAbM (1, 192, 320, 331), however not all studies have found this (345).

It may be important to study the influence of the TKR during difference points within the gait cycle. At the time of peak vGRF, TKR patients experienced a 1.06 %BW*height decrease in KAbM at six months. During this study, healthy controls had a significantly lower KAbM (2.7 %BW*height) during peak vGRF, compared to pre-surgery patients (4.07 %BW*height), and statistically similar KAbM compared to post-surgery (3.01 %BW*height) (193). This finding is

important to show how TKR can return patients to a loading pattern that is similar to those in healthy controls.

Effects of TKR on Ramp Walking

Two studies have reported findings for TKR patients during ramp walking (258, 335). The results of this thesis indicate that similar to trends seen in level walking and stair negotiation, TKR patients exhibit decreased total stance phase knee flexion ROM (42.8°) compared to healthy controls (48.6°), and less peak stance phase knee flexion (18.1°) in the replaced limb compared to non-replaced (23.2°) and healthy controls (26.3°). Sagittal plane knee kinetics were also significantly different. The loading-response KEM was significantly lower in the operated limb (-0.58 Nm/kg) compared to the non-operated limbs (-0.75 Nm/kg) and healthy controls (-0.91 Nm/kg). The push-off peak KEM was also lower in the operated limb (-0.45 Nm/kg) compared to the non-operated (-0.58 Nm/kg), but not difference than healthy controls (-0.53 Nm/kg) (258). No frontal plane kinematics or kinetics were presented in this study.

More recently, Wen (335) studied the effects of TKR on uphill and downhill walking on a ramp at set three different degrees of inclination: 5°, 10°, and 15°. Further, this study examined differences between replaced and non-replaced limbs of TKR patients. The results of this study indicate significant differences between limbs of TKR patients as well as significant differences between TKR patients and healthy controls.

During uphill walking, TKR patients exhibited lower knee extension ROM in both the replaced (4.4°) and non-replaced (3.9°) at 5°, compared to both limbs of healthy controls (10.9° and 11.3°). At 10°, the replaced limb of TKR patients had significantly lower knee extension ROM (17.3°) compared to non-replaced (19.8°). Both limbs of TKR patients had significantly lower knee extension ROM at 10° compared to both limbs of healthy controls (28.4° and 26.5°).

There were no limb differences between replaced (29.8°) and non-replaced (31.5°) limbs at 15°, however both limbs of healthy controls exhibited greater knee extension ROM (40.1° and 39.4°). No significant differences were found between TKR patients and healthy controls during downhill walking.

In the frontal plane, there were significant differences in peak KEM between replaced and non-replaced limbs, as well as between replaced limbs of TKR patients and healthy controls, during level, uphill, and downhill walking. During level walking, there were no limb differences between peak KEM in replaced (0.33 Nm/kg) and non-replaced (0.35 Nm/kg); however, each limb of healthy controls had significantly higher peak KEM (0.49 Nm/kg and 0.57 Nm/kg). This trend continues at 5° as replaced (0.30 Nm/kg) and non-replaced (0.32 Nm/kg) limbs were not different, and both limbs of healthy controls were significantly higher (0.52 Nm/kg and 0.58 Nm/kg). As the incline increases to 10°, significant between limb differences appear in TKR patients. The replaced limb (0.39 Nm/kg) was significantly lower than the non-replaced limb (0.52 Nm/kg); each of these were significantly lower than both limbs of healthy controls (0.67 Nm/kg and 0.72 Nm/kg). This discrepancy continued at 15° where the replaced limb (0.45 Nm/kg) and non-replaced limb (0.61 Nm/kg) were significantly lower than the limbs of the healthy controls (0.73 Nm/kg and 0.84 Nm/kg).

During downhill walking, there are two peak KEMs, loading-response and push-off response. Peak loading response KEM exhibited the most differences between limbs and groups. At 5°, the replaced limb had a significantly lower loading-response KEM (0.44 Nm/kg) compared to the control limb (0.53 Nm/kg). Further, healthy controls had a significantly larger loading-response KEM in one limb (0.68 Nm/kg). At 10°, the between limb differences for TKR patients continued with a peak loading-response KEM in the replaced limb of 0.58 Nm/kg and

0.75 Nm/kg in the non-replaced limb. The replaced limb was significantly lower than both limbs in the healthy controls (0.81 Nm/kg and 0.89 Nm/kg). Between group differences were not apparent at 15°, however, in TKR patients, the replaced limb exhibited lower loading-response peak KEM (0.75 Nm/kg) compared to the non-replaced limb (0.94 Nm/kg).

No group or limb differences were found for push-off peak KEM during level walking and at 5°. At 10°, TKR patients exhibited significant between limb push-off peak KEM with the replaced limb peak KEM of 0.69 Nm/kg and the non-replaced limb at 0.83 Nm/kg. This difference continued at 15° with replaced (0.98 Nm/kg) being significantly lower than non-replaced (1.12 Nm/kg). Additionally, the replaced limb of the TKR patients was significantly lower than one limb of the healthy controls (1.20 Nm/kg). In the frontal plane, no significant differences were found during level, uphill, or downhill walking.

The results of these studies indicate that the quadriceps avoidance gait seen in TKR patients during level walking may also be present during ramp walking. In order to assess the differences between level walking, stair negotiation, and ramp walking, a comprehensive study examining these three gait types may be beneficial. Results from a study with all three of these ambulation types may indicate whether or not it may be beneficial for a TKR patient to use a ramp rather than stairs. Also, this could indicate that physical therapy could be beneficial to patients by increasing the difficulty of gait from level ground walking, then up and down a ramp, and finally use stairs to regain a healthy level of mobility.

Effects of TKR on EMG

To date, few studies have examined EMG signal during early stages of recovery from TKR surgery. However, many studies have demonstrated that there is a decrease in quadriceps and hamstring muscle strength immediately following TKR (145, 184, 214, 238, 308, 313). At

one month following TKR, quadriceps muscle force was decreased between 42% (145) to 62% (214), and hamstrings muscle force was decreased by 34% (145) and 48% (308). These decreases may continue up to six months following surgery (308), however, by one year these decreases no longer exist.

Two types of EMG characteristics that have been researched in early TKR recovery are CCI and timing of signal. Three studies found that the CCI was significantly higher in TKR patients compared to healthy controls (187, 308, 313). Prior to surgery and at one-month post-TKR, quadriceps and hamstring CCI in the operated limb was significantly higher than healthy controls (313). This study also found that the non-operated limb had a higher CCI than healthy controls one month following TKR. Two studies found that quadriceps muscles were activated longer into the gait cycle in TKR patients than in healthy controls (187, 313).

Effects of TKR on Stair Negotiation

Stair negotiation is a common activity that many people perform on a regular basis. However, this activity may be more difficult for patients who have underwent TKR. Many previous studies have examined the capacity of TKR patients to perform this task (27, 30, 32, 56, 95, 104, 142, 151, 190, 192, 197, 198, 230, 244, 251, 277, 305, 306, 337). This section focuses on the differences in knee joint kinematics and kinetics of TKR patients during stair negotiation.

During stair ascent, many significant differences can be found between TKR patients and asymptomatic controls. In the sagittal plane, patients tend to have decreased knee flexion at initial contact (27, 56, 95, 190, 244, 306). The value at initial contact for TKR varies widely between studies from 33.6° to 65.9° (190, 306). However, asymptomatic controls tend to have an initial contact knee flexion angle between 50.5° (190) and 68.9° (306). Due to this decreased knee flexion, many studies have found that TKR patients tend to have lower ROM through

stance phase (27, 32, 56, 95, 306). Knee flexion ROM during stance phase for the replaced limb of TKR patients has been found to range from 48.4° (27) to 55.1° (306), while control limbs of healthy participants tend to range from 55.8°(306) to 56.7° (56, 95). As seen here, this is a small difference, which explains why additional studies found no difference in flexion ROM (337). Differences in participant height and the height of each step may play a significant role in the ROM of the participants, making cross-study comparisons difficult.

Ouellet et al. (230) found that TKR patients had significantly lower (two TKR groups: 59.0° and 54.0°) maximum knee flexion angle during stance phase of stair ascent, compared to asymptomatic controls (62.0°). During swing phase, multiple studies have found that TKR patients exhibit a significantly lower maximum knee flexion angle, compared to controls (56, 95, 244, 277). Maximum swing phase knee flexion for TKR patients ranged from 73.1°(95) to 89.0° (277), while asymptomatic control limbs had maximums ranging from 85.5° (27) to 95.0° (277).

Conflicting reports are present on sagittal plane knee moments of TKR patients during stair ascent. Multiple studies have found significant reductions in the internal peak KEMs in TKR patients, compared to healthy controls (27, 56, 95, 197, 245). This, along with a reduction in muscle force production in the quadriceps (251), demonstrates a common quadriceps avoidance pattern commonly seen in these patients (209). However, not all studies have found this to be significant (32, 277, 306, 337). Peak sagittal plane knee moments in TKR patients have been reported to range from 2.7 %BW*Ht (197) to 3.3 %BW*Ht (56), while healthy controls had moments ranging from 3.8 %BW*Ht (197) to 6.5 %BW*Ht (95).

Due to the positive effects of increased walking speed on vertical GRF , the speed of stair ascent and descent can play a significant role in the findings of the sagittal plane moments in these studies (149). Similar to level walking, many studies found reductions in stair ascent speed

in TKR patients, compared to controls (27, 56, 95, 192). However, this difference is not present in all studies (306).

In the frontal plane, the most commonly reported variable is the peak KAbM. As previously discussed, this variable is often studied in knee OA and TKR literature due to its influence on the loading of the medial compartment of the knee, the most common location for knee OA. Conflicting reports between KAbM of TKR and asymptomatic controls can be found. Studies have indicated that TKR patients may have lower peak KAbM than healthy controls with moments ranging from $-1.8 \%BW*Ht$ (56, 95) to $-3.13 \%BW*Ht$ (192), compared to controls $-2.7 \%BW*Ht$ (56, 95) to $4.69 \%BW*Ht$ (192). However, the patients in this study ascended slower than the controls, which would act to reduce this moment. Other studies have found higher peak KAbM in TKR patients ($-3.8 \%BW*Ht$) compared to healthy controls ($-2.7 \%BW*Ht$) (27). This increase was found despite a significantly reduced ascent speed in TKR patients (0.33 m/s versus 0.39 m/s). Further studies have found no significant difference between these groups (277, 306).

Fewer studies have examined differences between these groups during stair descent. In the sagittal plane, only one study has examined the knee extension angle at contact (56). This study found that the knee of TKR patients were significantly less extended at contact (2.6°) than the controls (10.9°). Three studies have identified that TKR patients have significantly reduced peak knee flexion during stance phase (30, 104, 197). TKR patients had a peak knee flexion angle of 91.0° , while controls had a peak of 94.1° (104). Given these reduced angles, it is expected to find reduced flexion ROM between these groups. While one study (56) found no difference in sagittal plane ROM, two studies found TKR patients to have significantly reduced

ROM (32, 337). The ROM for TKR patients ranged from 84° (32) to 88° (337), while controls have ROM of 96° (337) to 97° (32).

Multiple studies have found that there are no differences in peak knee flexion moment during the stance phase of stair descent in TKR patients compared to healthy controls (56, 104, 277, 306). However, two studies have found TKR patients to have significantly lower peak KEMs during stance phase while descending (197, 337). McClelland et al. (197) reported TKR patients to have a loading-response peak KEM of 2.6 %BW*Ht and a push-off peak of 5.6 %BW*Ht. asymptomatic controls had peaks of 3.2 %BW*Ht and 6.1 %BW*Ht, respectively. Similar to stair ascent, this potential decrease in KEM may indicate a quadriceps avoidance gait pattern.

Similar to the knee flexion moment, there are conflicting reports of the KAbM of TKR patients during stair descent. Three studies found no differences between these groups (56, 277, 306). However, Fenner et al. (104) found that TKR patients had a loading-response KAbM of 0.45 Nm/kg, while controls had a 0.57 Nm/kg peak loading-response KAbM, a significant difference.

Biomechanics of Bilateral TKR Patients

To date, few studies have focused on biomechanical differences between bilateral TKR patients, unilateral TKR patients, and healthy controls. Multiple studies using bilateral TKR patients focused on patients with different implant designs and how they affect knee joint biomechanics differently (206, 226, 253, 289). This review will focus on studies that had examined clinical status using common clinical evaluations (i.e. WOMAC, Knee Society Score, FJS, SF-12) and differences between bilateral TKR patients and either healthy controls or

unilateral TKR patients. To the author's knowledge, no studies have currently examined differences in bilateral and unilateral TKR patients.

The first study to examine bilateral TKR patients (32) examined muscular strength and gait analysis of patients with cruciate-retaining and cruciate-substituting replacement types. The authors concluded that there were no significant differences in knee flexion moments, knee ROM, and EMG activity during level walking and stair negotiation. This is an important finding because it demonstrates that both implant types can perform similarly during these two types of motions.

The next study to examine bilateral TKR patients examined biomechanical differences in patients who underwent staged versus simultaneous knee replacement (35). After a minimum of two years following the most recent surgery, this study found that there was no difference in isometric strength, peak knee extension or flexion moments, step length, stance time, or swing time. There were, however, staged TKR patients had significantly less knee flexion ROM and a significantly lower loading-response GRF than healthy controls and simultaneous TKR patients. This study is important because it concludes that there are minimal differences in biomechanical outcomes following staged and simultaneous TKR surgeries.

Two recent studies examined functional capacities following bilateral TKR (132, 182). Huang et al. (132) found that unilateral and bilateral TKR patients achieve similar scores for the WOMAC and SF-36. Lizaur-Utrilla et al. (182) examined the functional scores of the first and second knee to be replaced in staged bilateral TKR patients. This study found that both knees achieved similar ROM, WOMAC, and SF-12 (physical portion) scores at 6, 12, and 24 months post-TKR. At 24 months, SF-12 (mental portion) and patient satisfaction was significantly better (i.e. more satisfied) for the second knee.

Two studies have examined gait biomechanics of bilateral TKR patients in comparison to healthy (asymptomatic) controls during level walking (253, 262). Renaud et al. (253) found that TKR patients had more flexed knees at heel strike, less flexion through swing phase, increased loading-response knee varus angle, increased knee varus angle during swing phase, and less knee internal rotation during stance, when compare to asymptomatic controls. Ro et al. (262) found that bilateral TKR patients walked significantly slower, generated a significantly lower peak KEM, and had significantly less knee ROM than healthy controls.

One study to date has examined differences in unilateral and bilateral TKR patients during stair negotiation. McClelland et al. (197) studied sagittal plane mechanics of these patients. This study found no differences between unilateral and bilateral TKR patients for maximum knee flexion during ascent and descent and peak knee flexion moments during ascent and descent.

Principal Component Analysis

Biomechanical data collections provide an extraordinary amount of data. This is because the data collected (i.e. marker trajectories and GRF), as well as data that is calculated (i.e. joint angles, joint moments, and joint powers) and data that is estimated (i.e. musculoskeletal modeling), are represented as waveforms over time. Typical analyses of biomechanical data include examining values of the waveform at pre-determined events; such as local maxima, minima, heel-strike, and toe-off (265). Following the identification of these values, between and within group/subject comparisons are often made to determine if these values significantly differ between groups of individuals, or, as is often the case in knee OA and TKR studies, between limbs (77, 79, 265).

When analyzing biomechanical data by extracting discrete parameters, information regarding waveform characteristics may be lost (76). One technique used in biomechanical research is principal component analysis (PCA). PCA performs an orthogonal transformation on a set of correlated variables into a smaller number of uncorrelated variables, known as principal components (PC). PCA is valuable in biomechanical analysis because it compresses the size of the data into independent components and only a few components are required to represent the original data (76). Further, PCA is valuable because of its ability to detect changes in overall waveform magnitude throughout a given time, its ability to detect changes in the timing of local peaks (time-shift), and its ability to detect differences in local peaks between different waveforms.

To calculate principal components, original waveform data is represented in matrix form,

$$X = \begin{bmatrix} x_{11} & \cdots & x_{1p} \\ \vdots & \ddots & \vdots \\ x_{n1} & \cdots & x_{np} \end{bmatrix}$$

Equation 1. Sample input data matrix for PCA

Where each row of matrix X is time series data from a participant (n = number of time series and rows) and each column is the data value at one instant in time (p = number of time points) (76). Time series data is commonly viewed in waveform, so the changes in the values over time can be seen. In biomechanical gait data sets, these time series typically indicate how variables of interest (i.e. joint angles and moment) change throughout the entire gait cycle (stance and swing) or just during stance phase (if swing data is not of interest). Gait data is typically time-normalized to 101 data points, representing 100% of the gait cycle or stance phase. Next either a covariance matrix, or a correlation matrix is formed to represent the variance in the data. A correlation matrix is formed when the data has been mean-centered and scaled to unit variance, removing

effects of measurement differences when using differing units (76). This is done by subtracting the mean of the waveform from each time point (zero-centered) and then dividing by the standard deviation. This gives a unitless score of distance away from the mean. This matrix can be given the title of matrix S for further calculations. Eigenvector decomposition of the covariance matrix (or correlation matrix, matrix S) results in an orthogonal transformation matrix, U . The columns of U are the eigenvectors of the matrix S , these are also known as the loading vectors. To find the variation associated with the PCs, a matrix, D , is formed by the following,

$$U^t S U = D.$$

The diagonal components of matrix D are the eigenvalues of matrix S . U^t is the transposed matrix U . The number of potential eigenvalues, and thus PCs, is equal to the minimum between the number of observations (n), or time points (p). The principal component matrix, Z , is then formed by first subtracting the mean of matrix X from matrix X , then pre-multiplying the resultant matrix with matrix U (76).

$$Z = [X - \bar{X}]U$$

As previously stated, one of the benefits of PCA is to reduce the number of important variables by identifying the variables that are most important throughout the gait cycle. While the PCA will calculate all possible PCs, not all PCs provide a large amount of variation explained. Once the PCA is ran, the output orders the PCs from most variance explained (PC1) to second most explained (PC2), and so forth for the total number of PCs. For example, if there are 30 PCs generated, the 30th PC will explain the 30th highest amount of variation (or the lowest amount in this example). Further reduction in associated variables can be obtained by only selecting the PCs that explain the highest percentage of variation in the data. A commonly

reported value for a cut-off of the number of PCs to retain is to retain the minimum number that account for 90% of the variation (42, 76-79, 168, 265).

Once the minimum number of retained PCs is determined, the next step in PCA is to interpret the meaning behind each of the retained PCs. Interpretation is often performed by inspecting shape of the loading vector of each PC along with the raw data (input data) of the participants who were two standard deviations (95th percentile, high and 5th percentile, low) away from the mean PC score (42, 76-78, 165, 265). A visual comparison is performed to determine how these waveforms differ. Brandon et al. (42) suggests that the best way to interpret the biomechanical meaning of a PC is to compare regions of high and low waveforms where the PC loading vector has a large positive or large negative magnitude. If the high waveform is vertically shifted from the low waveform, the PC indicates a magnitude difference. If the PC loading vector has a large positive peak aligned with one peak, but no large magnitude at a second peak, the PC is indicating a difference in the magnitude of the local peak, rather than an overall vertical shift. This is known as a “difference feature.” A phase shift, indicating a difference in the timings of peaks in waveforms, is found when the PC loading vector is off-set from the peak of the mean data waveform. Typically, a phase shift is indicated when the PC loading vector will have a large positive peak before the peak in the raw data, and a negative peak following the peak in the data (42).

Following interpretation of the biomechanical meaning of the PCs, a statistical analysis can be performed to determine if specific participants differ from others. For example, a t-test can be performed to determine if patients with knee OA vary significantly from healthy controls. This is done by first calculating the PC scores and comparing the scores of the individuals for each PC. A PC score is calculated by projecting the original data onto the PC. The original data

is multiplied by the transpose of the PC matrix, containing all retained PCs. These scores show how each patient varies due to the first PC. A t-test then uses the PC scores to determine differences in groups (77).

The use of PCA has become more prevalent in biomechanical research in recent years. PCA has been used to analyze waveforms of patients including stroke (37, 212), Parkinson's disease (81), knee OA (41, 50, 77-79, 97, 110, 121, 144, 155, 159, 180, 254-256, 263, 264, 273), and TKR (12, 15, 78, 120, 122, 194, 204, 205, 262, 318). Other studies have focused on non-patients such as runners (26, 40, 107, 221, 229, 241, 242, 249). This review will focus on studies that have focused on knee OA and TKR patients. While most studies to date have focused on using PCA for level walking tasks, three studies (194, 252, 318) have used PCA on participants during stair negotiation. One of these studies (252) was performed on older adults who were healthy.

Reid et al. (252) examined healthy young and older adults during stair ascent using PCA. They found that the older adults had a lower posterior-anterior force throughout stance, a higher mediolateral force throughout stance, decreased loading-response and push-off response peak vertical force, decreased knee flexion angle throughout stance, increased knee external adduction moment throughout stance, increased peak knee external flexion moment during early stance, decreased peak knee external flexion moment during late stance, decreased knee external internal rotation moment throughout stance.

An early study by Deluzio et al. (79) focused on determining the usefulness of PCA on biomechanical data sets. A more recent study by Deluzio and Astephen (77) used PCA to describe differences between healthy participants and those with knee OA. This study found that knee OA patients exhibited significantly different waveforms at the knee. Specifically, knee OA

patients had a lower knee flexion angle throughout the entire gait cycle, lower range of motion throughout gait, lower loading-response knee external flexion moment magnitude, lower push-off response KEM, higher knee external adduction moment throughout stance, but a lower loading-response knee external adduction moment.

These results are similar to those found by Astephen et al. (14), who also measured EMG activity in knee OA patients. OA patients had lower early stance knee external flexion moment, higher mid-late stance knee external flexion moment magnitude, higher mid-stance and lower late stance hip external adduction moment, lower RF EMG activity during early, higher RF EMG activity during mid to late stance, higher VM EMG activity throughout stance, higher early-stance plantarflexion angle, lower late-stance dorsiflexion angle, decreased peak knee flexion at late stance, peak knee flexion angle occurred later in stance phase, higher overall hip flexion moment magnitude, higher mid-stance knee external adduction moment, lower late-state knee external adduction moment, greater ankle dorsiflexion moments in early stance, smaller dorsiflexion moments in late stance, smaller overall magnitude of knee internal rotation moment, and greater VL EMG activity throughout stance. In contrast, Brandon and Deluzio (41) found decreased hip adduction moment magnitudes in knee OA patients, with similar increases in knee external adduction moment magnitudes and decreased internal rotation knee moments.

Resende et al. (254) studied the power generation and absorption of knee OA patients and found that women with knee OA absorbed and generated less energy at the hip and ankle joints, and absorbed less energy at the knee when compared to the asymptomatic group. Changes in the moments and power generation and absorption at the hip may lead to increased pelvis motion.

Linley et al. (180) found that OA patients had increased ROM at the pelvis during stance.

Despite the advantages of using PCA to examine the differences between asymptomatic controls and knee OA patients, Hatfield et al. (121) found that significant group differences could be determined using only peak and impulse value information, rather than entire waveforms of data. Therefore, it is suggested that the PC demonstrating a change in magnitude may not provide information unique from peak analysis. However, PCs that describe other differences (i.e. phase shifts and difference features) may provide useful information that analysis of local maxima or minima may not.

In addition to PCA of knee OA patients, multiple studies have used this technique on knee replacement patients. One of the first studies, similar to knee OA, was performed by Deluzio et al. (78). This study used pre-operation and post-operation waveforms of bone-on-bone forces, net joint reaction moments, and knee angles during gait of 13 unicompartmental TKR patients. Comparisons of these waveforms were made to determine if they differ from similar waveforms of asymptomatic controls. The authors then checked the waveforms of the eight variables (three forces, three moments, and two angles) for deviation from the “normal” waveforms of the asymptomatic controls. If the variable was within normal limits, they received a gait score of “1”, if not, they received a “0.” No significant change in the gait scores was found.

Mandeville et al. (194) used PCA to determine what variable most clearly differentiates asymptomatic controls to end-stage knee OA patients, and the same patients six-months post-TKR operation. They found that when the patients’ knees were replaced, the knee external adduction moment during gait was not as important as it was during pre-operation. This indicates success in returning the moment to healthy levels.

Hatfield et al. (120) used PCA to determine differences in the waveforms of knee biomechanics in TKR patients. They found that TKR patients had a decreased overall and midstance knee external adduction moment magnitude, and increased knee flexion angle magnitude, increased in early stance knee external flexion moment, increased late stance KEM, and a decrease in the early stance knee external rotation moment.

Astephen et al. (15) examined how sex affects knee joint biomechanics and neuromuscular control following knee replacement. Women had lower pre-operation and post-operation knee flexion angle from late stance to mid-swing. Pre-operatively, men had lower external flexion moment magnitude throughout stance than post-operatively and both pre- and post-operation women. Men also had higher knee external adduction moments during stance than women.

Trinler et al. (318) examined how stair ascent and descent with different dimensions affects both TKR patients and healthy controls. Interestingly, this study found no differences between the knee flexion angle, knee adduction angle, knee external flexion moment, knee external adduction moment, or knee power of the TKR patients and the healthy controls. However, it was determined that the height of the staircase (17 cm versus 21 cm) did have a significant influence on each of these variables.

Recently, Ro et al. (262) used PCA to evaluate the differences in bilateral TKA patients before and after surgery to healthy controls. PCA was used only on the waveforms of the knee flexion angle. The results indicated that following surgery, bilateral TKR patients had higher overall knee flexion angle throughout stance and greater ROM.

This review has demonstrated the usefulness of PCA in biomechanical analysis. Due to the limited number of PCA analyses on patients with unilateral TKR, further research is

warranted to determine how this population differs from healthy adults. Further, a PCA examination of differences between bilateral TKR, unilateral TKR, and healthy adults may be useful in determining how TKR most profoundly effects gait. While many studies have been performed on TKR patients using local maxima and minima, very few have examined three-dimensional waveforms of the joint motions of this patient population. As pointed out by Hatfield et al. (121), PCA can provide insight into how these patients are moving differently than their asymptomatic counterparts, which can be critical in providing insight to how to clinically address issues following TKR surgery.

Each of the studies previously discussed in this section generated a PCA model for each variable and analyzed the findings independently. However, other researchers have found that combining variables (i.e. multivariate) into one data matrix may provide a more robust analysis of movement (39, 158, 221). When this approach is used, the variability of the variables of interest described by a PC identifies correlated changes, while other PCs remain uncorrelated (39). The process of generating the input matrix follows the same path as with univariate PCA. First, correlation matrixes of each of the variables of interest are generated. These matrices are concatenated together horizontally, increasing the number of columns. For example, if a researcher has identified a certain number of variables of interest (v), the researcher would first generate v correlation matrixes with the dimensions $(n \times p)$, as stated previously. Concatenation of these matrices would form a new matrix with dimensions of $n \times (p \times v)$. PCA is then performed on this new, larger matrix.

The resultant PCs will contain the variation explained by each variable and therefore will have a length of $(p \times v)$. From this point, the researcher can identify which PC to interpret. This is done by performing t-tests on the PC scores. For example, Kobayashi et al. (158) compared

the scores of faller and non-fallers and found that only the fifth PC had significantly different scores between the groups. Once significant PCs are identified, the researcher can interpret the individual variables that comprise the PC (39, 158). This is done in the same manner as previously discussed (42, 76, 77). To date, there has been no research using this method of PCA on patients with knee OA or knee joint replacements.

Chapter III

Materials and Methods

Study One, Two, and Three

Participants

Potential bilateral TKR patients were identified via database inspection carried out at the Tennessee Orthopedic Clinics (TOC). TKR procedures were all performed by the same surgeon. Once potential participants were identified, the TOC sent out recruitment letters introducing the study to the patients and recommending the patients to contact the principal investigator. Patients who contacted the principal investigator were screened via inclusion and exclusion criteria over the phone (Table 1).

Patients who met the criteria were invited to participate in a data collection session. Unilateral TKR and healthy participants were collected during previous studies conducted in our lab (306, 322, 335). Inclusion and exclusion criteria were similar for unilateral patients. All unilateral patients had cruciate-retaining implants. For each study, 15 patients were randomly selected via a random number generator in MATLAB. A separate random draw was performed for each study. An *a priori* power analysis was performed using previous reports of KEMs in bilateral TKR patients, compared to healthy controls (262). This analysis indicated a minimum of 15 participants were needed per group to achieve a beta of 0.8, while using an alpha of 0.05. The effect size indicated from this literature was 1.1. All participants signed an informed consent document and all procedures were approved by the Institutional review Board at The University of Tennessee, Knoxville.

Instrumentation

Three-dimensional (3D) kinematics were collected using a 12-camera motion analysis system (240 Hz, Vicon Motion Analysis Inc., Oxford, UK). All participants wore standardized running shoes (Air Zoom Pegasus 34, Nike). Anatomical markers were placed bilaterally on the 1st and 5th metatarsal heads, distal end of the 2nd toes, medial and lateral malleoli and femoral epicondyles, greater trochanters, iliac crests, and acromion processes. Semi-rigid thermoplastic shells, each with four retroreflective markers, were used for motion tracking. These shells were placed bilaterally on the lateral shanks and thighs, on the dorsal aspect of each midfoot, as well as the distal posterior trunk. Further, the pelvis was tracked using a pair of shells, each with two retroreflective markers, placed on the posterior pelvis, along the line from the posterior superior iliac spine to the iliac crests. Force platforms (1200 Hz, BP600600 and OR-6-7, American Mechanical Technology Inc., Watertown, MA, USA) measured 3D ground reaction force (GRF) and moments during over-ground walking and stair negotiation. An instrumented 3-step staircase (FP-Stairs, American Mechanical Technology Inc., Watertown, MA, USA), with two additional steps to ensure continuous motion, was bolted independently on to the two force platforms and used to during stair negotiation to collect GRF data in conjunction with the force platforms (Figure 1). The rise, run, and width of the staircase was 17.8 cm, 29.9 cm, and 60.0 cm, respectively. A handrail, on the right-hand side during stair ascent, was available in case of balance loss. Two sets of photocells (63501 IR, Lafayette Instrument Inc., IN, USA) and Universal Timer and Software (Model 35930, Lafayette Instrument Inc., IN, USA) monitored the time for the participants to complete each trial. The photocells were set three meters apart, at the shoulder height of the participant, during over-ground walking and at the 1st and 4th steps during

stair negotiation. Time was then converted to speed given the time it took to cover the required distance.

In addition to the motion capture data, participants were asked to fill out forms to assess their capacity to perform physical activity, pain, functional capacity, and satisfaction. The surveys to collect this data include the physical activity readiness questionnaire (PAR-Q), KOOS, KSS, and a patient satisfaction survey.

Experimental Procedures

Upon arrival, participants were asked to sign and fill out an informed consent, PAR-Q, KOOS, KSS, and patient satisfaction survey. Once all forms were completed, participants were asked to change into the testing shoes and tight-fitting spandex shorts. Participants then proceeded to warm-up at a self-selected pace on a treadmill for three minutes.

A single static trial was then captured to apply the marker set file and record body weight using the Nexus data collection software on the VICON system (Vicon Motion Analysis Inc., Oxford, UK). Once the static trial was checked for missing markers and completeness, anatomical markers were removed. Due to the setup time required for the staircase, stair negotiation trials were performed first. Participants were allowed up to five practice trials for stair negotiation and level walking trials. Average speed ($\pm 10\%$) was calculated from practice trials and used to monitor gait speed during data collection to ensure gait speed to fall within the time range for consistency. Participants performed five trials of six different over-ground, ascent, and descent conditions.

For level walking, the testing conditions included contacting the first force platform with the foot of the first TKR limb and contacting the first force platform with the foot of the second TKR limb. The condition order (first/second TKR) was randomized. Trials were repeated if the

incorrect foot was used to step on the force platform, the foot was outside the boundaries of the force platform, if the participant alters their gait to actively target the force platform, or if the predetermined time range was not achieved.

For stair negotiation, these conditions include beginning ascent/descent with the foot of the first TKR limb on the first step and beginning ascent/descent with the foot of the second TKR limb on the first step. First and second replaced limbs refers to the order in which they were replaced. The participant began stair ascent conditions three steps away from the staircase to simulate a natural approach to a staircase. While descent always followed ascent to minimize the number of trials performed, the beginning foot (first/second TKR limb) was randomized within ascent and descent conditions, respectively. The second step, during ascent, was the step used for data analysis, this same step was used as the step of interest during descent. The first two steps during descent are not instrumented and was used in case of altered biomechanics during the first two steps during descent. Participants were instructed to use step-over-step manner. Trials were repeated if the incorrect foot was used to step on the first step, if the participant altered their gait to actively target the staircase, if the step-over-step manner was not used, if the handrail was used, or if the predetermined time range was not achieved.

Data Analysis (Study One and Two)

Three-dimensional (3D) marker trajectory and analog data (GRF) were exported from Vicon Neexus and imported to Visual 3D (V6, C-Motion, Inc., Germantown, MD, USA). A fourth-order Butterworth zero-lag low-pass filter with a cutoff of frequency of 8 Hz was used to filter marker trajectory and GRF data for kinematic and joint moment analysis. A separate filter fourth-order Butterworth zero-lag low-pass filter with a cutoff of frequency of 50 Hz was used to filter GRF data for analysis of GRFs. 3D kinematic and kinetic computations for over-ground

and stair negotiation data was performed using Visual 3D. 3D angular kinematic and kinetic computations were performed using the joint coordinate system (118) with a Cardan rotational sequence (X-Y-Z). The convention of the joint angles and moments were defined using the right-hand rule. Positive values at the ankle, knee, and hip include: dorsiflexion, inversion, internal rotation, knee/hip adduction, knee extension, and hip flexion. Joint moments were calculated as internal moments and expressed in the proximal segment reference system. Customized computer programs (VB_V3D and VB_Table, MS Visual Basic 6.0, USA) were used to identify and organize critical values and events. These critical values were averaged across the five trials for each condition, providing a single mean for statistical comparison. Joint moments and GRF were normalized to participant's body mass (Nm/kg) and body weight (BW), respectively.

Data Analysis (Study Three)

In study three, principal component analysis (PCA) was used to identify differences in kinematic and kinetic waveforms of bilateral TKR and unilateral TKR patients, as well as healthy controls. For the present study, a single PCA on a data matrix that includes all variables of interest was used. These variables of interest include: sagittal and frontal plane knee angles and moments throughout stance, and vertical GRF, of the 1st replaced limbs of bilateral patients, the replaced limb of unilateral patients, and a randomly selected limb of asymptomatic controls. Similar to the PCAs performed by Boyer et al. (39) and Kobayashi et al. (158), our PCA identified principal components (PCs) that contains variables that are correlated to one another. Performing a PCA in this fashion allowed us to identify how variations within multiple variables work congruently to distinguish our groups.

For this study, each of the selected variables of each trial was time normalized to 101 data points (0 to 100% of stance phase). To account for measurement differences, each trial was

scaled to unit variance to account for differences in units across the variables. This is done by calculating a z-score. A z-score is calculated by subtracting the mean trial vector from each individual trial (mean-centered) and then dividing by the standard deviation of the trials at each time point. This gives each trial a unitless score of distance away from the mean (76). Once the all variables are scaled, each trial for each participant was ensemble averaged was combined into a single average trial per participant. Average trials for all participants were combined into a single data matrix. This scaled data matrix is called a correlation matrix (76). The different variables are concatenated horizontally, while participants are added as rows.

The correlation matrix (S) for the PCA consisted of 15 1st replaced bilateral limbs, 15 replaced unilateral limbs, and 15 randomly selected controls limbs. Five trials for each participant were included. Therefore, the correlation matrix consisted of 45 rows (45 participants' limbs) and 505 columns (5 variables*101 time points per variable). The PCA was performed on this matrix.

Briefly, PCA performs an eigenvector decomposition of the correlation matrix. Eigenvector decomposition of matrix S results in an orthogonal transformation matrix, U. The columns of U are the eigenvectors of the matrix S, these are also known as the PC loading vectors. These PCs are vectors that indicate the direction of variance in the data. To find the variation associated with the PCs, a matrix, D, is formed by the following,

$$U^t S U = D.$$

The diagonal components of matrix D are the eigenvalues of matrix S. U^t is the transposed matrix U. The eigenvalues measure the variation explained by each principal component. Variation explained by each PC is calculated by dividing the eigenvalue for the PC by the sum of the diagonal elements of matrix D (76). The total number of PCs generated is

equal to the smaller of either the number of variables or the number of participants. For example, if there are 100 variables for 20 participants, the maximum number of PCs generated was 20. However, only the PCs that explain the most variation is needed for analysis. For this study, we will keep the number of PCs required to explain 90% of the variance in the data (42, 76-79, 168, 265).

PCA was performed on this data matrix using MATLAB (R2017a, MathWorks, Matick, MA, USA). PCA output includes a set of eigenvectors (PCs), percentage explained by each PC, and PC scores for each limb in the data set.

Statistical Analysis (Study One and Two)

A 2 x 2 (limb x group) mixed model analysis of variance (ANOVA), using IBM SPSS Statistics (version 24) at an alpha level of 0.05 set *a priori*, was performed to detect kinematic and kinetic differences between and within groups during the over-ground walking and stair ascent and descent, separately. Post-hoc comparisons were performed on significant interactions and main effects using a Holm-Bonferroni adjustment. Adjusted p-values for the six hypotheses tested were: 0.008, 0.01, 0.013, 0.017, 0.025, and 0.05. Cohen's d was calculated and reported for all t-tests, effect sizes are considered small (0.2), medium (0.5), and large (0.8) according to the guidelines by Cohen. (69). Further, partial eta-squared was reported for ANOVA results, with small, medium, and large effect sizes as 0.01, 0.09, and 0.25, respectively (86).

Statistical Analysis (Study Three)

A one-way ANOVA, using IBM SPSS Statistics (version 24), at an alpha level of 0.05 set *a priori*, was used for each retained PC. This was used to identify differences between the replaced limb unilateral TKR patients and the first replaced limb of bilateral TKR patients for each PC. Input for the ANOVA was the PC scores for each limb. PCs that include significant

group differences were included for further analysis, while PCs that include no group differences were discarded.

Once significant PCs are identified, the researcher can interpret the individual variables that comprise the PC (39, 158). This is done in the same manner as described in previous studies (42, 76, 77). Waveforms associated with significant group differences were interpreted via representative extremes (42, 76). Representative extreme waveforms were first generated by multiplying the standard deviation of each PC score with its corresponding loading vector. The extreme waveform corresponding to a high PC score was then generated by adding this new vector to the overall mean vector, while the low PC score waveform was generated by subtracting this vector instead. A visual comparison is performed to determine how these waveforms differ. Brandon et al. (42) suggests that the best way to interpret the biomechanical meaning of a PC is to compare regions of high and low waveforms where the PC loading vector has a large positive or large negative magnitude. If the high waveform is vertically shifted from the low waveform, the PC indicates a magnitude difference. If the PC loading vector has a large positive peak aligned with one peak, but no large magnitude at a second peak, the PC is indicating a difference in the magnitude of the local peak, rather than an overall vertical shift. This is known as a “difference feature.” A phase shift, indicating a difference in the timings of peaks in waveforms, is found when the PC loading vector is off-set from the peak of the mean data waveform. Typically, a phase shift is indicated when the PC loading vector will have a large positive peak before the peak in the raw data, and a negative peak following the peak in the data (42).

Although the studies describing the interpretation of PCA on biomechanical variables used a single-variable approach, multi-variate PCA can be analyzed in the same way. Each

variable within each PC is analyzed individually for its influence on the PC. This is done by sectioning the PC vector into sections that are associated with different variables. Therefore, for this study each PC was separated into 7 different pieces, each with 101 time points. The approach described above was then used to analyze how each variable affects the PC. This was done for each PC that identified significant group differences.

Chapter III Appendix: Tables

Table 1. Inclusion and Exclusion Criteria for Bilateral TKR Patients

Exclusion Criteria:	Inclusion Criteria:
<input type="checkbox"/> Diagnosed osteoarthritis at the ankle or hip joint as reported by the patient.	<input type="checkbox"/> Men and women between the ages of 50 and 75.
<input type="checkbox"/> Any additional lower extremity joint replacement.	<input type="checkbox"/> Total knee replacement in two knees.
<input type="checkbox"/> Any lower extremity joint arthroscopic surgery or intra-articular injection within past 3 months.	<input type="checkbox"/> At least 12-months from the second TKR.
<input type="checkbox"/> Systemic inflammatory arthritis (rheumatoid arthritis, psoriatic arthritis) as reported by the patient.	<input type="checkbox"/> No more than 10-years from the first TKR
<input type="checkbox"/> BMI greater than 40.	<input type="checkbox"/> Cruciate retaining TKR.
<input type="checkbox"/> Neurologic disease (e.g. Parkinson's disease, stroke patients) as reported by the patient.	
<input type="checkbox"/> Any additional major lower extremity injuries/surgeries except for the replaced knees.	
<input type="checkbox"/> Inability to walk without a walking aid.	
<input type="checkbox"/> Any visual conditions affecting gait or balance.	
<input type="checkbox"/> Women who are pregnant or nursing.	
<input type="checkbox"/>	

Chapter IV

Are Level Walking Biomechanics Different Between Bilateral and Unilateral Total Knee Replacement Patients?

Abstract

Background: Due to the high risk of a bilateral total knee arthroplasty (TKR) following unilateral TKR, this study was performed to investigate bilateral TKR patients. Specifically, we examined biomechanical differences between the 1st replaced and 2nd replaced limbs of bilateral patients. Further, we examined bilateral TKR effects on hip, knee, and ankle biomechanics, compared to the replaced and non-replaced limbs of unilateral patients.

Methods: Fifteen bilateral patients (69.23±5.23 years, 1.73±0.09 m, 95.56±15.24 kg) and fifteen unilateral TKR patients (68.67±6.18 years, 1.73±0.10 m, 87.72±15.70 kg) were analyzed while performing level walking. A repeated measures one-way ANOVA was performed to analyze between-limb differences within the bilateral TKR group. A 2 x 2 (Limb X Group) ANOVA was used to determine differences between bilateral and unilateral patients.

Results: The 2nd replaced limb exhibited a lower peak loading-response knee extension moment than the first replaced limb. No other kinematic or kinetic differences were found. Bilateral patients exhibited lower loading-response knee extension moments, knee abduction moments, and dorsiflexion moments, compared to unilateral patients. Bilateral patients also exhibited lower push-off peak hip flexion moments and vertical GRF. Bilateral patients had higher survey scores, indicating increased functional capacity compared to unilateral patients.

Conclusion: Differences between 1st and 2nd replaced limbs of bilateral patients may indicate different adaptation strategies used following a second TKR. Significant group differences indicate adaptations that are different between these groups, and that it may be inadvisable to use these groups in conjunction with one another in gait analysis.

Keywords: arthroplasty, gait, knee, hip, ankle

Introduction

The majority of estimated 8.6 million people with severe knee OA in the United States are likely to receive a recommendation for total knee replacement (TKR). It is expected that by 2030, 3.5 million TKR surgeries will be performed each year (161). Between 37% and 46% of unilateral TKR patients will undergo TKR in the contralateral limb within 20 years (203, 279, 291). Given the trend of increasing total TKR surgeries, and the high percentage of TKR patients eventually needing their contralateral limb replaced, it is important that we understand how the presence of bilateral knee replacements alters lower extremity gait biomechanics.

Limited research has examined level walking biomechanics of bilateral TKR patients (32, 35, 253, 262). Borden et al. (35) found staged bilateral TKR patients had lower knee flexion range of motion (ROM) and peak loading-response vertical GRF than asymptomatic controls and simultaneous TKR patients. Bolanos et al. (32) found no differences in peak knee extension moment (KEM) and ROM between cruciate-retaining and cruciate-substituting implants in patients who had undergone simultaneous (one staged) TKR. Renaud et al. (253) compared kinematics of two different types of cruciate-substituting TKR implants and found that the 2nd replaced limb had less adduction ROM from initial contact to midstance. No joint kinetics were reported. These studies tend to agree that bilateral patients exhibit significantly lower peak KEMs (32, 35, 262), and had significantly less knee ROM than asymptomatic controls (32, 35, 253, 262). It is currently unknown if significant time between replacements causes altered biomechanics between the 1st and 2nd replaced limbs. Investigating this may be beneficial as advancements in TKR designs and degradation of older TKRs may generate differences between these limbs.

Reduced peak internal knee extension (173, 190, 300, 321) and abduction (KAbM) (8, 205) moments have also been reported in the replaced limb of unilateral TKR patients, compared to asymptomatic controls and their non-replaced limbs. The reduction in peak KEMs is often referred as a quadriceps avoidance gait (177, 209). This avoidance gait may be associated with reduced quadriceps strength prior to and following TKR (139, 308, 348, 349), as well as a kinesiophobia due to a pain-related fear of the movement task (106).

The presence of an implant may produce altered joint kinematics and kinetics in the remaining joints (i.e. hip and ankle) in lower limb of TKR patients. Two studies have examined how knee replacement affects hip and ankle kinematics and kinetics (29, 173). Levinger et al. (2013) found no differences in the hip joint kinematics or kinetics between unilateral TKR patients and asymptomatic controls. However, higher peak dorsiflexion angles were found in the replaced limb of the unilateral patients. No kinetic differences were identified at the ankle. These results conflict with the recent study by Biggs et al. (29), which found increased hip flexion angles throughout gait, reduced hip adduction ROM, reduced peak hip external flexion moments, and a loss of the biphasic nature of the hip adduction moment, compared to asymptomatic controls. The unilateral TKR patients exhibited increased dorsiflexion and ankle internal rotation moments during the first half of stance, lower dorsiflexion and internal rotation moments during the second half of stance. To our knowledge, hip and ankle differences between limbs of unilateral TKR patients and bilateral patients are currently unknown.

In addition to gait analysis, clinical outcomes for TKR patients are commonly assessed via the Knee Injury and Osteoarthritis Outcome Score (KOOS) (267), the Knee Society Scoring System (KSS) (285), and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (200). These scoring systems indicate that pain is decreased and functional capacity

is increased during common activities of daily living for TKR patients following surgery (47, 123, 157).

To our knowledge, no studies have examined differences of hip, knee, and ankle biomechanics between the 1st and 2nd replaced limbs of bilateral TKR patients in gait. Additionally, no studies have compared hip, knee, and ankle biomechanics of bilateral TKR patients to the replaced and non-replaced limbs of unilateral TKR patients. Previous research on TKR patients have either excluded bilateral TKR patients (108, 306) or included bilateral TKR patients within their patient population without examining interlimb differences in bilateral patients (300). If joint mechanics of the 1st and 2nd replaced limbs of bilateral TKR patients differ from those of unilateral TKR patients, it may not a good idea to include both bilateral and unilateral patients in same gait biomechanics study.

The primary purpose of this study was, therefore, to examine differences in knee joint biomechanics in both limbs of bilateral TKR patients and replaced and non-replaced limbs of unilateral TKR patients during level walking. A secondary purpose for this study was to examine ankle and hip joint biomechanics for potential compensatory movements. It was first hypothesized that bilateral TKR patients would have similar knee extension and abduction moments and ROM between the 1st and 2nd replaced limbs. Our second hypothesis was that bilateral TKR patients would exhibit similar knee extension and abduction moments and ROM compared to the replaced limb of unilateral TKR patients, but decreased KEMs and ROM compared to the non-replaced limb of unilateral TKR patients. Our final hypothesis was that bilateral and the replaced limb of unilateral patients would have similar hip and ankle sagittal plane moments, indicating similar compensations following TKR, but different moments than the non-replaced limb of unilateral patients.

Materials and Methods

Participants

For this study, fifteen (6 males) bilateral TKR patients (69.23 ± 5.23 years, 1.73 ± 0.09 m, 95.56 ± 15.24 kg) were recruited from a local orthopedic clinic. Eleven of the patients had staged bilateral replacements (73.36 ± 21.92 months since first TKR and 59.00 ± 25.11 months since second TKR) while four patients had simultaneous bilateral replacements (83.23 ± 35.26 months since TKR). Additionally, fifteen (8 male) unilateral TKR patients (68.67 ± 6.18 years, 1.73 ± 0.10 m, 87.72 ± 15.70 kg, 27.93 ± 12.03 months since TKR) were randomly selected from two previous studies conducted in our lab (322, 335). Inclusion criteria for all patients included men and women between 50 and 75, at least 12-months from most recent TKR, no more than 10 years since first TKR, cruciate retaining implant, and surgeries performed by the same surgeon. The exclusion criteria were: OA in hip or ankle, any additional lower extremity joint replacement, BMI greater than 40, neurological disease, and inability to walk or negotiate stairs without the use of a walking aid or handrail. An *a priori* power analysis was performed using a previous report of KEMs in bilateral TKR patients, compared to healthy controls (262). This analysis indicated a minimum of 15 participants was needed per group to achieve a beta of 0.8 and an alpha of 0.05, with an effect size of 1.1. All participants signed an informed consent document and all procedures were approved by the Institutional Review Board at The University of Tennessee, Knoxville.

Instrumentation

Three-dimensional (3D) kinematics were collected using a 12-camera motion analysis system (240 Hz, Vicon Motion Analysis Inc., Oxford, UK). All participants wore standardized running shoes. Anatomical markers were placed bilaterally on the 1st and 5th metatarsal heads,

distal end of the 2nd toes, medial and lateral malleoli and femoral epicondyles, greater trochanters, iliac crests, and acromion processes. Semi-ridged thermoplastic shells, each with four retroreflective markers, were used for motion tracking. These shells were placed bilaterally on the lateral shanks and thighs, on the dorsal aspect of each midfoot, as well as the distal posterior trunk. Further, the pelvis was tracked using a pair of shells, each with two retroreflective markers, placed on the posterior pelvis. The hip joint center was calculated at 25% of the distance between greater trochanters (333). A force platform (1200 Hz, BP600600, American Mechanical Technology Inc., Watertown, MA, USA) measured 3D ground reaction forces (GRF) and moments. Two sets of photocells (63501 IR, Lafayette Instrument Inc., IN, USA) and Universal Timer and Software (Model 35930, Lafayette Instrument Inc., IN, USA), set three meters apart, monitored the time for the participants to complete each trial.

Experimental Procedures

Upon arrival, participants were asked to fill out forms to assess their capacity to perform physical activity, pain, functional capacity, and satisfaction. The surveys used to collect this data were the physical activity readiness questionnaire (PAR-Q), the knee injury and osteoarthritis outcome score (KOOS) (267), the knee society scoring system (KSS) (285), and a patient satisfaction survey. Unilateral patients from one of the previous studies (322) performed the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (200). Participants then proceeded to warm-up at a self-selected pace on a treadmill for three minutes.

Participants were allowed up to five practice trials to familiarize themselves with the over-ground walking conditions. Average walking speed ($\pm 10\%$) was determined from practice trials and used to moderate data collection trials to ensure gait speed of actual test trials to fall

within the speed range for consistency. Participants performed 3-5 data collection trials for each of the level walking conditions.

The testing conditions included walking with the foot of the first TKR limb contacting the force platform and with the foot of the second TKR limb contacting the force platform, respectively. For the patients with simultaneous TKRs, limbs were randomly selected to correspond to “first” and “second” replaced limb. The condition order (first/second TKR) was randomized for all patients. Trials were repeated if the incorrect foot was used to step on the force platform, the foot was outside the boundaries of the force platform, if the participant altered their gait to actively target the force platform, or if the predetermined speed range was not achieved.

Data Analysis

3D kinematics and kinetic computations were performed using Visual 3D biomechanical software suite (C-Motion, Inc., Germantown, MD, USA). A fourth-order Butterworth low-pass filter was used to filter raw marker and moment data at cutoff frequencies of 8 Hz. A separate filter was performed on GRF data at 50Hz to aid in GRF analysis.. 3D angular kinematic and kinetic computations were performed using a Cardan rotational sequence (X-Y-Z) and conventions were defined using the right-hand rule. Positive values of the ankle, knee, and hip indicate dorsiflexion, inversion, internal rotation, knee/hip adduction, knee extension, and hip flexion. Joint moments were calculated as internal moments. A customized computer program (VB_V3D and VB_Table, MS Visual Basic 6.0, USA) was used to identify and organize critical values and events. These critical values were averaged across five trials for each condition and used in statistical comparison. Joint moments and GRF were normalized to participant mass (Nm/kg) and bodyweight (BW), respectively.

Statistical Analysis

To test our first hypothesis, a repeated measure one-way analysis of variance (ANOVA) was performed to identify kinematic and kinetic differences between 1st and 2nd replaced limbs of bilateral TKR patients. A 2 x 2 (limb x group) mixed model ANOVA was performed to detect kinematic and kinetic differences between bilateral and unilateral TKR groups. Both ANOVA tests had an alpha level of 0.05 set a priori. All statistical tests were performed using IBM SPSS Statistics (version 24). Observed power of main effects and interactions was reported as partial eta squared (η_p^2). Post-hoc comparisons were performed on significant interactions using a stepwise Holm-Bonferroni adjustment for multiple comparisons (64, 126). Cohen's *d* was calculated and reported for all t-tests, effect sizes are considered small (0.2), medium (0.5), and large (0.8) according to the guidelines by Cohen. (69). Further, partial eta-squared was reported for ANOVA main effects and interactions (86).

Results

Bilateral TKR patients recruited for this study were similar in age, height, and weight as the unilateral patients (Table 2). The average time since the first TKR of bilateral TKR patients was 10.5 months earlier than the second TKR ($p = 0.003$, $d = 1.30$). Further, times since surgery for the 1st replaced limb ($p < .001$, $d = 2.44$), and 2nd replaced limb ($p < .001$, $d = 1.69$), of bilateral patients was significantly longer than the replaced knee of the unilateral patients (Table 2). There were no differences in walking speed between groups (Table 2).

During the loading-response of stance phase, no leg ($p=0.133$) or group ($p=0.195$) main effect differences were found for vertical GRF (Table 3). During the push-off of stance phase, a significant group GRF main effect, showing decreased vertical GRF in bilateral TKR patients, was found ($F(1, 28) = 6.63$, $p = 0.016$, $\eta_p^2 = 0.191$).

At the knee, a limb×group interaction ($F(1, 27) = 5.76, p = 0.024, \eta_p^2 = 0.176$) was found for peak loading-response KEM (Table 3). A significant within-group difference was found, indicating the 1st replaced limb of bilateral patients had a significantly higher loading-response peak KEM, compared to the 2nd replaced ($p = 0.024, d = 0.925$). Post-hoc tests demonstrated that the peak moment for the 1st replaced ($p = 0.010, d = -1.03$) and 2nd replaced ($p < 0.001, d = -1.60$) limbs of bilateral patients were significantly lower than non-replaced limbs of unilateral patients. Furthermore, the peak moment for the 2nd replaced limb was lower than unilateral replaced limbs ($p = 0.001, d = -1.44$). A group main effect difference was also identified for the loading-response abduction moment ($F(1, 28) = 5.04, p = 0.033, \eta_p^2 = 0.153$). This main effect demonstrates that the bilateral group had lower loading-response peak KAbM than the unilateral group.

At the ankle, the peak loading-response dorsiflexion moment was significantly higher in the unilateral group ($F(1, 28) = 18.24, p < .001, \eta_p^2 = 0.394$, Table 3). No further significant group/limb main effects, or interactions, were found at the ankle.

The hip joint also exhibited kinetic differences in the sagittal plane. The push-off flexion moment was significantly lower in the bilateral group ($F(1, 28) = 7.78, p = 0.009, \eta_p^2 = 0.217$). A significant interaction in the hip adduction ROM was identified ($F(1, 28) = 4.25, p = .049, \eta_p^2 = 0.132$, Table 4). No significant post-hoc comparisons were found.

Discussion

The primary purpose of this study was to examine differences in knee joint biomechanics of both limbs of bilateral and unilateral TKR patients during level walking. Our first hypothesis was that the 1st and 2nd knee replacements of bilateral TKR patients would exhibit similar peak knee extension and abduction moments, as well as ROM. This hypothesis was partially

supported due to the 1st replaced limb of bilateral patients exhibiting significantly higher peak loading-response KEMs. This is in contrast to previous research, which has shown bilateral TKR patients exhibiting similar peak KEMs in each limb (32, 35).

When comparing the motions of both 1st and 2nd replaced knees, we found no differences in knee extension and abduction ROM through stance phase. This is a positive outcome as it suggests that both knees exhibit similar joint kinematic patterns during gait. However, the decreased peak KEM in the 2nd replaced limb may indicate a more complex recovery following a second replacement. The quadriceps avoidance gait, commonly associated with reductions in the KEM, seems to be more prevalent in the 2nd replacement limb of bilateral TKR patients. Silvia et al. (296) determined that reduced quadriceps strength was present in the replaced limb of unilateral patients 2.8 years following surgery, compared to asymptomatic controls. Huang et al. (130) found reduced quadriceps strength persisted up to 13 years following surgery. Our results also showed reduced loading-response peak KEM for the 1st replaced limb compared to replaced limb of unilateral TKR patients, these patients may have increased difficulties recovering quadriceps strength in the 2nd replaced limb.

Our second hypothesis, that bilateral TKR patients would have similar peak knee extension and abduction moments, and knee joint ROM during stance phase, as the replaced limb of unilateral TKR patients, was partially supported. The loading-response KEM was significantly lower in the bilateral TKR group. Post-hoc analysis indicated lower moments in both limbs of bilateral TKR patients, compared to the non-replaced limb of unilateral TKR patients. This was expected, as it is a similar finding as previous research on bilateral patients and asymptomatic controls (262). Unlike the study by Ro et al. (262), our bilateral patients did not walk significantly slower than the opposing group. Despite similar walking speeds, a lower extension

moment continued to persist in bilateral patients. This may indicate increased movement efficiency in the bilateral group, allowing for reduced moments while maintaining their walking speed. Further, the 2nd replaced limb of bilateral patients was significantly lower than the replaced limb of unilateral patients.

This decreased moment may be representative of a quadriceps avoidance that is more prevalent in the bilateral group. Similar to the previous discussion on the differences of this variable within the bilateral group, the presence of two knee replacements may cause an exaggerated quadriceps avoidance gait in bilateral patients. Further, non-significant differences between these groups may have helped to promote this difference. The bilateral patients walked slightly slower, and had a slightly lower loading-response peak vertical GRF, which may have collectively contributed to decreased loading-response peak KEMs (170). Despite this reduction in the loading-response moment, the push-off knee flexion moment was slightly (but non-significantly) higher in the bilateral group. Similarities in knee extension and abduction ROM between these groups indicate that they both groups use similar knee kinematic movement patterns during level walking.

Additionally, the unilateral group demonstrated no between-limb differences for the loading-response peak KEM. This is in contrast to previous research, which has demonstrated lower peak KEMs in the replaced limbs of unilateral patients, compared their non-replaced limbs, as well as asymptomatic controls (173, 190, 300, 321). A lack of differences for the loading-response peak KEM may be associated with the use of contralateral limbs of unilateral TKR patients. A recent study by Aljehani et. al. (4) found there were differences between limbs of unilateral TKR patients which depended on the presence of bilateral OA. This research found that the patients with bilateral OA had symmetrical, abnormal joint motions following unilateral

TKR. However, patients who were asymptomatic in the non-operated knee had asymmetrical joint motions, with increased initial contact knee flexion, less knee flexion and extension excursion, and decreased knee extension in non-replaced limb, compared to replaced. Therefore, their results suggested that contralateral limbs of TKR patients may not be as useful for comparisons as asymptomatic controls.

Further, the loading-response KAbM was lower in the bilateral group. This was an expected result as previous research comparing replaced and non-replaced limbs of unilateral TKR patients has shown the loading-response KAbM to be significantly lower in the replaced limb, compared to non-replaced (8, 75, 211). This peak has also been found to be smaller in the replaced limb of unilateral TKR patients, compared to asymptomatic controls (8, 23, 205). Reduced KAbM is a positive sign as increased KAbM is commonly associated with increased loading on the medial compartment of the knee (8, 211). The redistributed loading may be indicative of the excellent clinical outcomes of TKR procedures for our bilateral group. Our bilateral patients had much higher KOOS and KSS scores, compared to the unilateral group (Table 5), which indicates the bilateral group in our study had functionally adapted to living with a replacement to a greater extent than the unilateral group. This may be due to the significantly longer recovery time since surgery for both limbs of bilateral patients, compared to the replaced limb of unilateral patients. A previous study has found bilateral TKR patients may achieve higher functional scores than unilateral patients (18). Further, reduced KAbM is supported by previous research on between-limb differences of unilateral patients. There is conflicting evidence for the differences of asymptomatic controls and non-operated limbs. Alnahdi et al. (8) found no differences between control and non-replaced limbs. Milner and O'Bryan (211) found no difference between replaced and control limbs, but the non-replaced limb was higher than

both limbs. However, in our study, we found no differences in KAbM between replaced and non-replaced limbs of unilateral patients. This is similar to a recent study by Wen et al. (335) who found no difference in KAbM between the replaced and non-replaced limbs of unilateral patients during level walking.

In addition to examining the knee joint, our secondary purpose was to examine any differences between or within these groups at the ankle and hip. We hypothesized that bilateral patients would have similar hip and ankle kinematics and kinetics between 1st and 2nd replaced limbs, which was supported as ankle dorsiflexion/plantarflexion moments and hip extension/flexion and abduction moments, as well as ankle dorsiflexion/eversion and hip extension/adduction ROM were similar between limbs of the bilateral patients. A lack of differences between limbs indicates that these patients may have developed similar neuromuscular adaptations in both 1st and 2nd replaced limbs. This result also reflects the similar movement patterns at the knee. Further, the slightly (non-significant) higher loading-response hip extension moment in the 2nd replaced limb may be present to compensate for the lower loading-response KEM in the 2nd replaced limb.

Additional between-group differences were identified at the hip and ankle. During loading-response, the bilateral patients exhibited reduced dorsiflexion moments compared to the unilateral patients. Reduced dorsiflexion moments in bilateral patients was not expected. A recent study by Biggs et al. (29) found that the replaced limb of TKR patients had higher peak dorsiflexion moments, compared to asymptomatic controls. It was theorized that unilateral patients might have relied on increased dorsiflexion moments to compensate for muscle weakness at the knee joint. This indicates different compensation methods between these groups at the ankle. Biggs et al. (29) also found that the replaced limb of unilateral patients had reduced

peak hip external flexion moments, compared to asymptomatic controls. This contrasts with Levinger et al. (173), who found no differences in hip kinetics. Further, our study did not find different loading-response peak hip extension moments of bilateral patients compared to unilateral patients. However, bilateral patients exhibited lower push-off hip flexion moments, as well as push-off peak vertical GRF. These lower joint moments may be related to the high functional scores, and therefore higher functional capacity, of our bilateral patients, compared to the unilateral patients.

Differences in joint moments among the hip, knee, and ankle in bilateral patients may indicate that this patient population may compensate for their knee replacements using methods different than those of the unilateral patients. Researchers have found that unilateral TKR patients tend to increase their trunk angle while walking, compared to asymptomatic controls (177). While this variable was not examined in the present study, increased forward trunk lean may be present in this population in order to compensate for bilateral quadriceps weakness. However, no differences in hip extension ROM was found between groups in the present study, which is related to trunk angle, and therefore suggesting both groups may have altered their trunk angle similarly.

Limitations for this study include a longer time since surgery for bilateral patients, compared to unilateral patients. This increased length of time may be related to higher KOOS and KSS scores in our bilateral patients. These scores may not be representative of all bilateral TKR patients. Secondly, high body-weight of TKR patients may produce soft tissue motion artifacts level gait which are not representative of the underlying boney landmarks (125, 239).

Conclusion

During level walking, the bilateral group did demonstrate a lower loading-response KEM in the 2nd replaced limb. Aside from this difference, bilateral patients had similar loading-response and push-off hip, knee, and ankle joint sagittal- and frontal-plane joint moments, as well as ROM, between the 1st and 2nd replaced limb. We found that bilateral patients exhibited significantly lower loading-response KEMs, KAbM, loading-response dorsiflexion moments, and push-off hip flexion moments, compared to the unilateral patients. These results indicate that bilateral patient population may produce neuromuscular adaptations that are different than unilateral patients. Future research on how acute adaptations differ following 1st and 2nd replacements may be needed to understand why these groups differ. Further, research into more physically demanding daily activity, such as stair negotiation, may be warranted to examine how these patients differ. Finally, due to significant differences between bilateral and unilateral patients, it may be inadvisable to use bilateral TKR patients in conjunction with unilateral patients when examining their gait biomechanical adaptations.

Chapter IV Appendix: Tables

Table 2. Patient Demographics: mean \pm STD

	Bilateral	Unilateral	p
# of Patients	15 (M: 6)	15(M: 8)	-
Age (years)	69.40 \pm 5.04	68.67 \pm 6.18	0.724
Height (m)	1.73 \pm 0.09	1.73 \pm 0.10	0.614
Weight (kg)	95.56 \pm 15.24	87.73 \pm 15.70	0.297
Time Since First TKR (months)	76.00 \pm 25.11	27.93 \pm 12.03	<0.001
Time Since Second TKR (months)	65.47 \pm 28.98	-	<0.001
Walking Speed (m/s)	1.10 \pm 0.14	1.18 \pm 0.21	0.150

Bold: significant difference.

Table 3. Peak GRFs (N/kg) and Ankle, Knee, and Hip moments (Nm/kg): mean \pm STD

Variable	Bilateral		Unilateral		Limb p	Group p	Int. p
	First Replaced	Second Replaced	Replaced	Non-Replaced			
LR Vertical GRF	1.03 \pm 0.11	1.05 \pm 0.11	1.07 \pm 0.06	1.09 \pm 0.04	0.133	0.195	0.903
PO Vertical GRF	1.00 \pm 0.05	1.01 \pm 0.06	1.05 \pm 0.06	1.06 \pm 0.05	0.095	0.016	0.531
LR Knee Ext. Moment [#]	0.28 \pm 0.23 ^b	0.18 \pm 0.18 ^{a,b}	0.41 \pm 0.14	0.53 \pm 0.26	0.970	0.001	0.024
PO Knee Flex. Moment	-0.16 \pm 0.13	-0.19 \pm 0.16	-0.08 \pm 0.14	-0.14 \pm 0.13	0.105	0.161	0.481
LR Knee Abd. Moment	-0.35 \pm 0.08	-0.38 \pm 0.10	-0.46 \pm 0.10	-0.45 \pm 0.18	0.642	0.033	0.731
PO Knee Abd. Moment	-0.29 \pm 0.10	-0.26 \pm 0.11	-0.32 \pm 0.08	-0.36 \pm 0.16	0.604	0.128	0.360
LR DF Moment	0.17 \pm 0.05	0.18 \pm 0.07	0.30 \pm 0.11	0.27 \pm 0.07	0.217	<0.001	0.058
PO PF Moment	-1.32 \pm 0.12	-1.25 \pm 0.24	-1.30 \pm 0.16	-1.34 \pm 0.15	0.689	0.483	0.066
LR Hip Ext. Moment	-0.61 \pm 0.19	-0.65 \pm 0.19	-0.59 \pm 0.13	-0.55 \pm 0.14	0.907	0.251	0.151
PO Hip Flex. Moment	0.48 \pm 0.11	0.47 \pm 0.13	0.61 \pm 0.17	0.62 \pm 0.17	0.913	0.009	0.680
LR Hip Abd. Moment	-0.85 \pm 0.10	-0.89 \pm 0.13	-0.91 \pm 0.13	-0.92 \pm 0.19	0.459	0.300	0.566
PO Hip Abd. Moment	-0.82 \pm 0.12	-0.86 \pm 0.17	-0.85 \pm 0.11	-0.83 \pm 0.14	0.645	0.914	0.238

[#] Significantly different between the 1st and 2nd replaced limbs, ^a Significantly different from Unilateral Replaced following Holm Adjustment, ^b Significantly different from Unilateral Non-Replaced following Holm Adjustment, LR: Loading-Response, PO: Push-off Response, PF: Plantarflexion, DR: Dorsiflexion, Int.: Limb*Group Interaction, Bold: significant p-values.

Table 4. Ankle, Knee, and Hip ROM (deg): mean \pm STD

Variable	Bilateral		Unilateral		Limb p	Group p	Int. P
	First Replaced	Second Replaced	Replaced	Non- Replaced			
Knee Extension	-48.11 \pm 4.63	-47.45 \pm 5.23	-46.06 \pm 5.80	-47.15 \pm 6.26	0.826	0.511	0.381
Knee Abduction	3.80 \pm 1.90	3.31 \pm 1.61	4.28 \pm 1.12	3.42 \pm 0.86	0.066	0.648	0.856
Ankle Dorsiflexion	22.41 \pm 3.39	22.72 \pm 4.51	24.70 \pm 3.03	22.55 \pm 3.67	0.184	0.370	0.082
Ankle Eversion	-7.48 \pm 4.07	-7.73 \pm 3.78	-5.96 \pm 2.24	-7.23 \pm 3.63	0.393	0.286	0.565
Hip Extension	-35.07 \pm 7.11	-33.86 \pm 5.27	-34.33 \pm 6.08	-37.18 \pm 4.79	0.514	0.466	0.112
Hip Adduction	8.24 \pm 2.73	8.24 \pm 4.72	11.56 \pm 4.16	10.45 \pm 4.98	0.482	0.480	0.049

Int.: Limb*Group Interaction, Bold: significant p-values.

Table 5. KOOS and KSS Scores for Bilateral TKR patients.

		Bilateral	Unilateral
KOOS	Symptoms	94.33±7.29	81.30±20.28
	Stiffness	90.83±12.01	78.10±29.54
	Pain	95.19±9.71	75.00±25.86
	Function - Daily Living	94.12±8.78	82.72±23.23
	Function - Sports	81.50±21.87	25.00±17.80
	Quality of Life	85.42±20.55	62.50±26.52
KSS	Symptoms (25 points)	5.00±2.04	5.25±2.63
	Satisfaction (40 points)	38.67±3.68	23.50±10.75
	Expectation (15 points)	12.53±2.70	8.25±3.77
	Functional Activities (100 points)	86.00±12.80	68.50±23.70
WOMAC	Pain (500 mm)	-	74.45±85.30
	Stiffness (200 mm)	-	44.68±46.22
	Function (1,700 mm)	-	276.36±238.52
	Total (2,400 mm)	-	395.50±341.50

“-“: not available. Bilateral N=15, Unilateral: KOOS and KSS N=4, Unilateral WOMAC N=11.

Chapter V

Altered Biomechanics in Bilateral Total Knee Replacement Patients During Stair Negotiation

Abstract

Purpose: Many total knee replacement (TKR) patients will need to have a contralateral knee replacement. Biomechanical differences between 1st and 2nd replaced limbs of bilateral TKR have not been examined during stair negotiation. Additionally, it's unknown if hip and ankle biomechanics of bilateral patients are altered during stair negotiation. We examined hip, knee, and ankle biomechanics of 1st and 2nd replaced limbs bilateral patients, as well as replaced and non-replaced limbs of unilateral patients, during stair ascent and descent.

Methods: Fifteen bilateral TKR patients (69.40±5.04 years, 1.73±0.09 m, 95.56±15.24 kg) and fifteen unilateral TKR patients (64.93±5.11 years, 1.75±0.09 m, 89.18±17.55 kg) were recruited. Patients performed 3-5 trials of stair ascent and descent. The second step, during ascent, was the step of interest when analyzing each limb. A 2×2 (Limb×Group) ANOVA was performed to determine differences between limbs and groups.

Results: During ascent, bilateral patients exhibited decreased peak loading-response knee extension moment (KEM) and push-off plantarflexion moments. Unilateral replaced limb KEM was lower than non-replaced limbs. During descent, bilateral patients descended the staircase significantly slower, had lower peak loading-response vertical GRF and KEM, and push-off KEM. Bilateral patients had higher peak loading-response hip extension and push-off plantarflexion moments, and increased knee adduction range of motion.

Conclusion: Bilateral patients exhibited similar hip, knee, and ankle joint moments between 1st and 2nd replaced limbs. Substantial differences in hip, knee, and ankle biomechanics during stair negotiation in bilateral patients compared to unilateral patients may indicate a more complex adaptation strategy present in these patients.

Keywords: arthroplasty, gait, stair ascent, stair descent, hip, ankle

Introduction

The number of total-knee replacement (TKR) surgeries performed per year is expected to grow by 673% by 2030 (161). The goal of TKR is to reduce pain and improve functional capacity in patients with severe knee osteoarthritis (45, 330, 357). Unfortunately, risk for contralateral TKR in unilateral patients is between 37% and 46% within 20 years of the 1st replacement (203, 279, 291). Due to high risk for 2nd replacements, it is important to understand how bilateral knee replacements affects this population during activities of daily living.

Stair negotiation is often studied in biomechanics because of its relevance to daily living and more challenge over level walking. Several studies have examined how unilateral TKR patients negotiate stairs (142, 197, 306, 322), fewer have examined bilateral patients (32, 197). McClelland et al. (197) found no differences of maximum knee flexion angle or peak internal knee extension moments (KEM) between bilateral and unilateral patients during stair ascent and descent. No between-limb analyses were conducted for bilateral TKR patients. One study (32) examined bilateral TKR patients, with different implant designs in each limb, during stair negotiation. No differences were found in peak KEM and ROM between two implant designs. To our knowledge, no studies have examined biomechanical differences between 1st and 2nd replaced limbs of bilateral patients during stair negotiation.

During stair negotiation unilateral patients tend to have lower knee flexion ROM (27, 95), compared to asymptomatic controls. Further, they show reduced peak KEM during stair ascent (27, 197, 245) and descent (197, 337). Reduction of KEM may be a result of quadriceps avoidance, producing asymmetries between replaced and non-replaced limbs of unilateral patients, potentially leading to a need for a second TKR. Further, the loading-response knee abduction moment (KA_{BM}) in unilateral patients has been shown to be similar to controls during

ascent (306). Conflicting reports of push-off KAbM indicate this variable is not consistent for unilateral patients (56, 95, 306).

In addition to altered knee joint biomechanics, TKR may also produce altered mechanics in surrounding joints (i.e. hip and ankle). Fenner et al. (103) compared hip and ankle kinetics and kinematics of unilateral patients to asymptomatic controls. During ascent, unilateral patients had increased push-off peak hip extension moments, more extended hips at push-off, and increased peak dorsiflexion angles and decreased peak dorsiflexion moments at push-off. During descent, unilateral patients exhibited higher push-off peak hip extension moments and increased dorsiflexion at initial contact (104).

Differences in hip, knee, and ankle biomechanics between 1st and 2nd replaced limbs of bilateral patients during stair negotiation are unknown. No studies have examined hip, knee, and ankle kinematics and kinetics of bilateral patients compared to unilateral patients during stair negotiation. While some studies have excluded bilateral patients (306), other studies have not (197, 300). It is unknown if excluding bilateral patients from TKR research is necessary. The primary purpose of this study was to examine differences in knee biomechanics of 1st and 2nd replaced limbs of bilateral patients during stair negotiation; and compare differences in knee biomechanics of 1st and 2nd replaced limbs of bilateral patients, with replaced and non-replaced limbs of unilateral patients. The secondary purpose was to examine hip and ankle kinematics and kinetics of these patients.

We hypothesized that peak KEM, KAbM, and knee extension and abduction ROM would not be statistically different between 1st and 2nd replaced limbs of bilateral patients. We further hypothesized that 1st and 2nd replaced limbs of bilateral patients would have similar peak KEM and KAbM as replaced limbs, but lower KEM and KAbM compared to non-replaced limbs of

unilateral patients. Finally, we hypothesized that hip and ankle kinetics and kinematics would be similar between 1st and 2nd replaced limbs of bilateral patients and replaced limbs of unilateral patients, but hip extension moments would be higher compared to non-replaced limbs of unilateral patients.

Methods

Participants

Fifteen (9 female) bilateral TKR patients were recruited for this study from a local orthopedic clinic (Table 6). An additional fifteen (6 female) unilateral TKR patients from the same orthopedic clinic were randomly selected from two previous studies conducted in our lab (306, 322). Within the bilateral group, eleven patients had staged TKR surgeries and four patients had simultaneous TKR surgeries. Inclusion criteria and exclusion criteria for this study are found in Table 7. An *a priori* power analysis of KEM in bilateral TKR patients and healthy controls indicated a minimum of 15 participants per group were needed to achieve a beta of 0.80 and alpha of 0.05, with an effect size of 1.1 (262). All participants signed an informed consent document and all procedures were approved by the Institutional Review Board.

Instrumentation

A motion analysis system (240 Hz, Vicon Motion Analysis Inc., Oxford, UK) captured three-dimensional (3D) kinematics. Anatomical and tracking markers were used for 3D kinematic data collection (347). Ground reaction forces (GRF) were measured via an instrumented 3-step staircase (FP-Stairs, American Mechanical Technology Inc., Watertown, MA, USA) mounted on top of two force platforms (1200 Hz, American Mechanical Technology Inc., Watertown, MA, USA) (347).

Experimental Procedures

Bilateral patients warmed up by walking on a treadmill at a self-selected pace for three minutes. Patients wore standard neutral lab running shoes and performed up to five practice trials to obtain their preferred speed during ascent and descent. Gait speed during testing trials was monitored and maintained within $\pm 10\%$ of their preferred speeds. Three to five trials were collected for each of ascent and descent conditions. Unilateral patients followed similar data collection protocols.

Participants began stair ascent conditions three steps away from the staircase. The second step, during ascent, was used for data analysis. The four conditions included ascending and descending with either the 1st or 2nd replaced limb contacting the 2nd step. Four simultaneous TKR patients had their limbs randomly selected as 1st and 2nd replaced limb. Descent condition always followed ascent and testing order of 1st and 2nd TKR limbs was randomized within ascent and descent conditions, respectively. Participants were instructed to use step-over-step manner.

Data Analysis

Marker trajectory and analog data were exported to Visual 3D (V6, C-Motion, Inc., Germantown, MD, USA). A fourth-order Butterworth zero-lag low-pass filter was used to filter marker trajectory and GRF data at a cutoff frequency of 8 Hz for kinematic and joint moment analysis. A separate fourth-order Butterworth zero-lag low-pass filter was used to filter GRF at 50 Hz data for analysis of GRFs. 3D angular kinematic and kinetic computations were performed using the joint coordinate system (118) with a Cardan rotational sequence (X-Y-Z). The right-hand rule defined joint angle and moment conventions. Joint moments were calculated as internal moments and expressed in the proximal segment reference system. Joint moments and GRF were normalized to participant's body mass (Nm/kg) and body weight (BW), respectively.

Statistical Analysis

A one-way repeated measure analysis of variance (ANOVA) was performed to detect differences between 1st and 2nd replaced limbs of bilateral patients. A 2 x 2 (limb x group) mixed model ANOVA was performed to detect differences between limbs and between groups. All statistical tests were performed using IBM SPSS Statistics (version 24), with alpha level of 0.05 set a priori. Effect sizes of main effects and interactions was reported as partial eta squared (η_p^2). Post-hoc comparisons were performed on significant interactions. Independent sample t-tests were performed to identify between-group differences while paired-sample t-tests were used to determine differences between limbs of both groups. A step-wise Holm procedure was used in adjusting alpha level for multiple comparisons in post hoc tests (64, 126). Cohen's *d* was calculated and reported for all t-tests, using standard definitions for small, medium, and large effects (69).

Results

Bilateral patients were older than unilateral patients selected for this study ($p = 0.023$, $d = 0.881$, Table 6). Time since surgery was longer for the 1st knee replacement, compared to the 2nd replacement, in bilateral patients ($p = 0.003$, $d = 1.30$). Time since surgery was longer for the 1st replaced ($p < 0.001$, $d = 2.06$) and 2nd replaced ($p = 0.001$, $d = 1.41$) limbs of bilateral patients than replaced limbs of unilateral patients. Bilateral patients descended stairs slower than unilateral patients ($p = 0.007$, $\eta_p^2 = 0.234$, Table 6).

During ascent, a significant limb×group interaction was found for push-off peak vertical GRF ($p = 0.009$, $\eta_p^2 = 0.220$, Table 8). However, post-hoc test revealed no within- or between-group differences.

Peak loading-response KEM exhibited a significant limb*group interaction ($p = 0.004$, $\eta_p^2 = 0.263$, Table 8). Post-hoc tests show KEM was lower for 2nd replaced limbs of bilateral patients than non-replaced limbs of unilateral patients ($p = 0.010$, $d = 1.01$). Additionally, KEM for non-replaced limbs were higher than replaced limbs in unilateral patients ($p = 0.006$, $d = 1.18$).

At the ankle, a limb×group interaction ($p = 0.03$, $\eta_p^2 = 0.162$) for peak push-off plantarflexion moment was found (Table 8). Post-hoc tests showed that 2nd replaced limb of bilateral patients had a lower moment than non-replaced limb of unilateral patients ($p = 0.006$, $d = 1.09$). In addition, peak loading-response hip extension moments were higher in bilateral patients compared to unilateral ($p = 0.017$, $\eta_p^2 = .186$). A limb×group interaction was found for ankle plantarflexion ROM during ascent ($p = 0.012$, $\eta_p^2 = 0.205$, Table 9). Post-hoc analyses revealed no significant differences between groups, or between limbs, of bilateral and unilateral patients.

During descent, bilateral patients had lower peak loading-response vertical GRFs than unilateral patients ($p = 0.020$, $\eta_p^2 = 0.178$, Table 10). Additionally, peak loading-response KEM had a limb×group interaction ($p = 0.011$, $\eta_p^2 = 0.209$). Post-hoc tests revealed that KEM for 1st replaced limbs of bilateral patients were lower than both replaced ($p = 0.014$, $d = 0.98$) and non-replaced ($p < 0.001$, $d = 1.75$) limbs of unilateral patients. Further, KEM for 2nd replaced limbs of bilateral patients were lower than both replaced ($p = 0.010$, $d = 1.36$) and non-replaced ($p < 0.001$, $d = 2.17$) limbs of unilateral patients. Peak push-off KEM demonstrated a limb×group interaction ($p = 0.003$, $\eta_p^2 = 0.281$). Post-hoc analysis revealed that KEM of 1st ($p = 0.009$, $d = 1.04$) and 2nd ($p = 0.002$, $d = 1.30$) replaced limbs of bilateral patients were lower than non-replaced limbs of unilateral patients.

For ankle kinetics, a limb×group interaction was found for peak loading-response plantarflexion moment ($p = 0.026$, $\eta_p^2 = 0.164$, Table 10). Post-hoc tests show no within- or between-group differences. For peak push-off plantarflexion moment, there was a limb×group interaction ($p = 0.002$, $\eta_p^2 = 0.283$). Post-hoc comparisons demonstrated within group differences for both groups. This peak moment for 1st replaced limbs of bilateral patients were higher than the 2nd replaced ($p = 0.029$, $d = 0.90$). The peak moment for replaced limbs of unilateral patients was lower than nonreplaced limbs ($p = 0.037$, $d = 0.86$). Between group comparisons showed that moments for 1st replaced limbs of bilateral patients were higher than replaced ($p < 0.001$, $d = 2.34$) and non-replaced ($p = 0.004$, $d = 1.16$) limbs of unilateral patients. 2nd replaced limb was also higher than replaced limbs of unilateral patients ($p < 0.001$, $d = 1.56$). Hip loading-response extension moments were higher in bilateral patients ($p < 0.001$, $\eta_p^2 = .536$).

There was a limb main effect for the knee flexion ROM during descent showing lower ROM for 1st replaced limbs of bilateral and replaced limbs of unilateral patients compared the respective second replaced and non-replaced limbs ($p = 0.007$, $\eta_p^2 = 0.234$, Table 11). In the frontal plane, a limb×group interaction ($p = 0.016$, $\eta_p^2 = 0.189$) was present. Post-hoc tests show significantly greater knee adduction ROM for 2nd replaced limbs of bilateral patients, compared to non-replaced limbs of unilateral patients ($p = 0.004$, $d = 1.18$).

Discussion

Our first hypothesis that bilateral patients would have similar KEM, KAbMs, as well as similar extension ROM between 1st and 2nd replaced limbs, was supported. This shows that both replaced limbs have similar functional capacity and recovery following surgery. No significant difference in the KEM indicate similar quadriceps recovery between limbs.

Increases in KEM and KAbM indicate increased knee joint loading (189, 328). Lack of differences between 1st and 2nd replaced limbs suggests that bilateral patients are placing similar loads on both implants. Doing so may reduce potential risks of future revisions due to asymmetrical loads. Since one of the goals of TKR is to reduce knee joint loading in knee OA patients, it is promising that both limbs of bilateral patients appear to have similar loading-response and push-off peak KAbM during ascent (235) and lower loading-response and push-off peak KAbM compared to OA patients during descent (236). loading-response KEMs in 1st (1.00 ± 0.36 Nm/kg) and 2nd (0.96 ± 0.31 Nm/kg) replaced limbs of bilateral patients were greater than knee OA patients during stair ascent (0.63 Nm/kg) (230). Bilateral patients had similar push-off peak KEM (1st: 0.79 ± 0.25 Nm/kg and 2nd: 0.73 ± 0.25 Nm/kg) compared to knee OA patients during descent (0.71 Nm/kg) (236). This demonstrates that bilateral patients may regain quadriceps function above pre-surgery levels.

No significant differences between limbs of bilateral patients contrasts with previous research on level walking for this patient group (Chapter IV) During level walking, 1st replaced limbs of bilateral patients had higher peak KEM compared to 2nd replaced limbs. Given increased difficulty in stair negotiation, it is surprising that this difference has disappeared. A small quadriceps avoidance is seen in each limb during stair ascent, especially in 2nd replaced limbs, and may be exaggerated during descent, as these moments are much smaller than those of unilateral patients. These patients may have adapted to stair negotiation by reducing avoidance in 2nd replaced limbs in order to progress to the following steps. Therefore, increased difficulty in negotiating stairs may have prompted similar adaptations between 1st and 2nd replaced limbs during this activity.

Lack of differences between 1st and 2nd replaced limbs may also be related to the extended time from surgery for these bilateral patients. Average time since surgery for 1st replaced limbs was approximately 6.33 years, 5.46 years since 2nd replacement, an average of 3.2 years longer than unilateral patients. Given the longer time that bilateral patients have had replacements, any differences in acute adaptations between 1st and 2nd replaced limbs may no longer be present. Further research into acute adaptations following bilateral TKR is needed to determine short-term after-surgery effects on these limbs.

Our second hypothesis, that bilateral patients would have similar KEM, KAbM, and knee extension ROM as replaced limbs of unilateral patients, but decreased KEM and KAbM than non-replaced limbs of unilateral patients, was partially supported. During ascent, peak loading-response KEM of 2nd replaced limbs of bilateral patients was lower than non-replaced limbs of unilateral patients. Reductions in this moment in bilateral patients, compared to asymptomatic controls, has been found previously during level walking (262). Further, KEM of replaced limbs of unilateral patients was lower than their non-replaced limbs. This similar to previous studies (197, 245). This reduced moment is indicative of a quadriceps avoidance gait, possibly due to reductions in muscular strength or a fear of pain/discomfort. Interestingly, our results of this moment did not show differences between 1st replaced limbs of bilateral patients and non-replaced limbs of unilateral patients, while 2nd replaced limbs demonstrated differences. This may be indicative of the large standard deviation of this variable for 1st replaced limbs.

During stair descent, peak loading-response and push-off KEM were different than unilateral patients. Peak loading-response KEM moments were lower in 1st and 2nd replaced limbs of bilateral patients, compared to both limbs of unilateral patients. Further, push-off KEM was lower in both 1st and 2nd replaced limbs of bilateral patients, compared to non-replaced limbs

of unilateral patients. However, it is important to note that unilateral patients descended the staircase significantly faster than bilateral patients. Previous research indicates the direct relationship between changes in gait speed and changes in both GRF and joint moments (170). Reduced descent speeds in bilateral patients may have played a significant role in the decreased loading-response vertical GRF and both loading-response and push-off KEM. A repeated measure analysis of covariance (ANCOVA) was performed with descent speed as a covariate. The ANCOVA results demonstrated that group differences for loading-response peak vertical GRF became non-significant. However, group differences for both loading-response and push-off KEM were still present.

In the frontal plane, no kinetic differences were found during either ascent or descent. It was expected that bilateral patients would have similar peak KAbMs as replaced limbs of unilateral patients. No differences were identified for KAbM within unilateral patients. This is similar to previous research during stair negotiation (56).

Our hypothesis on hip and ankle biomechanics was partially supported. During ascent, we found minimal differences in hip and ankle moments and ROM between the 1st and 2nd replaced limbs of bilateral patients. However, during descent 1st replaced limbs exhibited higher push-off peak plantarflexion moments compared to 2nd replaced limbs. While this was the only significant between-limb difference for bilateral patients, a trend of higher plantarflexion moments ($p = 0.087$) in 1st replaced limbs can be seen during loading-response of descent. As previously stated, differences between 1st and 2nd replaced limbs may indicate altered joint loading strategies between limbs.

When comparing hip and ankle kinematics and kinetics, differences between bilateral and unilateral patients were identified. During ascent, bilateral patients exhibited increased loading-response hip extension moments, and lower push-off plantarflexion moments. During descent, however, bilateral patients exhibited higher push-off plantarflexion moments and loading-response hip extension moments. Increased hip extension moment during ascent and descent supports the findings of Fenner et al. (103, 104). However, this is in contrast to previous reports of no difference (306) or reductions (277) in hip extension moments in replaced limbs of unilateral patients compared to their non-replaced limbs and asymptomatic controls during stair ascent. Further, increased plantarflexion moments in bilateral patients, compared to unilateral patients, supports previous findings. The hip compensation strategy reflected in increased loading-response hip extension moments, which was more apparent during descent, may indicate that bilateral patients increase their reliance on this joint during stair ambulation, compared to unilateral patients. Importantly, increases in plantarflexion and hip extension moments were present in bilateral patients despite decreased stair descent speeds. Similar gait speeds may have produced even greater differences between these groups.

Implications for this study are that bilateral patients may have functional adaptations that are different than those of unilateral patients. This can be seen in lower KEM in bilateral patients which may be due to decreased muscular strength, and kinesiophobia. Despite these deficits, bilateral patients did not show a hesitancy in stair usage. Our bilateral patients reported an average 5.47 ± 2.42 days per week of stair usage. While the amount of stair usage for unilateral patients was unknown, it is clear that the alterations in joint moments in the bilateral group does not inhibit them from using stairs.

One limitation for this study is increased descent speed of unilateral patients. However, when controlling for the increased descent speed of unilateral patients, it did not affect the statistical outcome of key the loading variable, KEM. Bilateral patients had significantly longer recovery time since surgery and were significantly older. Increased age of implant and age of patients may have contributed to differences between these groups. Additionally, the increased body-weight of TKR patients may produce soft-tissue artifacts, corresponding to movement that are not exact representations of underlying bony landmarks (125, 239).

Conclusion

Bilateral patients exhibited similar hip, knee, and ankle joint moments between 1st and 2nd replaced limbs. Increased push-off plantarflexion moments in 1st replaced limbs, as well as non-significant differences in knee moments, may indicate that small adaptive differences following the 2nd knee replacement. Several differences between bilateral and unilateral patients were identified. During ascent, bilateral patients exhibited decreased push-off plantarflexion moments and increased loading-response hip extension moments. During descent, bilateral patients exhibited decreased loading-response vertical GRF, loading-response and push-off KEM, as well as increased push-off plantarflexion moments, loading-response hip extension moments, and knee abduction ROM.

Chapter V Appendix: Tables

Table 6. Patient Demographics: mean \pm STD.

	Bilateral		Unilateral		p
# of Patients	15 (F: 9)		15 (F: 6)		
Age (years)	69.40 \pm 5.04		64.93 \pm 5.11		0.023
Height (m)	1.73 \pm 0.09		1.75 \pm 0.09		0.614
Weight (kg)	95.56 \pm 15.24		89.18 \pm 17.55		0.297
Time Since First TKR (mo)	76.00 \pm 25.11		32.07 \pm 16.60		<0.001
Time Since Second TKR (mo)	65.47 \pm 28.98		-		0.001
	1 st	2 nd	Replaced	Non-Replaced	Group p
	Replaced	Replaced			
Ascent Speed (m/s) [#]	0.58 \pm 0.06	0.57 \pm 0.05	0.62 \pm 0.10	0.62 \pm 0.11	0.108
Descent Speed (m/s) [#]	0.52 \pm 0.04	0.50 \pm 0.06	0.59 \pm 0.11	0.59 \pm 0.11	0.007

Bold: p-values indicate significance. #: No significant limb main effect or interaction of group x limb were found.”

Table 7. Exclusion and Inclusion Criteria for Bilateral TKR Patients.

Exclusion Criteria	Inclusion Criteria
<ul style="list-style-type: none"> • Diagnosed osteoarthritis at the ankle or hip joint as reported by the patient. • Any additional lower extremity joint replacement. • Any lower extremity joint arthroscopic surgery or intra-articular injection within past 3 months. • Systemic inflammatory arthritis (rheumatoid arthritis, psoriatic arthritis) as reported by the patient. • BMI greater than 38. • Neurologic disease (e.g. Parkinson's disease, stroke patients) as reported by the patient. • Any additional major lower extremity injuries/surgeries except for the replaced knees. • Inability to walk or use stairs without a walking aid. • Women who are pregnant or nursing. • Any visual conditions affecting gait or balance. 	<ul style="list-style-type: none"> • Men and women between the ages of 50 and 75. • Total knee replacement in two knees. • At least 12-months from the second TKR. • No more than 10-years from the first TKR. • Cruciate retaining TKR.

Table 8. Ascent Peak GRFs (N/kg), and Ankle, Knee, and Hip moments (Nm/kg): mean \pm STD.

Variable	Bilateral		Unilateral		Limb p	Group p	Int. p
	First Replaced	Second replaced	Replaced	Non-Replaced			
LR Vertical GRF	1.02 \pm 0.08	1.02 \pm 0.07	0.98 \pm 0.05	1.02 \pm 0.06	0.083	0.489	0.108
PO Vertical GRF	1.14 \pm 0.10	1.12 \pm 0.10	1.13 \pm 0.09	1.20 \pm 0.09	0.106	0.207	0.009
LR Knee Ext. Moment	1.00 \pm 0.36	0.96 \pm 0.31 ^b	0.98 \pm 0.22 [#]	1.27 \pm 0.29	0.024	0.154	0.004
LR Knee Abd. Moment	-0.42 \pm 0.16	-0.39 \pm 0.22	-0.36 \pm 0.11	-0.36 \pm 0.18	0.716	0.344	0.739
PO Knee Abd. Moment	-0.32 \pm 0.21	-0.19 \pm 0.28	-0.27 \pm 0.15	-0.32 \pm 0.25	0.617	0.374	0.441
LR PF Moment	-0.52 \pm 0.20	-0.47 \pm 0.25	-0.52 \pm 0.13	-0.56 \pm 0.19	0.867	0.527	0.210
PO PF Moment	-1.01 \pm 0.18	-0.95 \pm 0.24 ^b	-1.08 \pm 0.09	-1.17 \pm 0.15	0.790	0.015	0.030
LR Hip Ext. Moment	-0.58 \pm 0.13	-0.60 \pm 0.15	-0.50 \pm 0.17	-0.45 \pm 0.14	0.471	0.017	0.220

^a Significantly different than Unilateral Replaced, ^b Significantly different than Unilateral Non-Replaced, [#] Significantly different from the contralateral limb of the same group difference. LR: Loading-Response, PO: Push-off Response, PF: Plantarflexion, Int.: Leg*Group Interaction, Bold: p-values indicate significance.

Table 9. Ascent Ankle, Knee, and Hip ROM (deg): mean \pm STD.

Variable	Bilateral		Unilateral		Limb p	Group p	Int. P
	First Replaced	Second Replaced	Replaced	Non-Replaced			
Knee Extension	54.18 \pm 5.73	52.87 \pm 6.65	54.21 \pm 5.58	58.39 \pm 4.77	0.293	0.095	0.050
Knee Abduction	-12.87 \pm 6.00	-13.90 \pm 6.77	-13.55 \pm 6.74	-11.03 \pm 6.68	0.797	0.436	0.208
Plantarflexion	-34.88 \pm 8.71	-33.26 \pm 9.12	-28.30 \pm 5.94	-32.73 \pm 8.34	0.223	0.206	0.012
Hip Extension	-49.45 \pm 6.88	-49.87 \pm 3.96	-49.56 \pm 3.53	-51.70 \pm 3.56	0.263	0.459	0.450

^a Significantly different than Unilateral Replaced, ^b Significantly different than Unilateral Non-Replaced, [#] Significant within-group difference. Int.: Leg*Group Interaction, Bold: p-values indicate significance.

Table 10. Descent Peak GRFs (N/kg) and Ankle, Knee, and Hip moments (Nm/kg): mean \pm STD.

Variable	Bilateral		Unilateral		Limb p	Group p	Int. p
	First Replaced	Second Replaced	Replaced	Non-Replaced			
LR Vertical GRF	1.40 \pm 0.21	1.34 \pm 0.15	1.51 \pm 0.24	1.56 \pm 0.22	0.864	0.020	0.110
PO Vertical GRF	0.96 \pm 0.08	0.94 \pm 0.09	0.89 \pm 0.06	0.92 \pm 0.07	0.640	0.089	0.099
LR Knee Ext. Moment	0.32 \pm 0.29 ^{a,b}	0.23 \pm 0.25 ^{a,b}	0.62 \pm 0.33	0.87 \pm 0.34	0.212	<0.001	0.011
PO Knee Ext. Moment	0.79 \pm 0.25 ^b	0.73 \pm 0.25 ^b	0.83 \pm 0.24	1.07 \pm 0.29	0.073	0.027	0.003
LR Knee Abd. Moment	-0.39 \pm 0.24	-0.54 \pm 0.23	-0.54 \pm 0.26	-0.51 \pm 0.24	0.291	0.375	0.173
PO Knee Abd. Moment	-0.32 \pm 0.24	-0.47 \pm 0.20	-0.38 \pm 0.22	-0.35 \pm 0.15	0.387	0.470	0.161
LR PF Moment	-1.10 \pm 0.15	-0.97 \pm 0.29	-0.94 \pm 0.25	-1.06 \pm 0.30	0.876	0.651	0.026
PO PF Moment	-1.28 \pm 0.15 ^{a,b,#}	-1.18 \pm 0.15 ^a	-0.99 \pm 0.09 [#]	-1.11 \pm 0.15	0.798	<0.001	0.002
LR Hip Ext. Moment	-0.86 \pm 0.19	-0.86 \pm 0.30	-0.34 \pm 0.29	-0.36 \pm 0.28	0.913	<0.001	0.800

^a Significantly different than Unilateral Replaced, ^b Significantly different than Unilateral Non-Replaced, [#] Significant within-group difference. LR: Loading-Response, PO: Push-off Response, PF: Plantarflexion, Int.: Leg*Group Interaction, Bold: p-values indicate significance.

Table 11. Descent Ankle, Knee, and Hip ROM (deg): mean \pm STD.

Variable	Bilateral		Unilateral		Limb p	Group p	Int. P
	First Replaced	Second Replaced	Replaced	Non-Replaced			
Knee Flexion	-78.30 \pm 5.27	-79.38 \pm 4.97	-80.06 \pm 4.05	-82.60 \pm 4.45	0.007	0.132	0.252
Knee Abduction	11.17 \pm 4.99	14.37 \pm 8.16 ^b	9.71 \pm 7.20	6.31 \pm 4.45	0.864	0.023	0.016
Plantarflexion	58.84 \pm 4.93	57.20 \pm 8.35	51.05 \pm 14.08	53.38 \pm 16.76	0.781	0.177	0.119
Hip Extension	18.10 \pm 4.17	19.20 \pm 3.91	18.54 \pm 3.64	18.64 \pm 5.01	0.242	0.952	0.171

^a Significantly different than Unilateral Replaced, ^b Significantly different than Unilateral Non-Replaced, [#] Significant within-group difference. Int.: Leg*Group Interaction, Bold: p-values indicate significance.

Chapter VI

Principal Component Analysis of Bilateral and Unilateral Total Knee Replacement

Patients During Level Walking

Abstract

Background: Many unilateral total knee replacement (TKR) patients will need a contralateral TKR. Differences in knee joint biomechanics between bilateral patients, unilateral patients, and asymptomatic controls is not well established. The purpose of this study was to examine knee joint differences in level walking between bilateral and unilateral patients, and asymptomatic controls, using principal component analysis.

Methods: Knee joints of 1st replaced limbs of 15 bilateral patients (69.40 ± 5.04 years, 1.73 ± 0.09 m, 95.56 ± 15.24 kg), 15 replaced limbs of unilateral patients (66.47 ± 6.15 years, 1.75 ± 0.10 m, 87.71 ± 14.29 kg), and 15 randomly selected limbs of asymptomatic controls (63.53 ± 9.50 years, 1.79 ± 0.10 m, 85.07 ± 19.59 kg) were analyzed during level walking. Principal component analysis examined knee joint sagittal- and frontal-plane kinematics and moments, and vertical GRF. A one-way analysis of variance analyzed differences between principal component scores of each group.

Results: TKR patients exhibited more flexed and abducted knees throughout stance, decreased sagittal knee range of motion (ROM), increased early-stance adduction ROM, decreased loading-response knee extension and push-off knee flexion moments, decreased loading-response and push-off peak knee abduction moment (KAbM), increased KAbM at midstance, increased midstance vertical ground reaction force (GRF), as well as decreased loading-response and push-off vertical GRF. Additionally, bilateral patients exhibited reduced sagittal knee ROM, increased adduction ROM, decreased sagittal knee moments throughout stance, decreased KAbM throughout stance, an earlier loading-response peak vertical GRF, and a decreased push-off vertical GRF, compared to unilateral patients.

Conclusion: TKR patients, especially bilateral patients had stiff knee motion in the sagittal-plane, increased frontal-plane joint laxity, and a quadriceps avoidance gait.

Keywords: arthroplasty, gait, PCA, knee extension moment, knee abduction moment

Introduction

In the United States, total knee replacement (TKR) is a common procedure that is expected to become even more commonplace in the future, with an estimated 3.5 million TKRs performed each year by 2030 (161). Within 10 to 20 years of initial surgery, approximately 37% to 46% of TKR patients require a 2nd replacement in the contralateral limb (203, 279, 291). Previous research indicates significant gait alterations due to unilateral TKR (8, 173, 190, 205, 300, 321). Given this, it is reasonable to expect further differences to be present following a contralateral TKR.

Previous research into unilateral TKR patients indicates that these patients walk with a stiff knee gait and a quadriceps avoidance gait (210, 354). A stiff knee gait is determined in this patient population due to the reduced sagittal-plane knee range of motion (ROM) (202). Further, a quadriceps avoidance is determined to be in this population due to reduced knee extension moments (173, 190, 211, 300, 321). This avoidance may be associated with reduced muscular strength, or kinesiophobia during gait (106, 139). This quadriceps avoidance has also been demonstrated in both limbs of bilateral patients (Chapter IV). A recent investigation on both limbs of bilateral patients showed decreased peak loading-response knee extension moments, compared to unilateral patients (Chapter IV). This may have indicated that bilateral patients demonstrate similar but enhanced quadriceps avoidance.

The aforementioned research used discrete events in order to analyze differences between unilateral patients and asymptomatic controls, or between bilateral and unilateral patients. While these analysis of these events, such as loading-response and push-off response, are commonplace and provide significant insight into how groups of people differ, information regarding waveform characteristics through the entire movement phase may be lost (76). In order to

perform a robust analysis of the entire waveform of biomechanical data, researchers can use principal component analysis (PCA), which identifies variations in waveform patterns and characteristics influencing variations in data.

This analysis technique has been used previously in TKR research (12, 15, 29, 78, 120, 122, 194, 204, 205, 262, 318). During level walking, unilateral TKR patients tend to exhibit reduced sagittal plane knee ROM, reduced knee extension and flexion moments, lower loading-response and push-off knee abduction moment (KAbM) (29). One study examined changes in the knee flexion angle of bilateral TKR patients before and after surgery (262). This study found that the patients had higher knee flexion angles and greater ROM throughout stance after TKR surgery. However, the bilateral patients exhibited decreased knee flexion ROM, compared to asymptomatic controls.

Previous research performing PCA on gait biomechanics of TKR patients generated separate PCA models for individual variables and therefore all results were independent of the others. However, other researchers have found that a more robust analysis of biomechanical data would be to combine the waveforms of all variables of interest (39, 158, 221). The variance within the variables of interest of a single principal component (PC) identifies correlated changes, while other PCs remain uncorrelated (39). To date, no study has used this multivariate approach to study gait biomechanical waveforms of TKR patients.

The purpose of this study was to examine knee joint biomechanical differences in level walking between bilateral patients, unilateral patients, and asymptomatic controls, using multivariate PCA. The PCA was performed to identify kinematic and kinetic features of entire stance-phase waveforms, and to compare the waveforms of these groups for differences. We hypothesized that bilateral and unilateral patients would have similar PC-scores, indicating no

differences in the waveforms. Secondly, we hypothesized that the PC-scores of bilateral and unilateral patients would differ significantly from those of asymptomatic controls, indicating significant differences in the waveforms.

Materials and Methods

Participants

Fifteen bilateral (6 male) and unilateral (8 male) patients, as well as fifteen asymptomatic (9 male) controls, participated in this study (Table 1). All patients were recruited from a local orthopedic clinic and were operated by the same surgeon. Unilateral patients and asymptomatic controls were selected randomly, using a random number generator in MATLAB, from previous studies (306, 322, 335). The 1st replaced limb for bilateral patients (76.00 ± 25.11 months since TKR), replaced limbs for unilateral patients (25.33 ± 15.09 months since TKR), and a randomly selected limb of asymptomatic controls were used for analysis. Inclusion criteria for this study included participants aged between 50 and 75, patients between 1- and 10-years post-op, and having the same surgeon. Patients were excluded if osteoarthritis (OA) or joint replacements were present in any additional lower extremity joints, BMI >40, any neurological disorder, or unable to walk without aid. All participants signed an informed consent and all procedures approved by the Institutional Review Board.

Instrumentation

A motion analysis system (240 Hz, Vicon Motion Analysis Inc., Oxford, UK) captured three-dimensional marker trajectories during level walking trials. The markers and their placements have been described previously (Chapter IV). Three-dimensional ground-reaction forces (GRF) and moments were measured via two force platforms (1200 Hz, BP600600, American Mechanical Technology Inc., Watertown, MA, USA). The gait speed for each trial

was monitored by two sets of photocells (63501 IR, Lafayette Instrument Inc., IN, USA) placed three meters apart, and electronic timers (54035A, Lafayette Instrument Inc., IN, USA)

Experimental Procedure

Patients were allowed up to five practice trials walking across the force platform to ensure consistent walking speed and foot placement. Average walking speed ($\pm 10\%$) was recorded from the practice trials and was used to control walking speed during data acquisition trials. Patients performed 3-5 data acquisition trials. Trials were repeated if the incorrect foot contacted the force platform, if the foot was outside the boundaries of the force platform, if patients visibly altered their gait to contact the force platform, or if the predetermined speed range was not met.

Data Analysis

A PCA was used to identify differences in kinematic and kinetic waveforms of bilateral patients, unilateral patients, and asymptomatic controls. For the present study, a single PCA on a data matrix that includes all variables of interest was used. These variables included: sagittal and frontal plane knee angles and moments and vertical ground reaction force (GRF). Similar to the PCAs performed by Boyer et al. (39) and Kobayashi et al. (158), our PCA identified principal components (PCs) contain variables that work in concert to generate the direction of variation of individual PCs. Performing a PCA in this fashion allowed us to identify how variations within multiple variables work congruently to distinguish our groups.

Individual trials for each participant was ensemble averaged to generate a single waveform, one corresponding to each of five variables, for each participant (42). To account for unit differences, each trial was scaled to unit variance to account for differences in units across the variables. This is done by calculating a z-score, a unitless distance from a mean (76). Each

ensemble average of each participant of the five variables, was then combined into a single data matrix. This scaled data matrix is called a correlation matrix (76). The different variables are concatenated horizontally, while participants are added as rows. The correlation matrix for the PCA consisted of 15 bilateral 1st replaced limbs, 15 unilateral replaced limbs, and 15 randomly selected controls limbs. Therefore, the correlation matrix consisted of 45 rows (45 patients) and 505 columns (5 variables*101 time points per variable). The multivariate PCA was performed on this matrix (39, 76).

Only the PCs that explain the most variation are included for analysis. For this study, we kept the number of PCs required to explain at least 90% of the variance in the data (76).

Waveforms associated with significant group differences were interpreted via representative extremes (42, 76). Representative extreme waveforms were first generated by multiplying the standard deviation of each PC score with its corresponding loading vector (LV). The extreme waveform corresponding to a high PC score was then generated by adding this new vector to the overall mean vector, while the low PC score waveform was generated by subtracting this vector instead. Each PC contains directions of variations for each variable, in the order it was placed into the PCA data matrix.

Statistical Analysis

PCA was performed using customized codes in MATLAB (R2017a, MathWorks, Matick, MA, USA). The output of the PCA was a set of eigenvectors (PCs), percentage explained by each PC, and PC scores for each limb in the data set. PC scores were grouped into bilateral, unilateral, and controls. A one-way analysis of variance (ANOVA) was performed on each retained PC to determine differences between the groups within each PC (24, IBM SPSS Statistics). Post-hoc independent samples t-tests were conducted on significant group effects.

Additionally, a one-way ANOVA was performed to detect differences in age, height, weight, and gait speed between the three groups. An independent samples t-test was performed to detect differences in time since TKR surgery for bilateral and unilateral patients.

Results

No differences in age, height, or weight, were found between bilateral, unilateral, and controls. Bilateral patients had significantly longer time since surgery (76.00 ± 25.11 months) than unilateral patients (25.3 ± 15.1 months, Table 1). Preferred walking speed was not different between bilateral and unilateral patients ($p = 0.386$). However, asymptomatic controls walked significantly faster than both bilateral ($p < 0.001$) and unilateral ($p = 0.010$) patients.

Eleven PCs were retained, accounting for 91.21% of the variation in the data. PC2, PC3 and PC5 were different between three participant groups and they accounted for 16.88%, 11.38%, and 5.38%, respectively (Table 2). Bilateral and unilateral patients had lower PC2 scores (both $p = 0.005$), as well as lower PC3 scores (both $p = 0.001$), compared to controls. Bilateral patients also had a lower PC5 ($p = 0.009$), compared to unilateral patients. PC5 scores were not different between bilateral patients and controls ($p = 0.085$), or between unilateral patients and controls ($p = 0.334$). PC1, which accounted for the largest variation in the dataset (35.83%), showed a trend of group differences ($p = 0.067$, Table 2).

Waveforms of the sagittal knee angle were reconstructed to isolate the variance captured by PCs 2, 3, and 5 (Figure 1G-I). PC2 LV was entirely positive, indicating a magnitude difference between the groups throughout stance with the largest variance occurring following midstance (Figure 1D). Inspection of the reconstructed waveforms (Figure 1G), and mean waveforms (Figure 1A-C), support that low-scoring participants (TKR) were less extended following midstance, especially so from 50-85% of stance. The PC3 LV exhibited negative

values before midstance and positive values following midstance, indicating a difference feature (Figure 1E). Reconstructed waveforms show TKR patients were less flexed in early stance, and less extended in late stance (Figure 1H). Therefore, TKR patients had less sagittal knee ROM. The LV for PC5 is negative during the first 15% of stance and is positive throughout the rest of stance (Figure 1F). Examination of the reconstructed waveforms shows unilateral patients were slightly more flexed during the 1st 15% of stance and were slightly more extended throughout the rest of stance, compared to bilateral patients (Figure 1I).

Waveforms of the frontal knee angle were reconstructed to isolate the variance captured by PCs 2, 3, and 5 (Figure 2G-I). PC2 LV of the frontal knee angle was entirely positive, indicating a magnitude shift. Largest variations between the groups occur prior to midstance (Figure 2D). Reconstructed waveforms support this shift in magnitude throughout stance. This can also be seen when looking at the mean waveforms of the groups (Figure 2 A-C). Bilateral patients were more abducted throughout stance (Figure 2G). The LV of PC3 transitions from positive at heel strike to a negative peak by approximately 10% (Figure 2E). Inspecting the reconstructed waveforms shows that both groups exhibited a peak adduction angle at approximately 20%. TKR patients were more abducted at heel strike, but more adducted at the peak adduction angle, compared to controls. This indicates that TKR patients go through a larger ROM from heel strike until peak adduction at approximately 20% of stance (Figure 2H). PC5 had a LV similar to PC3. The reconstructed waveforms indicated that bilateral patients had a larger ROM from heel strike to the peak adduction angle at 20% of stance, compared to unilateral patients.

Waveforms of the sagittal knee moment were reconstructed to isolate the variance captured by PCs 2, 3, and 5 (Figure 3G-I). PC2 LV for sagittal knee moment had small, positive

values before midstance, and large, negative values after midstance, indicating a peak difference feature (Figure 3D). Reconstructed waveforms show that the push-off knee flexion moment, occurring at approximately 70%, was decreased in TKR patients (Figure 3G). The LV of PC3 was highly positive during the loading-response, and slightly negative during push-off, indicating a peak difference feature (Figure 3E). High-scoring participants (controls) had higher loading-response knee extension moments (Figure 3H, A-C). PC5 LV was entirely positive, except approximately the last 2-3%. This indicates that high-scoring participants had higher values throughout stance (Figure 3F). Reconstructions show that, throughout the entirety of stance, sagittal knee moments of unilateral TKR patients was positively shifted, compared to bilateral patients. (Figure 3I).

Waveforms of the frontal knee moment were reconstructed to isolate the variance captured by PCs 2, 3, and 5 (Figure 4G-I). The multiple zero-crossings exhibited in the LV for PC2, with minimums at approximately 20% and 80% of stance, indicates similar differences between the groups during both loading-response and push-off (Figure 4D). Reconstructed waveforms support that peak loading-response and push-off KAbM was decreased in TKR patients (Figure 4 A-C, G). The LV for PC3 is entirely positive, indicating a magnitude shift, and that high-scoring patients had more positive values throughout gait (Figure 4E). However, the LV has the highest variation in the midstance. Reconstructed waveforms demonstrate that bilateral patients had increased knee abduction moments during midstance (Figure 4H). The LV for PC5 was almost entirely negative throughout stance, indicating a magnitude shift (Figure 4F). Reconstructed waveforms indicate increased KAbM throughout stance for unilateral patients, compared to bilateral (Figure 4I).

Waveforms of the vertical GRF were reconstructed to isolate the variance captured by PCs 2, 3, and 5 (Figure 5G-I). The LV for PC2 and PC3 were similar, with positive peaks during loading-response and push-off, and negative peaks in between. PC2 was determined to demonstrate the variance during midstance, while PC3 indicated greater variance during loading-response and push-off, because the loading-response and push-off peaks for the variance were higher in PC3 (Figure 5E), compared to PC2 (Figure 5D). Reconstructed waveforms show that TKR patients had higher midstance vertical GRF (Figure 5G), but lower loading-response and push-off peak vertical GRF (Figure 5H). These differences can be seen in the mean waveforms for each group (Figure 5 A-C). The LV for PC5 demonstrated two differences between bilateral and unilateral groups. Prior to midstance, the LV has negative and positive peaks that are off set from the loading-response vertical GRF peaks, indicating a temporal shift. At approximately 40% of stance, the LV briefly returns negative, and then has a positive peak that is aligned with the push-off vertical GRF peak (Figure 5F). Inspection of the reconstructed waveforms indicates that bilateral patients had an earlier loading-response peak vertical GRF, as well as a decreased push-off peak vertical GRF (Figure 5I).

Discussion

The purpose of this study was to use a multivariate PCA approach to examine the waveforms of bilateral and unilateral TKR patients, as well as asymptomatic controls. It was hypothesized that bilateral and unilateral patients would exhibit PC scores that were significantly different than the controls, but not different between the patient groups. The hypothesis of differences between patient groups and controls was partially supported, as PC scores for PC2 and PC3 were significantly different in the patients compared to controls, but not different from

each other. However, it was found that PC5 scores were significantly different between bilateral and unilateral groups.

In the sagittal plane, TKR patients had more flexed knee angles throughout stance, as well as a decreased sagittal-plane knee ROM. Reduced ROM, also referred to as a stiff knee gait, in TKR patients has been demonstrated previously (29, 202, 262). Biggs et al. (29) found that the replaced limb of unilateral patients had decreased ROM during stance, while Ro et al. (262), who examined only the right limb of bilateral patients, determined that bilateral patients also exhibited reduced ROM, compared to asymptomatic controls. Our study showed that both unilateral and bilateral patients exhibited reduced sagittal knee ROM (Figure 1G), with reduced peak flexion angles during at approximately 25% of stance and increased peak flexion angles at around 70% of stance. However, PC5 indicated bilateral patients had a lower ROM, compared to unilateral patients, demonstrating that bilateral patients had knees that were stiffer than unilateral patients. A recent study by Zeni et al. (354) shows that unilateral patients who exhibited a stiff knee gait pattern had increased risk of a contralateral TKR. A risk analysis revealed that for every 1° decrease in knee flexion/extension ROM, the risk for contralateral TKR was increased by 9.1%. Therefore, it may be possible that the patients with bilateral TKR may have had reduced ROM before the 2nd TKR, rather than a reduced ROM due to the 2nd TKR.

Sagittal plane knee moments were also different between TKR patients and asymptomatic controls. TKR patients appear to use a gait that avoids loading the knee joint throughout stance. In the first half of stance, the LV of PC3 shows greatly reduced peak knee extension moments. This has been previously established in TKR patients using PCA (29), and discrete variables (173, 190, 300, 321, 322, 335). Further, push-off peak knee flexion moments were significantly decreased in TKR patients. This reduction can be seen via visual inspection of

the mean waveforms of unilateral patients (Figure 3B) and asymptomatic controls (Figure 3C), where the peak flexion moment (negative) around approximately 70% for unilateral patients, is much smaller than the peak at this time for controls. All TKR patients attempted to reduce the loading of the knee joint. This may be due to muscle weakness, which may be associated with pain-related fear during gait and has been seen in previous TKR research (106, 139, 177, 209, 308, 348, 349). The loading vector for PC5 of the sagittal knee moment is entirely positive, as previously stated, and demonstrates that patients with higher PC scores (i.e. unilateral patients) had a waveform that was more positive, throughout gait. The positive magnitude shift in unilateral patients, indicated by PC5, appears to demonstrate bilateral patients may have an exaggerated quadriceps avoidance gait, compared to unilateral patients. This supports previous reports during level walking (Chapter IV).

In the frontal plane, patients exhibited more abducted knees throughout stance. As shown by the entirely positive LV of the frontal knee angle, participants with high PC2 scores (i.e. controls) had waveforms that were more positive throughout stance. This can be seen clearly when comparing the mean frontal-plane knee angles of bilateral patients (Figure 2A) to the mean angle of controls (Figure 2C). PC3 demonstrates that patients exhibited a greater ROM from heel strike to peak adduction at approximately 20% of stance (Figure 2A and 2C). Bilateral patients at heel-strike had approximately -3.5° of abduction, and -1° of abduction at 20% (an increase of 2.5°), whereas control patients appear to move through approximately 2° of adduction during the same time period. This increased ROM may indicate a laxer and more unstable joint. Further, PC5 shows that this ROM difference may be larger in bilateral patients, compared to unilateral patients. Visual inspection of the frontal plane knee angle of unilateral patients from a previous study supports our finding of an increased ROM during the first 20% of stance in

unilateral patients (192), as the patients from the study were also found to be more abducted at heel strike, and more adducted at the peak adduction angle at 20%. Most previous PCA research in TKR patients largely focuses on the sagittal plane (29, 262). Hatfield et al. (122) found no difference in the magnitude of the adduction angle throughout stance, which conflicts with our findings. Further, a PCA performed on unilateral TKR patients during stair ascent found that the patients had similar knee angles in the frontal plane, with a higher knee abduction ROM in patients, compared to asymptomatic controls, partially supporting our findings (304).

Significant differences in both loading-response and push-off peak KAbM between patients and controls were found. PC2 demonstrated that the most important difference in the frontal-plane joint moments between TKR and controls groups were the reduction in loading-response and push-off peak KAbM. The lower peaks can be seen when comparing the mean waveforms of bilateral patients (Figure 4A) and control (Figure 4C). These reductions have been previously reported between unilateral patients and controls (8, 205), as well as between these bilateral patients and other unilateral patients (Chapter IV). Further, waveforms of the TKR patients appears to be less definitively biphasic. A loss of the biphasic nature of this moment was also reported recently by Biggs et al. (29). Interestingly, PC3 demonstrated that both bilateral and unilateral patients had higher KAbM during midstance, compared to controls. The increase in midstance KAbM, along with the decrease loading-response and push-off KAbM, further indicates a loss of the biphasic nature of these waveforms. Further, unilateral patients had a negative vertical shift (greater KAbM) in the frontal plane moment throughout stance, compared to bilateral patients (Figure 4I, 4A and B). This indicates a lower KAbM throughout stance in bilateral patients. Both groups of TKR patients appear to walk in such a way as to maintain stability in the knee joint. Reduced sagittal plane ROM and reduced biphasic moment patterns in

both sagittal and frontal planes act to keep the knee joint as stationary as possible during gait. However, it appears that TKR patients may have reduced ability to maintain knee joint stability in the frontal plane, given the increased adduction ROM in early stance. Further the increased ROM and reduced KAbM of bilateral patients may demonstrate reduced stability control in the frontal-plane.

Interpretation of PC2 and PC3 for the vertical GRF proved difficult due to the similarities in the LV and reconstructed waveforms. PC2 and PC3 are likely demonstrating two sides of the same story: TKR patients had lower peak loading-response and push-off vertical GRF, but higher vertical GRF during midstance. Similar to the KAbM, we see a decrease in the overall biphasic pattern typically seen in this variable. PC3 was interpreted to exhibit the increased loading-response and push-off vertical GRF of controls because of the similarities of the peaks in the LV during loading-response and push-off, compared to the less typical shape of the peaks for PC2. The increased vertical GRF during midstance of TKR patients may have contributed to increased KAbM of patients during midstance. Further, the similarly increased midstance vertical GRF and KAbM, and subsequent loss of biphasic shape in these curves, is reflective of lower vertical displacement of the center of gravity and further indicates a stiff knee gait pattern of TKR patients. As stated previously, these patients may have adapted their gait in an attempt to improve the stability of the knee joint by lowering the amount of motion it goes through and potentially decreasing the vertical center of gravity displacement during midstance. Unfortunately, increased midstance vertical GRF and KAbM shows that TKR patients are not unloading their joints, while controls have a period of decreased joint loading. The increased risk of TKR, related to stiff knee gait, may be due to this consistent joint loading throughout stance of patients who exhibit this gait pattern (202).

The LV for PC5 of the vertical GRF exhibits a negative and positive peak aligned with the loading-response vertical GRF. This demonstrates a time-shift where bilateral patients exhibited an earlier loading-response peak vertical GRF. Additionally, the LV again crossed zero, becoming negative briefly, and once again returns to a positive peak, which is aligned with the push-off vertical GRF. This indicated the vertical GRF was higher during push-off in unilateral patients, compared to bilateral. This is supported by our previous findings (Chapter IV). It should be noted that controls walked faster than TKR patients, which likely increased their GRF (170). However, similar to Biggs et al. (29) we had elected not to controls for variations caused by this difference.

The application of PCA to biomechanical waveforms is an alternative to discrete variable analysis and provides a robust and detailed analysis. The features extracted reduce the data to its most important features, entire waveforms are considered, and the features within each PC are uncorrelated to features explained by other PCs (77). The reconstructed waveforms provides a visualization of how each PC effects the mean data, while being unaffected by variations due to additional PCs (42). Further, waveform analyses provided by PCA removes the subjectivity of choosing discrete variables (77). Further, the use of a multivariate PCA may be more robust than using multiple single-variable PCAs when attempting to describe differences between groups of people. This is because in order to observe significant differences between PC scores, sufficient variation must be present across all selected variables.

Noted limitations for this study include an increased time since surgery for bilateral patients, only the 1st replaced limb of bilateral patients was used for analysis, and increased gait speed of asymptomatic controls. Increased recovery time may have promoted compensations at the knee joint that were not present, or were different, in earlier periods following TKR. It is

unknown if 2nd replacements exhibited similar waveforms as the 1st replaced, however our previous research indicates minimal differences between 1st and 2nd replaced limbs in bilateral patients (Chapter IV).

Conclusion

The PCA used in this study demonstrated that significant differences are present between TKR patients (bilateral and unilateral) and asymptomatic controls, as well as between bilateral patients and unilateral patients. Further, while some findings were similar to those described by studies using discrete variables, the PCA provided additional insight into the overall waveforms of these participants. It was determined that TKR patients exhibited more flexed and abducted knees throughout stance, decreased sagittal knee ROM, increased early-stance adduction ROM, decreased loading-response knee extension and push-off knee flexion moments, decreased loading-response and push-off KAbM, increased KAbM at midstance, increased midstance vertical GRF, as well as decreased loading-response and push-off vertical GRF. Additionally, bilateral patients exhibited reduced flexion/extension knee ROM, increased adduction ROM, decreased flexion/extension knee moments throughout stance, decreased KAbM throughout stance, an earlier loading-response peak vertical GRF, and a decreased push-off vertical GRF, compared to unilateral patients. The clinical importance of these findings is that TKR patients, especially bilateral patients, were stiffer in the sagittal plane, had increased frontal plane joint laxity, and exhibited a quadriceps avoidance gait. Therefore, it may be important for clinicians to strengthen their pre-habilitation prior to a 2nd TKR, as well as rehabilitation following surgery. This study indicates that a 2nd TKR may produce significant alterations to the capabilities of the knee joint even during a basic task such as level walking. Further, increasing not only the muscular strength of all TKR patients, but their flexibility, may allow these patients to regain the

biphasic pattern of knee loading, potentially decreasing joint degradation. PCA research into the 2nd replaced limb of bilateral patients, non-replaced limbs of unilateral patients, as well as hip and ankle joint waveforms of TKR patients and asymptomatic controls, may be needed to further develop an understanding of altered gait due to unilateral and bilateral TKR.

Chapter VI Appendix: Tables and Figures.

Table 12. Demographic Information Between Bilateral, Unilateral, and Asymptomatic Controls.

	Bilateral	Unilateral	Control	p-value
# of Patients	15 (M: 6)	15 (M: 8)	15 (M: 9)	
Age (years)	69.4±5.04	66.47±6.15	63.53±9.50	0.092
Height (m)	1.73±0.09	1.75±0.10	1.79±0.10	0.190
Weight (kg)	95.56±15.24	87.71±14.29	85.07±19.59	0.209
Time Since TKR (months)	76.00±25.11	25.3±15.1	N/A	<0.001
Walking Speed (m/s)	1.10±0.14 ^a	1.18±0.13 ^a	1.34±0.16	<0.001

^a: Significantly different than asymptomatic controls. **Bold**: Indicates Significance.

Table 13. PCs Retained, Variance Explained, and PC-Scores for Bilateral TKR, Unilateral TKR, and Asymptomatic Controls.

PC	Variance Explained	Sum Variance Explained	Bilateral	Unilateral	Control	P-Values
1	35.83%	35.83%	-5.98±7.12	0.69±17.07	5.29±12.57	0.067
2	16.88%	52.71%	-3.02±8.25 ^a	-3.00±7.23 ^a	6.03±9.44	0.006
3	11.38%	64.08%	-2.89±6.30 ^a	-2.74±8.00 ^a	5.63±5.09	0.001
4	5.66%	69.74%	-0.83±7.51	0.09±3.91	0.74±4.09	0.731
5	5.38%	75.12%	-2.69±4.89 ^b	2.22±5.00	0.47±4.81	0.029
6	4.15%	79.27%	0.32±4.34	0.48±4.89	-0.79±4.69	0.719
7	2.98%	82.24%	-1.04±2.89	1.07±3.73	-0.03±4.75	0.340
8	2.81%	85.05%	0.38±3.51	-0.32±4.59	-0.06±3.30	0.880
9	2.53%	87.58%	1.47±3.58	-0.84±2.89	-0.63±3.94	0.146
10	2.07%	89.65%	0.90±3.40	-0.56±3.28	-0.34±3.03	0.423
11	1.56%	91.21%	0.64±2.87	-1.09±2.42	0.44±2.96	0.184

^a: Significantly different than asymptomatic controls. ^b: Significantly different than unilateral patients. **Bold**: Indicates Significance.

Figure 1. Sagittal knee angle principal components (PCs). Columns represent individual PCs and are ordered by percent variance explained. A-C: Mean waveforms for bilateral patients (A, solid/ red), unilateral patients (B, dotted/green) and asymptomatic controls (C, dashed/blue). D-F: Loading vectors for PC 2, 3 and 5. G-I: Reconstructed sagittal knee angles, reconstructed to demonstrate variance due to a single PC, of high (dashed, blue) and low (solid, red) percentiles. Positive- Extension.

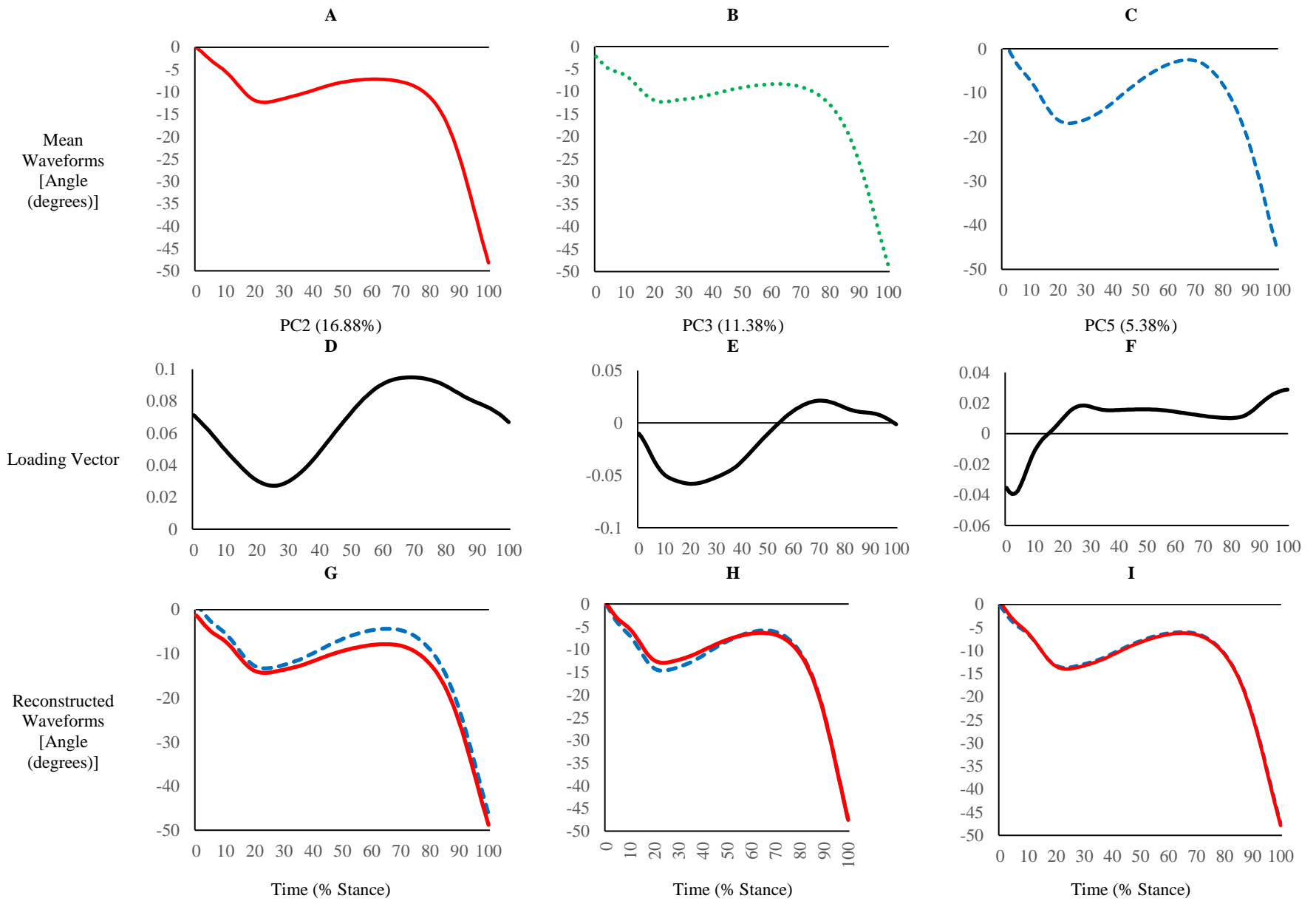


Figure 2. Frontal knee angle principal components (PCs). Columns represent individual PCs and are ordered by percent variance explained. A-C: Mean waveforms for bilateral patients (A, solid/ red), unilateral patients (B, dotted/green) and asymptomatic controls (C, dashed/blue). D-F: Loading vectors for PC 2, 3 and 5. G-I: Reconstructed sagittal knee angles, reconstructed to demonstrate variance due to a single PC, of high (dashed, blue) and low (solid, red) percentiles. Positive- Adduction.

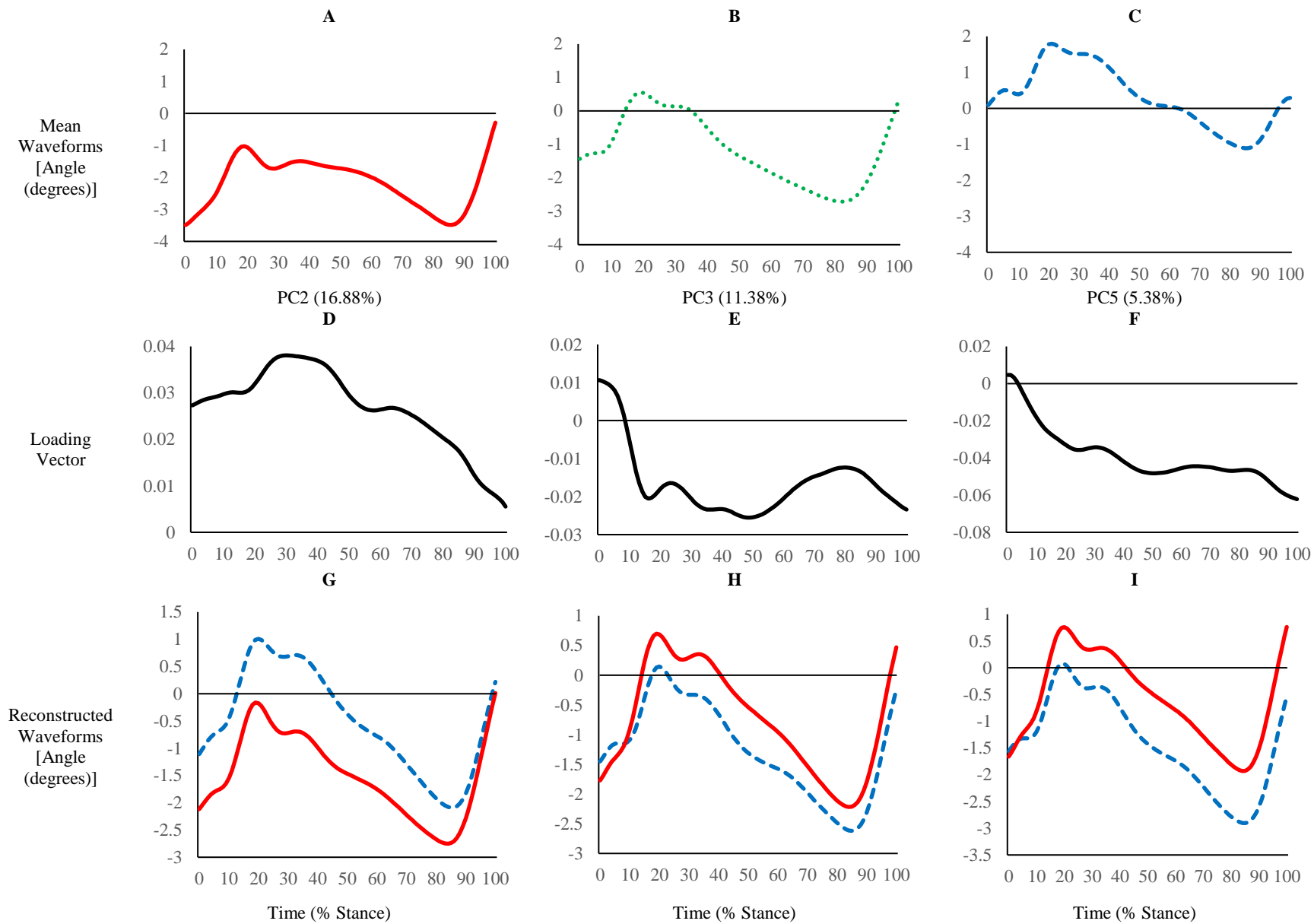


Figure 3. Sagittal knee moment principal components (PCs). Columns represent individual PCs and are ordered by percent variance explained. A-C: Mean waveforms for bilateral patients (A, solid/ red), unilateral patients (B, dotted/green) and asymptomatic controls (C, dashed/blue). D-F: Loading vectors for PC 2, 3 and 5. G-I: Reconstructed sagittal knee angles, reconstructed to demonstrate variance due to a single PC, of high (dashed, blue) and low (solid, red) percentiles. Positive – Extension.

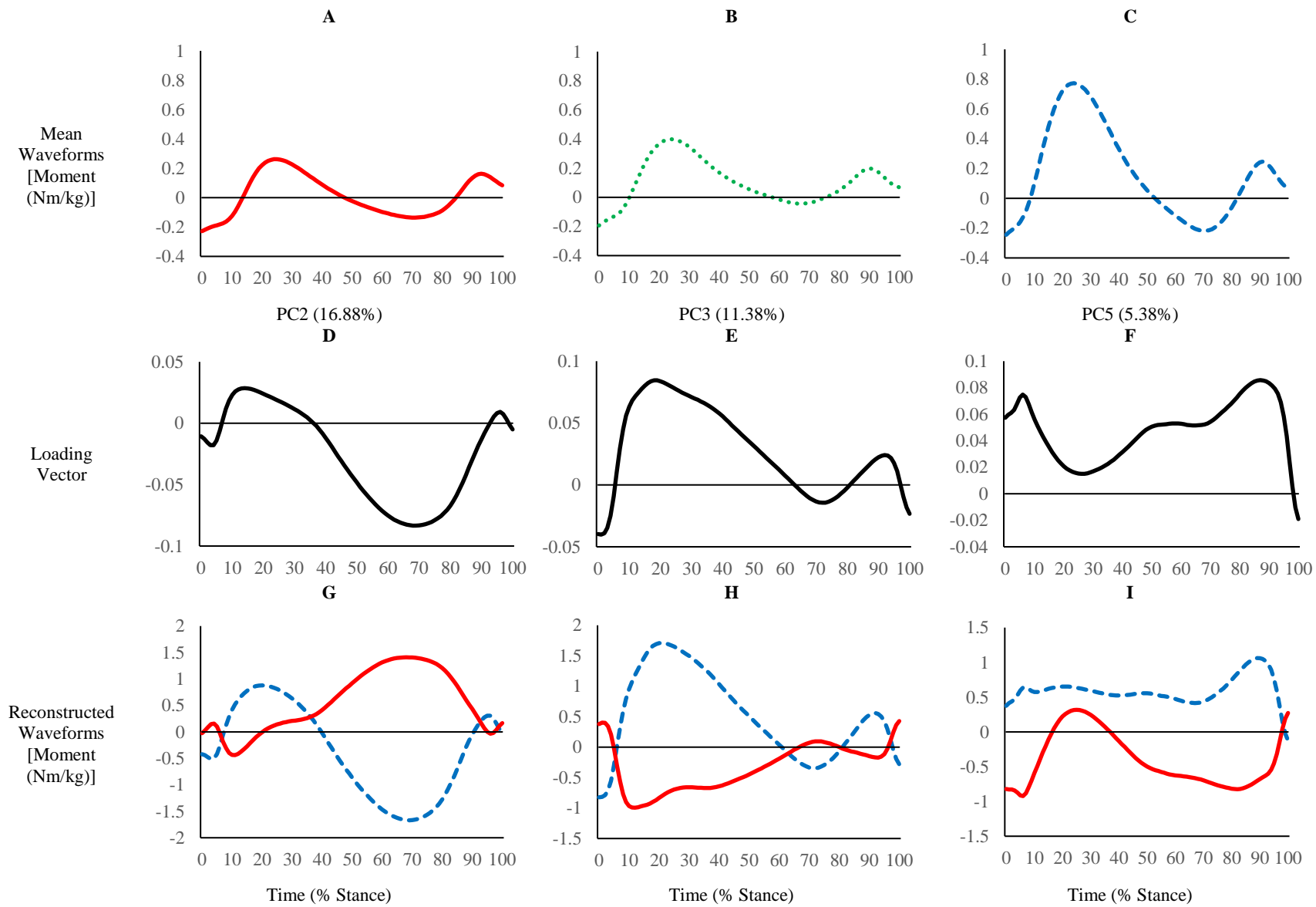


Figure 4. Frontal knee moment principal components (PCs). Columns represent individual PCs and are ordered by percent variance explained. A-C: Mean waveforms for bilateral patients (A, solid/ red), unilateral patients (B, dotted/green) and asymptomatic controls (C, dashed/blue). D-F: Loading vectors for PC 2, 3 and 5. G-I: Reconstructed sagittal knee angles, reconstructed to demonstrate variance due to a single PC, of high (dashed, blue) and low (solid, red) percentiles. Positive – Adduction.

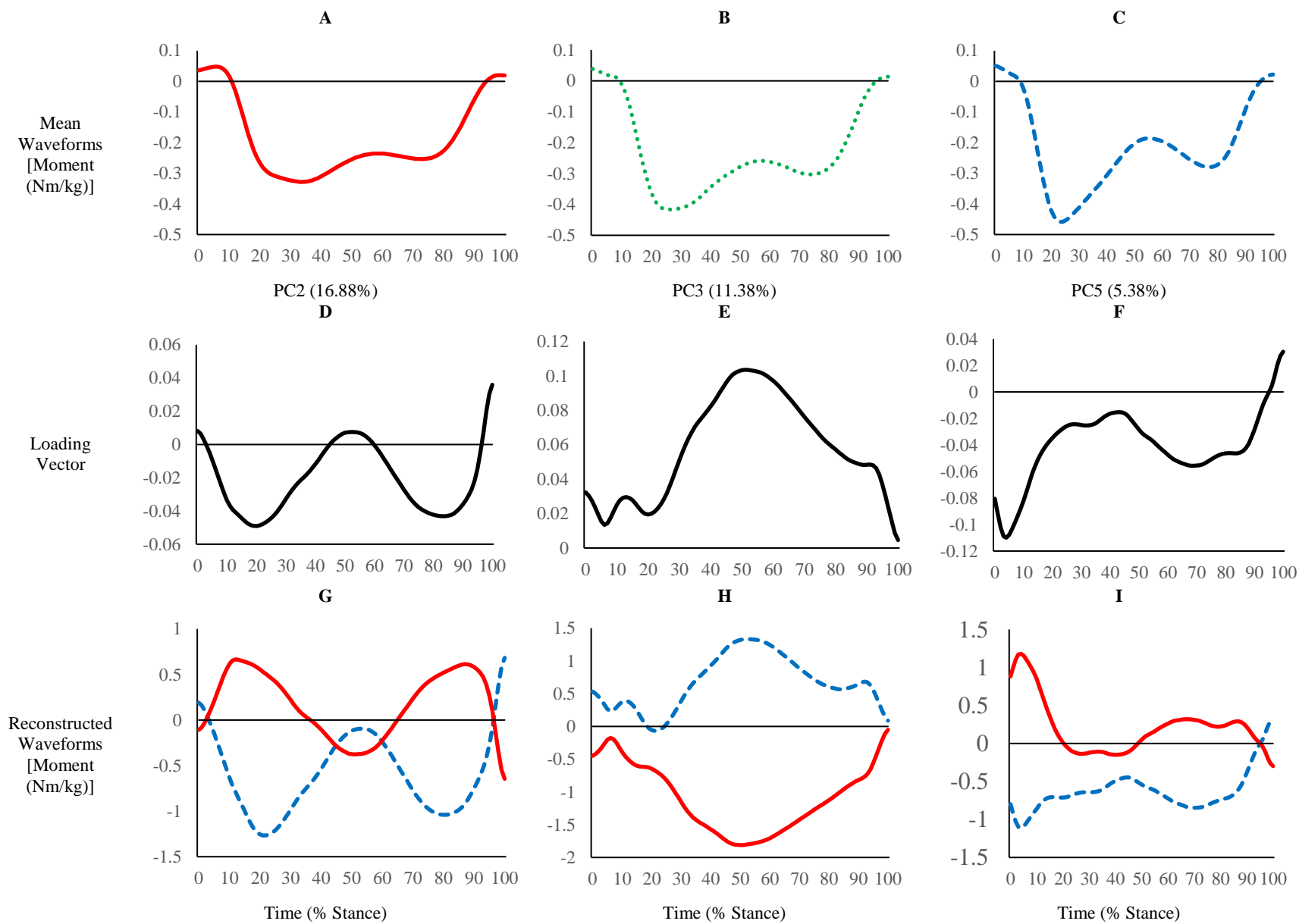
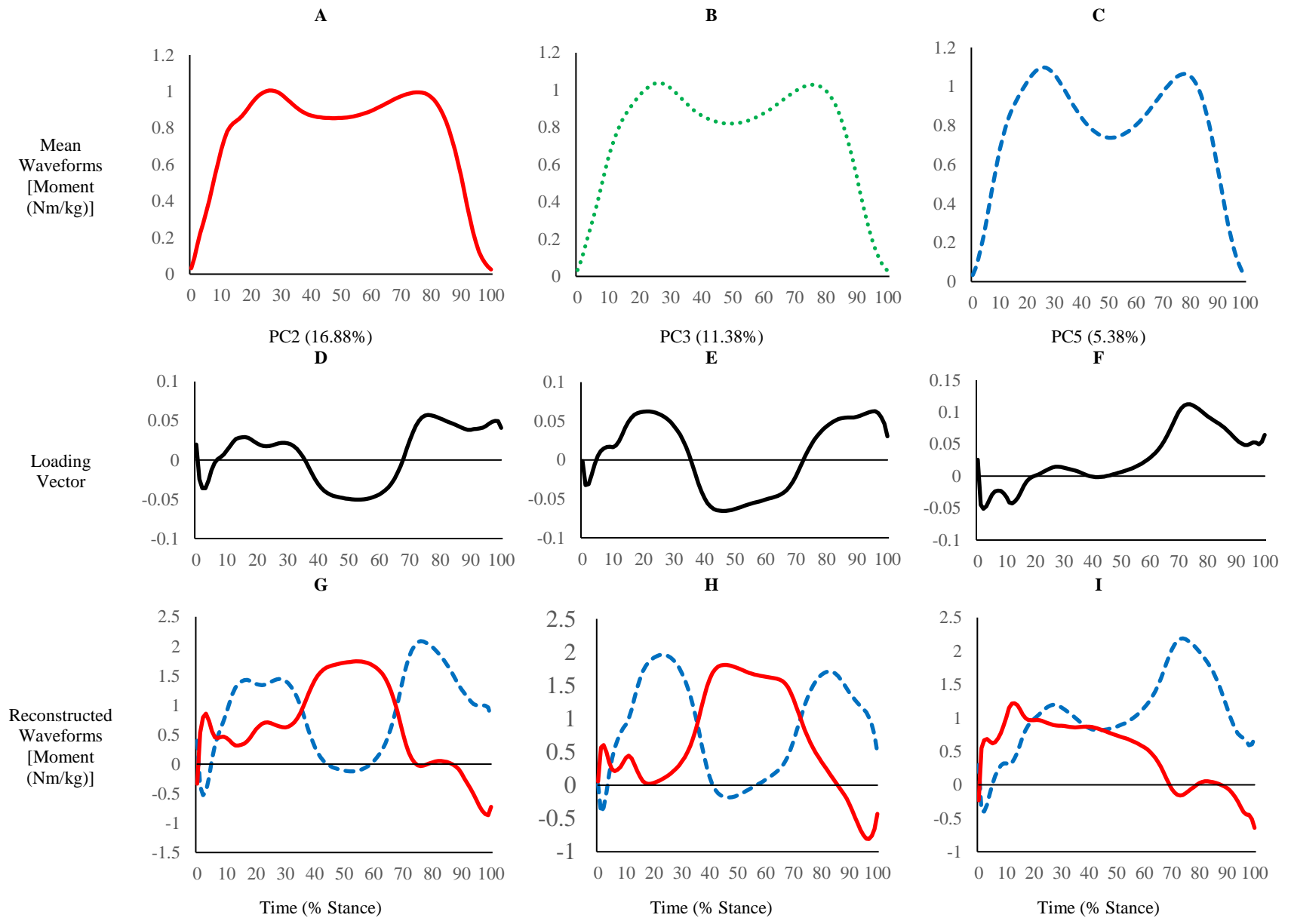


Figure 5. Vertical GRF knee angle principal components (PCs). Columns represent individual PCs and are ordered by percent variance explained. A-C: Mean waveforms for bilateral patients (A, solid/ red), unilateral patients (B, dotted/green) and asymptomatic controls (C, dashed/blue). D-F: Loading vectors for PC 2, 3 and 5. G-I: Reconstructed sagittal knee angles, reconstructed to demonstrate variance due to a single PC, of high (dashed, blue) and low (solid, red) percentiles.



Chapter VII

Conclusion

The purpose of this dissertation was to develop an understanding of how bilateral TKR effects lower extremity biomechanics during level walking and stair negotiation. The studies one and two demonstrated that bilateral patients exhibit a quadriceps avoidance gait during both level walking and stair negotiation. While unilateral TKR patients also demonstrate this adaptation, it appears to be more exaggerated in bilateral TKR patients. Study three demonstrates that both bilateral and unilateral TKR patients exhibit significant differences in knee joint biomechanics throughout stance phase of gait. Specifically, this study further demonstrates a quadriceps avoidance gait, as well as increased knee joint stiffness in the sagittal plane, while increased frontal plane laxity may be present in TKR patients. Again, bilateral patients appear to have exaggerated quadriceps avoidance, more stiff knees in the sagittal plane, and more lax joints in the frontal plane.

The findings of this dissertation have significant implications for the study of TKR patients. Primarily, this dissertation demonstrates that bilateral and unilateral patients should be studied as separate patient populations, and not combined into groups together, due to the significant differences in lower extremity biomechanics between these groups. This study shows that bilateral patients, while functionally as capable as unilateral patients, tend to exhibit gait adaptations that are exaggerated versions of what has been previously reported in unilateral patients..

These differences between unilateral and bilateral patients may be due to a compounding effect where the adaptations generated following the 1st TKR are still present when the 2nd TKR is placed and this causes more substantial adaptations. Future research into acute adaptations

prior to and following a staged 2nd TKR will help provide insight into how the two knee limbs interact. Additionally, research into bilateral patients who undergo simultaneous TKR will also be beneficial to determine which approach, simultaneous versus staged, provides patients with the best quality of life and return of normal gait functions.

Finally, while this dissertation is the first steps in generating knowledge about this bilateral TKR patient population, it also has significant clinical implications. The adaptations seen in bilateral patients, which are exaggerated versions of adaptation seen in unilateral patients (i.e. quadriceps avoidance and stiffness), may be able to be decreased or eliminated with proper pre-habilitation and rehabilitation. Orthopedic surgeons and physical therapists should be able to use the information provided in this dissertation and forthcoming manuscripts as reasons for building a more rigorous strength training and flexibility pre/rehabilitation protocol.

List of References

1. Abdel MP, Parratte S, Blanc G et al. No benefit of patient-specific instrumentation in TKA on functional and gait outcomes: a randomized clinical trial. *Clinical Orthopaedics and Related Research*. 2014;472(8):2468-76.
2. Al-Zahrani KS, Bakheit AM. A study of the gait characteristics of patients with chronic osteoarthritis of the knee. *Disability and Rehabilitation*. 2002;24(5):275-80.
3. Alentorn-Geli E, Samuelsson K, Musahl V, Green CL, Bhandari M, Karlsson J. The Association of Recreational and Competitive Running With Hip and Knee Osteoarthritis: A Systematic Review and Meta-analysis. *Journal of Orthopaedic and Sports Physical Therapy*. 2017;47(6):373-90.
4. Aljehani M, Madara K, Snyder-Mackler L, Christiansen C, Zeni JA, Jr. The contralateral knee may not be a valid control for biomechanical outcomes after unilateral total knee arthroplasty. *Gait & Posture*. 2019;70:179-84.
5. Allan R, Woodburn J, Telfer S, Abbott M, Steultjens MP. Knee joint kinetics in response to multiple three-dimensional printed, customised foot orthoses for the treatment of medial compartment knee osteoarthritis. *Journal of Engineering in Medicine*. 2017;231(6):487-98.
6. Allen KD, Chen JC, Callahan LF et al. Associations of occupational tasks with knee and hip osteoarthritis: the Johnston County Osteoarthritis Project. *Journal of Rheumatology*. 2010;37(4):842-50.
7. Allen KD, Golightly YM. State of the evidence. *Current opinion in rheumatology*. 2015;27(3):276-83.
8. Alnahdi AH, Zeni JA, Snyder-Mackler L. Gait after unilateral total knee arthroplasty: frontal plane analysis. *Journal of Orthopaedic Research*. 2011;29(5):647-52.
9. Andersson-Molina H, Karlsson H, Rockborn P. Arthroscopic partial and total meniscectomy: A long-term follow-up study with matched controls. *Arthroscopy : the journal of arthroscopic & related surgery : official publication of the Arthroscopy Association of North America and the International Arthroscopy Association*. 2002;18(2):183-9.
10. Andriacchi TP. Dynamics of knee malalignment. *Orthopedic Clinics of North America*. 1994;25(3):395-403.
11. Apostolopoulos A, Lалlos S, Mastrokalos D et al. Kinematic and kinetic analysis of the knee joint before and after a PCL retaining total knee replacement during gait and single step ascent. *Journal of long-term effects of medical implants*. 2011;21(4):339-48.
12. Ardestani MM, Moazen M. How human gait responds to muscle impairment in total knee arthroplasty patients: Muscular compensations and articular perturbations. *Journal of biomechanics*. 2016;49(9):1620-33.
13. 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. *Journal of Orthopaedic Research*. 2008;26(3):332-41.
14. Astephen JL, Deluzio KJ, Caldwell GE, Dunbar MJ, Hubley-Kozey CL. Gait and neuromuscular pattern changes are associated with differences in knee osteoarthritis severity levels. *Journal of biomechanics*. 2008;41(4):868-76.
15. Astephen Wilson JL, Dunbar MJ, Hubley-Kozey CL. Knee joint biomechanics and neuromuscular control during gait before and after total knee arthroplasty are sex-specific. *Journal of Arthroplasty*. 2015;30(1):118-25.

16. Badlani JT, Borrero C, Golla S, Harner CD, Irrgang JJ. The effects of meniscus injury on the development of knee osteoarthritis: data from the osteoarthritis initiative. *American Journal of Sports Medicine*. 2013;41(6):1238-44.
17. Baghaei Roodsari R, Esteki A, Aminian G et al. The effect of orthotic devices on knee adduction moment, pain and function in medial compartment knee osteoarthritis: a literature review. *Disability and Rehabilitation*. 2017;12(5):441-9.
18. Bagsby D, Pierson JL. Functional outcomes of simultaneous bilateral versus unilateral total knee arthroplasty. *Orthopedics*. 2015;38(1):e43-7.
19. Baliunas AJ, Hurwitz DE, Ryals AB et al. Increased knee joint loads during walking are present in subjects with knee osteoarthritis. *Osteoarthritis and Cartilage*. 2002;10(7):573-9.
20. Barbour KE, Hootman JM, Helmick CG et al. Meeting physical activity guidelines and the risk of incident knee osteoarthritis: a population-based prospective cohort study. *Arthritis care & research*. 2014;66(1):139-46.
21. Bejek Z, Paroczai R, Illyes A, Kiss RM. The influence of walking speed on gait parameters in healthy people and in patients with osteoarthritis. *Knee Surgery, Sports Traumatology, Arthroscopy*. 2005;14(7):612-22.
22. Bejek Z, Paroczai R, Szendroi M, Kiss RM. Gait analysis following TKA: comparison of conventional technique, computer-assisted navigation and minimally invasive technique combined with computer-assisted navigation. *Knee Surgery, Sports Traumatology, Arthroscopy*. 2011;19(2):285-91.
23. Benedetti MG, Catani F, Bilotta TW, Marcacci M, Mariani E, Giannini S. Muscle activation pattern and gait biomechanics after total knee replacement. *Clinical biomechanics*. 2003;18(9):871-6.
24. 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. *Annals of the Rheumatic Diseases*. 2011;70(10):1770-4.
25. Bennett HJ, Shen G, Cates HE, Zhang S. Effects of toe-in and toe-in with wider step width on level walking knee biomechanics in varus, valgus, and neutral knee alignments. *The Knee*. 2017;24(6):1326-34.
26. Benson LC, O'Connor KM. The Effect of Exertion on Joint Kinematics and Kinetics During Running Using a Waveform Analysis Approach. *Journal of applied biomechanics*. 2015;31(4):250-7.
27. Berti L, Benedetti MG, Ensini A, Catani F, Giannini S. Clinical and biomechanical assessment of patella resurfacing in total knee arthroplasty. *Clinical biomechanics*. 2006;21(6):610-6.
28. Beswick AD, Wylde V, Gooberman-Hill R, Blom A, Dieppe P. What proportion of patients report long-term pain after total hip or knee replacement for osteoarthritis? A systematic review of prospective studies in unselected patients. *BMJ Open*. 2012;2(1):e000435.
29. Biggs PR, Whatling GM, Wilson C, Metcalfe AJ, Holt CA. Which osteoarthritic gait features recover following total knee replacement surgery? *PloS one*. 2019;14(1):e0203417.
30. Bjerke J, Ohberg F, Nilsson KG, Foss OA, Stensdotter AK. Peak knee flexion angles during stair descent in TKA patients. *Journal of Arthroplasty*. 2014;29(4):707-11.

31. Blagojevic M, Jinks C, Jeffery A, Jordan KP. Risk factors for onset of osteoarthritis of the knee in older adults: a systematic review and meta-analysis. *Osteoarthritis and Cartilage*. 2010;18(1):24-33.
32. Bolanos AA, Colizza WA, McCann PD et al. A comparison of isokinetic strength testing and gait analysis in patients with posterior cruciate-retaining and substituting knee arthroplasties. *Journal of Arthroplasty*. 1998;13(8):906-15.
33. Bonnefoy-Mazure A, Armand S, Sagawa Jr Y, Suvà D, Miozzari H, Turcot K. Knee Kinematic and Clinical Outcomes Evolution Before, 3 Months, and 1 Year After Total Knee Arthroplasty. *The Journal of Arthroplasty*. 2017;32(3):793-800.
34. Boonstra MC, De Waal Malefijt MC, Verdonschot N. How to quantify knee function after total knee arthroplasty? *Knee*. 2008;15(5):390-5.
35. Borden LS, Perry JE, Davis BL, Owings TM, Grabiner MD. A biomechanical evaluation of one-stage vs two-stage bilateral knee arthroplasty patients. *Gait & Posture*. 1999;9(1):24-30.
36. Borjesson M, Weidenhielm L, Mattsson E, Olsson E. Gait and clinical measurements in patients with knee osteoarthritis after surgery: a prospective 5-year follow-up study. *The Knee*. 2005;12(2):121-7.
37. Boudarham J, Roche N, Pradon D, Bonnyaud C, Bensmail D, Zory R. Variations in kinematics during clinical gait analysis in stroke patients. *PloS one*. 2013;8(6):e66421.
38. Boudriot U, Paschalidis T, Schmitt J, Lengsfeld M. [Systematic analysis of ground reaction forces before and after hip and knee arthroplasty]. *Biomedizinische Technik. Biomedical engineering*. 2003;48(11):325-30.
39. Boyer KA, Federolf P, Lin C, Nigg BM, Andriacchi TP. Kinematic adaptations to a variable stiffness shoe: mechanisms for reducing joint loading. *Journal of biomechanics*. 2012;45(9):1619-24.
40. Boyer KA, Freedman Silvernail J, Hamill J. The role of running mileage on coordination patterns in running. *Journal of applied biomechanics*. 2014;30(5):649-54.
41. Brandon SC, Deluzio KJ. Robust features of knee osteoarthritis in joint moments are independent of reference frame selection. *Clinical biomechanics*. 2011;26(1):65-70.
42. Brandon SCE, Graham RB, Almosnino S, Sadler EM, Stevenson JM, Deluzio KJ. Interpreting principal components in biomechanics: Representative extremes and single component reconstruction. *Journal of Electromyography and Kinesiology*. 2013;23(6):1304-10.
43. Brosseau L, Taki J, Desjardins B et al. The Ottawa panel clinical practice guidelines for the management of knee osteoarthritis. Part two: strengthening exercise programs. *Clinical rehabilitation*. 2017;31(5):596-611.
44. Brouwer GM, van Tol AW, Bergink AP et al. Association between valgus and varus alignment and the development and progression of radiographic osteoarthritis of the knee. *Arthritis and rheumatism*. 2007;56(4):1204-11.
45. Brown GA. AAOS clinical practice guideline: treatment of osteoarthritis of the knee: evidence-based guideline, 2nd edition. *Journal of the American Academy of Orthopaedic Surgeons*. 2013;21(9):577-9.
46. Bruns J, Volkmer M, Luessenhop S. Pressure distribution at the knee joint. Influence of varus and valgus deviation without and with ligament dissection. *Archives of orthopaedic and trauma surgery*. 1993;113(1):12-9.

47. Bruyere O, Ethgen O, Neuprez A et al. Health-related quality of life after total knee or hip replacement for osteoarthritis: a 7-year prospective study. *Archives of orthopaedic and trauma surgery*. 2012;132(11):1583-7.
48. Butler RJ, Barrios JA, Royer T, Davis IS. Frontal-plane gait mechanics in people with medial knee osteoarthritis are different from those in people with lateral knee osteoarthritis. *Physical therapy*. 2011;91(8):1235-43.
49. Bytyqi D, Shabani B, Lustig S, Cheze L, Karahoda Gjurgjeala N, Neyret P. Gait knee kinematic alterations in medial osteoarthritis: three dimensional assessment. *International orthopaedics*. 2014;38(6):1191-8.
50. Calce SE, Kurki HK, Weston DA, Gould L. Principal component analysis in the evaluation of osteoarthritis. *American journal of physical anthropology*. 2017;162(3):476-90.
51. Calce SE, Kurki HK, Weston DA, Gould L. The relationship of age, activity, and body size on osteoarthritis in weight-bearing skeletal regions. *International Journal of Paleopathology*. 2018;22:45-53.
52. Calliess T, Bocklage R, Karkosch R, Marschollek M, Windhagen H, Schulze M. Clinical Evaluation of a Mobile Sensor-Based Gait Analysis Method for Outcome Measurement after Knee Arthroplasty. *Sensors*. 2014;14(9):15953.
53. Cameron KL, Driban JB, Svoboda SJ. Osteoarthritis and the Tactical Athlete: A Systematic Review. *Journal of athletic training*. 2016;51(11):952-61.
54. Carr AJ, Robertsson O, Graves S et al. Knee replacement. *Lancet (London, England)*. 2012;379(9823):1331-40.
55. Casartelli NC, Item-Glatthorn JF, Bizzini M, Leunig M, Maffiuletti NA. Differences in gait characteristics between total hip, knee, and ankle arthroplasty patients: a six-month postoperative comparison. *BMC musculoskeletal disorders*. 2013;14:176.
56. Catani F, Benedetti MG, De Felice R, Buzzi R, Giannini S, Aglietti P. Mobile and fixed bearing total knee prosthesis functional comparison during stair climbing. *Clinical biomechanics*. 2003;18(5):410-8.
57. Chang AH, Chmiel JS, Moision KC et al. Varus thrust and knee frontal plane dynamic motion in persons with knee osteoarthritis. *Osteoarthritis and Cartilage*. 2013;21(11):1668-73.
58. Chang AH, Moision KC, Chmiel JS et al. External knee adduction and flexion moments during gait and medial tibiofemoral disease progression in knee osteoarthritis. *Osteoarthritis and Cartilage*. 2015;23(7):1099-106.
59. Chang QZ, Sohmiya M, Wada N et al. Alternation of trunk movement after arthroplasty in patients with osteoarthritis of the knee. *Journal of Orthopaedic Science*. 2011;16(4):382-8.
60. Chapman K, Takahashi A, Meulenbelt I et al. A meta-analysis of European and Asian cohorts reveals a global role of a functional SNP in the 5' UTR of GDF5 with osteoarthritis susceptibility. *Human Molecular Genetics*. 2008;17(10):1497-504.
61. Chehab EF, Favre J, Erhart-Hledik JC, Andriacchi TP. Baseline knee adduction and flexion moments during walking are both associated with 5 year cartilage changes in patients with medial knee osteoarthritis. *Osteoarthritis and Cartilage*. 2014;22(11):1833-9.
62. Chehab EF, Favre J, Erhart-Hledik JC, Andriacchi TP. Baseline knee adduction and flexion moments during walking are both associated with 5year cartilage changes in

- patients with medial knee osteoarthritis. *Osteoarthritis and Cartilage*. 2014;22(11):1833-9.
63. Chen CP, Chen MJ, Pei YC, Lew HL, Wong PY, Tang SF. Sagittal plane loading response during gait in different age groups and in people with knee osteoarthritis. *American Journal of Physical Medicine & Rehabilitation*. 2003;82(4):307-12.
 64. Chen SY, Feng Z, Yi X. A general introduction to adjustment for multiple comparisons. *Journal of thoracic disease*. 2017;9(6):1725-9.
 65. Childs JD, Sparto PJ, Fitzgerald GK, Bizzini M, Irrgang JJ. Alterations in lower extremity movement and muscle activation patterns in individuals with knee osteoarthritis. *Clinical biomechanics*. 2004;19(1):44-9.
 66. Chu CR, Millis MB, Olson SA. Osteoarthritis: From Palliation to Prevention: AOA Critical Issues. *Journal of Bone and Joint Surgery*. 2014;96(15):e130.
 67. Chu M, Zhu X, Wang C et al. The rs4238326 polymorphism in ALDH1A2 gene potentially associated with non-post traumatic knee osteoarthritis susceptibility: a two-stage population-based study. *Osteoarthritis and Cartilage*. 2017;25(7):1062-7.
 68. Coggon D, Reading I, Croft P, McLaren M, Barrett D, Cooper C. Knee osteoarthritis and obesity. *International Journal of Obesity and Related Metabolic Disorders*. 2001;25(5):622-7.
 69. Cohen J. *Statistical power analysis for the behavioral sciences*. Routledge; 2013.
 70. Control CfD, Prevention. Cost of hospital discharges with common hospital operating room procedures in nonfederal community hospitals, by age and selected principle procedure: United States, selected years 2000-2012. In: 2015.
 71. Creaby MW, Bennell KL, Hunt MA. Gait Differs Between Unilateral and Bilateral Knee Osteoarthritis. *Archives of physical medicine and rehabilitation*. 2012;93(5):822-7.
 72. Cross M, Smith E, Hoy D et al. The global burden of hip and knee osteoarthritis: estimates from the global burden of disease 2010 study. *Annals Rheumatic Diseases*. 2014;73(7):1323-30.
 73. Culvenor AG, Felson DT, Niu J et al. Thigh Muscle Specific-Strength and the Risk of Incident Knee Osteoarthritis: The Influence of Sex and Greater Body Mass Index. *Arthritis care & research*. 2017;69(8):1266-70.
 74. de Vos BC, Landsmeer MLA, van Middelkoop M et al. Long-term effects of a lifestyle intervention and oral glucosamine sulphate in primary care on incident knee OA in overweight women. *Rheumatology*. 2017;56(8):1326-34.
 75. Debbi EM, Bernfeld B, Herman A et al. Frontal plane biomechanics of the operated and non-operated knees before and after unilateral total knee arthroplasty. *Clinical biomechanics*. 2015;30(9):889-94.
 76. Deluzio K, Harrison AJ, Coffey N, Caldwell GE. Analysis of Biomechanical Waveform Data. In. *Research Methods in Biomechanics, 2E: Human Kinetics*; 2013, pp. 317-37.
 77. Deluzio KJ, Astephen JL. Biomechanical features of gait waveform data associated with knee osteoarthritis: an application of principal component analysis. *Gait & Posture*. 2007;25(1):86-93.
 78. Deluzio KJ, Wyss UP, Costigan PA, Sorbie C, Zee B. Gait assessment in unicompartmental knee arthroplasty patients: Principal component modelling of gait waveforms and clinical status. *Human movement science*. 1999;18(5):701-11.

79. Deluzio KJ, Wyss UP, Zee B, Costigan PA, Serbie C. Principal component models of knee kinematics and kinetics: Normal vs. pathological gait patterns. *Human movement science*. 1997;16(2):201-17.
80. Deshpande BR, Katz JN, Solomon DH et al. Number of Persons With Symptomatic Knee Osteoarthritis in the US: Impact of Race and Ethnicity, Age, Sex, and Obesity. *Arthritis care & research*. 2016;68(12):1743-50.
81. Dillmann U, Holzoffer C, Johann Y et al. Principal Component Analysis of gait in Parkinson's disease: relevance of gait velocity. *Gait & Posture*. 2014;39(3):882-7.
82. Driban JB, Hootman JM, Sitler MR, Harris KP, Cattano NM. Is Participation in Certain Sports Associated With Knee Osteoarthritis? A Systematic Review. *Journal of athletic training*. 2017;52(6):497-506.
83. Duivenvoorden T, Brouwer RW, van Raaij TM, Verhagen AP, Verhaar JA, Bierma-Zeinstra SM. Braces and orthoses for treating osteoarthritis of the knee. *The Cochrane database of systematic reviews*. 2015;(3):Cd004020.
84. Duivenvoorden T, van Raaij TM, Horemans HL et al. Do laterally wedged insoles or valgus braces unload the medial compartment of the knee in patients with osteoarthritis? *Clinical Orthopaedics and Related Research*. 2015;473(1):265-74.
85. Ebert JR, Hambly K, Joss B, Ackland TR, Donnelly CJ. Does an unloader brace reduce knee loading in normally aligned knees? *Clinical Orthopaedics and Related Research*. 2014;472(3):915-22.
86. Ellis PD. *The essential guide to effect sizes: Statistical power, meta-analysis, and the interpretation of research results*. Cambridge University Press; 2010.
87. Englund M, Guermazi A, Lohmander LS. The meniscus in knee osteoarthritis. *Rheumatic diseases clinics of North America*. 2009;35(3):579-90.
88. Englund M, Lohmander LS. Risk factors for symptomatic knee osteoarthritis fifteen to twenty-two years after meniscectomy. *Arthritis and rheumatism*. 2004;50(9):2811-9.
89. Erhart-Hledik JC, Favre J, Andriacchi TP. New insight in the relationship between regional patterns of knee cartilage thickness, osteoarthritis disease severity, and gait mechanics. *Journal of biomechanics*. 2015;48(14):3868-75.
90. Evangelos E, Kay C, Ingrid M et al. Large-scale analysis of association between GDF5 and FRZB variants and osteoarthritis of the hip, knee, and hand. *Arthritis & Rheumatism*. 2009;60(6):1710-21.
91. Ezzat AM, Li LC. Occupational physical loading tasks and knee osteoarthritis: a review of the evidence. *Physiotherapy Canada*. 2014;66(1):91-107.
92. Fantini Pagani CH, Hinrichs M, Bruggemann GP. Kinetic and kinematic changes with the use of valgus knee brace and lateral wedge insoles in patients with medial knee osteoarthritis. *Journal of Orthopaedic Research*. 2012;30(7):1125-32.
93. Fantini Pagani CH, Potthast W, Bruggemann GP. The effect of valgus bracing on the knee adduction moment during gait and running in male subjects with varus alignment. *Clinical biomechanics*. 2010;25(1):70-6.
94. Fantini Pagani CH, Willwacher S, Benker R, Bruggemann GP. Effect of an ankle-foot orthosis on knee joint mechanics: a novel conservative treatment for knee osteoarthritis. *Prosthetics and orthotics international*. 2014;38(6):481-91.
95. Fantozzi S, Benedetti MG, Leardini A et al. Fluoroscopic and gait analysis of the functional performance in stair ascent of two total knee replacement designs. *Gait & Posture*. 2003;17(3):225-34.

96. Favre J, Erhart-Hledik JC, Andriacchi TP. Age-related differences in sagittal-plane knee function at heel-strike of walking are increased in osteoarthritic patients. *Osteoarthritis and Cartilage*. 2014;22(3):464-71.
97. Federolf PA, Boyer KA, Andriacchi TP. Application of principal component analysis in clinical gait research: Identification of systematic differences between healthy and medial knee-osteoarthritic gait. *Journal of biomechanics*. 2013;46(13):2173-8.
98. Felson DT. Obesity and vocational and avocational overload of the joint as risk factors for osteoarthritis. *Journal of Rheumatology*. 2004;70:2-5.
99. Felson DT. Osteoarthritis as a disease of mechanics. *Osteoarthritis and Cartilage*. 2013;21(1):10-5.
100. Felson DT, Lawrence RC, Dieppe PA et al. Osteoarthritis: new insights. Part 1: the disease and its risk factors. *Annals of Internal Medicine*. 2000;133(8):635-46.
101. Felson DT, Zhang Y, Anthony JM, Naimark A, Anderson JJ. Weight loss reduces the risk for symptomatic knee osteoarthritis in women. The Framingham Study. *Annals Internal Medicine*. 1992;116(7):535-9.
102. Felts E, Parratte S, Pauly V, Aubaniac JM, Argenson JN. Function and quality of life following medial unicompartmental knee arthroplasty in patients 60 years of age or younger. *Orthop Traumatol Surg Res*. 2010;96(8):861-7.
103. Fenner V, Behrend H, Kuster MS. Whole body gait function during stair ascending and level walking in patients following total knee arthroplasty. *International Journal of Physical Medicine and Rehabilitation*. 2014;2(5):1000231.
104. Fenner VU, Behrend H, Kuster MS. Joint Mechanics After Total Knee Arthroplasty While Descending Stairs. *Journal of Arthroplasty*. 2017;32(2):575-80.
105. Fernandes GS, Parekh SM, Moses J et al. Prevalence of knee pain, radiographic osteoarthritis and arthroplasty in retired professional footballers compared with men in the general population: a cross-sectional study. *British journal of sports medicine*. 2018;52(10):678-83.
106. Filardo G, Roffi A, Merli G et al. Patient kinesiphobia affects both recovery time and final outcome after total knee arthroplasty. *Knee Surgery, Sports Traumatology, Arthroscopy*. 2016;24(10):3322-8.
107. Foch E, Milner CE. The influence of iliotibial band syndrome history on running biomechanics examined via principal components analysis. *Journal of biomechanics*. 2014;47(1):81-6.
108. Fuchs S, Floren M, Skwara A, Tibesku CO. Quantitative gait analysis in unconstrained total knee arthroplasty patients. *International Journal of Rehabilitation Research*. 2002;25(1):65-70.
109. Gagnier JJ, Morgenstern H, Chess L. Interventions designed to prevent anterior cruciate ligament injuries in adolescents and adults: a systematic review and meta-analysis. *American Journal of Sports Medicine*. 2013;41(8):1952-62.
110. Gaudreault N, Mezghani N, Turcot K, Hagemester N, Boivin K, de Guise JA. Effects of physiotherapy treatment on knee osteoarthritis gait data using principal component analysis. *Clinical biomechanics*. 2011;26(3):284-91.
111. Gholami J, Mansournia MA, Davatchi F, Mohammad K, Hosseini H, Majdzadeh R. Are daily physical activities risk factors for knee osteoarthritis? *International journal of rheumatic diseases*. 2016;19(3):241-7.

112. Glass NA, Torner JC, Frey Law LA et al. The relationship between quadriceps muscle weakness and worsening of knee pain in the MOST cohort: a 5-year longitudinal study. *Osteoarthritis and Cartilage*. 2013;21(9):1154-9.
113. Gok H, Ergin S, Yavuzer G. Kinetic and kinematic characteristics of gait in patients with medial knee arthrosis. *Acta orthopaedica Scandinavica*. 2002;73(6):647-52.
114. Goodwin JS, Creighton RA, Pietrosimone BG, Spang JT, Blackburn JT. Medial Unloader Braces and Lateral Heel Wedges Do Not Alter Gait Biomechanics in Healthy Young Adults. *Journal of sport rehabilitation*. 2018:1-22.
115. Gossec L, Paternotte S, Maillefert JF et al. The role of pain and functional impairment in the decision to recommend total joint replacement in hip and knee osteoarthritis: an international cross-sectional study of 1909 patients. Report of the OARSI-OMERACT Task Force on total joint replacement. *Osteoarthritis and Cartilage*. 2011;19(2):147-54.
116. Gottlob CA, Baker CL, Jr., Pellissier JM, Colvin L. Cost effectiveness of anterior cruciate ligament reconstruction in young adults. *Clinical Orthopaedics and Related Research*. 1999;(367):272-82.
117. Griffin LY, Albohm MJ, Arendt EA et al. Understanding and preventing noncontact anterior cruciate ligament injuries: a review of the Hunt Valley II meeting, January 2005. *American Journal of Sports Medicine*. 2006;34(9):1512-32.
118. Grood ES, Suntay WJ. A joint coordinate system for the clinical description of three-dimensional motions: application to the knee. *Journal of Biomechanical Engineering*. 1983;105(2):136-44.
119. Hart HF, Collins NJ, Ackland DC, Cowan SM, Hunt MA, Crossley KM. Immediate Effects of a Brace on Gait Biomechanics for Predominant Lateral Knee Osteoarthritis and Valgus Malalignment After Anterior Cruciate Ligament Reconstruction. *American Journal of Sports Medicine*. 2016;44(4):865-73.
120. Hatfield GL, Hubley-Kozey CL, Astephen Wilson JL, Dunbar MJ. The effect of total knee arthroplasty on knee joint kinematics and kinetics during gait. *Journal of Arthroplasty*. 2011;26(2):309-18.
121. Hatfield GL, Stanish WD, Hubley-Kozey CL. Relationship between knee adduction moment patterns extracted using principal component analysis and discrete measures with different amplitude normalizations: Implications for knee osteoarthritis progression studies. *Clinical biomechanics*. 2015;30(10):1146-52.
122. Hatfield GL, Stanish WD, Hubley-Kozey CL. Three-dimensional biomechanical gait characteristics at baseline are associated with progression to total knee arthroplasty. *Arthritis care & research*. 2015;67(7):1004-14.
123. Hawker G, Wright J, Coyte P et al. Health-related quality of life after knee replacement. *Journal of Bone and Joint Surgery*. 1998;80(2):163-73.
124. Heiden TL, Lloyd DG, Ackland TR. Knee joint kinematics, kinetics and muscle co-contraction in knee osteoarthritis patient gait. *Clinical biomechanics*. 2009;24(10):833-41.
125. Holden JP, Orsini JA, Siegel KL, Kepple TM, Gerber LH, Stanhope SJ. Surface movement errors in shank kinematics and knee kinetics during gait. *Gait & Posture*. 1997;5(3):217-27.
126. Holm S. A simple sequentially rejective multiple test procedure. *Scandinavian Journal of Statistics*. 1979:65-70.

127. Hootman JM, FitzGerald S, Macera CA, Blair SN. Lower extremity muscle strength and risk of self-reported hip or knee osteoarthritis. *Journal of Physical Activity and Health*. 2004;1(4):321-30.
128. Hortobágyi T, Westerkamp L, Beam S et al. Altered hamstring-quadiceps muscle balance in patients with knee osteoarthritis. *Clinical biomechanics*. 2005;20(1):97-104.
129. Hsu RW, Himeno S, Coventry MB, Chao EY. Normal axial alignment of the lower extremity and load-bearing distribution at the knee. *Clinical Orthopaedics and Related Research*. 1990;(255):215-27.
130. Huang CH, Cheng CK, Lee YT, Lee KS. Muscle strength after successful total knee replacement: a 6- to 13-year followup. *Clinical Orthopaedics and Related Research*. 1996;(328):147-54.
131. Huang S-C, Wei IP, Chien H-L et al. Effects of severity of degeneration on gait patterns in patients with medial knee osteoarthritis. *Medical Engineering & Physics*. 2008;30(8):997-1003.
132. Huang Y-H, Lin C, Yang J-H et al. No difference in the functional improvements between unilateral and bilateral total knee replacements. *BMC musculoskeletal disorders*. 2018;19:87.
133. Hubley-Kozey CL, Deluzio KJ, Landry SC, McNutt JS, Stanish WD. Neuromuscular alterations during walking in persons with moderate knee osteoarthritis. *Journal of Electromyography and Kinesiology*. 2006;16(4):365-78.
134. Hubley-Kozey CL, Hill NA, Rutherford DJ, Dunbar MJ, Stanish WD. Co-activation differences in lower limb muscles between asymptomatic controls and those with varying degrees of knee osteoarthritis during walking. *Clinical biomechanics*. 2009;24(5):407-14.
135. Hunt MA, Wrigley TV, Hinman RS, Bennell KL. Individuals with severe knee osteoarthritis (OA) exhibit altered proximal walking mechanics compared with individuals with less severe OA and those without knee pain. *Arthritis care & research*. 2010;62(10):1426-32.
136. 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. *Journal of Orthopaedic Research*. 2002;20(1):101-7.
137. Hurwitz DE, Ryals AR, Block JA, Sharma L, Schnitzer TJ, Andriacchi TP. Knee pain and joint loading in subjects with osteoarthritis of the knee. *Journal of Orthopaedic Research*. 2000;18(4):572-9.
138. Iosifidis MI, Tsarouhas A, Fylaktou A. Lower limb clinical and radiographic osteoarthritis in former elite male athletes. *Knee Surgery, Sports Traumatology, Arthroscopy*. 2015;23(9):2528-35.
139. Ishii Y, Noguchi H, Sato J, Sakurai T, Toyabe SI. Quadriceps strength impairment in the mid- to long-term follow-up period after total knee arthroplasty. *Knee Surgery, Sports Traumatology, Arthroscopy*. 2017;25(11):3372-7.
140. Jafarnezhadgero AA, Oliveira AS, Mousavi SH, Madadi-Shad M. Combining valgus knee brace and lateral foot wedges reduces external forces and moments in osteoarthritis patients. *Gait & Posture*. 2018;59:104-10.
141. Jiang L, Tian W, Wang Y et al. Body mass index and susceptibility to knee osteoarthritis: A systematic review and meta-analysis. *Joint Bone Spine*. 2012;79(3):291-7.

142. Joglekar S, Gioe TJ, Yoon P, Schwartz MH. Gait analysis comparison of cruciate retaining and substituting TKA following PCL sacrifice. *The Knee*. 2012;19(4):279-85.
143. Johnson VL, Hunter DJ. The epidemiology of osteoarthritis. *Best practice & research. Clinical rheumatology*. 2014;28(1):5-15.
144. Jones L, Holt CA, Beynon MJ. Reduction, classification and ranking of motion analysis data: an application to osteoarthritic and normal knee function data. *Computer methods in biomechanics and biomedical engineering*. 2008;11(1):31-40.
145. Judd DL, Eckhoff DG, Stevens-Lapsley JE. Muscle strength loss in the lower limb after total knee arthroplasty. *American Journal of Physical Medicine & Rehabilitation*. 2012;91(3):220-6; quiz 7-30.
146. Kaufman KR, Hughes C, Morrey BF, Morrey M, An K-N. Gait characteristics of patients with knee osteoarthritis. *Journal of biomechanics*. 2001;34(7):907-15.
147. Kean CO, Hinman RS, Bowles KA, Cicuttini F, Davies-Tuck M, Bennell KL. Comparison of peak knee adduction moment and knee adduction moment impulse in distinguishing between severities of knee osteoarthritis. *Clinical biomechanics*. 2012;27(5):520-3.
148. Keays SL, Newcombe PA, Bullock-Saxton JE, Bullock MI, Keays AC. Factors involved in the development of osteoarthritis after anterior cruciate ligament surgery. *American Journal of Sports Medicine*. 2010;38(3):455-63.
149. Keller TS, Weisberger AM, Ray JL, Hasan SS, Shiavi RG, Spengler DM. Relationship between vertical ground reaction force and speed during walking, slow jogging, and running. *Clin Biomech (Bristol, Avon)*. 1996;11(5):253-9.
150. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. *Annals of the Rheumatic Diseases*. 1957;16(4):494-502.
151. Kelman GJ, Biden EN, Wyatt MP, Ritter MA, Colwell CW, Jr. Gait laboratory analysis of a posterior cruciate-sparing total knee arthroplasty in stair ascent and descent. *Clinical Orthopaedics and Related Research*. 1989;(248):21-5; discussion 5-6.
152. Kemnitz J, Wirth W, Eckstein F, Ruhdorfer A, Culvenor AG. Longitudinal change in thigh muscle strength prior to and concurrent with symptomatic and radiographic knee osteoarthritis progression: data from the Osteoarthritis Initiative. *Osteoarthritis and Cartilage*. 2017;25(10):1633-40.
153. Kerkhof HJ, Lories RJ, Meulenbelt I et al. A genome-wide association study identifies an osteoarthritis susceptibility locus on chromosome 7q22. *Arthritis and rheumatism*. 2010;62(2):499-510.
154. Khan SJ, Khan SS, Usman J, Mokhtar AH, Abu Osman NA. Combined effects of knee brace, laterally wedged insoles and toe-in gait on knee adduction moment and balance in moderate medial knee osteoarthritis patients. *Gait & Posture*. 2018;61:243-9.
155. Kirkwood RN, Resende RA, Magalhaes CM, Gomes HA, Mingoti SA, Sampaio RF. Application of principal component analysis on gait kinematics in elderly women with knee osteoarthritis. *Revista Brasileira de Fisioterapia*. 2011;15(1):52-8.
156. Ko SU, Ling SM, Schreiber C, Nesbitt M, Ferrucci L. Gait patterns during different walking conditions in older adults with and without knee osteoarthritis--results from the Baltimore Longitudinal Study of Aging. *Gait & Posture*. 2011;33(2):205-10.
157. Ko Y, Narayanasamy S, Wee HL et al. Health-related quality of life after total knee replacement or unicompartmental knee arthroplasty in an urban asian population. *Value*

- in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research*. 2011;14(2):322-8.
158. Kobayashi Y, Hobara H, Matsushita S, Mochimaru M. Key joint kinematic characteristics of the gait of fallers identified by principal component analysis. *Journal of biomechanics*. 2014;47(10):2424-9.
 159. Kotti M, Duffell LD, Faisal AA, McGregor AH. The complexity of human walking: a knee osteoarthritis study. *PloS one*. 2014;9(9):e107325.
 160. Kramers-de Quervain IA, Kampfen S, Munzinger U, Mannion AF. Prospective study of gait function before and 2 years after total knee arthroplasty. *Knee*. 2012;19(5):622-7.
 161. Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. *The Journal of bone and joint surgery. American volume*. 2007;89(4):780-5.
 162. Kutzner I, Kuther S, Heinlein B et al. The effect of valgus braces on medial compartment load of the knee joint - in vivo load measurements in three subjects. *Journal of biomechanics*. 2011;44(7):1354-60.
 163. Kutzner I, Trepczynski A, Heller MO, Bergmann G. Knee adduction moment and medial contact force--facts about their correlation during gait. *PloS one*. 2013;8(12):e81036.
 164. Landry SC, McKean KA, Hubley-Kozey CL, Stanish WD, Deluzio KJ. Knee biomechanics of moderate OA patients measured during gait at a self-selected and fast walking speed. *Journal of biomechanics*. 2007;40(8):1754-61.
 165. Landry SC, McKean KA, Hubley-Kozey CL, Stanish WD, Deluzio KJ. Neuromuscular and Lower Limb Biomechanical Differences Exist between Male and Female Elite Adolescent Soccer Players during an Unanticipated Run and Crosscut Maneuver. *The American journal of sports medicine*. 2007;35(11):1901-11.
 166. Lawrence RC, Felson DT, Helmick CG et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. *Arthritis & Rheumatism*. 2008;58(1):26-35.
 167. Lee IH. Biomechanical deficits in patients at 3 months following total knee arthroplasty. *Journal of back and musculoskeletal rehabilitation*. 2016;29(3):439-44.
 168. Lee M, Roan M, Smith B. An application of principal component analysis for lower body kinematics between loaded and unloaded walking. *Journal of biomechanics*. 2009;42(14):2226-30.
 169. Lefevre-Colau MM, Nguyen C, Haddad R et al. Is physical activity, practiced as recommended for health benefit, a risk factor for osteoarthritis? *Annals of physical and rehabilitation medicine*. 2016;59(3):196-206.
 170. Lelas JL, Merriman GJ, Riley PO, Kerrigan DC. Predicting peak kinematic and kinetic parameters from gait speed. *Gait & Posture*. 2003;17(2):106-12.
 171. Lespasio MJ, Piuzzi NS, Husni ME, Muschler GF, Guarino A, Mont MA. Knee Osteoarthritis: A Primer. *The Permanente journal*. 2017;21.
 172. Levinger P, Lai DT, Menz HB et al. Swing limb mechanics and minimum toe clearance in people with knee osteoarthritis. *Gait & Posture*. 2012;35(2):277-81.
 173. Levinger P, Menz HB, Morrow AD, Feller JA, Bartlett JR, Bergman NR. Lower limb biomechanics in individuals with knee osteoarthritis before and after total knee arthroplasty surgery. *Journal of Arthroplasty*. 2013;28(6):994-9.

174. Levinger P, Menz HB, Morrow AD et al. Knee biomechanics early after knee replacement surgery predict abnormal gait patterns 12 months postoperatively. *Journal of Orthopaedic Research*. 2012;30(3):371-6.
175. Lewek MD, Rudolph KS, Snyder-Mackler L. Control of frontal plane knee laxity during gait in patients with medial compartment knee osteoarthritis. *Osteoarthritis and Cartilage*. 2004;12(9):745-51.
176. Lewek MD, Scholz J, Rudolph KS, Snyder-Mackler L. Stride-to-stride variability of knee motion in patients with knee osteoarthritis. *Gait & Posture*. 2006;23(4):505-11.
177. Li K, Ackland DC, McClelland JA et al. Trunk muscle action compensates for reduced quadriceps force during walking after total knee arthroplasty. *Gait & Posture*. 2013;38(1):79-85.
178. Liebensteiner MC, Herten A, Gstoettner M, Thaler M, Krismer M, Bach CM. Correlation between objective gait parameters and subjective score measurements before and after total knee arthroplasty. *The Knee*. 2008;15(6):461-6.
179. Liikavainio T, Bragge T, Hakkarainen M, Karjalainen PA, Arokoski JP. Gait and muscle activation changes in men with knee osteoarthritis. *The Knee*. 2010;17(1):69-76.
180. Linley HS, Sled EA, Culham EG, Deluzio KJ. A biomechanical analysis of trunk and pelvis motion during gait in subjects with knee osteoarthritis compared to control subjects. *Clinical biomechanics*. 2010;25(10):1003-10.
181. Litwic A, Edwards MH, Dennison EM, Cooper C. Epidemiology and burden of osteoarthritis. *British medical bulletin*. 2013;105:185-99.
182. Lizaur-Utrilla A, Serna-Berna R, Vizcaya-Moreno MF, Martinez-Mendez D, Marco-Gomez L, Lopez-Prats FA. Comparison of Functional Outcomes Between the First and Second Knee in Staged Bilateral Total Knee Arthroplasty With Diverse Intervals Between Stages. *Journal of Arthroplasty*. 2018.
183. Lloyd DG, Buchanan TS, Besier TF. Neuromuscular biomechanical modeling to understand knee ligament loading. *Medicine and science in sports and exercise*. 2005;37(11):1939-47.
184. Lorentzen JS, Petersen MM, Brot C, Madsen OR. Early changes in muscle strength after total knee arthroplasty. A 6-month follow-up of 30 knees. *Acta orthopaedica Scandinavica*. 1999;70(2):176-9.
185. Losina E, Paltiel AD, Weinstein AM et al. Lifetime medical costs of knee osteoarthritis management in the United States: impact of extending indications for total knee arthroplasty. *Arthritis Care Research*. 2015;67(2):203-15.
186. Luc B, Gribble PA, Pietrosimone BG. Osteoarthritis prevalence following anterior cruciate ligament reconstruction: a systematic review and numbers-needed-to-treat analysis. *Journal of athletic training*. 2014;49(6):806-19.
187. Lundberg HJ, Rojas IL, Foucher KC, Wimmer MA. Comparison of Antagonist Muscle Activity During Walking Between Total Knee Replacement and Control Subjects Using Unnormalized Electromyography. *Journal of Arthroplasty*. 2016;31(6):1331-9.
188. Maleki M, Arazpour M, Joghtaei M, Hutchins SW, Aboutorabi A, Pouyan A. The effect of knee orthoses on gait parameters in medial knee compartment osteoarthritis: A literature review. *Prosthetics and orthotics international*. 2016;40(2):193-201.
189. Manal K, Gardinier E, Buchanan TS, Snyder-Mackler L. A more informed evaluation of medial compartment loading: the combined use of the knee adduction and flexor moments. *Osteoarthritis and Cartilage*. 2015;23(7):1107-11.

190. Mandeville D, Osternig LR, Chou LS. The effect of total knee replacement on dynamic support of the body during walking and stair ascent. *Clinical biomechanics*. 2007;22(7):787-94.
191. Mandeville D, Osternig LR, Chou LS. The effect of total knee replacement on dynamic support of the body during walking and stair ascent. *Clin Biomech (Bristol, Avon)*. 2007;22(7):787-94.
192. Mandeville D, Osternig LR, Lantz BA, Mohler CG, Chou L-S. The effect of total knee replacement on the knee varus angle and moment during walking and stair ascent. *Clinical biomechanics*. 2008;23(8):1053-8.
193. Mandeville D, Osternig LR, Lantz BA, Mohler CG, Chou LS. The effect of total knee replacement on the knee varus angle and moment during walking and stair ascent. *Clinical biomechanics*. 2008;23(8):1053-8.
194. Mandeville DS, Osternig LR, Lantz BA, Mohler CG, Chou LS. A multivariate statistical ranking of clinical and gait measures before and after total knee replacement. *Gait & Posture*. 2009;30(2):197-200.
195. Maradit Kremers H, Larson DR, Crowson CS et al. Prevalence of Total Hip and Knee Replacement in the United States. *Journal of Bone and Joint Surgery. American volume*. 2015;97(17):1386-97.
196. McCarthy I, Hodgins D, Mor A, Elbaz A, Segal G. Analysis of knee flexion characteristics and how they alter with the onset of knee osteoarthritis: a case control study. *BMC musculoskeletal disorders*. 2013;14:169.
197. McClelland JA, Feller JA, Menz HB, Webster KE. Patterns in the knee flexion-extension moment profile during stair ascent and descent in patients with total knee arthroplasty. *Journal of biomechanics*. 2014;47(8):1816-21.
198. McClelland JA, Webster KE, Feller JA. Variability of walking and other daily activities in patients with total knee replacement. *Gait & Posture*. 2009;30(3):288-95.
199. McClelland JA, Webster KE, Feller JA, Menz HB. Knee kinematics during walking at different speeds in people who have undergone total knee replacement. *Knee*. 2011;18(3):151-5.
200. McConnell S, Kolopack P, Davis AM. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC): a review of its utility and measurement properties. *Arthritis and rheumatism*. 2001;45(5):453-61.
201. McDermott ID, Amis AA. The consequences of meniscectomy. *The Journal of bone and joint surgery. British volume*. 2006;88(12):1549-56.
202. McGinnis K, Snyder-Mackler L, Flowers P, Zeni J. Dynamic joint stiffness and co-contraction in subjects after total knee arthroplasty. *Clinical biomechanics*. 2013;28(2):205-10.
203. McMahan M, Block JA. The risk of contralateral total knee arthroplasty after knee replacement for osteoarthritis. *Journal of Rheumatology*. 2003;30(8):1822-4.
204. McNair PJ, Boocock MG, Dominick ND, Kelly RJ, Farrington BJ, Young SW. A Comparison of Walking Gait Following Mechanical and Kinematic Alignment in Total Knee Joint Replacement. *Journal of Arthroplasty*. 2018;33(2):560-4.
205. Metcalfe AJ, Stewart CJ, Postans NJ et al. Abnormal loading and functional deficits are present in both limbs before and after unilateral knee arthroplasty. *Gait & Posture*. 2017;55:109-15.

206. Mikashima Y, Ishii Y, Takeda M, Noguchi H, Momohara S, Banks SA. Does mobile-bearing knee arthroplasty motion change with activity? *The Knee*. 2013;20(6):422-5.
207. Mills K, Hunt MA, Ferber R. Biomechanical deviations during level walking associated with knee osteoarthritis: a systematic review and meta-analysis. *Arthritis care & research*. 2013;65(10):1643-65.
208. Mills K, Hunt MA, Leigh R, Ferber R. A systematic review and meta-analysis of lower limb neuromuscular alterations associated with knee osteoarthritis during level walking. *Clinical biomechanics*. 2013;28(7):713-24.
209. Milner CE. Is gait normal after total knee arthroplasty? Systematic review of the literature. *Journal of orthopaedic science : official journal of the Japanese Orthopaedic Association*. 2009;14(1):114-20.
210. Milner CE. Is gait normal after total knee arthroplasty? Systematic review of the literature. *Journal of Orthopaedic Science*. 2009;14(1):114-20.
211. Milner CE, O'Bryan ME. Bilateral frontal plane mechanics after unilateral total knee arthroplasty. *Archives of physical medicine and rehabilitation*. 2008;89(10):1965-9.
212. Milovanovic I, Popovic DB. Principal component analysis of gait kinematics data in acute and chronic stroke patients. *Computational and mathematical methods in medicine*. 2012;2012:649743.
213. 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. *Annals of the Rheumatic Diseases*. 2002;61(7):617-22.
214. Mizner RL, Petterson SC, Stevens JE, Vandenborne K, Snyder-Mackler L. Early quadriceps strength loss after total knee arthroplasty. The contributions of muscle atrophy and failure of voluntary muscle activation. *Journal of Bone and Joint Surgery. American volume*. 2005;87(5):1047-53.
215. Mundermann 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 and rheumatism*. 2005;52(9):2835-44.
216. Nagano Y, Naito K, Saho Y et al. Association between in vivo knee kinematics during gait and the severity of knee osteoarthritis. *The Knee*. 2012;19(5):628-32.
217. Nagura T, Niki Y, Harato K, Mochizuki T, Kiriyama Y. Analysis of the factors that correlate with increased knee adduction moment during gait in the early postoperative period following total knee arthroplasty. *The Knee*. 2017;24(2):250-7.
218. Naili JE, Wretenberg P, Lindgren V, Iversen MD, Hedstrom M, Brostrom EW. Improved knee biomechanics among patients reporting a good outcome in knee-related quality of life one year after total knee arthroplasty. *BMC Musculoskelet Disord*. 2017;18(1):122.
219. Neogi T, Zhang Y. Epidemiology of osteoarthritis. *Rheumatic diseases clinics of North America*. 2013;39(1):1-19.
220. Nessler T, Denney L, Sampley J. ACL Injury Prevention: What Does Research Tell Us? *Current reviews in musculoskeletal medicine*. 2017;10(3):281-8.
221. Nigg BM, Baltich J, Maurer C, Federolf P. Shoe midsole hardness, sex and age effects on lower extremity kinematics during running. *Journal of biomechanics*. 2012;45(9):1692-7.
222. Noble PC, Gordon MJ, Weiss JM, Reddix RN, Conditt MA, Mathis KB. Does total knee replacement restore normal knee function? *Clin Orthop Relat Res*. 2005;(431):157-65.

223. Oiestad BE, Engebretsen L, Storheim K, Risberg MA. Knee osteoarthritis after anterior cruciate ligament injury: a systematic review. *American Journal of Sports Medicine*. 2009;37(7):1434-43.
224. Oiestad BE, Holm I, Gunderson R, Myklebust G, Risberg MA. Quadriceps muscle weakness after anterior cruciate ligament reconstruction: a risk factor for knee osteoarthritis? *Arthritis care & research*. 2010;62(12):1706-14.
225. Oiestad BE, Juhl CB, Eitzen I, Thorlund JB. Knee extensor muscle weakness is a risk factor for development of knee osteoarthritis. A systematic review and meta-analysis. *Osteoarthritis and Cartilage*. 2015;23(2):171-7.
226. Okamoto N, Breslauer L, Hedley AK, Mizuta H, Banks SA. In vivo knee kinematics in patients with bilateral total knee arthroplasty of 2 designs. *Journal of Arthroplasty*. 2011;26(6):914-8.
227. Oliveria SA, Felson DT, Reed JI, Cirillo PA, Walker AM. Incidence of symptomatic hand, hip, and knee osteoarthritis among patients in a health maintenance organization. *Arthritis and rheumatism*. 1995;38(8):1134-41.
228. Orishimo KF, Kremenec IJ, Deshmukh AJ, Nicholas SJ, Rodriguez JA. Does total knee arthroplasty change frontal plane knee biomechanics during gait? *Clinical Orthopaedics and Related Research*. 2012;470(4):1171-6.
229. Osis ST, Hettinga BA, Leitch J, Ferber R. Predicting timing of foot strike during running, independent of striking technique, using principal component analysis of joint angles. *Journal of biomechanics*. 2014;47(11):2786-9.
230. Ouellet D, Moffet H. Locomotor deficits before and two months after knee arthroplasty. *Arthritis and rheumatism*. 2002;47(5):484-93.
231. Palazzo C, Nguyen C, Lefevre-Colau MM, Rannou F, Poiraudreau S. Risk factors and burden of osteoarthritis. *Annals of physical and rehabilitation medicine*. 2016;59(3):134-8.
232. Palmer KT. Occupational activities and osteoarthritis of the knee. *British medical bulletin*. 2012;102:147-70.
233. Palmieri-Smith RM, Cameron KL, DiStefano LJ et al. The Role of Athletic Trainers in Preventing and Managing Posttraumatic Osteoarthritis in Physically Active Populations: a Consensus Statement of the Athletic Trainers' Osteoarthritis Consortium. *Journal of athletic training*. 2017;52(6):610-23.
234. Palotie A, Ott J, Elima K et al. PREDISPOSITION TO FAMILIAL OSTEOARTHROSIS LINKED TO TYPE II COLLAGEN GENE. *The Lancet*. 1989;333(8644):924-7.
235. Paquette MR, Klipple G, Zhang S. Greater Step Widths Reduce Internal Knee Abduction Moments in Medial Compartment Knee Osteoarthritis Patients During Stair Ascent. *Journal of applied biomechanics*. 2015;31(4):229-36.
236. Paquette MR, Zhang S, Milner CE, Klipple G. Does increasing step width alter knee biomechanics in medial compartment knee osteoarthritis patients during stair descent? *The Knee*. 2014;21(3):676-82.
237. Pengas IP, Assiotis A, Nash W, Hatcher J, Banks J, McNicholas MJ. Total meniscectomy in adolescents: a 40-year follow-up. *The Journal of bone and joint surgery. British volume*. 2012;94(12):1649-54.

238. Perhonen M, Komi PV, Häkkinen K, von Bonsdorff H, Partio H. Strength training and neuromuscular function in elderly people with total knee endoprosthesis. *Scandinavian Journal of Medicine & Science in Sports*. 1992;2(4):234-43.
239. Peters A, Galna B, Sangeux M, Morris M, Baker R. Quantification of soft tissue artifact in lower limb human motion analysis: A systematic review. *Gait & Posture*. 2010;31(1):1-8.
240. Petersen W, Ellermann A, Zantop T et al. Biomechanical effect of unloader braces for medial osteoarthritis of the knee: a systematic review (CRD 42015026136). *Archives of orthopaedic and trauma surgery*. 2016;136(5):649-56.
241. Phinyomark A, Hettinga BA, Osis S, Ferber R. Do intermediate- and higher-order principal components contain useful information to detect subtle changes in lower extremity biomechanics during running? *Human movement science*. 2015;44:91-101.
242. Phinyomark A, Osis S, Hettinga BA, Ferber R. Kinematic gait patterns in healthy runners: A hierarchical cluster analysis. *Journal of biomechanics*. 2015;48(14):3897-904.
243. Phinyomark A, Osis ST, Hettinga BA, Kobsar D, Ferber R. Gender differences in gait kinematics for patients with knee osteoarthritis. *BMC musculoskeletal disorders*. 2016;17:157.
244. Pollo FE, Jackson RW, Koeter S, Ansari S, Motley GS, Rathjen KW. Walking, chair rising, and stair climbing after total knee arthroplasty: patellar resurfacing versus nonresurfacing. *American Journal of Knee Surgery*. 2000;13(2):103-8; discussion 8-9.
245. Pozzi F, Snyder-Mackler L, Zeni J, Jr. Relationship between biomechanical asymmetries during a step up and over task and stair climbing after total knee arthroplasty. *Clinical biomechanics*. 2015;30(1):78-85.
246. Prieto-Alhambra D, Judge A, Javaid MK, Cooper C, Diez-Perez A, Arden NK. Incidence and risk factors for clinically diagnosed knee, hip and hand osteoarthritis: influences of age, gender and osteoarthritis affecting other joints. *Annals of the Rheumatic Diseases*. 2014;73(9):1659-64.
247. Pua YH, Seah FJ, Clark RA, Lian-Li Poon C, Tan JW, Chong HC. Factors associated with gait speed recovery after total knee arthroplasty: A longitudinal study. *Seminars in arthritis and rheumatism*. 2017;46(5):544-51.
248. Qin J, Barbour KE, Nevitt MC et al. Objectively Measured Physical Activity and Risk of Knee Osteoarthritis. *Medicine and science in sports and exercise*. 2018;50(2):277-83.
249. Rabiei M, Eslami M, Movaghar AF. The assessment of three-dimensional foot pronation using a principal component analysis method in the stance phase of running. *Foot*. 2016;29:11-7.
250. Rahman J, Tang Q, Monda M, Miles J, McCarthy I. Gait assessment as a functional outcome measure in total knee arthroplasty: a cross-sectional study. *BMC musculoskeletal disorders*. 2015;16:66.
251. Rasnick R, Standifird T, Reinbolt JA, Cates HE, Zhang S. Knee Joint Loads and Surrounding Muscle Forces during Stair Ascent in Patients with Total Knee Replacement. *PloS one*. 2016;11(6):e0156282.
252. Reid SM, Graham RB, Costigan PA. Differentiation of young and older adult stair climbing gait using principal component analysis. *Gait & Posture*. 2010;31(2):197-203.
253. Renaud A, Fuentes A, Hagemester N, Lavigne M, Vendittoli PA. Clinical and Biomechanical Evaluations of Staged Bilateral Total Knee Arthroplasty Patients with Two Different Implant Designs. *Open Orthopaedics Journal*. 2016;10:155-65.

254. Resende RA, Fonseca ST, Silva PL, Magalhaes CM, Kirkwood RN. Power at hip, knee and ankle joints are compromised in women with mild and moderate knee osteoarthritis. *Clinical biomechanics*. 2012;27(10):1038-44.
255. Resende RA, Kirkwood RN, Deluzio KJ, Hassan EA, Fonseca ST. Ipsilateral and contralateral foot pronation affect lower limb and trunk biomechanics of individuals with knee osteoarthritis during gait. *Clinical biomechanics*. 2016;34:30-7.
256. Resende RA, Kirkwood RN, Deluzio KJ, Morton AM, Fonseca ST. Mild leg length discrepancy affects lower limbs, pelvis and trunk biomechanics of individuals with knee osteoarthritis during gait. *Clinical biomechanics*. 2016;38:1-7.
257. Reyes C, Leyland KM, Peat G, Cooper C, Arden NK, Prieto-Alhambra D. Association Between Overweight and Obesity and Risk of Clinically Diagnosed Knee, Hip, and Hand Osteoarthritis: A Population-Based Cohort Study. *Arthritis & Rheumatology*. 2016;68(8):1869-75.
258. Reynolds S. Does total knee arthroplasty reproduce natural knee mechanics. Université d'Ottawa/University of Ottawa; 2013.
259. Richmond SA, Fukuchi RK, Ezzat A, Schneider K, Schneider G, Emery CA. Are joint injury, sport activity, physical activity, obesity, or occupational activities predictors for osteoarthritis? A systematic review. *Journal of Orthopaedic and Sports Physical Therapy*. 2013;43(8):515-b19.
260. Riordan EA, Little C, Hunter D. Pathogenesis of post-traumatic OA with a view to intervention. *Best practice & research. Clinical rheumatology*. 2014;28(1):17-30.
261. Rivière C, Ollivier M, Girerd D, Argenson JN, Parratte S. Does standing limb alignment after total knee arthroplasty predict dynamic alignment and knee loading during gait? *The Knee*.
262. Ro DH, Han H-S, Lee DY, Kim SH, Kwak Y-H, Lee MC. Slow gait speed after bilateral total knee arthroplasty is associated with suboptimal improvement of knee biomechanics. *Knee Surgery, Sports Traumatology, Arthroscopy*. 2018;26(6):1671-80.
263. Robbins SM, Astephen Wilson JL, Rutherford DJ, Hubble-Kozey CL. Reliability of principal components and discrete parameters of knee angle and moment gait waveforms in individuals with moderate knee osteoarthritis. *Gait & Posture*. 2013;38(3):421-7.
264. Robbins SM, Birmingham TB, Jones IC, Sischek EL, Dietzsch M, Giffin JR. Comparison of Gait Characteristics Between Patients With Nontraumatic and Posttraumatic Medial Knee Osteoarthritis. *Arthritis care & research*. 2016;68(9):1215-23.
265. Robertson G, Caldwell G, Hamill J, Kamen G, Whittlesey S. *Research methods in biomechanics, 2E*. Human Kinetics; 2013.
266. Roos EM, Arden NK. Strategies for the prevention of knee osteoarthritis. *Nature reviews. Rheumatology*. 2016;12(2):92-101.
267. Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynon BD. Knee Injury and Osteoarthritis Outcome Score (KOOS)—Development of a Self-Administered Outcome Measure. *Journal of Orthopaedic & Sports Physical Therapy*. 1998;28(2):88-96.
268. Rudolph KS, Schmitt LC, Lewek MD. Age-related changes in strength, joint laxity, and walking patterns: are they related to knee osteoarthritis? *Physical therapy*. 2007;87(11):1422-32.
269. Runhaar J, de Vos BC, van Middelkoop M, Vroegindewij D, Oei EH, Bierma-Zeinstra SM. Prevention of Incident Knee Osteoarthritis by Moderate Weight Loss in Overweight and Obese Females. *Arthritis care & research*. 2016;68(10):1428-33.

270. Runhaar J, Deroisy R, van Middelkoop M et al. The role of diet and exercise and of glucosamine sulfate in the prevention of knee osteoarthritis: Further results from the PREvention of knee Osteoarthritis in Overweight Females (PROOF) study. *Seminars in arthritis and rheumatism*. 2016;45(4 Suppl):S42-8.
271. Runhaar J, Koes BW, Clockaerts S, Bierma-Zeinstra SM. A systematic review on changed biomechanics of lower extremities in obese individuals: a possible role in development of osteoarthritis. *Obesity Reviews*. 2011;12(12):1071-82.
272. Runhaar J, Zhang Y. Can we prevent OA? Epidemiology and public health insights and implications. *Rheumatology*. 2018;57(suppl_4):iv3-iv9.
273. Rutherford DJ, Hubley-Kozey C, Stanish W. Hip abductor function in individuals with medial knee osteoarthritis: Implications for medial compartment loading during gait. *Clinical biomechanics*. 2014;29(5):545-50.
274. Rutherford DJ, Hubley-Kozey CL, Deluzio KJ, Stanish WD, Dunbar M. Foot progression angle and the knee adduction moment: a cross-sectional investigation in knee osteoarthritis. *Osteoarthritis and Cartilage*. 2008;16(8):883-9.
275. Rutherford DJ, Hubley-Kozey CL, Stanish WD. The neuromuscular demands of altering foot progression angle during gait in asymptomatic individuals and those with knee osteoarthritis. *Osteoarthritis and Cartilage*. 2010;18(5):654-61.
276. Rutherford DJ, Hubley-Kozey CL, Stanish WD, Dunbar MJ. Neuromuscular alterations exist with knee osteoarthritis presence and severity despite walking velocity similarities. *Clinical biomechanics*. 2011;26(4):377-83.
277. Saari T, Tranberg R, Zugner R, Uvehammer J, Karrholm J. Total knee replacement influences both knee and hip joint kinematics during stair climbing. *International orthopaedics*. 2004;28(2):82-6.
278. Sagawa Y, Jr., Armand S, Lubbeke A et al. Associations between gait and clinical parameters in patients with severe knee osteoarthritis: a multiple correspondence analysis. *Clinical biomechanics*. 2013;28(3):299-305.
279. Sanders TL, Maradit Kremers H, Schleck CD, Larson DR, Berry DJ. Subsequent Total Joint Arthroplasty After Primary Total Knee or Hip Arthroplasty: A 40-Year Population-Based Study. *The Journal of bone and joint surgery. American volume*. 2017;99(5):396-401.
280. Schmitt D, Vap A, Queen RM. Effect of end-stage hip, knee, and ankle osteoarthritis on walking mechanics. *Gait & Posture*. 2015;42(3):373-9.
281. Schmitt LC, Rudolph KS. Influences on knee movement strategies during walking in persons with medial knee osteoarthritis. *Arthritis and rheumatism*. 2007;57(6):1018-26.
282. Schnitzer TJ, Popovich JM, Andersson GBJ, Andriacchi TP. Effect of piroxicam on gait in patients with osteoarthritis of the knee. *Arthritis & Rheumatism*. 1993;36(9):1207-13.
283. Schuster P, Gesslein M, Schlumberger M et al. Ten-Year Results of Medial Open-Wedge High Tibial Osteotomy and Chondral Resurfacing in Severe Medial Osteoarthritis and Varus Malalignment. *American Journal of Sports Medicine*. 2018;46(6):1362-70.
284. Scuderi GR, Bourne RB, Noble PC, Benjamin JB, Lonner JH, Scott WN. The new Knee Society Knee Scoring System. *Clinical orthopaedics and related research*. 2012;470(1):3-19.
285. Scuderi GR, Bourne RB, Noble PC, Benjamin JB, Lonner JH, Scott WN. The new Knee Society Knee Scoring System. *Clinical Orthopaedics and Related Research*. 2012;470(1):3-19.

286. Segal NA, Glass NA, Felson DT et al. Effect of quadriceps strength and proprioception on risk for knee osteoarthritis. *Medicine and science in sports and exercise*. 2010;42(11):2081-8.
287. Segal NA, Torner JC, Felson D et al. Effect of thigh strength on incident radiographic and symptomatic knee osteoarthritis in a longitudinal cohort. *Arthritis and rheumatism*. 2009;61(9):1210-7.
288. Selistre LFA, Mattiello SM, Nakagawa TH, Gonçalves GH, Petrella M, Jones RK. The relationship between external knee moments and muscle co-activation in subjects with medial knee osteoarthritis. *Journal of Electromyography and Kinesiology*. 2017;33:64-72.
289. Seon JK, Song EK, Yoon TR, Park SJ, Bae BH, Cho SG. Comparison of functional results with navigation-assisted minimally invasive and conventional techniques in bilateral total knee arthroplasty. *Computer Aided Surgery*. 2007;12(3):189-93.
290. SHAFIZADEGAN Z, KARIMI MT, SHAFIZADEGAN F, REZAEIAN ZS. EVALUATION OF GROUND REACTION FORCES IN PATIENTS WITH VARIOUS SEVERITIES OF KNEE OSTEOARTHRITIS. *Journal of Mechanics in Medicine and Biology*. 2016;16(02):1650003.
291. Shao Y, Zhang C, Charron KD, Macdonald SJ, McCalden RW, Bourne RB. The fate of the remaining knee(s) or hip(s) in osteoarthritic patients undergoing a primary TKA or THA. *Journal of Arthroplasty*. 2013;28(10):1842-5.
292. Sharma L, Chang AH, Jackson RD et al. Varus Thrust and Incident and Progressive Knee Osteoarthritis. *Arthritis & Rheumatology*. 2017;69(11):2136-43.
293. Sharma L, Chmiel JS, Almagor O et al. The role of varus and valgus alignment in the initial development of knee cartilage damage by MRI: the MOST study. *Annals of the Rheumatic Diseases*. 2013;72(2):235-40.
294. Sharma L, Song J, Dunlop D et al. Varus and valgus alignment and incident and progressive knee osteoarthritis. *Annals of the Rheumatic Diseases*. 2010;69(11):1940-5.
295. Shelburne KB, Torry MR, Steadman JR, Pandy MG. Effects of foot orthoses and valgus bracing on the knee adduction moment and medial joint load during gait. *Clinical biomechanics*. 2008;23(6):814-21.
296. Silva M, Shepherd EF, Jackson WO, Pratt JA, McClung CD, Schmalzried TP. Knee strength after total knee arthroplasty. *Journal of Arthroplasty*. 2003;18(5):605-11.
297. Silverwood V, Blagojevic-Bucknall M, Jinks C, Jordan JL, Protheroe J, Jordan KP. Current evidence on risk factors for knee osteoarthritis in older adults: a systematic review and meta-analysis. *Osteoarthritis and Cartilage*. 2015;23(4):507-15.
298. Sirin AV, Patla AE. Myoelectric changes in the triceps surae muscles under sustained contractions. Evidence for synergism. *European journal of applied physiology and occupational physiology*. 1987;56(2):238-44.
299. Slemenda C, Heilman DK, Brandt KD et al. Reduced quadriceps strength relative to body weight: a risk factor for knee osteoarthritis in women? *Arthritis and rheumatism*. 1998;41(11):1951-9.
300. Smith AJ, Lloyd DG, Wood DJ. Pre-surgery knee joint loading patterns during walking predict the presence and severity of anterior knee pain after total knee arthroplasty. *Journal of Orthopaedic Research*. 2004;22(2):260-6.

301. Smith AJ, Lloyd DG, Wood DJ. A kinematic and kinetic analysis of walking after total knee arthroplasty with and without patellar resurfacing. *Clinical biomechanics*. 2006;21(4):379-86.
302. Snoeker BA, Bakker EW, Kegel CA, Lucas C. Risk factors for meniscal tears: a systematic review including meta-analysis. *Journal of Orthopaedic and Sports Physical Therapy*. 2013;43(6):352-67.
303. Spector TD, MacGregor AJ. Risk factors for osteoarthritis: genetics11Supported by Procter & Gamble Pharmaceuticals, Mason, OH. *Osteoarthritis and Cartilage*. 2004;12:39-44.
304. Standifird TW. Lower Extremity Biomechanics during Stair Ascent in Healthy and Total Knee Replacement Older Adults. In: Trace: Tennessee Research and Creative Exchange; 2015, pp. 81-93;119-49.
305. Standifird TW, Cates HE, Zhang S. Stair ambulation biomechanics following total knee arthroplasty: a systematic review. *Journal of Arthroplasty*. 2014;29(9):1857-62.
306. Standifird TW, Saxton AM, Coe DP, Cates HE, Reinbolt JA, Zhang S. Influence of Total Knee Arthroplasty on Gait Mechanics of the Replaced and Non-Replaced Limb During Stair Negotiation. *Journal of Arthroplasty*. 2017;31(1):278-83.
307. Stein T, Mehling AP, Welsch F, von Eisenhart-Rothe R, Jager A. Long-term outcome after arthroscopic meniscal repair versus arthroscopic partial meniscectomy for traumatic meniscal tears. *American Journal of Sports Medicine*. 2010;38(8):1542-8.
308. Stevens-Lapsley JE, Balter JE, Kohrt WM, Eckhoff DG. Quadriceps and hamstrings muscle dysfunction after total knee arthroplasty. *Clinical Orthopaedics and Related Research*. 2010;468(9):2460-8.
309. Studenski S, Perera S, Patel K et al. Gait speed and survival in older adults. *JAMA*. 2011;305(1):50-8.
310. Tadano S, Takeda R, Sasaki K, Fujisawa T, Tohyama H. Gait characterization for osteoarthritis patients using wearable gait sensors (H-Gait systems). *Journal of biomechanics*. 2016;49(5):684-90.
311. Tas S, Guneri S, Baki A, Yildirim T, Kaymak B, Erden Z. Effects of severity of osteoarthritis on the temporospatial gait parameters in patients with knee osteoarthritis. *Acta orthopaedica et traumatologica turcica*. 2014;48(6):635-41.
312. Thomas AC, Hubbard-Turner T, Wikstrom EA, Palmieri-Smith RM. Epidemiology of Posttraumatic Osteoarthritis. *Journal of athletic training*. 2017;52(6):491-6.
313. Thomas AC, Judd DL, Davidson BS, Eckhoff DG, Stevens-Lapsley JE. Quadriceps/hamstrings co-activation increases early after total knee arthroplasty. *The Knee*. 2014;21(6):1115-9.
314. Timmins KA, Leech RD, Batt ME, Edwards KL. Running and Knee Osteoarthritis: A Systematic Review and Meta-analysis. *American Journal of Sports Medicine*. 2017;45(6):1447-57.
315. Torio CM, Moore BJ. National Inpatient Hospital Costs: The Most Expensive Conditions by Payer, 2013: Statistical Brief #204. In. *Healthcare Cost and Utilization Project (HCUP) Statistical Briefs*. Rockville (MD): Agency for Healthcare Research and Quality (US); 2006.
316. Tran G, Smith TO, Grice A, Kingsbury SR, McCrory P, Conaghan PG. Does sports participation (including level of performance and previous injury) increase risk of

- osteoarthritis? A systematic review and meta-analysis. *British journal of sports medicine*. 2016.
317. Trepczynski A, Kutzner I, Bergmann G, Taylor WR, Heller MO. Modulation of the relationship between external knee adduction moments and medial joint contact forces across subjects and activities. *Arthritis & Rheumatology*. 2014;66(5):1218-27.
 318. Trinler UK, Baty F, Mundermann A et al. Stair dimension affects knee kinematics and kinetics in patients with good outcome after TKA similarly as in healthy subjects. *Journal of Orthopaedic Research*. 2016;34(10):1753-61.
 319. Turkiewicz A, Timpka S, Thorlund JB, Ageberg E, Englund M. Knee extensor strength and body weight in adolescent men and the risk of knee osteoarthritis by middle age. *Annals of the Rheumatic Diseases*. 2017;76(10):1657-61.
 320. Urwin SG, Kader DF, Caplan N, St Clair Gibson A, Stewart S. Gait analysis of fixed bearing and mobile bearing total knee prostheses during walking: do mobile bearings offer functional advantages? *The Knee*. 2014;21(2):391-5.
 321. Vahtrik D, Gapeyeva H, Ereline J, Paasuke M. Relationship between leg extensor muscle strength and knee joint loading during gait before and after total knee arthroplasty. *The Knee*. 2014;21(1):216-20.
 322. Valenzuela KA, Zhang S, Schroeder LE, Weinhandl JT, Cates HE. Increased knee loading in stair ambulation in patients dissatisfied with their total knee replacement. *Clinical biomechanics*. 2019;67:38-44.
 323. van der Straaten R, De Baets L, Jonkers I, Timmermans A. Mobile assessment of the lower limb kinematics in healthy persons and in persons with degenerative knee disorders: A systematic review. *Gait & Posture*. 2018;59:229-41.
 324. Verbeek J, Mischke C, Robinson R et al. Occupational Exposure to Knee Loading and the Risk of Osteoarthritis of the Knee: A Systematic Review and a Dose-Response Meta-Analysis. *Safety and health at work*. 2017;8(2):130-42.
 325. Vignon E, Valat JP, Rossignol M et al. Osteoarthritis of the knee and hip and activity: a systematic international review and synthesis (OASIS). *Joint, bone, spine : revue du rhumatisme*. 2006;73(4):442-55.
 326. Vina ER, Kwok CK. Epidemiology of osteoarthritis: literature update. *Current opinion in rheumatology*. 2018;30(2):160-7.
 327. Wallace IJ, Worthington S, Felson DT et al. Knee osteoarthritis has doubled in prevalence since the mid-20th century. *Proceedings of the National Academy of Sciences of the United States of America*. 2017;114(35):9332-6.
 328. Walter JP, D'Lima DD, Colwell CW, Jr., Fregly BJ. Decreased knee adduction moment does not guarantee decreased medial contact force during gait. *Journal of Orthopaedic Research*. 2010;28(10):1348-54.
 329. Warner SC, Valdes AM. Genetic association studies in osteoarthritis: is it fairytale? *Current opinion in rheumatology*. 2017;29(1):103-9.
 330. Weber KL, Jevsevar DS, McGrory BJ. AAOS Clinical Practice Guideline: Surgical Management of Osteoarthritis of the Knee: Evidence-based Guideline. *Journal of the American Academy of Orthopaedic Surgeons*. 2016;24(8):e94-6.
 331. Wegrzyn J, Parratte S, Coleman-Wood K, Kaufman KR, Pagnano MW. The John Insall award: no benefit of minimally invasive TKA on gait and strength outcomes: a randomized controlled trial. *Clinical Orthopaedics and Related Research*. 2013;471(1):46-55.

332. Weidow J, Tranberg R, Saari T, Karrholm J. Hip and knee joint rotations differ between patients with medial and lateral knee osteoarthritis: gait analysis of 30 patients and 15 controls. *Journal of Orthopaedic Research*. 2006;24(9):1890-9.
333. Weinhandl JT, O'Connor KM. Assessment of a greater trochanter-based method of locating the hip joint center. *Journal of biomechanics*. 2010;43(13):2633-6.
334. Weiss JM, Noble PC, Conditt MA et al. What functional activities are important to patients with knee replacements? *Clin Orthop Relat Res*. 2002;(404):172-88.
335. Wen C, Cates HE, Zhang S. Is knee biomechanics different in uphill walking on different slopes for older adults with total knee replacement? *Journal of biomechanics*. 2019;89:40-7.
336. Wiik AV, Aqil A, Brevadt M, Jones G, Cobb J. Abnormal ground reaction forces lead to a general decline in gait speed in knee osteoarthritis patients. *World journal of orthopedics*. 2017;8(4):322-8.
337. Wilson SA, McCann PD, Gotlin RS, Ramakrishnan HK, Wootten ME, Insall JN. Comprehensive gait analysis in posterior-stabilized knee arthroplasty. *Journal of Arthroplasty*. 1996;11(4):359-67.
338. Winby CR, Gerus P, Kirk TB, Lloyd DG. Correlation between EMG-based co-activation measures and medial and lateral compartment loads of the knee during gait. *Clinical biomechanics*. 2013;28(9-10):1014-9.
339. Winby CR, Lloyd DG, Besier TF, Kirk TB. Muscle and external load contribution to knee joint contact loads during normal gait. *Journal of biomechanics*. 2009;42(14):2294-300.
340. Wink AE, Gross KD, Brown CA et al. Varus thrust during walking and the risk of incident and worsening medial tibiofemoral MRI lesions: the Multicenter Osteoarthritis Study. *Osteoarthritis and Cartilage*. 2017;25(6):839-45.
341. Worsley P, Stokes M, Barrett D, Taylor M. Joint loading asymmetries in knee replacement patients observed both pre- and six months post-operation. *Clinical biomechanics*. 2013;28(8):892-7.
342. Wu X, Chu L, Xiao L et al. Early Spatiotemporal Patterns and Knee Kinematics during Level Walking in Individuals following Total Knee Arthroplasty. *Journal of healthcare engineering*. 2017;2017:7056469.
343. Xie F, Kovic B, Jin X, He X, Wang M, Silvestre C. Economic and Humanistic Burden of Osteoarthritis: A Systematic Review of Large Sample Studies. *Pharmacoeconomics*. 2016;34(11):1087-100.
344. Xing F, Lu B, Kuang MJ et al. A systematic review and meta-analysis into the effect of lateral wedge arch support insoles for reducing knee joint load in patients with medial knee osteoarthritis. *Medicine*. 2017;96(24):e7168.
345. Xu Y-m, Bai Y-h, Zhou J, Li Q-t, Liang J. Gait analysis in primary total knee arthroplasty with and without patellar resurfacing: A randomized control study. *Journal of Shanghai Jiaotong University*. 2010;15(5):632-6.
346. Yang HY, Hu WH, Jiang T, Zhao H. SMAD3 gene rs12901499 polymorphism increased the risk of osteoarthritis. *Bioscience reports*. 2018;38(3).
347. Yocum D, Weinhandl JT, Fairbrother JT, Zhang S. Wide step width reduces knee abduction moment of obese adults during stair negotiation. *Journal of biomechanics*. 2018;75:138-46.

348. Yoshida Y, Mizner RL, Ramsey DK, Snyder-Mackler L. Examining outcomes from total knee arthroplasty and the relationship between quadriceps strength and knee function over time. *Clinical biomechanics*. 2008;23(3):320-8.
349. Yoshida Y, Mizner RL, Snyder-Mackler L. Association between long-term quadriceps weakness and early walking muscle co-contraction after total knee arthroplasty. *The Knee*. 2013;20(6):426-31.
350. Yucesoy B, Charles LE, Baker B, Burchfiel CM. Occupational and genetic risk factors for osteoarthritis: a review. *Work (Reading, Mass.)*. 2015;50(2):261-73.
351. Zeng X, Ma L, Lin Z et al. Relationship between Kellgren-Lawrence score and 3D kinematic gait analysis of patients with medial knee osteoarthritis using a new gait system. *Scientific reports*. 2017;7(1):4080.
352. Zeni JA, Higginson JS. Differences in gait parameters between healthy subjects and persons with moderate and severe knee osteoarthritis: A result of altered walking speed? *Clinical biomechanics*. 2009;24(4):372-8.
353. Zeni JA, Higginson JS. Knee osteoarthritis affects the distribution of joint moments during gait. *The Knee*. 2011;18(3):156-9.
354. Zeni JA, Jr., Flowers P, Bade M, Cheuy V, Stevens-Lapsley J, Snyder-Mackler L. Stiff knee gait may increase risk of second total knee arthroplasty. *Journal of Orthopedic Research*. 2019;37(2):397-402.
355. Zeni JA, Jr., Higginson JS. Dynamic knee joint stiffness in subjects with a progressive increase in severity of knee osteoarthritis. *Clinical biomechanics*. 2009;24(4):366-71.
356. Zeni JA, Rudolph K, Higginson JS. Alterations in quadriceps and hamstrings coordination in persons with medial compartment knee osteoarthritis. *Journal of Electromyography and Kinesiology*. 2010;20(1):148-54.
357. Zhang W, Moskowitz RW, Nuki G et al. OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. *Osteoarthritis and Cartilage*. 2008;16(2):137-62.
358. Zhang Y, Jordan JM. Epidemiology of osteoarthritis. *Clinics in geriatric medicine*. 2010;26(3):355-69.
359. Zhao D, Banks SA, Mitchell KH, D'Lima DD, Colwell CW, Fregly BJ. Correlation between the knee adduction torque and medial contact force for a variety of gait patterns. *Journal of Orthopaedic Research*. 2007;25(6):789-97.
360. Zheng H, Chen C. Body mass index and risk of knee osteoarthritis: systematic review and meta-analysis of prospective studies. *BMJ Open*. 2015;5(12):e007568.

Appendices

Appendix A: Bilateral TKR Patient Characteristics

Table 14. Individual Patient Characteristics

Subject	Age	Gender	Height	Weight	BMI
1	62	Female	1.67	94.95	34.05
2	71	Female	1.71	111.43	38.11
3	74	Female	1.58	72.30	28.96
4	70	Female	1.66	81.35	29.52
5	69	Male	1.77	102.95	32.86
6	71	Female	1.69	74.70	26.15
7	58	Male	1.79	107.00	33.39
8	74	Male	1.83	99.41	29.68
9	73	Female	1.70	82.94	28.70
10	75	Male	1.78	94.41	29.80
11	65	Male	1.92	115.62	31.36
12	65	Female	1.71	80.12	27.40
13	73	Male	1.79	120.42	37.58
14	74	Female	1.62	88.09	33.57
15	67	Female	1.73	107.68	35.98

Appendix B: Unilateral Patient Characteristics – Study One

Table 15. Individual Patient Characteristics

Subject	Age	Gender	Height	Weight	BMI	Replacement Side
16	54	Male	1.88	114.17	32.48	Left
17	59	Female	1.70	78.90	27.30	Right
18	64	Male	1.80	102.55	31.83	Right
19	72	Male	1.68	109.07	38.64	Right
20	64	Female	1.72	91.95	31.26	Right
21	66	Female	1.71	73.70	25.35	Right
22	75	Male	1.76	79.85	25.78	Right
23	74	Male	1.85	79.61	23.26	Left
24	72	Female	1.67	85.83	30.78	Right
25	71	Male	1.89	104.59	29.28	Right
26	71	Male	1.77	106.32	34.13	Left
27	74	Female	1.62	68.00	25.91	Right
28	68	Male	1.75	72.60	23.71	Left
29	75	Female	1.65	79.38	29.12	Right
30	71	Female	1.55	69.40	28.92	Left

Appendix C: Unilateral Patient Characteristics – Study Two

Table 16. Individual Patient Characteristics

Subject	Age	Gender	Height	Weight	BMI	Replacement Side
16	70	Male	1.76	112.28	36.25	Left
17	64	Male	1.80	102.55	31.83	Right
18	68	Female	1.68	63.40	22.60	Right
19	72	Male	1.68	109.07	38.64	Right
20	64	Female	1.72	91.95	31.26	Right
21	66	Female	1.71	73.70	25.35	Right
22	67	Male	1.81	92.71	28.46	Right
23	65	Female	1.52	51.27	22.19	Left
24	71	Male	1.77	106.32	34.13	Left
25	63	Male	1.88	95.91	27.14	Left
26	62	Female	1.69	76.82	26.90	Right
27	51	Female	1.69	91.40	32.00	Left
28	64	Male	1.83	105.20	31.41	Right
29	60	Male	1.84	81.60	24.10	Left
30	67	Male	1.85	83.46	24.39	Left

Appendix D: Unilateral Patient and Asymptomatic Control Characteristics – Study Three

Table 17. Individual Unilateral Patient Characteristics

Subject	Age	Gender	Height	Weight	BMI	Replacement Side
16	71	Female	1.549	69.4	28.92	Left
17	73	Female	1.727	72.57	24.33	Right
18	59	Female	1.626	81.2	30.71	Left
19	54	Male	1.88	114.17	32.48	Left
20	57	Female	1.68	85.42	30.27	Right
21	70	Male	1.76	112.28	36.25	Left
22	67	Male	1.805	92.71	28.46	Right
23	74	Male	1.85	79.61	23.26	Left
24	72	Female	1.67	85.83	30.78	Right
25	71	Male	1.765	106.32	34.13	Left
26	70	Female	1.67	70.54	25.29	Right
27	63	Male	1.88	95.91	27.14	Left
28	62	Female	1.69	76.82	26.90	Right
29	67	Male	1.76	89.4	28.86	Right
30	67	Male	1.85	83.46	24.39	Left

Table 18. Individual Asymptomatic Control Characteristics

Subject	Age	Gender	Height	Weight	BMI
31	66	Male	1.91	117.66	32.42
32	73	Female	1.73	68.19	22.84
33	69	Male	1.68	66.50	23.67
34	71	Male	1.88	93.60	26.51
35	59	Male	1.91	79.20	21.82
36	57	Female	1.69	71.86	25.31
37	50	Female	1.76	99.18	32.02
38	71	Female	1.76	77.37	25.12
39	45	Male	1.80	91.82	28.34
40	63	Male	1.95	127.27	33.47
41	51	Female	1.65	58.51	21.49
42	63	Female	1.63	63.95	24.07
43	68	Male	1.89	92.19	25.81
44	68	Male	1.82	93.44	28.36
45	79	Male	1.82	75.30	22.86

Appendix E: Informed Consent

Informed Consent Form

Effects of Bilateral Total Knee Replacement on Knee Joint Biomechanics During Level Walking and Stair Negotiation

Investigators: Derek Yocum

Faculty Advisor: Dr. Songning Zhang

Address: Biomechanics/Sports Medicine Lab
The University of Tennessee Knoxville
1914 Andy Holt Avenue
Knoxville, TN 37996

Phone: 865-974-2091

Introduction

You are invited to participate in a research study because you've had bilateral total knee replacements (TKR) and are between 50 and 75 years old. The primary purpose of this study is to learn the differences in how the knee works during level and stair walking in individuals who've had a single knee replacement, and those who've had two knee replacements. Please ask the study staff to explain any words or information that you do not clearly understand. Before agreeing to be in this study, it is important that you read and understand the following explanation of the procedures, risks, and benefits.

Testing Protocol

If you agree to participate in the study, you will attend one study test session at the Biomechanics/Sports Medicine Lab on the UT campus. The test session will take about 2 hours to complete. You will need to wear shorts and t-shirt for the study procedures. Your shorts should be close-fitting, so we can see how your body moves during the study procedures. If you do not have a close-fitting short, we will provide a spandex laboratory short.

At the start of the test session, you will complete the patient satisfaction score, and a few survey forms [knee injury and osteoarthritis outcome score (KOOS), Knee Society Scoring system score (KSS), and Physical Activity Readiness Survey (PAR-Q)]. Following completion of the surveys, you will change into appropriate testing attire and footwear. Height and weight will be recorded. You will walk on the treadmill for 3 minutes to get ready for the exercises. You will then be asked to perform an up-and-go test in which you will get out of a chair, walk about 9 feet, and walk back to the chair,

After completion of the aforementioned test, you will be asked to complete level and stair walking tests. An EMG electrode will be placed on several lower limb muscles on you. You will be asked to perform several movements to test the electrode attachment for the muscles. The electrodes are used to record the electrical signals of the muscles and will not discharge any electrical shock to you. Reflective markers will be placed on your body using double-sided tapes. You will then perform 5 successful tests for each of three walking test movement conditions: level walking, stair ascent, and stair descent. Tests need to be completed at your own preferred speed. You will be asked to rate your knee pain before and after each of the three walking conditions.

None of the instruments will interfere with your ability to do the test. The cameras used for motion capture will not record images of you and will record digital coordinates of the reflective markers placed on your body. If you have any further questions, interests or concerns

about any equipment to be used in this test, please feel free to ask the investigators or other research personnel.

Potential Risks

Risks for participating in the study are minimal so they are no greater than your daily activities. You can practice all of the exercises before the testing and hold on to the hand rail during the exercises if needed. In order to prevent potential falls and trips, the staircase include a handrail on the right side for support and balance if needed. The balance system also has a handrail for support. You may experience minor skin irritation where the adhesive electrodes are placed. You may also experience some muscle soreness and tightness which are common when participating in physical activities.

If any injury should occur during the course of testing, standard first aid procedures will be administered if needed. At least one researcher with a basic knowledge of first aid procedures will be present. In the unlikely event a physical injury is suffered as a result of participation in this study, the University of Tennessee does not "automatically" reimburse subjects for medical claims or other compensation. If physical injury is suffered in the course of research, please talk to Derek Yocum (974-2091) or Songning Zhang (974-4716). Breach of confidentiality is a potential risk, however, we have taken measures to prevent this.

Benefits

You may not benefit from your participation in this study directly. If you want, you can receive your individual study information to share with your personal physician in case it might be helpful to your future health care. Identifying the gait abnormalities following bilateral TKR may be also beneficial in improving future TKR designs, and surgical and rehabilitation methods in order to achieve higher levels of patients' functions after their knee joint replacements and future improvements of TKR implants.

Confidentiality

Only the principal investigator, and qualified lab personnel will have access to the respective subject information and data. Data will be stored on hard drives of password protected computers in the Biomechanics/Sports Medicine Lab and will be backed up onto DVDs and/or portable hard drives and erased from the hard drives after the completion of the study. All subject data will be coded numerically and referred to only by the code and not by subject's name.

The results will be shared in the form of presentations, and/or publications. Subject information sheets, informed consent, and backup data DVDs and/or portable hard drives will be stored in a locked file cabinet in Biomechanics/Sports Medicine Laboratory. The information sheets including the consent forms and other forms containing subject's identity information will be destroyed six years after the completion of the study. If subject decide to withdraw from the study, their information sheet, consent form and data with the identity will be destroyed. The cameras used in the study do not capture images of the subjects.

Use of Personal Health Information for Research Purposes

Under federal privacy regulations, you have the right to determine who may review or use your personal health information (also called "protected health information" or PHI). This includes information that can identify you. For example, it can include your name, phone number,

birthdate and medical record number. The PHI that researchers will receive, review and use in this research study may include information such as:

- Information provided by you
- Medical history
- Treatment records
- Diagnostic information/tests
- Demographic information

If you choose to be in this research study and sign this consent form, you are giving your permission to your health care providers, listed below, to share your PHI with the research team at The University of Tennessee, and for the research team to review and use your PHI for the research study.

- Tennessee Orthopaedic Clinics

Your PHI, which might identify you, may be shared with or used by:

- The Institutional Review Board (IRB) at The University of Tennessee, Knoxville

However, some of these organizations or institutions listed above do not have the same obligations to protect your PHI. Your PHI will only be used and/or given to others:

- To do the research described in this consent form;
- To study the results of the research; and
- To see if the research was done correctly.

Your PHI will be used until the research ends and all required monitoring has been completed. You may withdraw or take away your permission to use and share your PHI at any time. You can do this by sending written notice to the researchers listed on this consent form. When you withdraw your permission, no new PHI will be shared or used after that date. However, information that has already been collected may still be used to complete the research.

You have the right to see and copy your PHI that is shared or used in this research study. However in order to complete the research, your access to this PHI may be temporarily suspended while the research is in progress. When the study is completed, you will be able to access to this information. If you do not permit use of your PHI you cannot participate in this research study. If you withdraw your permission for use of your PHI, you may not be able to stay in the study. However, your decision to permit, not permit, or withdraw your permission for use of your PHI will not affect your relationship with The University of Tennessee or the services you and your family receive in any way.

Compensation

While there is no direct compensation for participation, you can park on campus for free.

Contact Information

If you have questions at any time about the study or the procedures or if you experience adverse effects as a result of participating in this study, you may contact the researcher, Derek Yocum, or the faculty advisor Dr. Songning Zhang at 865-974-2091 or at the address shown above. If you have questions about your rights as a participant, contact the University of Tennessee, IRB Compliance Officer at (865) 974-7697 or utkirb@utk.edu.

Participation

Your participation in this study is voluntary; you may decline to participate without penalty or loss of benefits to which you are otherwise entitled. You may be withdrawn from the

study by the investigator if it is determined that you do not meet the eligibility criteria or you answer yes to any of the questions on the PAR-Q.

If you decide to participate, you may withdraw from the study at anytime without penalty and without loss of benefits to which you are otherwise entitled. If you withdraw from the study before data collection is completed your data will be returned to you or destroyed.

CONSENT

I have read the above information. I have received a copy of this form. I agree to participate in this study.

Participant's name _____ Participant's signature _____ Date _____

Investigator's signature _____ Date _____ Subject # _____

Appendix F: Recruitment Letter

Tennessee Orthopaedic Foundation for Education and Research
9405 Park West Blvd.
Knoxville, Tennessee 37923
Office: (865) 373-1811

July 22, 2019

(Patient Name, Address)

Dear

I am writing to you about a research project at the University of Tennessee on how patients with two knee replacements perform daily activities such as walking, stair climbing, and other activities similar to exercises that you performed in physical therapy. Because you've had two total knee replacements, you might be eligible to participate in this study. The study may help the medical community better understand the effects of two knee replacements on patients' ability to perform daily living tasks, and how this effects other joints in the legs.

If you are interested in participating in this project, please contact Derek Yocum (dyocum@vols.utk.edu) or Dr. Songning Zhang (szhang@utk.edu) by email or by phone (865) 974-2091 at the University of Tennessee. There are multiple time slots available and they will work around your schedule.

I am associated with this research but you are not obligated to participate. Your future care at Tennessee Orthopaedic Clinics will not be affected by your decision regarding this research opportunity. Thank you in advance for your consideration.

Thank you,

Harold E. Cates

Harold E. Cates, M.D.

Appendix G: Physical Activity Readiness Questionnaire

PHYSICAL ACTIVITY READINESS QUESTIONNAIRE (PAR-Q)

Regular physical activity is fun and healthy, and increasingly more people are starting to become more active every day. Being more active is very safe for most people. However, some people should check with their doctor before they start becoming much more physically active.

If you are planning to become much more physically active than you are now, start by answering the seven questions in the box below. If you are between the ages of 15 and 69, the PAR-Q will tell you if you should check with your doctor before you start. If you are over 69 years of age and you are not used to being very active, check with your doctor.

No **Yes**

- | | | |
|--------------------------|--------------------------|--|
| <input type="checkbox"/> | <input type="checkbox"/> | 1. Has your doctor ever said that you have a heart condition <u>and</u> that you should only do physical activity recommended by a doctor? |
| <input type="checkbox"/> | <input type="checkbox"/> | 2. Do you feel pain in your chest when you do physical activity? |
| <input type="checkbox"/> | <input type="checkbox"/> | 3. In the past month, have you had chest pain when you were not doing physical activity? |
| <input type="checkbox"/> | <input type="checkbox"/> | 4. Do you lose your balance because of dizziness or do you ever lose consciousness? |
| <input type="checkbox"/> | <input type="checkbox"/> | 5. Do you have a bone or joint problem that could be made worse by a change in your physical activity? |
| <input type="checkbox"/> | <input type="checkbox"/> | 6. Is your doctor currently prescribing drugs (for example water pills) for your blood pressure of heart condition? |
| <input type="checkbox"/> | <input type="checkbox"/> | 7. Do you know of <u>any other reason</u> why you should not do physical activity? |

Please note: If your health changes so that you then answer YES to any of these questions, tell your fitness or health professional. Ask whether you should change your physical activity plan.

If you answered YES to one or more questions

Talk to your doctor by phone or in person BEFORE you start becoming much more physically active or BEFORE you have a fitness appraisal. Tell your doctor about the PAR-Q and which questions you answered YES.

- You may be able to do any activity you want as long as you start slowly and build up gradually. Or you may need to restrict your activities to those which are safe for you. Talk to your doctor about the kinds of activities you wish to participate in and follow his/her advice.
- Find out which community programs are safe and helpful for you.

If you answered NO to all questions

If you have answered NO honestly to all PAR-Q questions, you can be reasonably sure that you can:

- Start becoming much more physical active – begin slowly and build up gradually. This is the safest and easiest way to go.
- Take part in a fitness appraisal – this is an excellent way to determine your basic fitness so that you can plan the best way for you to live actively.

I understand that my signature signifies that I have read and understand all the information on the questionnaire, that I have truthfully answered all the questions, and that any question/concerns I may have had have been addressed to my complete satisfaction.

Name (please print)

Signature

Delay becoming much more active if:

- You are not feeling well because of a temporary illness such as a cold or a fever – wait until you feel better, or

If you are or may be pregnant – talk to your doctor before you start becoming more active.

Date

Appendix H: Individual Results for Select Variables – Level Walking

Table 19. Level Walking Loading-Response Vertical Ground Reaction Force (BW)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	1.192±0.034	1.185±0.026	16	1.079±0.017	1.081±0.032
2	0.834±0.012	0.841±0.023	17	1.185±0.023	1.133±0.057
3	1.074±0.078	1.152±0.062	18	1.116±0.021	1.105±0.024
4	0.932±0.024	0.959±0.024	19	1.033±0.031	1.106±0.021
5	0.975±0.028	1.084±0.036	20	1.042±0.010	1.078±0.034
6	0.977±0.013	1.036±0.008	21	1.033±0.020	1.179±0.022
7	1.107±0.031	1.146±0.039	22	1.146±0.057	1.094±0.017
8	1.122±0.023	0.990±0.032	23	1.033±0.005	1.065±0.030
9	0.993±0.020	0.970±0.024	24	0.998±0.017	1.056±0.021
10	1.300±0.035	1.216±0.032	25	1.108±0.012	1.135±0.050
11	1.061±0.032	1.167±0.053	26	0.984±0.013	1.007±0.012
12	1.007±0.016	0.974±0.022	27	1.072±0.038	1.025±0.008
13	0.991±0.015	1.051±0.038	28	1.090±0.025	1.113±0.022
14	0.941±0.012	0.957±0.008	29	1.032±0.021	1.050±0.014
15	0.998±0.045	1.008±0.018	30	1.119±0.045	1.115±0.015
Average	1.034±0.114	1.049±0.106	Average	1.071±0.056	1.089±0.045

Table 20. Level Walking Push-off Response Vertical Ground Reaction Force (BW)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	1.104±0.002	1.126±0.009	16	1.080±0.010	1.088±0.009
2	0.885±0.009	0.859±0.012	17	1.099±0.014	1.089±0.029
3	1.034±0.014	1.066±0.018	18	1.109±0.026	1.113±0.015
4	1.006±0.017	1.041±0.071	19	0.973±0.024	0.997±0.019
5	1.045±0.014	1.065±0.019	20	1.006±0.015	1.007±0.007
6	1.048±0.013	1.028±0.012	21	1.056±0.021	1.132±0.030
7	1.006±0.005	0.988±0.006	22	1.105±0.029	1.141±0.033
8	0.986±0.029	0.973±0.019	23	1.017±0.018	1.055±0.010
9	0.978±0.009	0.968±0.011	24	0.946±0.013	1.022±0.013
10	0.918±0.016	0.969±0.013	25	1.070±0.009	1.073±0.023
11	0.975±0.019	0.986±0.015	26	0.972±0.012	0.985±0.012
12	1.014±0.010	1.040±0.014	27	1.093±0.050	1.083±0.025
13	0.987±0.014	0.979±0.009	28	1.098±0.019	1.083±0.020
14	1.007±0.004	0.971±0.011	29	1.032±0.018	0.988±0.022
15	1.050±0.012	1.073±0.006	30	1.103±0.025	1.095±0.015
Average	1.003±0.054	1.009±0.064	Average	1.050±0.056	1.063±0.052

Table 21. Level Walking Dorsiflexion ROM (degrees)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	28.512±0.313	28.002±0.607	16	20.982±1.621	19.705±1.235
2	18.472±1.557	18.526±1.012	17	25.506±1.201	21.976±2.316
3	18.072±2.579	16.827±1.474	18	27.260±1.715	28.591±1.224
4	22.584±1.049	21.440±2.732	19	27.429±1.919	22.949±0.727
5	20.457±0.865	22.267±1.274	20	21.537±0.770	19.443±1.022
6	20.973±1.940	19.661±0.968	21	27.109±1.143	13.916±0.879
7	20.072±0.401	22.675±1.947	22	24.467±1.771	24.695±0.780
8	25.855±1.170	31.330±1.544	23	28.419±0.874	20.988±0.844
9	23.950±0.087	23.667±0.805	24	25.562±0.663	22.950±1.590
10	28.273±0.949	31.298±0.874	25	20.844±0.428	19.421±1.076
11	18.560±2.195	19.138±1.441	26	24.973±0.840	21.541±1.284
12	24.648±0.977	17.638±1.275	27	17.980±2.948	25.180±2.050
13	22.585±0.541	21.765±0.583	28	27.541±0.998	27.326±2.588
14	23.601±0.870	24.854±1.590	29	25.756±0.755	23.931±1.662
15	19.587±1.755	21.639±0.722	30	25.137±1.819	25.705±1.179
Average	22.414±3.389	22.715±4.515	Average	24.700±3.028	22.555±3.673

Table 22. Level Walking Eversion ROM (degrees)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	-17.373±0.961	-3.807±1.300	16	-8.778±0.875	-11.870±0.906
2	-4.897±1.683	-5.166±1.456	17	-7.164±1.564	-12.460±1.014
3	-4.639±2.851	-14.798±2.446	18	-4.416±0.761	-3.917±0.434
4	-11.071±1.828	-6.759±2.533	19	-7.048±1.721	-8.152±1.322
5	-6.978±1.471	-7.000±1.469	20	-7.890±1.470	-10.078±1.640
6	-12.530±1.631	-12.292±1.165	21	-3.008±0.962	-2.173±1.070
7	-7.068±1.898	-5.060±1.511	22	-5.135±0.936	-8.368±1.939
8	-1.039±1.157	-7.791±1.920	23	-2.001±0.826	-4.534±0.750
9	-4.872±1.263	-9.388±0.774	24	-5.617±0.647	-2.917±0.417
10	-8.435±0.752	-3.081±1.899	25	-6.593±1.111	-12.774±1.446
11	-6.708±1.078	-8.383±1.252	26	-3.333±1.450	-5.289±1.344
12	-4.835±1.306	-4.200±1.969	27	-7.463±2.151	-9.525±3.324
13	-8.606±1.289	-14.227±1.961	28	-5.146±0.902	-3.279±1.097
14	-9.792±1.112	-3.969±1.931	29	-5.593±0.685	-8.395±0.901
15	-3.380±2.301	-10.055±0.551	30	-10.223±1.289	-4.775±1.739
Average	-7.481±4.068	-7.732±3.783	Average	-5.961±2.242	-7.234±3.629

Table 23. Level Walking Loading-Response Dorsiflexion Moment (Nm/kg)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	0.181±0.026	0.117±0.019	16	0.255±0.018	0.253±0.018
2	0.231±0.015	0.228±0.033	17	0.393±0.022	0.259±0.013
3	0.232±0.018	0.172±0.021	18	0.382±0.019	0.292±0.011
4	0.139±0.010	0.139±0.006	19	0.253±0.027	0.195±0.030
5	0.138±0.033	0.167±0.037	20	0.264±0.023	0.277±0.024
6	0.111±0.013	0.134±0.005	21	0.374±0.014	0.309±0.017
7	0.206±0.010	0.205±0.020	22	0.496±0.022	0.393±0.027
8	0.104±0.012	0.115±0.010	23	0.399±0.017	0.370±0.033
9	0.139±0.013	0.134±0.020	24	0.214±0.015	0.247±0.020
10	0.154±0.009	0.107±0.011	25	0.298±0.021	0.306±0.035
11	0.265±0.015	0.389±0.025	26	0.361±0.037	0.320±0.032
12	0.125±0.007	0.185±0.013	27	0.094±0.009	0.165±0.039
13	0.108±0.014	0.159±0.004	28	0.218±0.025	0.174±0.012
14	0.177±0.009	0.182±0.018	29	0.159±0.014	0.221±0.033
15	0.226±0.019	0.213±0.006	30	0.336±0.018	0.214±0.021
Average	0.169±0.052	0.176±0.070	Average	0.300±0.105	0.266±0.067

Table 24. Level Walking Push-off Response Plantarflexion Moment (Nm/kg)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	-1.394±0.036	-1.518±0.045	16	-1.480±0.012	-1.466±0.005
2	-1.101±0.019	-1.123±0.027	17	-1.332±0.023	-1.365±0.054
3	-1.179±0.040	-1.286±0.029	18	-1.487±0.048	-1.497±0.019
4	-1.305±0.044	-1.491±0.252	19	-1.132±0.045	-1.224±0.038
5	-1.355±0.012	-1.402±0.009	20	-1.181±0.020	-1.256±0.024
6	-1.329±0.014	-1.250±0.010	21	-1.376±0.033	-1.460±0.059
7	-1.452±0.022	-1.380±0.027	22	-1.457±0.047	-1.669±0.039
8	-1.373±0.046	-0.818±0.014	23	-1.312±0.053	-1.291±0.036
9	-1.257±0.028	-1.173±0.019	24	-1.063±0.016	-1.194±0.039
10	-1.175±0.043	-0.653±0.032	25	-1.434±0.024	-1.400±0.025
11	-1.496±0.032	-1.421±0.024	26	-1.077±0.033	-1.126±0.045
12	-1.314±0.042	-1.192±0.030	27	-1.335±0.066	-1.297±0.023
13	-1.333±0.034	-1.304±0.014	28	-1.469±0.024	-1.420±0.109
14	-1.175±0.020	-1.248±0.020	29	-1.082±0.024	-1.094±0.019
15	-1.493±0.033	-1.467±0.018	30	-1.287±0.033	-1.400±0.015
Average	-1.315±0.120	-1.248±0.242	Average	-1.300±0.156	-1.344±0.153

Table 25. Level Walking Knee Extension ROM (degrees)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	-49.494±0.652	-49.316±1.934	16	-53.000±0.554	-54.746±1.356
2	-43.349±2.205	-40.622±1.923	17	-48.677±1.153	-47.050±2.307
3	-47.483±0.845	-40.320±1.552	18	-47.421±0.833	-56.688±1.505
4	-46.624±2.184	-47.108±3.453	19	-41.989±1.335	-48.935±1.345
5	-45.374±2.110	-43.699±1.530	20	-47.374±0.690	-50.757±1.079
6	-43.358±2.764	-45.074±2.275	21	-43.858±0.350	-32.122±1.696
7	-58.583±2.440	-58.478±1.794	22	-50.588±0.762	-53.196±1.323
8	-50.817±2.216	-56.604±1.795	23	-57.528±3.509	-47.306±1.751
9	-42.710±1.919	-48.234±1.694	24	-44.730±1.053	-48.485±1.320
10	-49.483±2.797	-49.175±1.339	25	-49.773±1.425	-50.001±1.789
11	-52.204±1.538	-49.647±1.330	26	-48.059±3.564	-45.133±1.937
12	-48.000±2.054	-42.528±0.686	27	-34.470±1.710	-42.814±4.613
13	-55.262±1.851	-49.316±1.433	28	-40.080±2.958	-42.085±4.871
14	-44.341±1.517	-48.649±2.317	29	-39.376±2.140	-48.520±0.780
15	-44.501±3.203	-43.032±1.133	30	-44.026±2.893	-39.386±2.165
Average	-48.106±4.633	-47.454±5.232	Average	-46.063±5.797	-47.148±6.256

Table 26. Level Walking Knee Abduction ROM (degrees)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	5.943±0.310	2.748±1.176	16	4.644±0.194	4.189±0.327
2	4.347±0.297	3.827±0.453	17	4.603±0.774	-
3	6.730±0.413	6.945±1.094	18	3.875±0.364	2.302±0.261
4	1.040±0.426	0.980±0.631	19	5.405±0.807	-
5	3.694±0.548	4.952±0.404	20	3.858±0.535	-
6	1.876±0.525	1.155±0.474	21	4.766±0.217	4.678±0.449
7	2.621±0.608	2.132±0.349	22	2.192±0.937	2.650±0.528
8	1.894±0.812	3.935±0.669	23	6.007±1.475	3.973±0.356
9	5.785±0.294	2.896±0.421	24	3.937±0.526	2.301±0.416
10	1.490±0.422	3.061±0.372	25	3.711±0.711	3.744±0.642
11	2.414±0.411	1.500±0.236	26	2.697±0.655	3.449±0.500
12	4.435±0.624	3.778±0.433	27	4.944±1.500	-
13	-	-	28	-	2.417±0.349
14	5.774±0.122	4.027±0.598	29	3.364±0.826	3.763±0.194
15	5.106±2.319	4.447±0.412	30	5.886±0.519	4.181±0.516
Average	3.796±1.902	3.313±1.614	Average	4.278±1.117	3.423±0.859

Table 27. Level Walking Loading-Response Knee Extension Moment (Nm/kg)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	0.181±0.039	0.236±0.128	16	0.516±0.031	0.338±0.038
2	0.298±0.035	0.151±0.038	17	0.532±0.054	0.719±0.017
3	0.265±0.172	-0.022±0.045	18	0.538±0.068	0.720±0.052
4	-0.009±0.035	-0.042±0.039	19	0.606±0.028	0.686±0.059
5	0.182±0.067	0.224±0.031	20	0.305±0.056	0.577±0.048
6	0.046±0.034	0.158±0.037	21	0.132±0.029	1.155±0.074
7	0.682±0.080	0.483±0.077	22	0.460±0.056	0.520±0.069
8	0.328±0.099	0.005±0.084	23	-	0.686±0.068
9	0.135±0.065	0.123±0.057	24	0.519±0.053	0.496±0.032
10	0.859±0.067	0.626±0.153	25	0.507±0.045	0.663±0.082
11	0.382±0.050	0.037±0.060	26	0.348±0.063	0.212±0.058
12	0.186±0.081	0.236±0.062	27	0.252±0.093	0.315±0.044
13	0.175±0.027	0.221±0.066	28	0.277±0.111	0.241±0.073
14	0.367±0.018	0.121±0.031	29	0.362±0.033	0.260±0.037
15	0.134±0.044	0.111±0.039	30	0.368±0.026	0.306±0.031
Average	0.281±0.229	0.178±0.180	Average	0.409±0.137	0.526±0.257

Table 28. Level Walking Push-off Response Knee Extension Moment (Nm/kg)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	0.064±0.041	0.039±0.022	16	0.053±0.031	0.008±0.019
2	-0.153±0.021	-0.267±0.029	17	-0.095±0.033	-0.123±0.041
3	-0.197±0.017	-0.244±0.068	18	-0.022±0.029	-0.180±0.054
4	-0.253±0.066	-0.376±0.112	19	0.151±0.056	-0.102±0.036
5	-0.043±0.072	-0.070±0.106	20	-0.045±0.020	0.055±0.012
6	-0.163±0.081	-0.020±0.037	21	-0.141±0.029	-0.275±0.063
7	-0.017±0.040	-0.086±0.075	22	0.070±0.044	-0.049±0.034
8	-0.162±0.057	-0.240±0.153	23	-0.262±0.024	-0.163±0.052
9	-0.133±0.026	-0.184±0.034	24	0.059±0.041	-0.108±0.059
10	-0.192±0.039	0.126±0.184	25	-0.351±0.041	-0.271±0.015
11	-0.223±0.036	-0.338±0.035	26	-0.114±0.031	-0.352±0.070
12	-0.224±0.046	-0.287±0.036	27	-0.188±0.078	0.063±0.135
13	-0.144±0.038	-0.147±0.027	28	-0.146±0.026	-0.116±0.006
14	-0.096±0.044	-0.235±0.043	29	0.065±0.065	-0.184±0.008
15	-0.520±0.022	-0.482±0.033	30	-0.243±0.066	-0.294±0.030
Average	-0.164±0.130	-0.187±0.163	Average	-0.081±0.145	-0.139±0.125

Table 29. Level Walking Loading-Response Knee Abduction Moment (Nm/kg)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	-0.395±0.021	-0.176±0.005	16	-0.536±0.017	-0.531±0.016
2	-0.384±0.027	-0.364±0.020	17	-0.567±0.052	-0.534±0.028
3	-0.344±0.070	-0.448±0.055	18	-0.552±0.014	-0.507±0.023
4	-0.429±0.038	-0.408±0.040	19	-0.500±0.028	-0.344±0.011
5	-0.272±0.026	-0.332±0.039	20	-0.443±0.017	-0.547±0.028
6	-0.275±0.011	-0.384±0.036	21	-0.591±0.020	-0.472±0.024
7	-0.349±0.021	-0.549±0.060	22	-0.511±0.027	-0.541±0.029
8	-0.372±0.060	-0.356±0.011	23	-0.341±0.013	-0.584±0.051
9	-0.200±0.020	-0.278±0.011	24	-0.450±0.011	-0.367±0.013
10	-0.259±0.017	-0.574±0.030	25	-0.558±0.017	-0.630±0.040
11	-0.283±0.033	-0.446±0.038	26	-0.302±0.010	-0.415±0.022
12	-0.528±0.019	-0.465±0.027	27	-0.243±0.052	-0.012±0.041
13	-0.352±0.015	-0.334±0.027	28	-0.464±0.039	-0.727±0.071
14	-0.416±0.020	-0.271±0.019	29	-0.401±0.046	-0.318±0.026
15	-0.372±0.044	-0.362±0.013	30	-0.372±0.040	-0.152±0.018
Average	-0.349±0.082	-0.383±0.104	Average	-0.455±0.105	-0.445±0.185

Table 30. Level Walking Push-off Response Knee Abduction Moment (Nm/kg)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	-	-0.058±0.027	16	-0.469±0.028	-0.403±0.012
2	-0.229±0.027	-0.238±0.006	17	-0.425±0.034	-0.560±0.037
3	-0.385±0.015	-0.102±0.021	18	-0.356±0.025	-0.515±0.011
4	-0.412±0.028	-0.484±0.093	19	-0.317±0.027	-0.377±0.037
5	-0.149±0.000	-0.262±0.039	20	-0.328±0.014	-0.407±0.026
6	-0.201±0.037	-0.257±0.032	21	-0.363±0.020	-0.280±0.056
7	-0.458±0.025	-0.397±0.036	22	-0.318±0.044	-0.379±0.018
8	-0.123±0.047	-0.275±0.047	23	-0.216±0.027	-0.356±0.025
9	-	-0.179±0.005	24	-0.250±0.015	-0.257±0.008
10	-0.237±0.014	-0.419±0.018	25	-0.388±0.028	-0.603±0.016
11	-0.252±0.025	-0.171±0.016	26	-0.204±0.020	-0.278±0.028
12	-	-0.331±0.025	27	-0.241±0.036	-0.055±0.016
13	-0.338±0.021	-0.241±0.019	28	-0.346±0.026	-0.575±0.042
14	-0.338±0.024	-0.248±0.029	29	-0.342±0.025	-0.227±0.024
15	-0.302±0.039	-0.205±0.025	30	-0.259±0.025	-0.109±0.027
Average	-0.285±0.105	-0.258±0.115	Average	-0.321±0.076	-0.359±0.163

Table 31. Level Walking Hip Extension ROM (degrees)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	-36.787±0.679	-27.747±0.740	16	-28.065±0.742	-30.985±0.949
2	-38.292±0.757	-34.940±1.173	17	-40.775±0.854	-43.479±2.476
3	-32.548±1.347	-40.253±1.470	18	-37.271±1.093	-37.810±0.375
4	-37.621±0.629	-31.991±1.285	19	-36.591±1.569	-33.652±0.584
5	-36.016±0.803	-36.618±1.643	20	-29.163±1.179	-32.564±0.513
6	-22.820±0.895	-32.584±1.192	21	-44.977±0.831	-46.345±1.148
7	-29.106±16.483	-30.507±1.176	22	-28.915±0.770	-38.180±1.852
8	-28.503±0.817	-26.650±2.012	23	-29.314±0.634	-37.766±0.458
9	-30.754±0.867	-23.773±0.915	24	-32.993±0.269	-34.384±0.680
10	-40.109±2.787	-37.614±1.743	25	-30.734±0.444	-42.666±1.389
11	-34.356±1.560	-39.274±2.066	26	-32.044±1.688	-34.097±1.363
12	-35.477±0.730	-36.870±1.140	27	-29.963±1.342	-32.916±1.231
13	-28.972±1.067	-40.354±1.544	28	-30.880±1.030	-35.417±1.919
14	-41.428±0.459	-38.643±0.607	29	-35.685±1.122	-33.748±0.529
15	-53.226±3.773	-30.033±1.460	30	-47.609±2.519	-43.733±1.232
Average	-35.068±7.110	-33.857±5.273	Average	-34.332±6.084	-37.183±4.788

Table 32. Level Walking Hip Abduction ROM (degrees)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	5.470±0.778	2.734±1.035	16	16.639±0.152	14.909±0.423
2	12.805±0.903	13.389±1.706	17	10.222±0.331	7.230±0.822
3	8.774±1.017	9.822±0.649	18	17.994±0.919	13.994±0.728
4	7.341±6.716	4.460±0.601	19	19.249±1.102	20.572±0.693
5	8.027±0.787	10.964±2.258	20	10.847±0.722	10.458±0.409
6	9.811±1.425	1.201±0.720	21	10.651±0.857	13.022±0.873
7	8.455±1.067	11.807±2.101	22	9.921±0.664	13.020±0.784
8	8.923±0.311	7.356±1.684	23	13.824±0.287	15.938±0.213
9	8.220±0.435	9.754±2.150	24	12.049±0.912	9.177±0.860
10	8.116±0.377	2.786±1.186	25	12.636±0.566	11.714±0.480
11	6.643±0.932	8.269±5.084	26	10.879±1.653	9.606±0.426
12	5.681±0.780	5.667±0.943	27	6.209±0.708	3.696±0.733
13	6.453±1.710	6.752±0.712	28	10.080±2.093	3.990±2.745
14	14.776±0.666	9.228±1.550	29	3.637±1.491	3.784±0.438
15	4.109±0.928	19.466±0.734	30	8.524±1.172	5.600±0.756
Average	8.240±2.735	8.244±4.720	Average	11.557±4.157	10.447±4.985

Table 33. Level Walking Loading-Response Hip Extension Moment (Nm/kg)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	-0.529±0.020	-1.010±0.044	16	-0.705±0.045	-0.662±0.034
2	-0.557±0.047	-0.455±0.047	17	-0.424±0.027	-0.460±0.047
3	-0.459±0.031	-0.681±0.070	18	-0.710±0.034	-0.598±0.046
4	-0.669±0.019	-0.722±0.023	19	-0.413±0.033	-0.304±0.023
5	-0.547±0.067	-0.628±0.068	20	-0.580±0.027	-0.530±0.040
6	-0.467±0.046	-0.677±0.009	21	-0.823±0.031	-0.693±0.025
7	-0.667±0.027	-0.594±0.022	22	-0.816±0.043	-0.818±0.031
8	-0.872±0.041	-0.653±0.046	23	-0.605±0.040	-0.343±0.041
9	-0.508±0.053	-0.504±0.074	24	-0.467±0.017	-0.423±0.034
10	-1.089±0.050	-1.000±0.066	25	-0.586±0.034	-0.630±0.097
11	-0.821±0.058	-0.757±0.053	26	-0.533±0.022	-0.615±0.078
12	-0.420±0.020	-0.369±0.035	27	-0.429±0.045	-0.586±0.005
13	-0.666±0.021	-0.848±0.077	28	-0.627±0.022	-0.707±0.082
14	-0.450±0.028	-0.448±0.032	29	-0.515±0.028	-0.431±0.009
15	-0.464±0.118	-0.465±0.030	30	-0.562±0.066	-0.462±0.024
Average	-0.612±0.189	-0.654±0.194	Average	-0.586±0.132	-0.551±0.145

Table 34. Level Walking Push-off Response Hip Flexion Moment (Nm/kg)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	0.652±0.046	0.211±0.023	16	0.644±0.025	0.688±0.025
2	0.378±0.023	0.431±0.015	17	0.784±0.042	0.705±0.029
3	0.517±0.023	0.393±0.041	18	0.759±0.039	0.665±0.037
4	0.446±0.014	0.397±0.022	19	0.501±0.039	0.508±0.027
5	0.509±0.038	0.552±0.056	20	0.517±0.030	0.580±0.027
6	0.429±0.013	0.330±0.039	21	0.828±0.038	0.910±0.094
7	0.537±0.035	0.549±0.050	22	0.716±0.041	0.676±0.081
8	0.328±0.044	0.419±0.063	23	0.355±0.046	0.650±0.016
9	0.288±0.008	0.305±0.029	24	0.605±0.021	0.667±0.016
10	0.522±0.031	0.564±0.025	25	0.630±0.013	0.510±0.045
11	0.461±0.050	0.610±0.049	26	0.322±0.045	0.382±0.037
12	0.552±0.012	0.564±0.013	27	0.949±0.046	0.941±0.051
13	0.398±0.031	0.509±0.027	28	0.475±0.020	0.352±0.073
14	0.568±0.028	0.623±0.025	29	0.538±0.039	0.532±0.027
15	0.688±0.141	0.637±0.013	30	0.547±0.050	0.508±0.032
Average	0.485±0.111	0.473±0.129	Average	0.611±0.174	0.618±0.165

Table 35. Level Walking Loading-Response Hip Abduction Moment (Nm/kg)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	-0.839±0.015	-0.545±0.047	16	-0.871±0.028	-0.948±0.027
2	-0.972±0.038	-0.875±0.042	17	-0.929±0.065	-1.075±0.054
3	-0.890±0.103	-1.046±0.055	18	-0.917±0.035	-0.854±0.026
4	-0.771±0.032	-0.932±0.038	19	-0.937±0.050	-0.783±0.032
5	-0.705±0.039	-0.815±0.068	20	-1.040±0.019	-1.005±0.020
6	-0.982±0.002	-1.061±0.044	21	-1.089±0.028	-1.323±0.031
7	-0.950±0.032	-1.036±0.056	22	-0.864±0.027	-0.874±0.039
8	-0.982±0.093	-0.762±0.018	23	-0.775±0.020	-1.048±0.039
9	-0.928±0.026	-0.947±0.015	24	-0.934±0.013	-0.781±0.022
10	-0.736±0.043	-0.947±0.065	25	-1.053±0.025	-0.856±0.064
11	-0.787±0.055	-0.799±0.045	26	-0.657±0.026	-0.704±0.037
12	-0.948±0.022	-0.915±0.024	27	-0.744±0.016	-0.530±0.034
13	-0.742±0.023	-0.947±0.056	28	-0.794±0.079	-0.992±0.102
14	-0.786±0.033	-0.925±0.026	29	-1.052±0.078	-0.843±0.037
15	-0.734±0.113	-0.776±0.019	30	-1.046±0.077	-1.159±0.032
Average	-0.850±0.104	-0.889±0.134	Average	-0.913±0.130	-0.918±0.194

Table 36. Level Walking Push-off Response Hip Abduction Moment (Nm/kg)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	-0.556±0.000	-0.450±0.041	16	-0.885±0.024	-0.940±0.025
2	-0.957±0.033	-0.871±0.023	17	-0.845±0.050	-0.880±0.034
3	-0.884±0.028	-1.065±0.029	18	-0.819±0.020	-0.745±0.009
4	-0.900±0.025	-0.941±0.114	19	-0.885±0.048	-0.727±0.044
5	-0.788±0.008	-0.990±0.025	20	-0.978±0.031	-0.903±0.033
6	-0.993±0.034	-1.045±0.038	21	-0.898±0.011	-1.007±0.052
7	-0.902±0.028	-0.994±0.025	22	-0.755±0.022	-0.940±0.045
8	-0.709±0.054	-0.724±0.048	23	-0.765±0.027	-0.946±0.027
9	-0.875±0.009	-0.922±0.039	24	-0.807±0.018	-0.614±0.023
10	-0.700±0.018	-0.723±0.039	25	-0.924±0.052	-0.765±0.006
11	-0.712±0.034	-0.689±0.053	26	-0.565±0.027	-0.567±0.016
12	-0.927±0.029	-0.875±0.035	27	-0.880±0.055	-0.716±0.031
13	-0.807±0.028	-0.764±0.019	28	-0.870±0.033	-0.865±0.073
14	-0.928±0.010	-0.973±0.030	29	-1.039±0.027	-0.775±0.031
15	-0.732±0.196	-0.941±0.012	30	-0.814±0.038	-1.075±0.041
Average	-0.825±0.122	-0.864±0.166	Average	-.849±0.109	-0.831±0.144

Appendix I: Individual Results for Select Variables – Stair Ascent

Table 37. Stair Ascent Loading-Response Vertical Ground Reaction Force (BW)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	1.178±0.056	1.131±0.026	16	0.883±0.026	0.999±0.013
2	0.836±0.019	0.881±0.024	17	0.996±0.011	1.026±0.020
3	1.026±0.034	1.117±0.002	18	1.011±0.021	1.071±0.038
4	0.995±0.013	0.982±0.012	19	0.976±0.035	0.952±0.005
5	1.035±0.071	1.051±0.026	20	0.934±0.018	0.997±0.014
6	0.964±0.017	0.981±0.015	21	0.969±0.006	1.036±0.011
7	1.001±0.018	1.062±0.015	22	1.000±0.037	1.054±0.034
8	1.143±0.032	1.029±0.019	23	1.026±0.027	1.074±0.022
9	0.961±0.011	1.049±0.013	24	0.937±0.024	1.018±0.026
10	1.128±0.037	1.090±0.028	25	0.926±0.058	1.003±0.018
11	1.024±0.051	1.049±0.024	26	0.996±0.018	0.948±0.030
12	1.019±0.014	0.992±0.011	27	1.025±0.030	0.892±0.024
13	0.970±0.013	0.961±0.025	28	1.045±0.021	1.074±0.015
14	0.993±0.024	0.964±0.021	29	0.951±0.027	1.150±0.032
15	0.975±0.027	0.934±0.026	30	1.047±0.008	1.054±0.024
Average	1.017±0.084	1.018±0.070	Average	0.981±0.048	1.023±0.063

Table 38. Stair Ascent Push-off Response Vertical Ground Reaction Force (BW)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	1.345±0.031	1.311±0.049	16	1.035±0.037	1.106±0.022
2	0.969±0.027	0.948±0.033	17	1.186±0.053	1.105±0.014
3	1.104±0.044	1.129±0.023	18	1.106±0.061	1.161±0.060
4	1.197±0.066	1.099±0.018	19	1.182±0.061	1.156±0.072
5	1.231±0.104	1.176±0.074	20	1.165±0.015	1.248±0.031
6	1.114±0.079	1.038±0.071	21	0.993±0.036	1.147±0.025
7	1.052±0.019	1.072±0.030	22	1.216±0.074	1.389±0.054
8	1.254±0.116	1.314±0.103	23	1.098±0.068	1.211±0.050
9	1.100±0.005	1.105±0.033	24	0.995±0.032	1.121±0.054
10	1.089±0.074	1.067±0.072	25	1.119±0.050	1.339±0.129
11	1.059±0.077	1.010±0.095	26	1.261±0.042	1.241±0.032
12	1.085±0.028	1.070±0.023	27	1.317±0.045	1.145±0.011
13	1.081±0.027	1.162±0.052	28	1.086±0.025	1.226±0.079
14	1.142±0.013	1.135±0.056	29	1.044±0.013	1.296±0.028
15	1.215±0.032	1.122±0.041	30	1.131±0.022	1.139±0.043
Average	1.136±0.096	1.117±0.099	Average	1.129±0.094	1.202±0.087

Table 39. Stair Ascent Plantarflexion ROM (degrees)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	-29.060±0.776	-31.682±1.239	16	-28.415±1.172	-42.368±1.643
2	-43.619±3.041	-41.079±2.512	17	-26.402±1.615	-30.550±2.184
3	-51.488±2.623	-40.453±3.071	18	-31.477±1.377	-28.335±2.031
4	-34.329±1.574	-40.804±3.782	19	-34.801±1.753	-38.323±1.543
5	-29.203±2.579	-29.937±3.630	20	-30.274±2.444	-38.673±2.368
6	-45.096±0.868	-44.265±2.016	21	-23.883±5.060	-40.969±2.111
7	-35.690±1.196	-35.951±1.752	22	-21.039±2.121	-21.922±4.336
8	-20.228±0.965	-12.650±2.099	23	-31.419±2.005	-41.353±3.108
9	-33.025±2.175	-31.875±2.623	24	-31.057±2.011	-32.372±4.799
10	-21.847±0.966	-16.308±4.423	25	-18.740±4.086	-17.855±4.113
11	-33.176±1.911	-29.639±1.367	26	-41.964±2.991	-40.358±0.906
12	-34.779±3.204	-39.160±1.175	27	-27.728±1.493	-33.739±1.563
13	-28.795±1.329	-28.393±2.115	28	-22.972±2.721	-22.499±1.043
14	-37.919±2.738	-35.547±1.954	29	-22.917±1.353	-39.140±1.300
15	-44.990±2.038	-41.144±1.475	30	-31.386±1.958	-22.519±1.864
Average	-34.883±8.714	-33.259±9.121	Average	-28.298±5.945	-32.732±8.338

Table 40. Stair Ascent Loading-Response Plantarflexion Moment (Nm/kg)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	-0.528±0.058	-0.707±0.150	16	-0.455±0.049	-0.444±0.087
2	-0.250±0.080	-0.334±0.057	17	-0.333±0.030	-0.594±0.114
3	-0.700±0.099	-0.908±0.041	18	-0.750±0.247	-0.600±0.162
4	-0.581±0.050	-0.838±0.036	19	-0.343±0.074	-0.477±0.397
5	-0.437±0.050	-0.513±0.204	20	-0.385±0.056	-0.298±0.077
6	-0.488±0.140	-0.198±0.049	21	-0.629±0.237	-0.885±0.100
7	-0.513±0.110	-0.351±0.053	22	-0.571±0.181	-0.657±0.148
8	-0.619±0.111	-0.259±0.083	23	-0.426±0.142	-0.241±0.159
9	-0.447±0.047	-0.472±0.053	24	-0.755±0.096	-0.880±0.069
10	-0.257±0.183	-0.148±0.138	25	-0.468±0.090	-0.500±0.163
11	-0.971±0.106	-0.875±0.105	26	-0.416±0.089	-0.700±0.073
12	-0.350±0.147	-0.236±0.122	27	-0.597±0.106	-0.417±0.051
13	-0.500±0.055	-0.389±0.031	28	-0.607±0.136	-0.494±0.133
14	-0.348±0.337	-0.347±0.056	29	-0.531±0.118	-0.410±0.123
15	-0.816±0.127	-0.515±0.076	30	-0.526±0.064	-0.743±0.279
Average	-0.520±0.198	-0.473±0.251	Average	-0.519±0.133	-0.556±0.192

Table 41. Stair Ascent Push-off Response Plantarflexion Moment (Nm/kg)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	-1.096±0.031	-1.329±0.061	16	-0.993±0.041	-1.127±0.062
2	-0.907±0.061	-0.944±0.031	17	-1.094±0.106	-1.237±0.042
3	-0.856±0.040	-1.004±0.066	18	-1.254±0.066	-1.341±0.063
4	-1.133±0.025	-1.236±0.033	19	-0.963±0.048	-0.981±0.043
5	-1.071±0.071	-1.004±0.173	20	-1.092±0.024	-1.176±0.043
6	-1.087±0.130	-0.903±0.090	21	-1.023±0.041	-1.146±0.053
7	-0.970±0.062	-0.904±0.081	22	-1.055±0.086	-1.342±0.035
8	-1.039±0.070	-0.563±0.048	23	-0.972±0.067	-1.017±0.043
9	-1.080±0.023	-0.976±0.016	24	-	-
10	-0.598±0.049	-0.343±0.079	25	-1.154±0.043	-1.479±0.099
11	-1.253±0.105	-1.044±0.087	26	-1.041±0.035	-1.143±0.040
12	-0.972±0.118	-0.857±0.123	27	-1.195±0.028	-0.901±0.028
13	-0.969±0.065	-0.968±0.117	28	-1.195±0.067	-1.103±0.063
14	-0.792±0.039	-1.000±0.023	29	-1.022±0.062	-1.137±0.059
15	-1.336±0.064	-1.112±0.047	30	-1.134±0.034	-1.206±0.029
Average	-1.011±0.181	-0.946±0.239	Average	-1.085±0.091	-1.167±0.152

Table 42. Stair Ascent Knee Extension ROM (degrees)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	45.276±1.167	47.229±1.890	16	49.496±2.869	63.002±1.573
2	46.377±3.344	52.400±2.675	17	42.851±2.447	59.178±1.808
3	55.290±3.596	39.505±1.825	18	52.127±1.001	59.595±3.278
4	64.399±2.367	66.605±2.380	19	58.939±1.655	53.137±1.287
5	56.858±0.344	60.520±4.422	20	57.114±1.135	53.759±1.579
6	49.517±1.212	52.208±1.242	21	57.186±1.646	62.426±0.352
7	52.167±2.314	48.864±1.261	22	62.448±8.253	56.926±3.005
8	49.820±1.776	54.676±2.111	23	52.421±3.130	58.546±1.880
9	57.392±0.781	48.995±1.955	24	50.049±3.033	54.052±3.824
10	64.498±1.396	57.528±3.350	25	63.615±0.899	51.857±4.286
11	48.443±2.688	47.926±1.216	26	58.746±2.094	66.129±2.636
12	55.167±1.714	56.830±1.469	27	50.324±1.632	66.990±1.047
13	54.409±0.603	46.873±0.724	28	55.417±1.765	52.945±2.073
14	56.174±1.482	55.345±1.435	29	53.210±2.109	57.435±1.493
15	56.954±2.954	57.588±1.961	30	49.159±1.343	59.925±3.344
Average	54.183±5.733	52.873±6.648	Average	54.207±5.579	58.393±4.774

Table 43. Stair Ascent Knee Abduction ROM (degrees)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	-	-7.544±1.477	16	-2.590±0.384	-23.779±0.468
2	-8.821±1.196	-9.076±1.473	17	-22.868±1.030	-10.462±0.808
3	-4.985±1.706	-29.225±0.446	18	-10.812±1.145	-3.992±1.313
4	-14.537±0.590	-21.982±2.628	19	-21.185±1.945	-0.974±0.547
5	-23.649±0.856	-9.451±1.626	20	-23.726±1.386	-13.384±1.449
6	-8.706±1.876	-8.373±2.535	21	-5.492±1.303	-7.290±1.237
7	-12.620±1.563	-21.207±0.783	22	-14.814±8.685	-10.976±0.996
8	-20.603±1.786	-18.299±0.147	23	-2.371±0.893	-1.220±0.637
9	-10.051±0.783	-11.704±0.469	24	-20.472±0.870	-17.884±1.654
10	-14.139±0.986	-18.611±1.497	25	-12.915±1.778	-6.573±1.535
11	-20.374±2.417	-27.982±0.756	26	-10.241±1.458	-12.938±1.050
12	-5.580±0.878	-6.095±0.640	27	-11.767±0.469	-16.442±1.324
13	-18.164±0.912	-21.468±0.554	28	-15.576±1.657	-9.669±0.847
14	-6.123±1.878	-9.894±1.456	29	-15.021±1.998	-20.585±1.377
15	-11.842±1.306	-17.081±2.176	30	-13.407±0.600	-9.337±2.780
Average	-12.871±6.002	-13.901±6.770	Average	-13.551±6.743	-11.034±6.682

Table 44. Stair Ascent Loading-Response Knee Extension Moment (Nm/kg)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	0.616±0.043	0.798±0.060	16	0.815±0.068	1.422±0.009
2	0.596±0.055	0.567±0.072	17	1.203±0.031	1.429±0.052
3	0.901±0.048	0.583±0.130	18	1.047±0.050	1.124±0.062
4	0.943±0.073	0.737±0.089	19	0.976±0.028	0.984±0.034
5	1.281±0.121	1.256±0.084	20	0.670±0.021	1.303±0.033
6	0.706±0.068	1.038±0.045	21	0.820±0.031	1.335±0.057
7	1.243±0.084	1.509±0.053	22	1.391±0.131	1.678±0.164
8	1.755±0.085	1.410±0.059	23	0.800±0.085	1.147±0.068
9	0.727±0.043	0.858±0.045	24	0.819±0.043	0.890±0.032
10	1.663±0.090	1.377±0.027	25	0.707±0.072	1.537±0.038
11	1.206±0.099	1.161±0.072	26	0.976±0.024	0.866±0.088
12	0.973±0.039	0.974±0.024	27	1.101±0.040	0.801±0.030
13	0.812±0.008	0.818±0.023	28	1.246±0.034	1.410±0.114
14	0.895±0.052	0.673±0.025	29	0.897±0.056	1.754±0.036
15	0.731±0.020	0.685±0.013	30	1.259±0.046	1.336±0.054
Average	1.003±0.358	0.963±0.313	Average	0.982±0.220	1.268±0.292

Table 45. Stair Ascent Loading-Response Knee Abduction Moment (Nm/kg)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	-0.055±0.039	-0.229±0.049	16	-0.645±0.048	-0.591±0.032
2	-0.472±0.030	-0.245±0.021	17	-0.443±0.027	-0.545±0.067
3	-0.502±0.038	-0.427±0.054	18	-0.185±0.037	-0.149±0.036
4	-0.447±0.044	-0.700±0.050	19	-0.374±0.041	-0.528±0.024
5	-0.599±0.017	-0.021±0.050	20	-0.403±0.017	-0.587±0.027
6	-0.471±0.033	-0.212±0.034	21	-0.295±0.021	-0.455±0.045
7	-0.519±0.037	-0.416±0.031	22	-0.378±0.077	-0.493±0.050
8	-0.255±0.076	-0.659±0.073	23	-0.384±0.036	-0.189±0.036
9	-0.282±0.027	-0.140±0.024	24	-0.469±0.022	-0.363±0.029
10	-0.470±0.046	-0.660±0.049	25	-0.310±0.024	-0.233±0.038
11	-0.383±0.060	-0.412±0.036	26	-0.302±0.057	-0.519±0.072
12	-0.284±0.040	-0.663±0.020	27	-0.205±0.019	-0.088±0.017
13	-0.632±0.031	-0.277±0.018	28	-0.367±0.034	-0.191±0.026
14	-0.277±0.020	-0.541±0.060	29	-0.298±0.030	-0.291±0.056
15	-0.630±0.042	-0.220±0.034	30	-0.345±0.014	-0.161±0.030
Average	-0.419±0.162	-0.388±0.217	Average	-0.360±0.111	-0.359±0.181

Table 46. Stair Ascent Push-off Response Knee Abduction Moment (Nm/kg)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	0.014±0.063	-0.107±0.032	16	-0.668±0.052	-0.237±0.011
2	-0.442±0.048	-0.124±0.036	17	-0.139±0.019	-0.676±0.035
3	-0.446±0.059	-0.004±0.043	18	-	-0.093±0.023
4	-0.231±0.048	-0.606±0.064	19	-	-0.511±0.039
5	-0.440±0.046	0.212±0.000	20	-	-0.601±0.060
6	-0.366±0.014	-	21	-0.126±0.011	-0.469±0.030
7	-0.551±0.015	-0.031±0.022	22	-0.248±0.044	-0.698±0.023
8	0.023±0.001	-0.464±0.039	23	-0.296±0.031	-0.063±0.018
9	-0.226±0.018	0.070±0.032	24	-0.376±0.029	-0.232±0.029
10	-0.433±0.041	-0.242±0.018	25	-0.316±0.034	-0.164±0.060
11	-0.295±0.051	0.076±0.137	26	-0.188±0.060	-0.475±0.046
12	-0.100±0.082	-0.662±0.049	27	-0.260±0.025	0.110±0.045
13	-0.514±0.023	-0.057±0.019	28	-0.124±0.041	-0.233±0.051
14	-0.115±0.017	-0.482±0.030	29	-0.228±0.032	-
15	-0.645±0.068	-	30	-0.252±0.023	-0.099±0.017
Average	-0.318±0.206	-0.186±0.281	Average	-0.268±0.148	-0.317±0.253

Table 47. Stair Ascent Hip Extension ROM (degrees)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	-41.877±0.504	-53.046±1.061	16	-53.509±1.328	-51.485±1.732
2	-44.514±0.917	-43.466±1.707	17	-42.115±1.688	-55.009±1.612
3	-35.532±1.886	-44.516±0.708	18	-48.952±1.802	-50.746±2.222
4	-57.754±2.554	-53.676±2.279	19	-53.199±1.594	-47.312±1.306
5	-54.779±1.868	-51.718±3.651	20	-50.936±1.707	-49.540±1.815
6	-43.669±1.742	-51.543±1.306	21	-47.191±0.971	-57.437±0.851
7	-48.562±0.473	-52.798±2.271	22	-55.187±8.134	-57.661±1.892
8	-49.634±1.664	-46.908±0.639	23	-53.683±2.002	-44.561±1.280
9	-49.650±0.759	-43.821±0.725	24	-49.626±1.428	-49.201±0.770
10	-60.704±0.614	-52.348±1.037	25	-52.218±2.429	-51.826±6.097
11	-42.907±1.490	-48.620±1.616	26	-48.377±0.744	-51.023±1.913
12	-55.602±0.990	-46.151±0.642	27	-46.477±2.656	-49.949±1.611
13	-48.114±0.624	-52.577±1.273	28	-46.531±2.401	-53.510±0.987
14	-53.433±0.878	-55.823±1.004	29	-47.546±1.371	-51.501±1.355
15	-54.945±1.622	-51.000±1.229	30	-47.928±2.718	-54.740±1.787
Average	-49.445±6.878	-49.867±3.964	Average	-49.565±2.1982	-51.700±1.815

Table 48. Stair Ascent Loading-Response Hip Extension Moment (Nm/kg)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	-0.640±0.110	-0.928±0.112	16	-0.248±0.035	-0.273±0.020
2	-0.458±0.026	-0.604±0.014	17	-0.507±0.054	-0.532±0.071
3	-0.395±0.062	-0.823±0.114	18	-0.548±0.058	-0.492±0.075
4	-0.655±0.114	-0.592±0.049	19	-0.327±0.010	-0.212±0.033
5	-0.395±0.074	-0.418±0.062	20	-0.736±0.040	-0.585±0.054
6	-0.535±0.040	-0.751±0.061	21	-0.750±0.070	-0.678±0.114
7	-0.480±0.035	-0.434±0.011	22	-0.595±0.048	-0.460±0.028
8	-0.816±0.028	-0.518±0.059	23	-0.318±0.054	-0.250±0.050
9	-0.681±0.030	-0.622±0.044	24	-0.488±0.022	-0.466±0.042
10	-0.573±0.059	-0.454±0.041	25	-0.457±0.068	-0.267±0.112
11	-0.617±0.033	-0.550±0.057	26	-0.379±0.041	-0.370±0.036
12	-0.599±0.100	-0.504±0.042	27	-0.301±0.055	-0.614±0.042
13	-0.795±0.014	-0.702±0.029	28	-0.662±0.053	-0.495±0.042
14	-0.557±0.060	-0.473±0.057	29	-0.744±0.077	-0.525±0.065
15	-0.539±0.059	-0.590±0.044	30	-0.509±0.034	-0.487±0.054
Average	-0.582±0.125	-0.598±0.148	Average	-0.505±0.048	-0.447±0.056

Appendix J: Individual Results for Select Variables – Stair Descent

Table 49. Stair Descent Loading-Response Vertical Ground Reaction Force (BW)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	1.782±0.018	1.483±0.148	16	1.118±0.101	1.476±0.061
2	1.143±0.054	1.123±0.052	17	1.619±0.088	1.550±0.051
3	1.349±0.114	1.399±0.116	18	1.810±0.066	1.917±0.060
4	1.343±0.074	1.371±0.041	19	1.640±0.034	1.658±0.088
5	1.384±0.228	1.327±0.157	20	1.534±0.056	1.462±0.065
6	1.150±0.086	1.228±0.061	21	1.359±0.052	1.415±0.038
7	1.170±0.054	1.157±0.048	22	1.404±0.179	1.599±0.133
8	1.425±0.094	1.099±0.088	23	1.680±0.329	1.613±0.166
9	1.482±0.083	1.444±0.038	24	1.023±0.052	1.116±0.063
10	1.766±0.211	1.270±0.132	25	1.418±0.079	1.614±0.070
11	1.168±0.078	1.268±0.065	26	1.697±0.081	1.670±0.144
12	1.297±0.049	1.371±0.069	27	1.393±0.049	1.279±0.102
13	1.485±0.071	1.561±0.047	28	1.527±0.113	1.334±0.101
14	1.612±0.067	1.399±0.097	29	1.507±0.091	1.802±0.138
15	1.378±0.095	1.561±0.038	30	1.899±0.061	1.830±0.229
Average	1.396±0.206	1.337±0.146	Average	1.508±0.236	1.556±0.216

Table 50. Stair Descent Push-off Response Vertical Ground Reaction Force (BW)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	1.123±0.043	1.180±0.012	16	0.947±0.012	0.912±0.027
2	0.834±0.036	0.825±0.039	17	0.905±0.031	0.912±0.037
3	0.993±0.032	0.904±0.026	18	0.777±0.013	0.907±0.027
4	1.006±0.044	0.921±0.034	19	0.887±0.051	0.913±0.030
5	0.928±0.047	0.965±0.086	20	0.907±0.031	0.969±0.049
6	0.957±0.065	0.939±0.045	21	0.885±0.020	1.037±0.037
7	1.027±0.016	0.977±0.037	22	0.898±0.039	1.028±0.054
8	1.093±0.047	1.014±0.015	23	0.839±0.052	0.939±0.029
9	0.940±0.034	0.890±0.043	24	0.998±0.030	0.990±0.022
10	0.930±0.039	0.863±0.050	25	0.828±0.100	0.911±0.096
11	0.876±0.031	0.904±0.041	26	0.940±0.033	0.826±0.045
12	0.954±0.021	1.011±0.056	27	0.981±0.025	0.844±0.032
13	0.953±0.020	0.910±0.026	28	0.918±0.013	0.909±0.038
14	0.869±0.031	0.919±0.023	29	0.780±0.053	0.845±0.095
15	0.849±0.018	0.867±0.029	30	0.868±0.061	0.845±0.049
Average	0.955±0.084	0.939±0.085	Average	0.890±0.065	0.919±0.065

Table 51. Stair Descent Plantarflexion ROM (degrees)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	58.015±0.602	55.262±1.337	16	58.824±1.411	66.735±1.233
2	62.402±1.371	61.157±1.405	17	68.714±1.203	66.431±0.721
3	58.910±0.553	62.685±2.479	18	57.780±2.074	61.568±0.647
4	58.088±2.628	62.997±3.165	19	55.498±0.608	60.099±1.019
5	55.101±3.270	53.584±2.746	20	61.865±1.882	68.688±1.101
6	58.957±3.595	60.832±2.543	21	60.178±0.812	68.021±1.316
7	58.353±3.731	57.769±1.296	22	63.308±3.302	61.585±1.607
8	64.191±1.471	51.521±1.943	23	65.482±2.385	72.813±1.339
9	59.955±0.806	59.928±0.752	24	61.206±1.606	66.648±0.902
10	52.204±1.037	33.855±4.595	25	24.479±4.390	30.295±2.361
11	53.254±3.099	54.984±1.857	26	35.757±1.059	36.749±2.790
12	52.401±2.633	63.274±1.414	27	32.375±1.408	25.431±13.602
13	55.534±0.575	48.211±0.989	28	40.308±9.590	44.857±9.253
14	68.159±0.941	67.506±0.803	29	36.258±1.547	42.165±11.416
15	67.041±1.662	64.438±1.176	30	43.692±9.150	28.598±5.416
Average	58.838±4.926	57.200±8.348	Average	51.048±14.083	53.379±16.762

Table 52. Stair Descent Loading-Response Plantarflexion Moment (Nm/kg)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	-1.124±0.071	-1.205±0.159	16	-0.787±0.152	-0.959±0.102
2	-0.797±0.068	-0.684±0.107	17	-1.087±0.125	-1.170±0.109
3	-1.330±0.054	-1.255±0.153	18	-1.176±0.070	-1.348±0.138
4	-1.070±0.165	-1.430±0.038	19	-0.699±0.075	-0.971±0.170
5	-1.172±0.441	-0.717±0.187	20	-0.831±0.120	-1.299±0.133
6	-1.071±0.166	-0.851±0.164	21	-0.930±0.047	-1.297±0.076
7	-1.043±0.119	-0.912±0.134	22	-0.618±0.250	-0.955±0.086
8	-0.943±0.078	-0.509±0.026	23	-0.942±0.199	-0.679±0.137
9	-1.234±0.073	-1.019±0.112	24	-0.418±0.049	-0.740±0.039
10	-1.110±0.427	-0.387±0.025	25	-0.918±0.191	-1.437±0.112
11	-0.943±0.218	-1.078±0.095	26	-1.418±0.107	-1.602±0.203
12	-1.004±0.076	-1.139±0.094	27	-1.052±0.079	-0.566±0.109
13	-1.205±0.081	-1.031±0.126	28	-1.067±0.133	-0.852±0.180
14	-1.064±0.038	-1.130±0.156	29	-1.182±0.157	-0.977±0.213
15	-1.368±0.105	-1.189±0.151	30	-1.007±0.226	-0.978±0.167
Average	-1.099±0.150	-0.969±0.291	Average	-0.942±0.249	-1.055±0.295

Table 53. Stair Descent Push-off Response Plantarflexion Moment (Nm/kg)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	-1.299±0.065	-1.432±0.070	16	-0.975±0.047	-1.049±0.024
2	-1.007±0.040	-0.979±0.026	17	-1.144±0.059	-1.144±0.074
3	-1.225±0.052	-1.050±0.027	18	-0.986±0.011	-1.203±0.032
4	-1.142±0.064	-1.308±0.041	19	-0.875±0.046	-1.075±0.050
5	-1.403±0.108	-1.341±0.088	20	-0.841±0.047	-1.260±0.069
6	-1.242±0.063	-1.092±0.095	21	-1.031±0.030	-1.389±0.053
7	-1.547±0.096	-1.248±0.343	22	-0.981±0.054	-1.303±0.103
8	-1.458±0.054	-1.304±0.028	23	-1.032±0.045	-1.000±0.029
9	-1.230±0.034	-1.076±0.018	24	-0.910±0.059	-1.006±0.036
10	-1.342±0.093	-0.932±0.032	25	-0.932±0.050	-1.241±0.225
11	-1.332±0.135	-1.340±0.053	26	-1.061±0.042	-1.025±0.054
12	-1.258±0.072	-1.171±0.078	27	-1.139±0.043	-0.881±0.081
13	-1.382±0.019	-1.197±0.014	28	-1.034±0.103	-1.135±0.110
14	-1.006±0.056	-1.081±0.039	29	-0.921±0.040	-0.954±0.153
15	-1.285±0.038	-1.155±0.025	30	-1.059±0.078	-0.952±0.077
Average	-1.277±0.149	-1.181±0.146	Average	-0.995±0.089	-1.108±0.147

Table 54. Stair Descent Knee Extension ROM (degrees)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	-61.509±1.046	-68.575±1.732	16	-79.736±0.807	-80.337±1.896
2	-81.059±1.489	-81.741±2.576	17	-79.359±0.260	-80.224±2.025
3	-81.588±1.241	-80.071±0.716	18	-78.754±1.337	-85.110±1.698
4	-81.592±0.622	-82.747±0.595	19	-76.861±1.658	-81.966±0.368
5	-79.083±3.691	-82.541±1.590	20	-83.544±2.295	-88.573±1.113
6	-77.761±2.293	-76.678±1.894	21	-77.057±2.564	-80.284±0.514
7	-78.963±0.718	-85.346±1.151	22	-82.498±3.229	-84.115±2.462
8	-76.749±1.174	-79.795±1.363	23	-89.131±2.055	-89.691±2.623
9	-79.152±0.747	-77.441±1.708	24	-78.646±2.128	-81.210±1.280
10	-78.931±2.245	-75.221±2.450	25	-82.242±4.143	-78.113±3.165
11	-72.820±4.397	-72.368±2.256	26	-83.632±1.170	-82.777±2.239
12	-81.680±2.456	-83.911±2.003	27	-80.622±1.000	-89.886±2.327
13	-80.039±0.792	-75.487±1.370	28	-71.355±1.068	-75.974±1.907
14	-80.302±1.090	-85.300±1.389	29	-80.865±1.114	-84.646±2.219
15	-83.211±0.933	-83.519±2.948	30	-76.615±2.138	-76.075±2.649
Average	-78.296±5.269	-79.383±4.966	Average	-80.061±4.054	-82.599±4.448

Table 55. Stair Descent Knee Abduction ROM (degrees)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	6.601±3.904	11.605±1.617	16	5.775±0.857	13.55±1.087
2	14.763±1.635	9.850±0.919	17	18.517±0.948	5.919±1.872
3	6.125±0.670	34.214±2.356	18	14.329±1.615	1.988±1.778
4	18.665±0.691	13.296±0.613	19	10.414±0.360	1.379±0.311
5	13.229±1.574	9.393±0.365	20	23.212±1.132	9.805±1.671
6	18.097±1.188	11.183±1.446	21	12.841±0.554	12.17±0.864
7	0.569±1.017	17.688±0.607	22	14.066±1.003	1.332±0.992
8	10.893±0.996	-0.911±0.674	23	8.000±1.552	8.507±1.037
9	13.352±1.014	17.779±1.095	24	16.190±1.100	10.60±4.115
10	6.314±1.596	10.417±3.314	25	0.365±1.761	4.056±2.278
11	11.439±2.538	20.446±1.890	26	13.975±1.678	4.441±1.788
12	8.076±1.788	4.791±0.464	27	1.840±0.471	11.07±2.851
13	10.517±1.795	22.235±0.573	28	4.927±1.585	-0.17±1.003
14	16.518±1.902	17.086±1.313	29	0.150±0.601	2.725±1.018
15	12.403±2.232	16.527±0.758	30	1.108±1.315	7.325±1.601
Average	11.171±4.990	14.373±8.160	Average	9.714±7.204	6.315±4.452

Table 56. Stair Descent Loading-Response Knee Extension Moment (Nm/kg)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	-0.119±0.022	-0.065±0.072	16	0.320±0.096	0.834±0.071
2	0.057±0.065	0.081±0.082	17	0.925±0.171	0.674±0.166
3	0.419±0.399	-0.120±0.230	18	0.947±0.131	1.161±0.168
4	0.308±0.096	0.101±0.123	19	0.859±0.072	0.884±0.096
5	0.259±0.210	0.572±0.127	20	0.244±0.106	1.077±0.142
6	-0.048±0.160	0.136±0.081	21	0.614±0.077	1.133±0.149
7	0.406±0.094	0.231±0.029	22	0.843±0.262	0.983±0.258
8	0.579±0.125	0.215±0.104	23	0.397±0.200	0.908±0.214
9	0.181±0.109	0.182±0.073	24	0.047±0.073	0.176±0.070
10	1.141±0.187	0.727±0.152	25	0.218±0.059	0.903±0.266
11	0.405±0.183	0.579±0.111	26	0.553±0.114	0.165±0.122
12	0.340±0.100	0.218±0.109	27	0.744±0.088	0.637±0.355
13	0.306±0.047	0.404±0.084	28	0.981±0.147	0.953±0.080
14	0.320±0.148	0.149±0.072	29	0.421±0.104	1.455±0.153
15	0.184±0.230	-0.017±0.113	30	1.149±0.103	1.040±0.113
Average	0.316±0.293	0.226±0.245	Average	0.617±0.332	0.866±0.345

Table 57. Stair Descent Push-off Response Knee Extension Moment (Nm/kg)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	0.627±0.077	0.518±0.011	16	0.826±0.031	1.276±0.033
2	0.422±0.018	0.546±0.010	17	1.082±0.059	1.262±0.097
3	0.618±0.460	0.570±0.039	18	0.819±0.015	1.038±0.029
4	0.741±0.022	0.644±0.032	19	0.881±0.069	0.924±0.056
5	0.867±0.208	1.170±0.106	20	0.410±0.044	1.134±0.056
6	0.750±0.032	0.895±0.073	21	0.847±0.075	1.408±0.057
7	1.150±0.027	0.979±0.107	22	1.258±0.056	1.610±0.031
8	1.402±0.126	1.176±0.031	23	0.671±0.079	0.919±0.065
9	0.723±0.029	0.599±0.022	24	0.698±0.012	0.756±0.027
10	1.054±0.053	0.804±0.052	25	0.512±0.070	1.339±0.118
11	0.906±0.068	0.870±0.053	26	0.682±0.061	0.422±0.053
12	0.800±0.067	0.722±0.046	27	1.062±0.070	0.805±0.021
13	0.651±0.022	0.540±0.039	28	1.174±0.054	1.089±0.131
14	0.685±0.061	0.473±0.037	29	0.630±0.026	1.020±0.129
15	0.500±0.045	0.391±0.017	30	0.968±0.072	1.084±0.085
Average	0.793±0.255	0.726±0.247	Average	0.834±0.242	1.072±0.293

Table 58. Stair Descent Loading-Response Knee Abduction Moment (Nm/kg)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	-0.444±0.023	0.022±0.047	16	-0.538±0.037	-0.781±0.026
2	-0.305±0.029	-0.606±0.031	17	-0.787±0.039	-0.535±0.043
3	-0.287±0.061	-0.593±0.086	18	-0.688±0.063	-0.046±0.064
4	-0.722±0.044	-0.519±0.049	19	-0.829±0.042	-0.353±0.040
5	-0.277±0.084	-0.650±0.028	20	-0.804±0.045	-0.602±0.047
6	-0.071±0.034	-0.578±0.042	21	-0.630±0.020	-0.334±0.045
7	-0.287±0.025	-0.676±0.044	22	-0.687±0.093	-0.613±0.051
8	-0.809±0.032	-0.219±0.054	23	-0.275±0.120	-0.580±0.049
9	-0.086±0.033	-0.603±0.059	24	-0.225±0.030	-0.507±0.035
10	-0.234±0.086	-0.806±0.058	25	-0.261±0.043	-0.862±0.049
11	-0.269±0.030	-0.738±0.037	26	-0.826±0.033	-0.522±0.042
12	-0.723±0.040	-0.416±0.066	27	-0.127±0.034	-0.294±0.058
13	-0.362±0.017	-0.765±0.016	28	-0.772±0.018	-0.204±0.051
14	-0.725±0.070	-0.269±0.046	29	-0.309±0.014	-0.478±0.061
15	-0.312±0.017	-0.627±0.027	30	-0.272±0.063	-0.957±0.097
Average	-0.394±0.238	-0.536±0.226	Average	-0.535±0.260	-0.511±0.244

Table 59. Stair Descent Push-off Response Knee Abduction Moment (Nm/kg)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	-0.446±0.113	-0.110±0.149	16	-0.547±0.042	-0.677±0.040
2	-0.308±0.020	-0.542±0.059	17	-0.608±0.033	-0.275±0.037
3	-0.060±0.055	-0.750±0.033	18	-0.317±0.009	-
4	-0.766±0.084	-0.364±0.024	19	-0.617±0.066	-0.272±0.031
5	-0.140±0.034	-0.473±0.068	20	-0.512±0.027	-0.280±0.036
6	-0.153±0.018	-0.499±0.034	21	-0.580±0.012	-0.334±0.052
7	-0.224±0.030	-0.720±0.038	22	-0.544±0.025	-0.316±0.035
8	-0.680±0.109	-0.190±0.030	23	-0.094±0.067	-0.341±0.069
9	-0.020±0.030	-0.514±0.019	24	-0.280±0.030	-0.608±0.026
10	-0.125±0.079	-0.726±0.044	25	-0.043±0.040	-0.433±0.063
11	-0.152±0.034	-0.617±0.042	26	-0.580±0.060	-0.267±0.019
12	-0.598±0.034	-0.348±0.036	27	-0.098±0.037	-0.283±0.030
13	-0.272±0.024	-0.580±0.035	28	-0.563±0.049	-0.058±0.015
14	-0.564±0.050	-0.204±0.013	29	-0.146±0.055	-0.299±0.111
15	-0.255±0.050	-0.453±0.072	30	-0.194±0.050	-0.437±0.086
Average	-0.318±0.236	-0.473±0.199	Average	-0.382±0.219	-0.349±0.153

Table 60. Stair Descent Hip Extension ROM (degrees)

Subject Number	Bilateral		Subject Number	Unilateral	
	1 st Replaced	2 nd Replaced		Replaced	Non-Replaced
1	9.046±4.166	29.784±2.623	16	17.025±1.104	23.698±1.626
2	16.884±3.435	20.185±1.069	17	17.083±2.030	24.359±2.070
3	12.565±1.282	19.145±2.854	18	16.034±3.050	21.264±3.876
4	19.005±2.348	17.084±1.012	19	14.499±3.056	17.001±4.068
5	22.367±4.426	23.028±4.783	20	19.190±1.663	14.452±5.709
6	18.297±2.272	20.621±2.093	21	13.697±1.338	19.345±6.726
7	17.682±1.317	23.740±2.306	22	20.682±3.646	25.274±7.553
8	20.953±1.167	18.858±1.293	23	18.564±2.415	12.704±8.063
9	18.245±1.176	16.905±1.199	24	21.529±4.902	10.409±9.166
10	22.709±4.058	15.552±2.694	25	26.688±2.974	18.113±10.947
11	10.812±2.123	14.523±0.914	26	21.837±3.589	22.634±11.554
12	20.857±3.621	17.521±3.354	27	15.846±2.389	24.284±12.204
13	21.266±0.750	17.363±1.666	28	14.023±1.515	17.049±13.336
14	20.210±2.650	15.998±2.801	29	18.920±1.991	10.439±14.451
15	20.537±2.467	17.638±3.440	30	22.497±4.062	18.529±15.898
Average	18.096±4.173	19.196±3.912	Average	18.541±0.378	18.637±5.006

Table 61. Stair Descent Loading-Response Hip Extension Moment (Nm/kg)

Subject Number	Bilateral		Subject Number	Unilateral	
	1st Replaced	2nd Replaced		Replaced	Non-Replaced
1	-1.252±0.064	-1.610±0.231	16	-0.211±0.052	-0.288±0.030
2	-0.956±0.057	-0.843±0.030	17	-0.088±0.051	-0.156±0.022
3	-0.655±0.070	-1.065±0.091	18	-0.149±0.024	0.005±0.105
4	-0.844±0.044	-0.886±0.038	19	-0.264±0.059	-0.210±0.048
5	-0.688±0.139	-0.630±0.153	20	-0.949±0.033	-0.975±0.040
6	-1.010±0.090	-1.124±0.050	21	-0.198±0.046	-0.395±0.075
7	-0.753±0.074	-0.646±0.054	22	-0.705±0.132	-0.795±0.079
8	-0.930±0.118	-0.652±0.062	23	-0.317±0.051	-0.314±0.057
9	-0.836±0.079	-0.844±0.035	24	-0.716±0.043	-0.689±0.059
10	-1.165±0.411	-0.682±0.148	25	-0.116±0.085	-0.036±0.075
11	-0.884±0.101	-0.669±0.089	26	-0.202±0.216	-0.305±0.082
12	-0.754±0.112	-0.850±0.081	27	0.117±0.100	-0.434±0.141
13	-0.930±0.053	-1.232±0.090	28	-0.371±0.225	-0.133±0.219
14	-0.510±0.053	-0.392±0.088	29	-0.667±0.087	-0.467±0.217
15	-0.778±0.081	-0.733±0.037	30	-0.297±0.258	-0.159±0.245
Average	-0.863±0.191	-0.857±0.300	Average	-0.342±0.290	-0.357±0.280

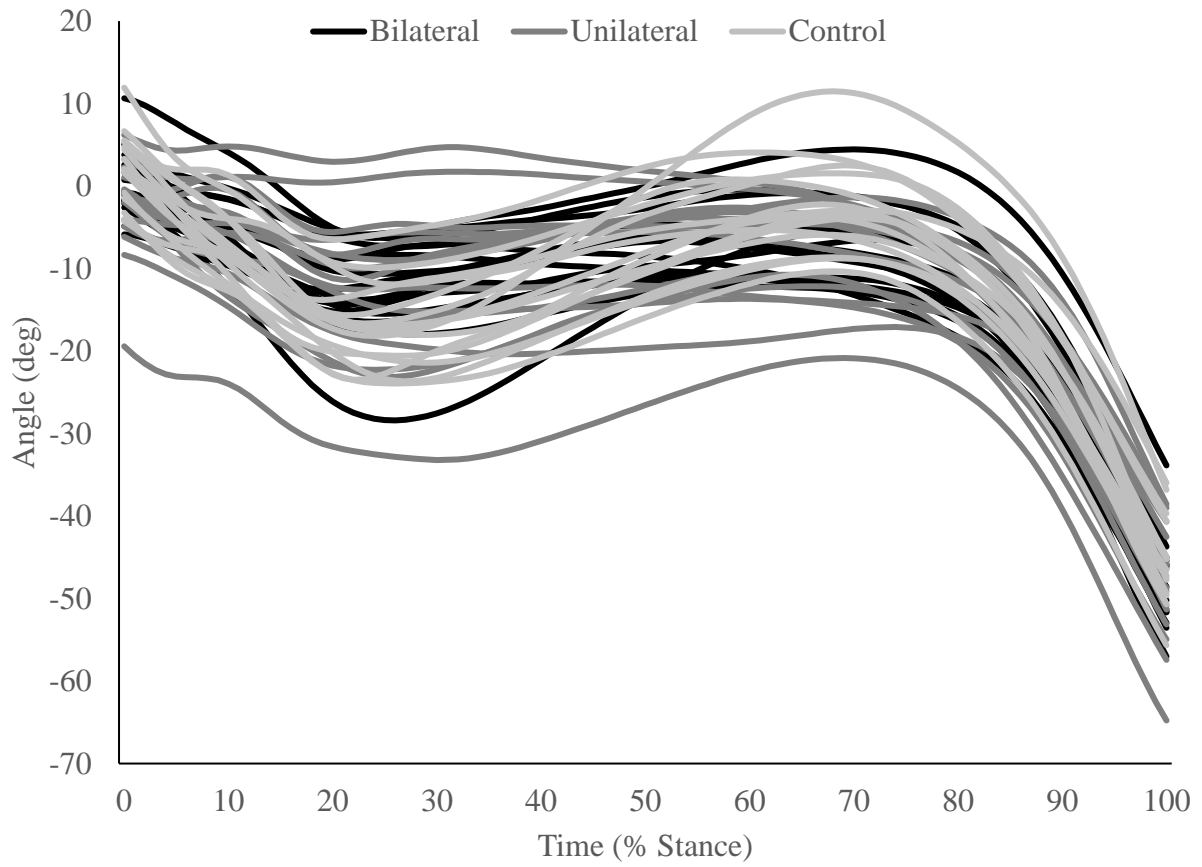


Figure 6. Individual waveforms of sagittal-plane knee angle in bilateral, unilateral, and control.

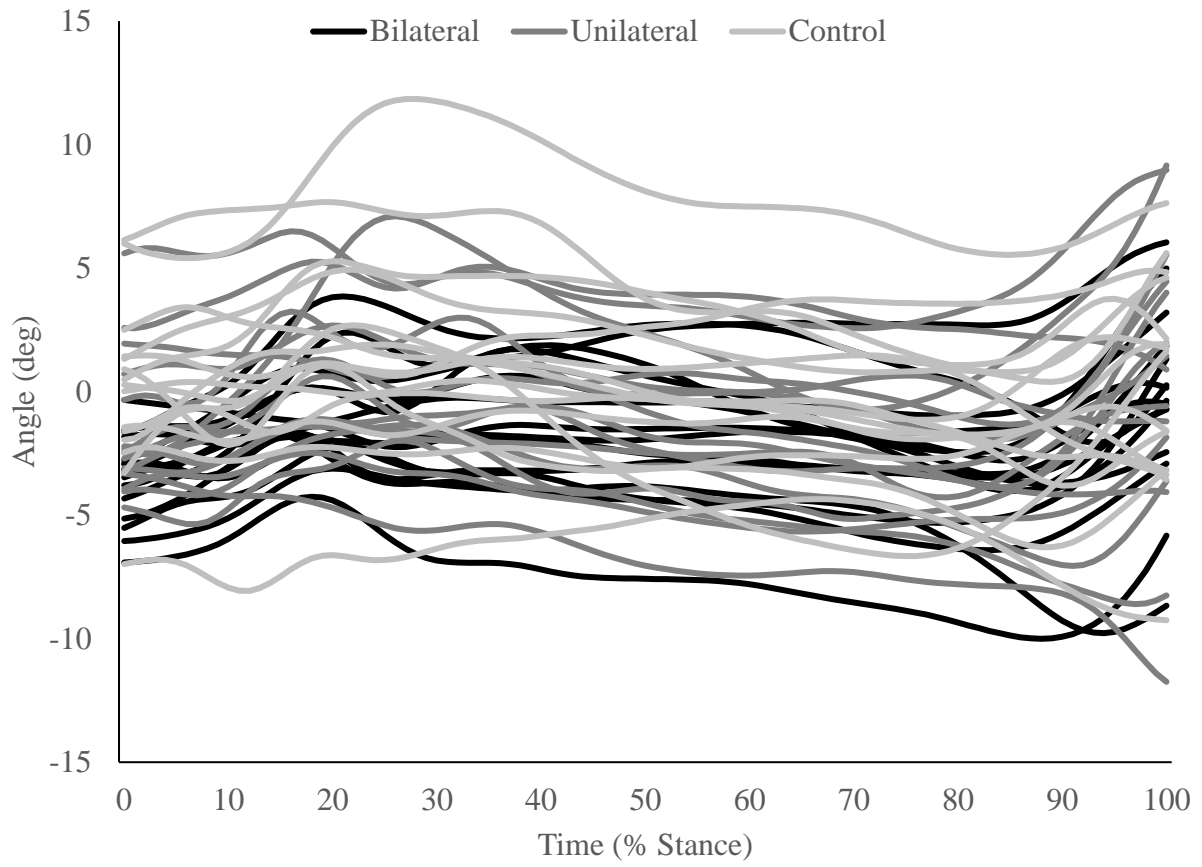


Figure 7. Individual waveforms of frontal-plane knee angle in bilateral, unilateral, and control.

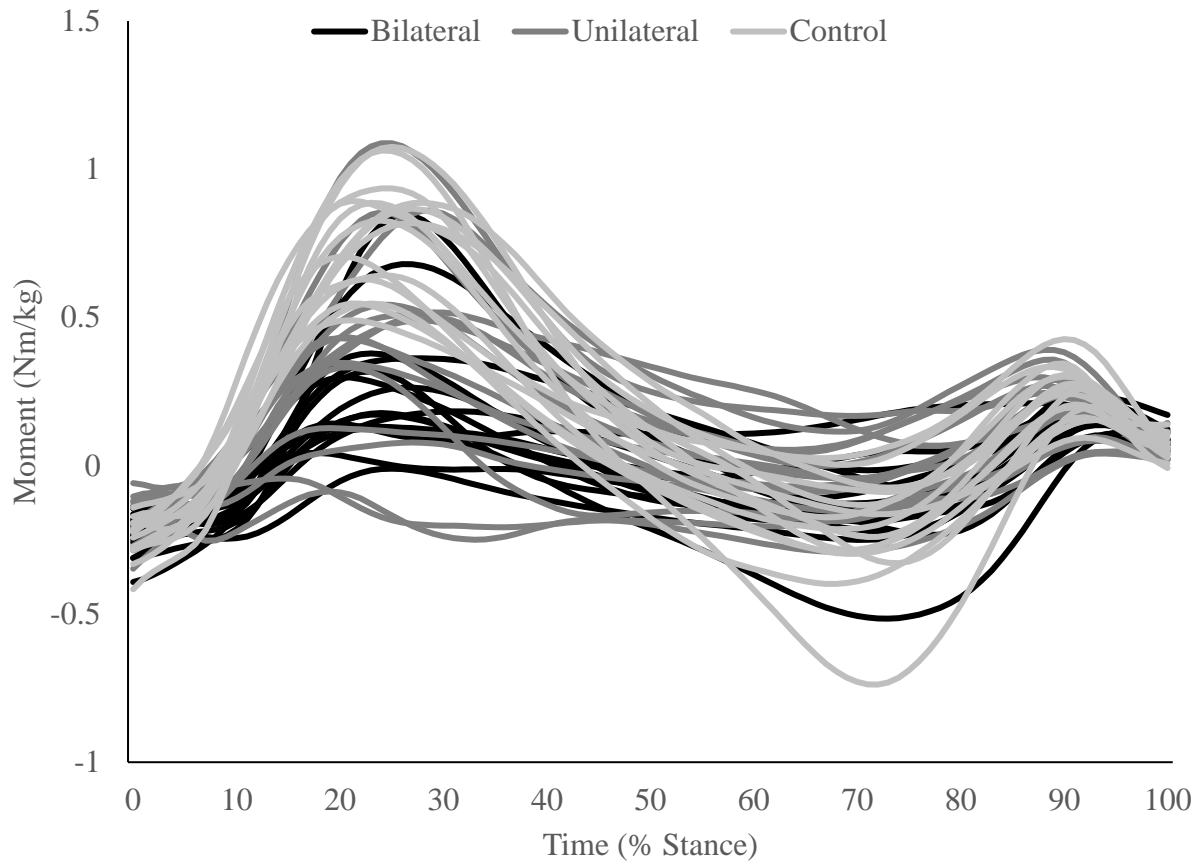


Figure 8. Individual waveforms of sagittal-plane knee moment in bilateral, unilateral, and control.

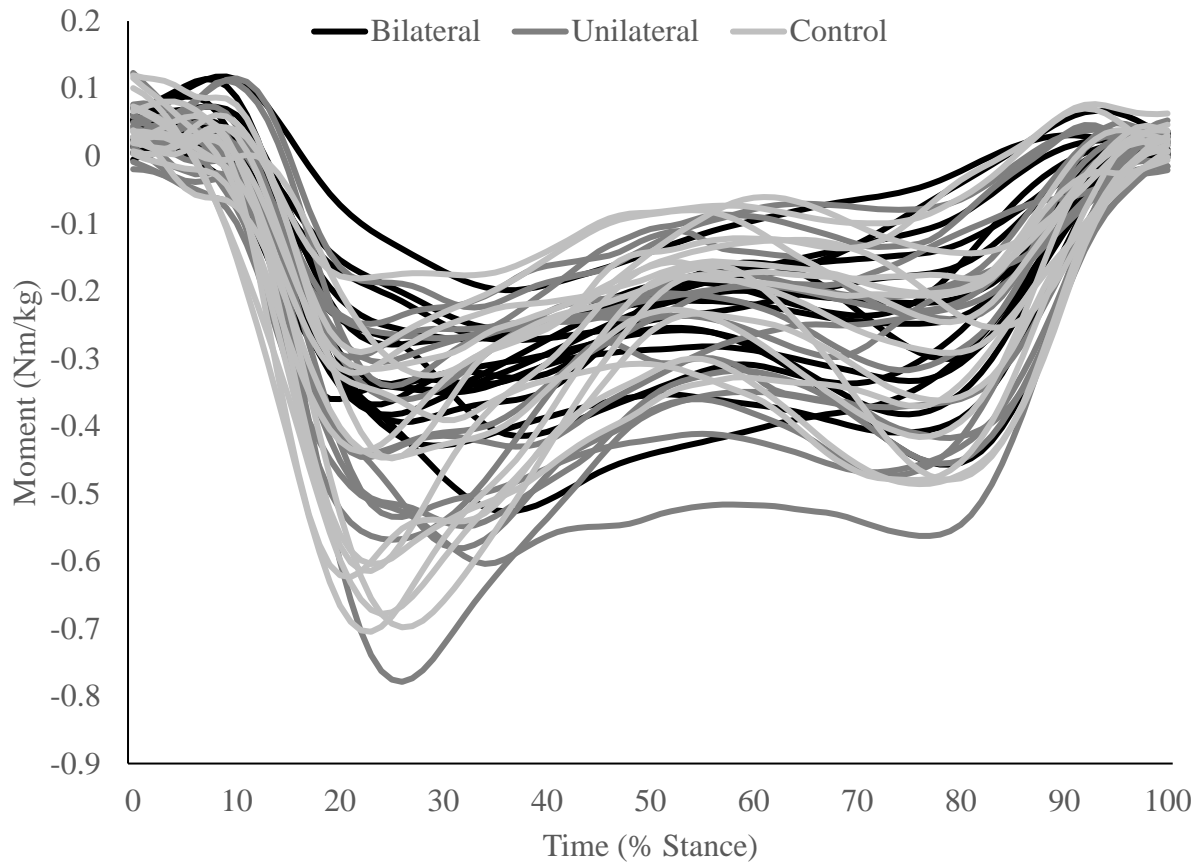


Figure 9. Individual waveforms of frontal-plane knee moment in bilateral, unilateral, and control.

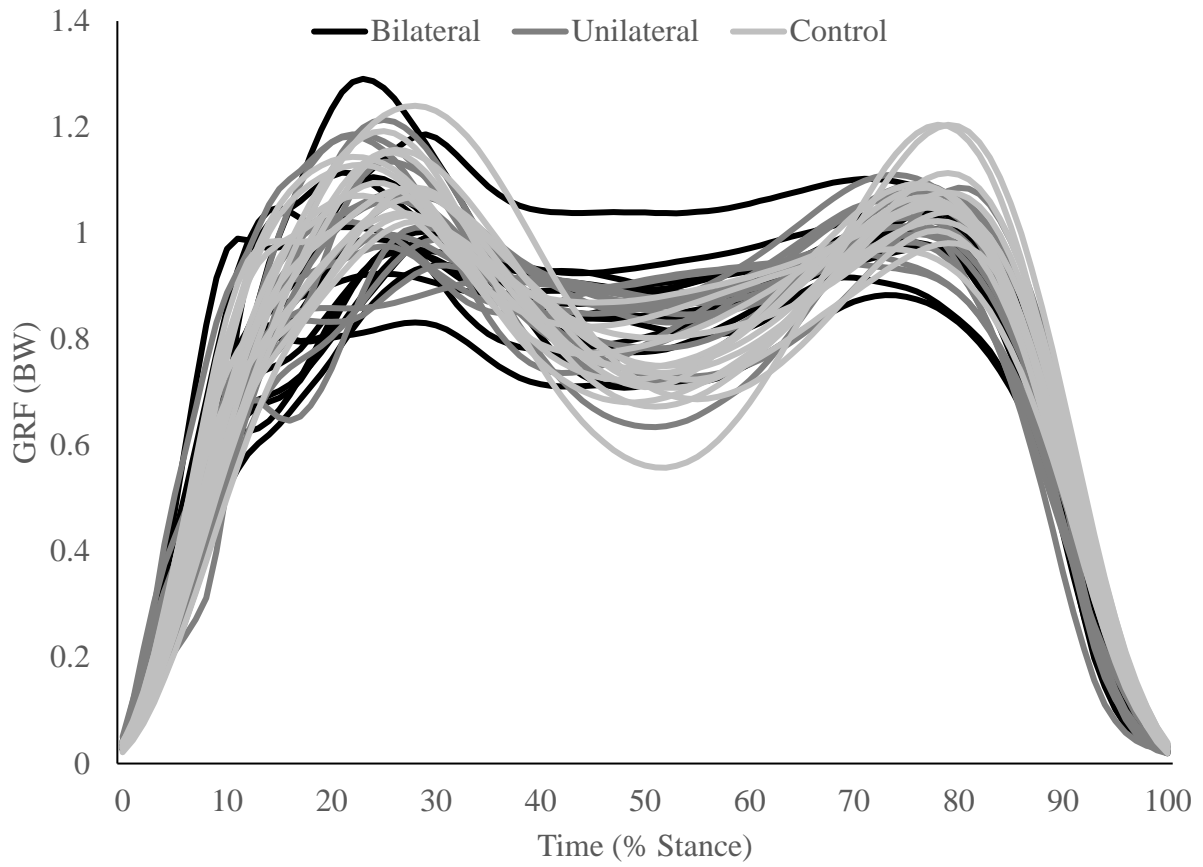


Figure 10. Individual waveforms of vertical GRF in bilateral, unilateral, and control.

Vita

Derek Yocum was born in Wabash, IN, in 1990 to Dewayne and Denise Yocum. He is the youngest of two children. He graduated from North Miami High School in 2009. Derek first attended Huntington University and later would graduate from Ball State university with a degree in Exercise Science in 2013. Derek then attended the University of Tennessee for both a Master's and PhD degrees in Biomechanics, which he finished in 2019. Derek accepted a tenure-track assistant professor position at Albion College in Albion, MI.