BIOMECHANICAL AND CLINICAL INFLUENCES ON RECOVERY AND OSTEOARTHRITIS PROGRESSION AFTER TOTAL KNEE ARTHROPLASTY

by

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A dissertation submitted to the Faculty of the University of Delaware in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Biomechanics and Movement Science

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABSTRACT

Total knee arthroplasty (TKA) is the most common treatment for end-stage knee osteoarthritis (OA). Despite reduced pain in the operated limb, strength, biomechanical and functional deficits persist after TKA. Such long-term deficiencies may contribute to the non-random progression of end-stage OA and joint replacement, most commonly in the contralateral cognate joint. Therefore, it is imperative for clinicians to understand the impairments and joint movement strategies that contribute to long term dysfunction and risk for contralateral TKA.

The overall goal of this work is to determine the asymmetrical movement and impairments that contribute to short- and long-term dysfunction and ultimately contralateral TKA use. The central hypothesis is that operated limb function will improve, while non-operated limb function will decline with time, leading to more symmetrical movement in the sagittal plane and less symmetrical movement in the frontal plane. Such biomechanical limb asymmetries, along with clinical impairments, will ultimately determine functional outcomes and contralateral TKA use.

This work will help to advance the understanding of post-surgical outcomes in the TKA population. A definitive characterization of short- and long-term joint biomechanics will be determined, filling a critical gap in the literature. In addition, clinicians will be able to better address poor functional outcomes associated with TKA by determining how disability is influenced not only by physical impairments, but also by irregular movement between limbs. Such unresolved abnormalities may ultimately contribute to the unacceptably high rate of contralateral TKA. Therefore, determining

the factors that lead to additional surgery may aid clinicians in developing targeted rehabilitation protocols designed to decrease the risk for contralateral TKA.

Chapter 1

BIOMECHANICAL AND CLINICAL CHARACTERISTICS OF UNILATERAL TOTAL KNEE ARTHROPLASTY AND ITS RELATIONSHIP WITH DYSFUNCTION AND CONTRALATERAL TOTAL KNEE ARTHROPLASTY

Degradation of Articular Cartilage

The forces experienced by the joint are the summation of the forces that result from ground reaction forces and the forces generated by surrounding muscle activity. Joint forces are a consequence of normal movement and are an essential component of joint health under normal circumstances. Forces are distributed throughout the articulating segments via articular cartilage, a deformable tissue that covers the proximal and distal bone surfaces. Articular cartilage is a composite of organic matrix and water and is extremely hydrophilic. This property of cartilage contributes to its ability to supporting the substantial loads experienced during a wide range of dynamic activities.

Cartilage deformation during loading conditions increases the joint contact area and distributes the loads across a larger area. In healthy joints, this process of deformation and load bearing occurs with little to no wear to the cartilage matrix. However, with traumatic injury or wear over time, changes in the cartilage surface can result in changes in tissue function and properties, ultimately leading to progressive deterioration known as osteoarthritis (OA)[1]. Models of anterior cruciate ligament (ACL) transection have indicated that altered joint mechanics and mechanical instability are primary risk factors for the onset and progression of OA[1].

OA is the most common form of arthritis, and most commonly affects weight-bearing joints. OA can be defined in three ways: 1) Clinically, which is based on self-reported symptoms (i.e. – swelling, pain, and stiffness) and physician-observed abnormalities (i.e. – joint tenderness, swelling, limited joint motion, and pain with motion)[2]; 2) Radiographically, which is based on the presence of osteophytes, thinning of joint cartilage, and altered bone geometry[3]; and 3)

Symptomatic, which is based on the presence of pain in addition to radiographic evidence of OA[4]. Symptomatic knee OA occurs in approximately 16% of the US population[5], and the lifetime risk of knee OA for an individual is 44.7%, which increases with a past history of injury or obesity[6].

Use of Total Knee Arthroplasty and Long Term Outcomes

Total knee arthroplasty (TKA) is a common surgical procedure used to manage the pain and the related dysfunction associated with end-stage knee OA. Of those diagnosed with symptomatic knee OA, over half will require at least one TKA procedure in their lifetime[7]. The number of primary TKA surgeries has increased by 161.5% from 1991 to 2010 and is expected to grow to a projected 3.48 million procedures by 2030, with a disproportionate increase in patients under the age of 45[8–10].

The presence of pain due to end-stage knee OA is commonly associated with alterations in muscle coordination strategies[11], lower extremity weakness[12], asymmetrical joint loading[13], and asymmetrical movement strategies that shift the demand off of the affected joint[14]. Prior to TKA surgery, patients with end-stage knee OA walk with 7% less knee flexion and have functional performance scores that are 19-33% worse than healthy individuals[15]. Success after surgery and rehabilitation is often defined by pain relief, improved knee flexion range of motion (ROM), and improved functional ability measured with performance-based tests and patient-reported outcomes[16]. However, long-term deficits remain well after the TKA surgery.

Three to six months after TKA, quadriceps muscles are 40-41% weaker in the operated limb compared to the non-operated limb and 42-54% weaker than healthy limbs[17–19]. Operated knee biomechanics are also abnormal, with reduced flexion excursions, flexion moments, and adduction moments compared to the non-operated limb[19–21]. Self-reported and performance-based functional deficits are present as well. Three months after TKA, patients still have KOS scores that are 22% lower than age-matched healthy subjects without knee pain, as well as 9-10% worse performance on the timed-up-and-go test (TUG), are 23-25% slower on the stair climbing test (SCT), and walk 12-19% shorter distances on the six minute walk test (6MW) compared to healthy individuals[17,19].

One year after TKA, functional performance does improve compared to the 3 month time point[18]. Similar improvements are also seen in quadriceps strength and extension ROM[18]; however, even one year after TKA, the operated limb remains 14% weaker than the non-operated limb and 26% weaker than healthy limbs[17]. Likewise, functional outcomes remain limited at this time when compared to healthy control subjects. Patients one year after TKA report 11% lower functional ability and are 7-16% worse on performance-based tests when compared to healthy controls[18]. This is concerning since most surgeons and clinicians consider individuals fully recovered by one year and patients are no longer routinely followed by orthopedic or rehabilitative care after this time.

Beyond 1 year, the non-operated limb begins to show signs of deterioration. By three years after TKA, quadriceps on the non-affected side are weaker than the operated limb and patients report 120% more pain in the non-operated limb[22]. The progressive deficits in the non-operated knee are associated with progressive functional impairments and performance that is 15%-26% worse compared to healthy controls[22,23].

Physical Impairments, Asymmetrical Movement, Functional Deficits, and Future Status of Non-Operated Limb

There are several theories as to why there is a progressive decline in the non-operated joints. Although aging may reduce strength and functional ability, the rapid decline in strength and increase in pain suggests that additional factors are driving the progressive changes in the non-operated limb. Persistent movement asymmetries that overload the non-operated joints may contribute to contralateral OA and subsequent TKA on this side. In a seminal study, Shakoor and colleagues[24] determined that end-stage OA in the lower extremities progresses non-randomly and the most common joint to be replaced following initial TKA is the contralateral knee joint, followed by the contralateral hip joint. The incidence of contralateral OA progression is substantial. Nearly 50% of individuals require contralateral TKA[25] within 18 years of baseline. Concernedly, the mean time to TKA progression in the contralateral limb was only 3.1 years and 26.8% required a successive arthroplasty within 2 years. This dramatic utilization of a secondary procedure is a significant public health concern and the procedures represent a substantial socioeconomic burden.

The progression of primary knee OA can take decades to develop and can be considered a chronic condition. During this time, patients often adopt altered movement patterns that progress as pain, weakness, and OA severity also increases[14,26,27]. Individuals with knee OA typically have reduced sagittal excursions and moments that correspond to reduced quadriceps strength and activation[28]. There is also a progressive increase in medial compartment loading with OA progression as measured by the external adduction moment, which is a surrogate of knee loading at the medial tibio-femoral compartment[29]. After TKA surgery, patients experience slight improvements in joint movement and significant improvements in pain[16,30]; however, asymmetrical patterns persist[20,21]. Such persistent asymmetrical movement patterns that offload the operated limb due to reduced variability of movement can put patients at risk for long-term dysfunction and injury. By three years after TKA, some of the movement asymmetry is resolved. Although it appears that movement symmetry improves over time, the increase in symmetry is due in part to worsening of the non-affected limb[19].

Despite the success of TKA, movement asymmetries persist and functional deficits tend to decline with longer term follow-ups. In order to better improve quality of life for TKA patients, it is essential to first determine the factors that are predictive of long-term functional success. Currently, it is unclear just how muscle strength, joint ROM, and knee biomechanics influence functional ability and patient reported outcomes. Understanding these relationships is essential because if such factors are found to significantly influence function, then clinicians may be able to develop better rehabilitative protocols designed to specifically address the factors that improve quality of life for patients living with TKA. Furthermore, it is unclear if the influence of such factors is limb dependent. With the non-operated limb being at risk for long-term OA development and progression after unilateral TKA surgery, it is possible that physical impairments and truncated joint motion in the non-operated limb could become limiting factors in long-term functional ability and perception. Therefore, establishing how each limb contributes to function may help clinicians develop protocols designed not only to treat operated limb dysfunction, but also prevent deterioration in the non-operated limb.

The long-term habitual utilization of asymmetrical loading may put the contralateral knee joint at risk for developing OA. It is possible that these movement asymmetries are perpetuated and enhanced by asymmetrical strength, joint contracture, or learned motor patterns that were adopted in the presence of pain and weakness prior to surgery. If modifiable predictors of contralateral TKA use can be identified, clinicians may be able to develop rehabilitation protocols designed to prevent long-term disability after TKA. Therefore, the goals of this study are to 1) characterize short- and longer-term movement patterns following TKA, 2) determine if physical impairments and movement patterns are related to poor functional outcomes following TKA, and 3) determine the clinical and biomechanics factors that predict contralateral TKA. This study will address the short- and long-term between-limb impairments and movement differences that impact functional ability and typify the unilateral TKA population. The short term time point included subjects 6 months after surgery. Six months after surgery is the time at which 1) most patients have been discharged from rehabilitation, 2) many patients resume regular daily activities, and 3) most patients are stable in terms of recovery[31,32]. Our two year time point represents an important stage in recovery and is the time at which some patients begin to experience a decline in function that may be associated with negative changes in the non-operated limb. This study is significant because it will lay the groundwork for rehabilitation treatments that address residual impairments and asymmetries, with the intention of improving operated limb function, as well as preserving the integrity of the non-operated joints.

Specific Aims

The overall goal of this work was to identify the asymmetrical movement patterns and clinical impairments that contribute to short- and long-term dysfunction and contralateral TKA use.

Aim 1: Identify movement asymmetries during gait in a large cross-sectional sample of subjects 6 months, 1 year, and 2 years after unilateral TKA.

Hypothesis 1.1: Two years after TKA, subjects will have more symmetry between limbs than subjects 1 year and 6 months after TKA, as a result of larger operated knee angles, excursions, and moments and smaller non-operated knee angles, excursions, and moments in the sagittal plane.

Hypothesis 1.2: Two years after TKA, subjects will have more asymmetry between limbs than subjects 1 year and 6 months after TKA, as a result of smaller operated knee moments and larger non-operated knee moments in the frontal plane.

Aim 2: Determine the relationship between clinical impairments, gait biomechanics and functional outcomes in a large cross-sectional sample of subjects 6 months, 1 year, and 2 years after unilateral TKA.

Hypothesis 2.1: Quadriceps strength and range of motion will influence functional outcomes 6 months, 1 year, and 2 years after TKA.

Hypothesis 2.2: Quadriceps strength and range of motion will influence biomechanical outcomes at 6 months, 1 year, and 2 years after TKA.

Hypothesis 2.3: Biomechanical variables will influence functional outcomes after accounting for quadriceps strength and range of motion at 6 months, 1 year, and 2 years after TKA.

Aim 3: Identify biomechanical and clinical predictors of future contralateral TKA use in subjects with primarily unilateral disease at baseline.

Hypothesis 3.1: Clinical impairments and knee biomechanics on the operated limb will predict contralateral TKA 2.5 years after unilateral TKA.

Hypothesis 3.2: Clinical impairments and knee biomechanics on the non-operated limb will predict contralateral TKA 2.5 years after unilateral TKA.

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Chapter 2

LONG-TERM BIOMECHANICAL OUTCOMES IN THE SAGITTAL AND FRONTAL PLANES AFTER TOTAL KNEE ARTHROPLASTY: A CROSS-SECTIONAL STUDY

Abstract

Objective: Prior to unilateral total knee arthroplasty (TKA), patients tend to walk with an asymmetrical movement pattern that unloads the affected knee and overloads the unaffected knee. However, after surgery, such adaptations may persist, putting patients at risk for long-term dysfunction. The purpose of this study was to examine the short- and long-term sagittal and frontal plane knee biomechanics of the unilateral TKA population.

Methods: Two hundred nineteen subjects participated in a cross-sectional study 6 months, 1 year, or 2 years after unilateral TKA surgery. Twenty healthy controls were also included for comparison. Outcome measures include knee angle (KA) at initial contact (IC), peak knee flexion (PKF), and peak knee extension (PKE), knee moment (KM) at PKF and PKE, knee excursion (KE) at weight acceptance (WA) and midstance (MS), and peak and average knee adduction moment (PKAM, KAM_{ave}).

Results: Up to 2 years after unilateral TKA, subjects exhibit asymmetrical movement patterns during walking. The operated knee exhibited reduced kinetic and kinematic movement in the sagittal plane throughout midstance and lower kinetics in the frontal plane throughout stance compared to the non-operated knee.

Conclusion: Similar to movement patterns that typify the OA population, subjects continue to adopt movement patterns that overload the non-operated knee and underload the operated knee after unilateral TKA surgery. Such lasting asymmetries may reflect unresolved unilateral impairments and may put the unilateral TKA population at risk for contralateral knee OA development, progression, and future TKA.

Introduction

Osteoarthritis (OA) is a progressive disorder that is characterized by pain, weakness and degeneration of the articular cartilage in weight-bearing joints[1]. As the symptoms of OA progress, individuals adopt asymmetrical movement patterns that reduce the demand on the affected joint[2] and increase the forces on the contralateral joints[3], resulting in a predictable progression of OA throughout the lower extremities[4]. Total knee arthroplasty (TKA) is a successful surgical procedure that results in a high degree of patient satisfaction a significant reduction in joint pain[5,6]. Of those diagnosed with symptomatic knee OA, over half will require at least one TKA procedure in their lifetime[7]. Although TKA relieves pain and improves quality of life, abnormal movement patterns remain[8–10]. Concernedly, the persistence of these movement abnormalities[11] may perpetuate disuse atrophy or even increase the risk of OA progression in the contralateral knee[12]. The pattern of movement asymmetries coincides closely with the pattern of subsequent joint replacement in which the contralateral knee is most likely to be overloaded during walking and also the most likely to be replaced next[4].

Success after surgery and rehabilitation is often defined by reduced physical impairments and improved patient satisfaction and functional ability[5,6,13]. Movement abnormalities are not often quantified as a metric of success, although asymmetrical movement patterns are associated with worse functional performance after TKA[14]. Three to six months after TKA, patients continue to move with lower flexion excursions and lower flexion moments on the operated knee[10,11,15]; however, there is little evidence about longer-term recovery of movement function after TKA. The few studies that have evaluated movement and functional recovery beyond 1 year, have shown that the non-operated limb begins to show signs of decline that includes progressive quadriceps weakness and pain[10,16]. Although initial evidence suggests some patients may improve movement symmetry several years after TKA, preliminary evidence suggests that the increase in interlimb symmetry may be the result of decline on the non-operated side, not solely improvements in the operated knee.

To date there have been few large-scale studies that have evaluated movement patterns in the operated and non-operated limbs of patients at varying stages of recovery after TKA throughout stance phase of gait. Therefore, the purpose of this was to evaluate sagittal and frontal plane interlimb kinetics and kinematics at the knee in a unilateral TKA population. We hypothesized that: 1) subjects would have greater sagittal plane symmetry as a result of larger knee angles, excursions, and moments in the operated limb and smaller knee angles, excursions, and moments in the non-operated limb 2 years after TKA compared to 1 year and 6 months, and 2) despite larger sagittal plane angles, excursions, and moments, subjects 2 years after TKA would still demonstrate knee angle, excursion, and moment deficits in the operated limb compared to a control group. We also hypothesized that 3) subjects would have greater frontal plane asymmetry as a result of smaller moments in the operated limb and larger moments in the non-operated limb 2 years after TKA compared to 1 year and 6 months, and 4) frontal plane moments in the non-operated knee would exceed that of the controls.

Methods

Study design

This was a cross-sectional study design (Figure 1). Subjects participated in two testing sessions several days apart. The first testing session was conducted in the University of Delaware Physical Therapy Clinic. The second testing session was conducted in the University of Delaware Physical Department Motion Analysis Laboratory.

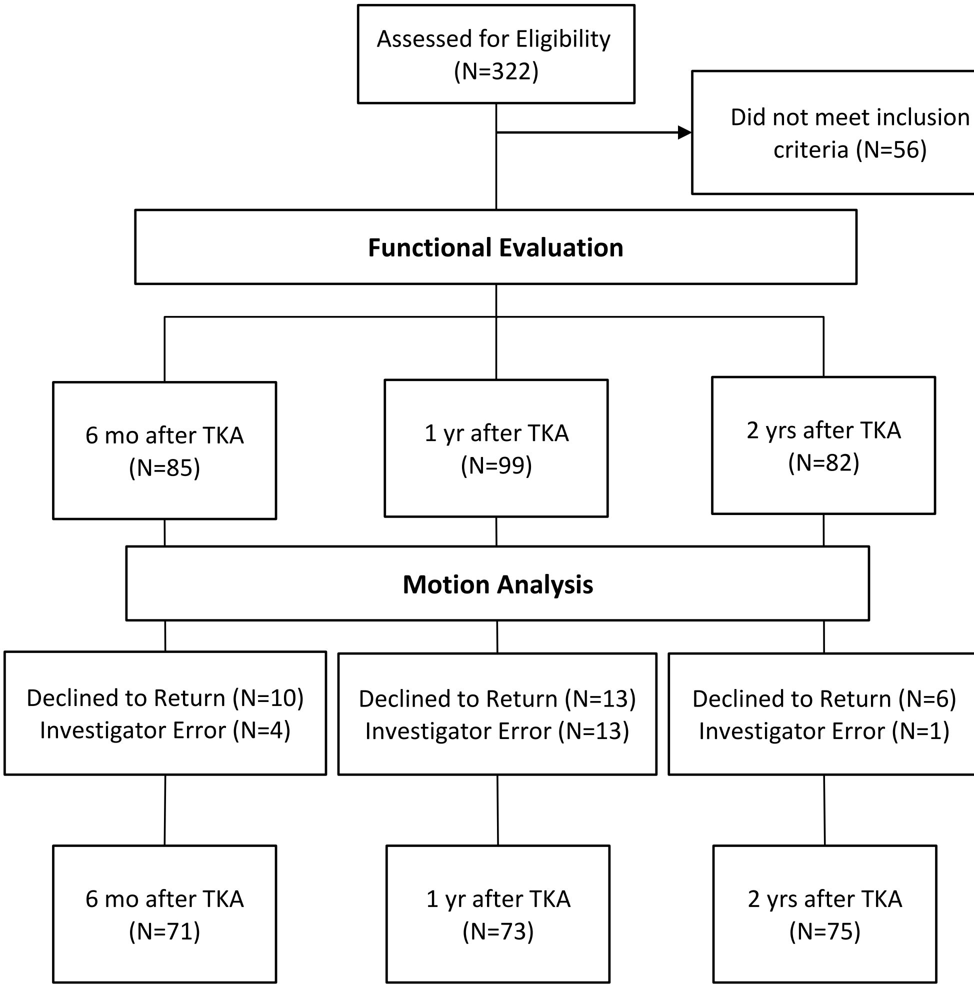

Figure 1 Study Flow Diagram

Subjects

Seventy-one subjects 6 months after unilateral TKA, 73 subjects 1 year after unilateral TKA, and 75 subjects 2 years after unilateral TKA were recruited for this study. Subjects were excluded if they had a known history of uncontrolled or insulin controlled diabetes; neurological, vascular, or cardiac problems that limit function; greater than mild osteoarthritis or other orthopedic conditions affecting the non-operated lower extremity that may limit function; >4/10 pain on the non-operated knee; planned staged TKA, orthopedic problems of the operated lower extremity, other than the TKA, that may limit function; or a Body Mass Index (BMI) of 40 or greater. All subjects signed informed consent forms approved by the Human Subjects Review Board at the University of Delaware prior to participation.

The healthy group of older adults consisted of 20 subjects who reported no knee pain or injury. Controls were excluded if they had a known history of uncontrolled or insulin controlled diabetes; neurological, vascular, or cardiac problems that limit function, surgery in the lower extremities, >4/10 pain in either knee, or musculoskeletal involvement in the lower extremities or the spine that limited their physical function, or BMI 40 or greater. Because we are comparing operated and non-operated limbs in our surgical groups, operated and non-operated limbs were randomly assigned for our control group. All subjects signed informed consent forms approved by the Human Subjects Review Board at the University of Delaware prior to participation.

Clinical Impairment Measures

Quadriceps Strength: For quadriceps strength testing, subjects performed a maximal voluntary isometric contraction (MVIC). Patients were seated on an isokinetic dynamometer (Kincom, Chattecx Corp, Harrison, TN), with a measuring arm secured to the ankle, the hip was fixed at 90° flexion, and the knee was fixed at 75° flexion. The peak volitional force generated was used to quantify quadriceps strength, and was normalized to BMI to account for anthropometric differences between individuals.

Active extension Range of Motion: Active extension ROM (AROMe) of the knee joint was measured using a long arm goniometer. Subjects were placed in a supine position with the distal arm aligned with the lateral malleolus and the proximal arm aligned with the greater trochanter. Subjects were instructed to actively extend their knee. The maximal extension angle was recorded, with positive values indicating flexion, zero indicating full extension, and negative values indicating hyperextension.

Motion Analysis

Joint kinematics and kinetics during walking were measured using an 8 camera infrared motion capture system (VICON, Oxford Metrics, London, England) synchronized with force plates (Bertec Corp., Worthington, OH). Sixteen 16 mm-millimeter spherical retro-reflective markers were placed bilaterally on the acromion, iliac crest, greater trochanter, medial and lateral femoral condyle, medial and lateral malleolus, and head of the 5th metatarsal to identify joint centers. Segments were defined using marker clusters fixed on rigid thermoplastic shells and were secured on the lower legs and thighs, and on the trunk and pelvis. Two additional retro-reflective markers were placed on the heels. Marker data were sampled at 120 Hz, while force data were collected at 1,080 Hz. Standing calibration was performed prior to walking trials to identify joint centers with respect to the coordinate system of each segment. Following the standing calibration, subjects were asked to walk over a 13m walkway at a self-selected speed (±5%) across force platforms embedded in the walkway, with clear contact of only one foot on each force plate. Subjects were allowed several practice walks until reaching a consistent self-selected speed prior to data collection. Five trials were collected for each subject.

Data Management

Marker trajectories and force plate data were low pass filtered at 6 Hz and 40 Hz, respectively, using a second-order phase-corrected Butterworth filter. Joint angles were calculated using Euler XYZ sequence corresponding to a flexion/extension, abduction/adduction, and internal/external rotation sequence. Gait events (initial contact, toe-off) were identified using a 20N force plate threshold. External joint moments were calculated using inverse dynamics and were normalized to body mass and height (N·m/kg·m). Trials were time normalized to 100% stance and averaged for statistical analysis. Kinematics and kinetics calculations were performed using a custom LabView program (National Instruments, Austin, TX) and Visual 3D 4.91.0 software (C-motion Inc., Rockville, MD). Primary kinematic outcomes include knee angle (KA) at initial contact (IC), peak knee flexion (PKF), and peak knee extension (PKE). Knee excursions (KE) during weight acceptance (WA) (change in knee flexion from IC to PKF) and midstance (MS) (change in knee extension from PKF to PKE) were also calculated. Primary kinetic outcomes include external knee moments (KM) at PKF and PKE, and peak and average knee adduction moment (PKAM, KAM_{ave}) were calculated for each limb.

Statistical Analysis

Differences between limbs across groups were assessed using a 4x2 (group x limb) mixed design ANOVA. Independent t-test or paired t-test was used to for post hoc testing when the interaction effect was significant. Metrics that were not limb specific were analyzed using one-way ANOVA to determine between group differences. All analyses were performed with SPSS 21. Significance level was set at 0.05.

Results

All three TKA groups had significantly more mass (6mo, $p<0.001$; 1yr, $p=0.002$; 2yr, $p=0.002$) and BMI (6mo, $p<0.001$; 1yr, $p<0.001$; 2yr, $p<0.001$) than the healthy group. There were no differences in age and height between groups (Table 1). The 6mo and 2yr TKA groups walked significantly slower than the healthy group (6mo, $p=0.006$; 2yr, $p=0.016$). There was a significant interaction effect for quadriceps strength ($F(3,235)=8.438$, $p<0.001$). Post-hoc analysis revealed the operated limb was weaker than the non-operated limb 6mo ($p<0.001$), 1yr ($p<0.001$), and 2yrs ($p=0.006$) after TKA. The operated limb was also stronger in the healthy group compared to the 6mo ($p<0.001$), 1yr ($p=0.003$), and 2 yrs ($p=0.003$) groups. There was also a significant interaction effect for extension ROM ($F(3,235)=4.952$, $p=0.002$). Post-hoc analysis revealed the operated limb had less extension than the non-operated limb 6mo ($p<0.001$) and 2yrs ($p=0.010$) after TKA. The healthy group also had greater operated knee extension than the 6mo ($p<0.001$), 1yr ($p=0.018$), and 2yrs ($p=0.019$) groups and greater non-operated knee extension than the 1yr group (p=0.028). The 6mo group also had greater non-operated knee extension than the 1yr group (p=0.040).

Table 1 Anthropometric, Strength, and Range of Motion Measures (Negative AROMe values indicate hyperextension, * significant difference from non-operated limb (p<0.05), #significant difference from all TKA groups (6mo, 1yr, 2yr) (p<0.05), ¶ significant difference from 6 mo group (p<0.05), ‡ significant difference from 1 yr group (p<0.05), ‖ significant difference from 2 yr group (p<0.05))

Variable		6 months (N=71)	1 year (N=73)	2 year (N=75)	Healthy (N=20)
Age (yr)		69.30±7.89	66.48±8.19	68.39±6.60	67.10±7.50
Sex (Female/Male)		35/36	36/37	38/37	13/7
Height (m)		1.70±0.09	1.70±0.09	1.69±0.10	1.66±0.08
Weight (kg)		91.03±21.25	88.85±17.52	88.66±20.73	70.36±17.94#
BMI (kg/m²)		31.24±5.91	30.78±5.12	31.29±4.96	25.20±4.41#
Walking Speed (m/s)		1.28±0.17	1.32±0.18	1.29±0.17	1.42±0.15¶‖
Quad Strength (N/BMI)	Operated	17.43±6.90*	18.40±6.74*	18.44±6.84*	23.64±6.56#
	Non-Operated	21.64±7.99	21.45±8.02	19.99±6.94	22.30±5.51
Extension ROM (°) ¶	Operated	1.11±4.79*	-0.16±3.80	-0.19±4.29*	-2.70±3.03#
	Non-Operated	-2.21±3.38‡	-1.01±3.56	-1.52±3.56	-2.95±3.17‡

Knee Kinematics

Weight Acceptance

Mean time series curves for knee angle in the sagittal plane can be found in Figure 2. There was a significant interaction effect for KA at IC ($F(3,235)=4.600$, $p=0.004$) (Table 2). Post-hoc analysis revealed the operated limb had 4.34°, 1.47°, and 2.00° less extension than the non-operated limb 6mo ($p<0.001$), 1yr ($p=0.020$), and 2yrs ($p=0.001$) after TKA, respectively. In addition, the 6 mo group had 2.30° and 3.90° less operated knee extension than the 1yr ($p=0.011$) and healthy ($p=0.005$) groups. For KA at PKF, there was a significant interaction effect ($F(3,235)=2.829$, $p=0.039$) (Table 2). Post-hoc analysis revealed the operated limb had

1.53° less peak flexion at 6mo ($p=0.027$) and 1.33° less peak flexion at 2yrs ($p=0.047$) compared to the non-operated limb. Additionally, the 1yr group had 2.02° less operated knee flexion compared to the 2yr group ($p=0.033$). There was an interaction effect for KE at WA ($F(3,235)=4.338$, $p=0.005$) (Table 2). Post-hoc analysis revealed the operated limb had 2.81° and 2.44° less flexion excursion at 6mo ($p<0.001$) and 1yr ($p<0.001$), respectively, compared to the non-operated knee. In addition, the healthy group had 4.41°, 3.40°, and 2.34° more operated knee flexion excursion than the 6mo ($p<0.001$), 1yr ($p=0.001$), and 2yr ($p=0.016$) groups, respectively.

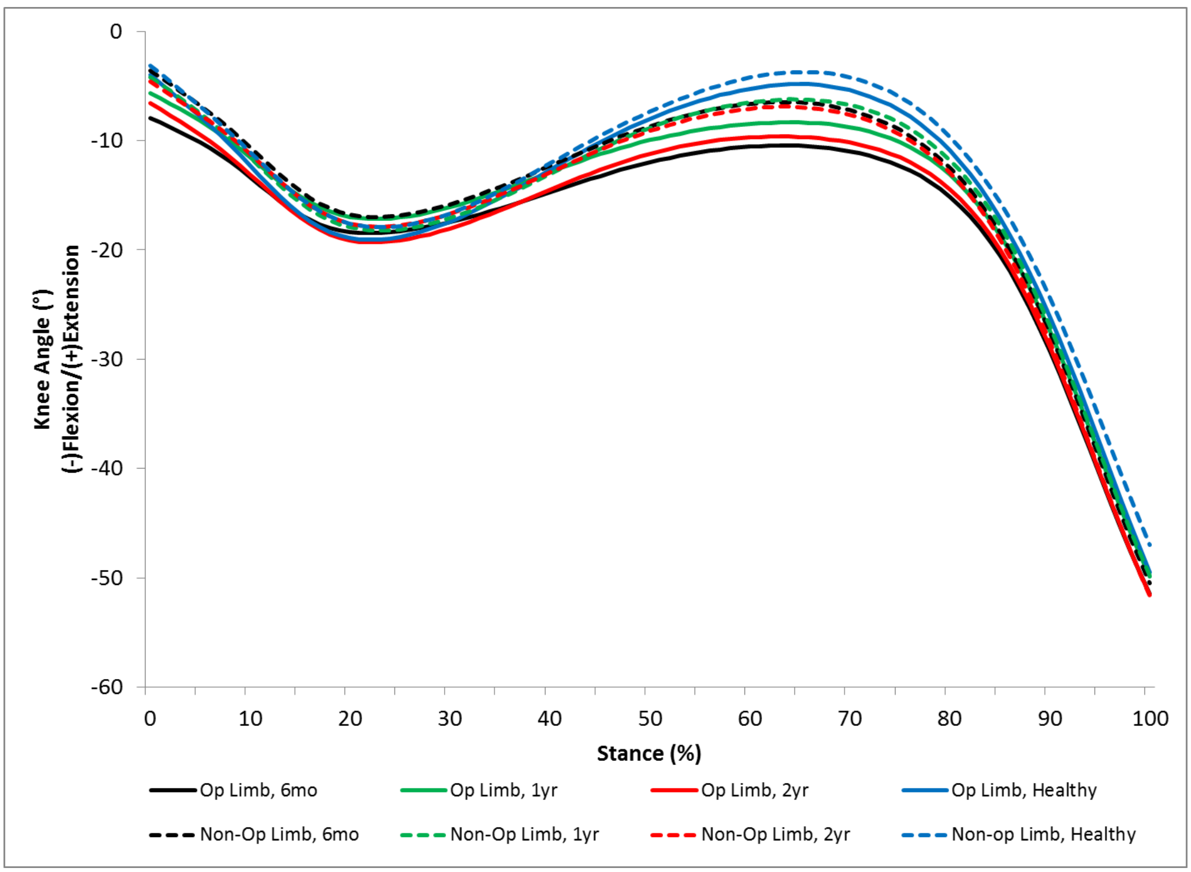

Figure 2 Sagittal Knee Angle during Stance Phase of Gait

Table 2 Kinetic and kinematic variables during stance phase of gait (*significant difference from non-operated knee (p<0.05), ¶ significant difference from 6 mo group (p<0.05), ‡ significant difference from 1 yr group (p<0.05), ‖ significant difference from 2 yr group (p<0.05)), # significant difference from all TKA groups (6mo, 1yr, 2yr) (p<0.05)

	6 Months	**1 year**	**2 years**	**Healthy**
KA at IC (°)				
Operated	-7.94±5.37*	-5.64±5.16*¶	-6.60±5.46*	-4.05±6.14¶
Non-Operated	-3.60±5.78	-4.17±5.75	-4.60±5.05	-3.27±5.20
KA at PKF (°)				
Operated	-18.76±5.46*	-17.46±6.17‖	-19.48±5.23*	-19.27±6.72
Non-Operated	-17.22±6.42	-18.44±6.63	-18.15±5.86	-18.34±5.78
KA at PKE (°)				#
Operated *	-10.05±5.95	-7.79±5.98	-9.25±5.77	-4.52±7.29
Non-Operated	-6.05±5.94	-5.70±7.72	-6.59±5.14	-3.58±6.37
KE at WA (°)				
Operated	10.82±3.77*	11.82±3.89*	12.88±3.95¶	15.23±3.19#
Non-Operated	13.63±4.93	14.26±4.16	13.58±4.98	15.07±3.58
KE at MS (°)				
Operated	8.71±4.29*	9.68±4.29*	10.22±4.92*¶	14.75±4.89#
Non-Operated	11.17±5.24	12.74±5.46	11.55±5.67	14.76±3.97
KM at PKF (N·m/kg·m)				¶‡
Operated	0.34±0.15	0.32±0.15	0.38±0.15	0.44±0.17
Non-Operated	0.32±0.18	0.33±0.19	0.34±0.19	0.41±0.14
KM at PKE (N·m/kg·m)				#
Operated *	-0.01±0.11*	-0.04±0.11*	-0.03±0.11*	-0.13±0.12#
Non-Operated	-0.06±0.11	-0.08±0.14	-0.07±0.10	-0.14±0.09
PKAM (N·m/kg·m)				
Operated	-0.29±0.11*	-0.26±0.25*	-0.30±0.11*	-0.41±0.12#
Non-Operated	-0.36±0.14	-0.38±0.15	-0.40±0.13	-0.38±0.11
KAM_{ave} (N·m/kg·m)				
Operated	-0.15±0.06*	-0.15±0.06*	-0.15±0.06*	-0.19±0.06#
Non-Operated	-0.18±0.08	-0.19±0.09	-0.20±0.08	-0.16±0.05

Midstance

Mean time series curves for knee angle in the sagittal plane can be found in Figure 2. There was no significant interaction effect for KA at PKE (F(3,235)=4.664, p=0.176). However, there was a significant main effect of limb (F(1,235)=24.765, p<0.001), where the operated limb had 2.42° less extension than the non-operated limb (Table 2). There was also a significant main effect of group ($F(3,235)=3.615$, $p=0.014$), where the healthy group had 4.00°, 2.69°, and 3.87° more extension than the 6mo ($p=0.003$), 1yr ($p=0.045$), and 2yr ($p=0.004$) groups, respectively. For KE at MS, there was a significant interaction effect ($F(3,235)=2.811$, $p=0.040$) (Table 2.2). Post-hoc analysis revealed the operated limb had 2.46°, 3.07°, and 1.33° less extension excursion than the non-operated limb 6mo ($p<0.001$), 1yr ($p<0.001$), and 2yrs ($p=0.022$) after TKA, respectively. In addition, the healthy group had 6.04°, 5.08°, and 4.53° more operated knee extension excursion than the 6mo ($p<0.001$), 1yr ($p<0.001$), and 2yr ($p<0.001$) groups, respectively. The 2yr group also had 1.52° more operated knee extension excursion than the 6mo group ($p=0.045$).

Knee Kinetics

Sagittal Plane

Mean time series curves for knee moment in the sagittal plane can be found in Figure 3. For KM at PKF, there was no interaction effect ($F(3,235)=1.084$, $p=0.357$), or effect of limb ($F(1,235)=2.181$, $p=0.141$). There was a significant effect of group ($F(3,235)=2.96$, $p=0.033$), with the healthy group having 0.10 N·m/kg·m and 0.10 N·m/kg·m more knee flexion moment than the 6mo ($p=0.010$) and 1yr ($p=0.008$) groups, respectively (Table 2). There was no significant interaction effect for KM at PKE ($F(3,235)=0.621$, $p=0.602$). However, there was a significant main effect of limb ($F(1,235)=14.866$, $p<0.001$), where the operated knee had 0.04 N·m/kg·m less extension moment than the non-operated knee (Table 2). There was also a significant main effect of group ($F(3,235)=6.154$, $p<0.001$), where the healthy group had 0.10 N·m/kg·m, 0.08 N·m/kg·m, 0.09 N·m/kg·m more extension moment than the 6mo ($p<0.001$), 1yr ($p=0.002$), and 2yr ($p<0.001$) groups, respectively (Table 2).

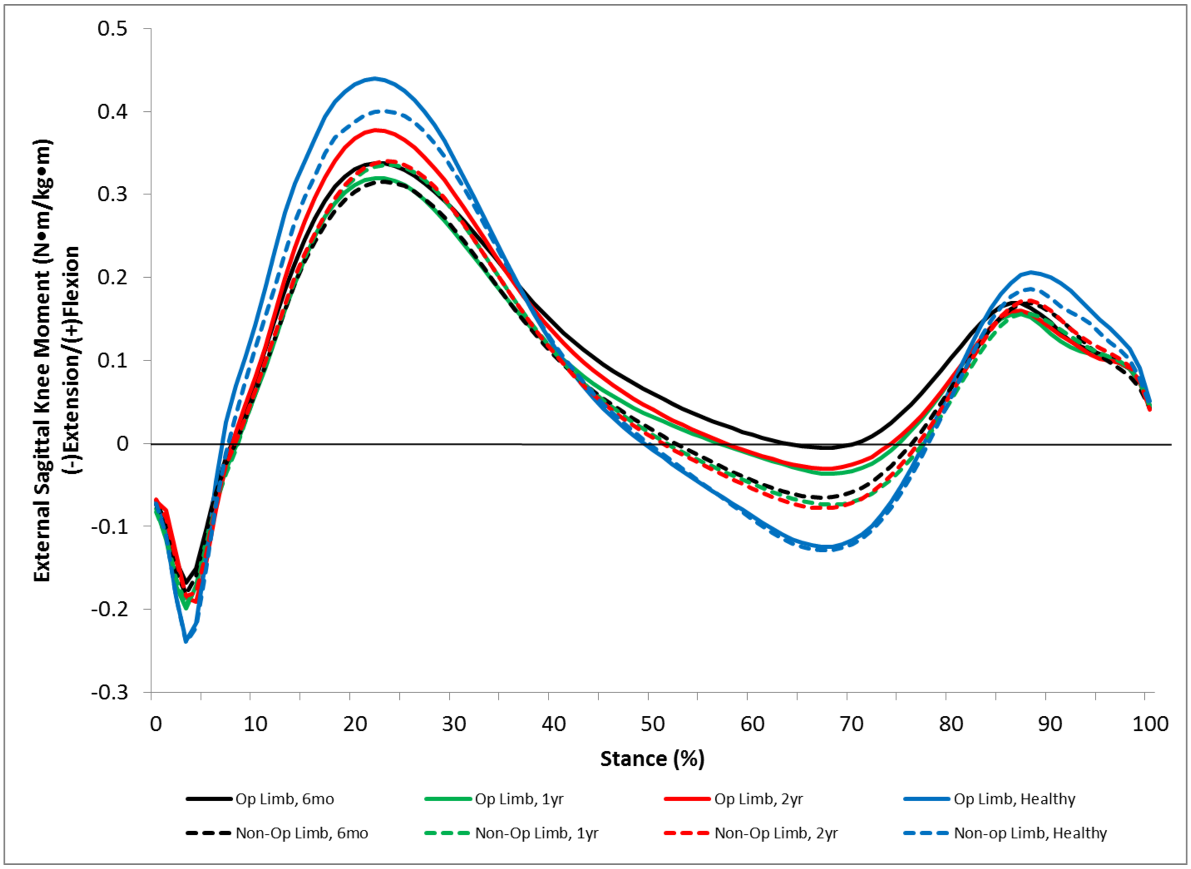

Figure 3 External Sagittal Knee Moment during Stance Phase of Gait

Frontal Plane

Mean time series curves for external knee moment in the frontal plane can be found in Figure 4. For PKAM, there was a significant interaction effect ($F(3,235)=3.751$, $p=0.012$) (Table 2). Post-hoc analysis revealed the operated limb had 0.07 N·m/kg·m, 0.12 N·m/kg·m, and 0.10 N·m/kg·m less peak adduction moment than the non-operated limb 6mo ($p=0.001$), 1yr ($p<0.001$), and 2yrs ($p<0.001$) after TKA, respectively. In addition, the healthy group had 0.13 N·m/kg·m, 0.15 N·m/kg·m, and 0.12 N·m/kg·m more operated knee peak adduction moment than the 6mo ($p=0.003$), 1yr ($p<0.001$), and 2yr ($p=0.006$) groups, respectively. For KAM_{ave}, there was a significant interaction effect ($F(3,235)=4.659$, $p=0.003$) (Table 2). Post-hoc analysis revealed the operated limb had 0.03 N·m/kg·m, 0.04 N·m/kg·m, and 0.05 N·m/kg·m less average adduction moment than the non-operated limb 6mo ($p=0.001$), 1yr ($p<0.001$), and 2yrs (p<0.001) after TKA, respectively. In addition, the healthy group had 0.04 N·m/kg·m, 0.04 N·m/kg·m, and 0.04 N·m/kg·m more operated knee peak adduction moment than the 6mo (p=0.008), 1yr (p=0.007), and 2yr (p=0.006) groups, respectively.

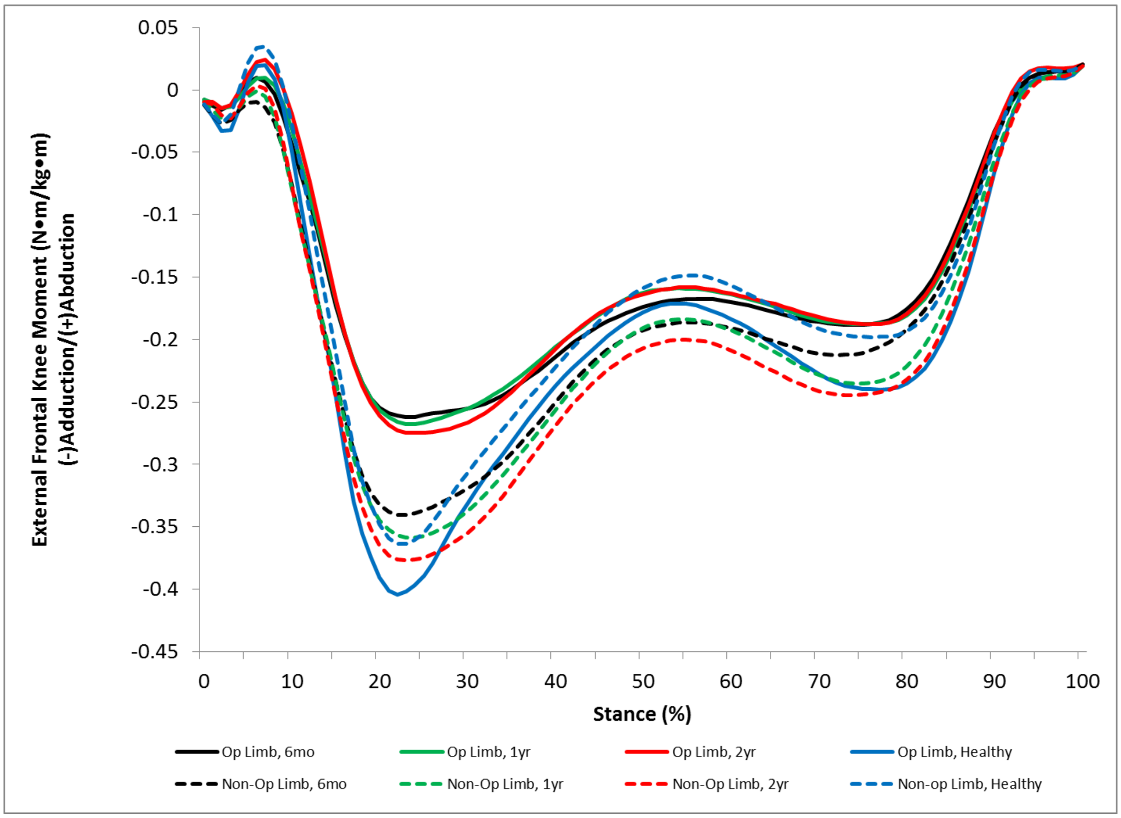

Figure 4 External Frontal Knee Moment during Stance Phase of Gait

Discussion

The results of this study partially support our hypothesis that individuals 2 years after TKA will have more symmetrical sagittal plane movement than those 6 months and 1 year after surgery. Six months after TKA, the operated knee had 75% less extension at IC, 25% less extension excursion, and 159% less peak extension moment than the non-operated knee. One year after surgery, the operated knee had 30% less extension at IC, 27% less extension excursion, and 70% less peak extension moment than the non-operated knee. Two years after TKA, the operated knee had 36% extension at IC, 12% less extension excursion, and 93% less peak extension moment than the non-operated knee. It appears that extension asymmetries are larger 6 months after surgery compared to 1 year and 2 years after surgery. The fact that the 1 and 2 year groups had less asymmetry was due primarily to greater operated knee extension, as opposed to less non-operated knee extension at the 1 and 2 year points. Compared to the 6 month group, the operated knee had 34% more knee extension at IC 1 year after TKA and 16% more extension excursion 2 years after TKA. However, there were no significant differences in extension angles in the non-operated knee.

Although there was more symmetry in the 1 and 2 year groups, deficits in the operated knee and interlimb asymmetries remained at these later time points. As noted in this study and in previous work, normal gait biomechanics consist of an almost fully extended knee and a biphasic sagittal knee moment that acts as an external knee extension moment during midstance [17,18]. In this study, all TKA groups had knees that remained substantially flexed during midstance and the magnitude of the extension deficit was greater on the operated side. This sagittal moment pattern known as "quadriceps overuse", where a flexion moment remains throughout stance, is particularly pronounced in the operated knee 6 months after TKA. The mean operated knee angles at PKE in the TKA groups ranged from 7.79° to 10.05°, which was significantly less than the 4.5° in the healthy group. Similar results were also seen for the knee angle at IC. As the heel strikes the ground, the knee should approach full extension. In our healthy sample and in the non-operated limb of our TKA group, knee angle during IC was within 3.60°-4.60° of full extension. However, in all of the TKA groups, the operated knee remained significantly more flexed (5.64°-7.94°). Clinicians should be aware that this is a pervasive biomechanical asymmetry that does not seem to resolve, even 2 years after TKA. This difference may be attributed to less active knee extension ROM in the TKA group, unresolved quadriceps weakness that developed prior to surgery, or learned motor patterns that were adopted prior to or early after surgery. It is also possible that feeling of instability or pain when the knee is in full extension contribute to the altered movement patterns that are characterized by decreased extension at initial contact and throughout midstance. Future work should identify the motor or physical impairments that contribute to the altered movement patterns observed at all time points after TKA.

There was a significant difference between the groups for knee flexion excursion during gait, particularly in the operated limb during weight acceptance. Six months after TKA, subjects had 23% less knee flexion excursion in the operated limb compared to the non-operated limb, but only modest differences existed between limbs 2 years after TKA. The 2 year group had only 7% less knee flexion excursion in the operated limb when compared to the non-operated limb. The greater knee excursion symmetry at 2 years was attributed to greater knee flexion excursion in the operated limb, and not less knee flexion in the non-operated side. The 2 year group had 17% greater operated knee flexion excursion compared to the 6 month group and no discernable difference in the non-operated knee. Despite greater knee flexion excursion symmetry 2 years after TKA, the 2 year group still had less knee flexion excursion than the healthy cohort. Knee flexion excursion is an important metric of walking performance in this population. During the weight acceptance phase, body weight is transferred to the stance limb and the quadriceps must actively counteract the external knee flexion moment generated by the ground reaction forces. Normal gait mechanics require that the quadriceps act like a shock absorber and attenuate the external force by going into knee flexion. Prior to surgery, reduced knee flexion excursion is the hallmark strategy to compensate for the pain and weakness associated with end-stage OA. This stiff-legged gait pattern reduces the external knee flexion moment and in turn, decreases the need for quadriceps activity. It is possible that the greater magnitude in operated limb knee flexion excursion and the greater symmetry in this biomechanical outcome arise as a result of the greater quadriceps strength and strength symmetry. Although we did not see any significant differences in strength between the TKA groups, subjects 2 years after TKA were only 8% weaker on the operated side compared to their non-operated side, whereas subjects 6 months after TKA were 20% weaker. Previous research has shown that improved strength symmetry is correlated to improved sagittal plane symmetry [9,15] and may be one explanation for what may be perceived as more normal gait pattern 2 years after TKA.

One notable difference between healthy controls and all TKA groups was the knee biomechanics at midstance. The healthy group had more 51%, 42%, and 36% more operated knee extension excursion than the 6 month, 1 year, and 2 year groups, respectively. Such deficits in excursion angles, along with deficits in peak knee extension angle and moment during midstance is meaningful, because few studies have evaluated knee kinematics during this phase of gait. Most analyses of knee biomechanics in the TKA population has focused on the weight acceptance phase of gait. While it is important to examine joint movement strategies during this phase, with the knee in a weight bearing, yet unstable position, it is also important to understand joint mechanics during a phase of single limb support that requires joint stability. The present study shows that during midstance, the TKA population exhibits reduced sagittal plane kinematics and kinetics compared to healthy individuals. Such extension deficits during midstance, coupled with persistent quadriceps weakness, indicates unresolved knee instability, putting people at a higher risk for knee buckling and overall physical function [19,20].

The results of this study also partially support our hypothesis that individuals 2 years after TKA will have more asymmetrical frontal plane knee mechanics due to reduced operated limb loading and higher non-operated limb loading. Asymmetrical peak and average adduction exists at all three time points. Six months after TKA, there was a 22% difference between limbs in the peak adduction moment and an 18% difference between limbs in the average adduction moment. Two years after TKA, there was 29% difference between limbs for both peak and average adduction moment. At both time points the non-operated limb had greater adduction moments compared to the operated limb, but 2 years after TKA the difference between limbs was 35-50% greater than at 6 months. Similarly, peak and mean adduction moments were 11% larger 2 years after TKA compared to 6 months in the non-operated limb. Furthermore, the operated limb had 24% less mean adduction moment, and 34%, 45%, and 31% less peak adduction moment 6 months, 1 year, and 2 years after surgery compared to the healthy group.

Interestingly, there were no significant differences between surgical groups and healthy controls in non-operative knee adduction moment. While it is commonly believed that reductions in knee joint loading are invariably accompanied by contralateral knee joint overloading, the present study shows otherwise. Such persistent patterns of loading deficits in the operated knee and normal loading in the non-operated knee may be indicative of a movement strategy that underloads the operated knee without overloading the non-operated knee (Figure 4). Because the joints of the lower limb are linked, changes in knee joint movement during the stance phase of gait are inevitably compensated for by changes in cognate and non-cognate joint movement in the ipsilateral and contralateral limbs. Therefore, it is possible that the TKA population in this study utilized a movement strategy that increased joint loading in their hips and ankles to offload the operated knee. However, after unilateral TKA, subsequent joint replacement surgery is most likely to occur in the contralateral knee[4,21,22], following a predictable pattern of OA development and progression and abnormally high knee joint loading [12,23]. Therefore, it is possible that the TKA population in the present study may actually utilize a contralateral knee joint overloading strategy. However, the time from surgery at which these individuals were tested may not be long enough to observe a significant difference in non-operated knee adduction moment from the healthy cohort. Although the difference was not significant, the surgical groups had 0.02-0.04 N·m/kg·m more average adduction moment than the healthy group. With a longer follow-up time, we may have seen greater adduction movements in the non-operated knee.

It is important to also consider the influence of walking speed on knee adduction moment. Subjects in the 6 month and 2 year TKA groups walked 10% slower than healthy controls. Faster gait speed is related to higher joint moments[24,25], so the fact that non-operated knee adduction moments did not exceed the control group may be a result of walking speed and may under-represent the true biomechanical disease state. If the subjects were forced to walk at faster speeds, it is possible and likely that the adduction moments would be greater than a comparable healthy population. Additionally, slower walking speeds also imply greater duration of loading through longer stance times. Although in this study we only analyzed the peak and time-normalized average adduction moments, longer duration of loads in the medial compartment may also negatively affect joint physiology.

Although this study provides insight into the biomechanical asymmetries that continue after TKA, there are several limitations. The cross sectional nature of this study does not allow us to determine cause and effect, nor does it allow us to make conclusions about how changes in movement patterns occur on an individual level. In this study, we did not evaluate movement patterns prior to TKA and prior to rehabilitation; therefore, we cannot identify how the surgery or subsequent rehabilitation interventions influenced sagittal plane mechanics. Although we anticipated that we would see decrease in function and changes in the movement patterns of the non-operated limb, we did not observe a trend towards worse movement or function on the contralateral limb. Future work should evaluate bilateral performance longer than 2 years after TKA to capture and quantify the potential negative changes that have been shown in the contralateral limb with longer-term follow-ups[10].

In summary, although subjects 2 years after TKA demonstrated better movement symmetry for knee flexion excursion during weight acceptance, the majority of variables remained significantly different between limbs and between surgical and healthy groups. Reduced operated knee extension at initial contact and midstance and knee adduction moments throughout stance were primary movement abnormalities seen in all TKA groups. In addition, the lack of differences between TKA and healthy subjects for frontal plane measures in the non-operated knee may be attributed to differences in walking speed. Future work should identify the causes for pervasive abnormal movement strategies after TKA.

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Chapter 3

CLINICAL AND BIOMECHANICAL PREDICTORS OF FUNCTIONAL OUTCOMES 6 MONTHS, 1 YEAR, AND 2 YEARS AFTER TOTAL KNEE ARTHROPLASTY

Abstract

Objective: Identifying how clinical impairments influence biomechanical and functional outcomes is imperative to develop appropriate rehabilitation strategies that reduce short- and long-term disability. Therefore, the purpose of this study was to determine relationships between clinical impairments and sagittal plane mechanics on functional outcomes after unilateral TKA surgery. We hypothesized that clinical impairments would predict functional ability and that biomechanical metrics would improve the prediction of functional performance after accounting for clinical impairments.

Methods: Two hundred nineteen subjects participated in a cross-sectional study 6 months, 1 year, or 2 years after unilateral TKA surgery. All subjects underwent three dimensional gait analysis, clinical testing, and functional testing. Clinical outcomes include isometric quadriceps strength testing and active extension range of motion (AROMe). Functional outcomes include stair climbing test, timed-up-and-go, six minute walk, and Knee Outcome Survey-Activities of Daily Living Scale (KOS-ADLS) questionnaire. Biomechanical outcomes include knee angle (KA) at initial contact (IC), peak knee flexion (PKF), and peak knee extension (PKE), knee moment (KM) at PKF and PKE, and knee excursion (KE) at weight acceptance (WA) and midstance (MS). Relationships between contralateral TKA and activity level and socioeconomic status were also determined.

Results: Bilateral clinical impairments are predictive of functional outcomes and bilateral knee mechanics 6 months, 1 year, and 2 years after TKA surgery. However, beyond the influence of clinical impairments, bilateral knee mechanics were also predictive of function at all

three time points, particularly at 2 years after TKA. Operated knee biomechanics during weight acceptance phase predicted 4.9-7.4% of the variance of self-reported function, while non-operated knee biomechanics throughout stance predicted 3.2-6.1% of the variance of six minute walk (6MW) test.

Conclusion: This study provides evidence of the short- and long-term influence of bilateral clinical impairments and knee biomechanics on functional outcomes after TKA surgery. Although clinicians should work to resolve deficits in the operated limb, they should also seek to maintain non-operated limb function. Long-term self-reported function is primarily dependent on operated knee extension and biomechanics during midstance. Therefore, improvements in the status of the operated knee drive improved long-term post-operative functional perception. However, with long-term 6MW performance primarily dependent on non-operated knee strength and biomechanics throughout stance, future declines in non-operated knee function can result in poor functional ability. Furthermore, in addition to treating the physical impairments that typify post-operative knee function, clinicians should also focus on normalizing knee joint movement patterns, as this is a vital component to improving functional outcomes following unilateral TKA.

Introduction

Osteoarthritis (OA) is a common degenerative disease of articular cartilage in the weight-bearing joints. Symptomatic knee OA (radiographic OA accompanied by pain) occurs in approximately 16% of the US population[1], and the lifetime risk of knee OA for an individual is 44.7%, which increases with age, a past history of injury, or obesity[2]. Total knee arthroplasty (TKA) is a surgical procedure used to manage the pain and the dysfunction associated with end-stage knee OA. The number of primary TKA surgeries has increased by 161.5% from 1991 to 2010 and is expected to grow to a projected 3.48 million procedures by 2030, with a disproportionate increase in patients under the age of 45[3–5].

Success after surgery and rehabilitation is often defined by pain relief, increased knee flexion range of motion (ROM), and improvements in performance-based functional tests and patient-reported outcomes[6–9]. Although most individuals report improved function compared to pre-operative status, abnormal joint movement patterns, physical impairments, and functional deficits still remain after TKA when compared to healthy controls[10–14]. Understanding the causes for residual biomechanical and functional deficits will allow clinicians to develop targeted rehabilitation strategies that reduce disability after TKA.

After TKA, the quadriceps muscles in the operated limb remain weaker than the non-operated limb and weaker than healthy controls[15–17]. This weakness may account for, or be perpetuated by, abnormal movement patterns that reduce reliance on the operated limb[16,18]. Six months after TKA there is a plateau in functional performance although functional scores remain lower than age-matched control subjects[13]. Concernedly, functional ability declines at longer term follow-up[19–21]. This may, in part, be a normal consequence of aging, but the functional decline may also be related to the decline in strength and increase in pain on the contralateral limb that begins by 3 years after surgery[16,22]. Continual overloading of the non-operated knee may expedite contralateral OA on the contralateral side and partially explain the decline in function of this knee by three years after the index TKA. Therefore, it is important to assess how the operated and non-operated knees influence functional ability and biomechanical asymmetry at longer-term follow-ups.

There is some evidence that has supported a connection between physical impairments, abnormal knee joint movement, and functional deficits. Several studies have examined the relationship between quadriceps strength and functional performance. Bilateral quadriceps weakness is correlated to worse functional performance prior to and 1 month after TKA surgery[23]. Three months and 6 months after TKA, quadriceps weakness is correlated to poor functional performance[17,24], and accounts for 19-30% of the variance in functional performance 1 and 2 years after surgery[22]. And 3 years after TKA, with declining strength and increasing pain, non-operated limb physical impairments account for 19-28% of the variance of functional performance[22]. However, few studies have explored the relationship between knee ROM and function. In a study of an institutionalized elderly population, limited extension ROM is correlated to impaired ambulation[25]. Before surgery and 1 month after TKA surgery, reduced operated knee extension ROM is correlated to worse self-reported function and worse self-reported and performance-based function at 1 year[23,26]. Therefore, physical impairments and functional deficits appear to be related in the TKA population, however, the influence of strength and joint range of motion on functional outcomes is unclear. This relationship between physical limitations and the ability or perceived ability to perform a task is important, because if impairments are found to influence function, then rehabilitation protocols targeted to improve weakness and ROM can be implemented in order to best improve quality of life for patients living with TKA.

Few studies have reported on the relationships between quadriceps strength and knee joint biomechanics. Greater strength asymmetries are correlated to greater knee flexion excursion asymmetries 3 months after TKA[17,18]. And in a recent study by Yoshida and colleagues[16], from 3 months to 3 years after TKA, subjects had improved flexion excursion and flexion moment symmetry coincident with improved quadriceps strength symmetry, although it is unclear whether the improvements in biomechanical symmetry were due to resolved operated limb impairments or developing non-operated limb impairments. However, no one has examined the relationship between knee extension ROM and joint biomechanics during a dynamic task. The relationship between the knee joint during a weight bearing (ie – walking) and a non-weight bearing (ie – active extension ROM) task is intuitive. Limited available joint ROM can impact the joint's kinematic and kinetic ability during a dynamic task. Therefore, physical impairments and joint biomechanics appear to be related in the TKA population, however, the influence of strength and joint range of motion on joint biomechanics remains unknown. This relationship between physical limitations and joint movement during a task is important, because if impairments are found to influence abnormal joint movement, then it is possible that clinicians can interrupt the adapted movement strategies that may lead to contralateral OA and TKA.

Even fewer studies have examined the relationship between biomechanics and function. Yoshida and colleagues[17]and Farquhar and colleagues[15] have reported improved symmetrical peak knee flexion angle and moment coinciding with and improved performance-based and self-reported function 1 year after TKA, yet the relationship between joint movement and functional ability remains unclear. This is also a crucial connection to make, because if movement asymmetries are found to influence functional outcomes, then it is possible that clinicians are missing a vital component to improving mobility beyond just resolving physical impairments.

Identifying the clinical and biomechanical measures that are related to disability is imperative to developing appropriate interventions and preventing longer-term functional decline. Therefore, the purpose of this study was to determine how clinical impairments and sagittal plane mechanics influence functional outcomes after unilateral TKA surgery. We hypothesize that limb-specific physical impairments will be related to worse functional outcomes via movement abnormalities 6 months, 1 year, and 2 years after TKA surgery. These time points were selected to also determine if these relationships differ based on time from surgery. In particular, we hypothesize that muscle weakness and joint contracture will be related to worse patient reported and performance-based functional outcomes and smaller sagittal plane knee angles and moments, and truncated sagittal knee movement will be related to worse function, over and above the influence of clinical impairments.

Methods

Study design

This study was designed as a cross-sectional study (Figure 5). Subjects participated in two testing sessions several days apart. The first testing session was conducted in the University of Delaware Physical Therapy Clinic. The second testing session was conducted in the University of Delaware Physical Department Motion Analysis Laboratory.

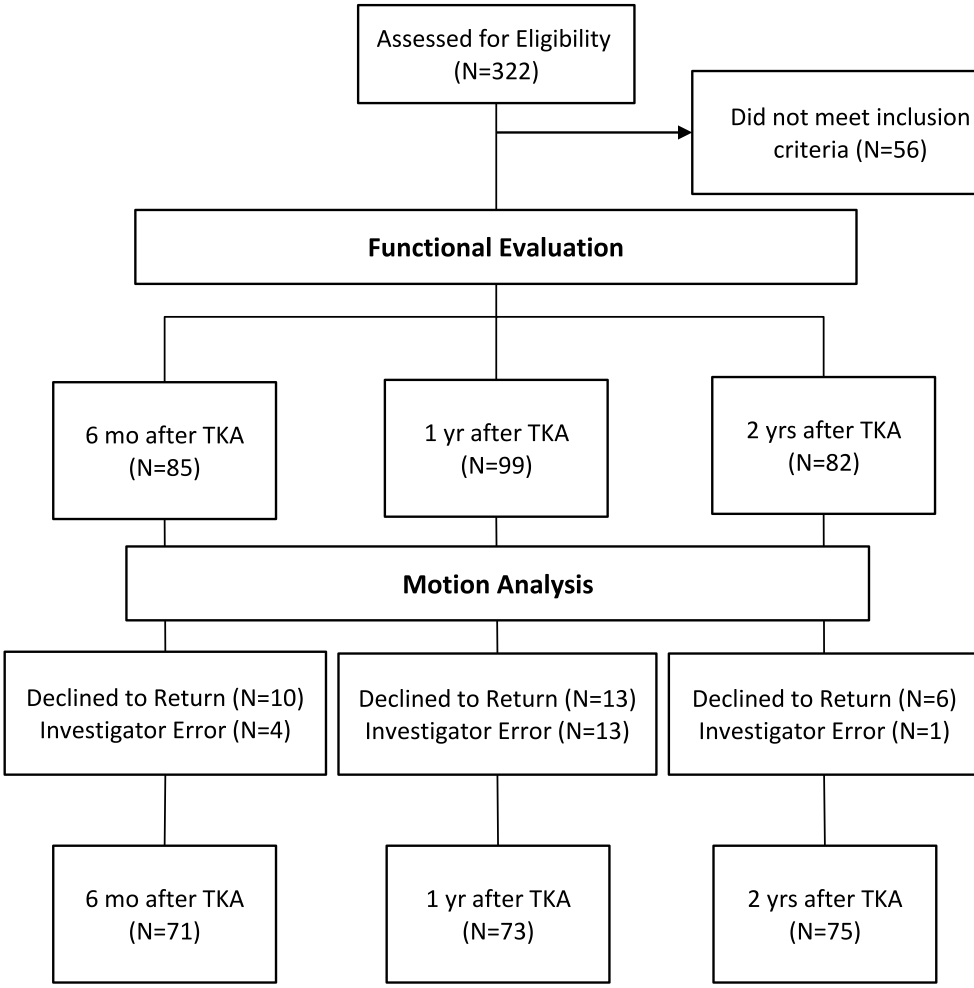

Figure 5 Study Flow Diagram

Subjects

Seventy-one subjects 6 months after unilateral TKA, 74 subjects 1 year after unilateral TKA, and 75 subjects 2 years after unilateral TKA were recruited for this study (Table 3). Subjects were excluded if they had a known history of uncontrolled or insulin controlled diabetes; neurological, vascular, or cardiac problems that limit function; greater than mild osteoarthritis or other orthopedic conditions affecting the non-operated lower extremity that may limit function; >4/10 pain on the non-operated knee; planned staged TKA, orthopedic problems of the operated lower extremity, other than the TKA, that may limit function; or a Body Mass

Index (BMI) of 40 or greater. All subjects signed informed consent forms approved by the Human Subjects Review Board at the University of Delaware prior to participation.

Functional Testing

Weight and height were measured and BMI was calculated for each subject. Functional performance based testing included Timed-Up-And-Go (TUG), Stair Climbing Test (SCT), and Six-Minute Walk (6MW). TUG is a test of mobility, strength, and balance that measures the amount of time it takes to rise from a standard height chair (46 cm), walk 3 m, and return to a seated position in the same chair. One practice trial was performed, followed by two recorded trials. This test is used to assess mobility, strength, and balance and has been commonly used in the OA and TKA populations[27]. SCT is a test that measures the time it takes to ascend and descend 12 7in high steps. A hand rail was available for subjects to use during testing. One practice trial was performed, followed by two recorded trials. During 6MW, subjects walk at a self-selected pase for as long of a distance they can walk, on level ground, for 6 min. This is a test of endurance and mobility over long distances. All tests are commonly used in the OA and TKA populations [27]. Subjects were instructed to walk as quickly and as safely as possible for all tests.

Self-reported function was assessed using the Knee Outcomes Survey-Activities of Daily Living (KOS-ADLS). The KOS-ADLS is a knee specific self-reported outcome measure that determines functional limitation in individuals with a variety of pathological disorders of the knee. The survey has 14 items with scores from 0 to 5. A percentage score is totaled, with a higher score indicating greater self-perceived functional ability. KOS-ALDS is a valid, reliable, and responsive measure of functional performance after TKA[28,29].

Clinical Impairment Measures

For quadriceps strength testing, subjects performed a maximal voluntary isometric contraction (MVIC). Patients were seated on an isokinetic dynamometer (Kincom, Chattecx

Corp, Harrison, TN), with a measuring arm secured to the ankle, the hip was fixed at 90° flexion, and the knee was fixed at 75° flexion. The peak volitional force generated was used to quantify quadriceps strength, and normalized to BMI to account for anthropometric differences between individuals.

Active extension ROM (AROMe) of the knee joint was measured using a long arm goniometer. Subjects were placed in a supine position with the distal arm aligned with the lateral malleolus and the proximal arm aligned with the greater trochanter. Subjects were instructed to actively extend their knee. The maximal extension angle was recorded, with positive values indicating flexion, zero indicating full extension, and negative values indicating hyperextension.

Motion Analysis

Joint kinematics and kinetics during walking were measured using an 8 camera infrared motion capture system (VICON, Oxford Metrics, London, England) synchronized with force plates (Bertec Corp., Worthington, OH). Sixteen 16 mm-millimeter spherical retro-reflective markers were placed bilaterally on the acromion, iliac crest, greater trochanter, medial and lateral femoral condyle, medial and lateral malleolus, and head of the 5th metatarsal to identify joint centers. Segments were defined using marker clusters fixed on rigid thermoplastic shells and will be secured on the lower leg and thigh bilaterally, and on the trunk and pelvis. Two additional retro-reflective markers were placed bilaterally on the heel. Marker data were sampled at 120 Hz, while the force platforms data were collected at 1,080 Hz. Standing calibration was performed prior to walking trials to identify joint centers with respect to the coordinate system of each segment. Following the standing calibration, subjects were asked to walk over a 13m walkway at a self-selected speed (±5%) across force platforms embedded in the walkway, with clear contact of only one foot on each force plate. Subjects were allowed several practice walks until reaching a consistent self-selected speed prior to data collection. Five trials were collected for each subject.

Marker trajectories and force plate data were low pass filtered at 6 Hz and 40 Hz, respectively, using a second-order phase-corrected Butterworth filter. Joint angles will be calculated using Euler XYZ sequence corresponding to a flexion/extension, abduction/adduction, and internal/external rotation sequence. Gait events (initial contact, toe-off) were identified using a 20N force plate threshold. External joint moments were calculated using inverse dynamics and were normalized to body mass and height (N·m/kg·m). Trials were time normalized to 100% stance and averaged for statistical analysis. Kinematics and kinetics calculations were performed using a custom LabView program (National Instruments, Austin, TX) and Visual 3D 4.91.0 software (C-motion Inc., Rockville, MD). Knee angle (KA) at initial contact (IC), peak knee flexion (PKF), and peak knee extension (PKE) will be determined, and Knee excursions (KE) during weight acceptance (WA) (change in knee flexion from IC to PKF) and midstance (MS) (change in knee extension from PKF to PKE) will be calculated. External knee moments (KM) at PKF and PKE were also calculated for each limb.

Statistical Analysis

Pearson correlation coefficients were used to determine the bivariate correlation between the variables. Hierarchical regression models were used to determine the relationship between clinical impairments, biomechanical measures, and functional outcomes, beyond the influence of age and BMI. Separate models were created for each limb and group. We expected age and BMI to predict outcomes, therefore, age and BMI were entered into the regression model first. To test the first hypothesis, the independent variables were the clinical measures, which were entered into the model in the following order: AROMe, then quadriceps strength to determine how much influence strength has on function beyond the influence of ROM. The dependent variables were the functional outcomes (TUG, SCT, 6MW, operated KOS). For the second hypothesis, the independent variables were the clinical measures, with AROMe entered first, followed by quadriceps strength, and the dependent variables were the sagittal knee biomechanical variables (KA at IC, KA at PKF, KA at PKE, KM at PKF, KM at PKE, KE at

WA, KE at MS). For the third hypothesis, after entering the clinical variables into the model (AROMe, quadriceps strength), the independent variables were biomechanical, and the dependent variables were the functional outcomes. Each biomechanical variable was entered separately into each model to determine the predictive value of joint biomechanics on functional outcomes, beyond the influence of clinical impairments. Changes in the R^2 value between each step (ΔR^2) were assessed for significance. Regressions models were tested for linearity, normality, homoscedasticity and multicollinarity. Differences between limbs across groups were assessed using a 3x2 (group x limb) mixed design ANOVA. Independent t-test or paired t-test was used to for post hoc testing when the interaction effect was significant. Metrics that were not limb specific were analyzed using one-way ANOVA to determine between group differences. All analyses were performed with SPSS 21. Significance level was set at 0.05.

Results

Healthy individuals were lighter, had lower BMI and had significantly better functional performance scores than those in the TKA groups (Table 3).

Clinical Measures

KOS score, extension ROM, and quadriceps strength on the operated limb was significantly lower than the non-operated limb in all three TKA groups (Table 3). Operated limb KOS score and quadriceps strength was greater in healthy group compared to the 6mo, 1yr, and 2yr groups. Operated limb extension ROM was greater in healthy group compared to 6 months after TKA. Non-operated KOS score was greater in healthy group compared 1 year and 2 years after TKA.

Table 3 Anthropometric data, Functional Outcomes, Strength and Extension Range of Motion, and Kinematic and Kinetic Variables. Negative extension range of motion indicates hyperextension. (* significant difference from non-operated limb, ‖ significant difference from 6 months, † significant difference from 1 year, # significant difference from 2 year, ‡significant difference from 6 months, 1 year, and 2 year groups ($p<0.05$))

Variable	**6 months (N=71)**		**1 year (N=73)**		**2 year (N=75)**	
Age (yr)	69.30±7.89		66.48±8.19		68.39±6.60	
Sex (Female/Male)	35/36		36/37		38/37	
Height (m)	1.70±0.09		1.70±0.09		1.69±0.10	
Weight (kg)	91.03±21.25		88.85±17.52		88.66±20.73	
BMI (kg/m^2)	31.24±5.91		30.78±5.12		31.29±4.96	
TUG (s)	8.38±1.81		8.06±1.74		8.29±2.00	
SCT (s)	14.10±4.39		12.75±3.51		13.62±4.73	
6MW (m)	546.85±88.47		542.33±81.06		537.46±83.73	
	Operated	**Non-Operated**	**Operated**	**Non-Operated**	**Operated**	**Non-Operated**
KOS	0.84±0.13*	0.92±0.10	0.85±0.13*	0.89±0.12	0.84±0.13*	0.88±0.15
Quad Strength (N/BMI)	17.43±6.90*	21.64±7.99	18.40±6.74*	21.45±8.02	18.44±6.84*	19.99±6.94
Extension ROM (°) ¶	1.11±4.79*	-2.21±3.38	-0.16±3.80*	-1.01±3.56	-0.19±4.29*	-1.52±3.56
KFA at IC (°)	-7.94±5.37*	-3.60±5.78	-5.64±5.16*	-4.17±5.75	-6.60±5.46*	-4.60±5.05
KFA at PKF (°)	-18.76±5.46*	-17.22±6.42	-17.46±6.17	-18.44±6.63	-19.48±5.23	-18.15±5.86
KFA at PKE (°)	-10.05±5.95*	-6.05±5.94	-7.79±5.98*	-5.70±7.72	-9.25±5.77*	-6.59±5.14
KFE at WA (°)	10.82±3.77*	13.63±4.93	11.82±3.89*	14.26±4.16	12.88±3.95‖	13.58±4.98
KFE at MS (°)	8.71±4.29*	11.17±5.24	9.68±4.29*	12.74±5.46	10.22±4.92*	11.55±5.67
KFM at PKF (N·m/kg·m)	0.34±0.15	0.32±0.18	0.32±0.15	0.33±0.19	0.38±0.15	0.34±0.19
KFM at PKE (N·m/kg·m)	-0.01±0.11*	-0.06±0.11	-0.04±0.11*	-0.08±0.14	-0.03±0.11*	-0.07±0.10

43

Kinematics and Kinetics

Knee angles at initial contact and peak knee extension, knee excursion at midstance, and knee moment at peak knee extension were significantly lower in the operated knee compared to the non-operated knee for all three surgical groups (Table 3). Knee excursion during weight acceptance was significantly lower in the operated knee compared to the non-operated knee 6 months and 1 year after surgery. Peak knee flexion angle was significantly larger in the operated knee compared to the non-operated knee 6 months after TKA. Operated knee peak extension angle, knee excursion at midstance, and peak extension moment was significantly larger in healthy controls compared to all three surgical groups. Operated knee angle at initial contact, non-operated knee excursion at midstance, and non-operated peak flexion moment was significantly larger in the healthy group compared to 6 months after TKA. Excursion at weight acceptance was significantly larger in the healthy group compared to 6 months and 1 year after TKA. Additionally, healthy controls exhibited significant asymmetries, with the operated knee having less peak flexion angle, less peak flexion moment, and more peak extension moment compared to the non-operated knee.

Clinical Impairments Predicting Functional Outcomes

Younger age and lower BMI were related to better functional performance in all three TKA groups (Table 4, 5). Regression analysis demonstrated that age and BMI were significant predictors of functional performance in all three TKA groups, explaining a greater amount of the variance 2 years after TKA compared to the 6 months and 1 year (Tables 6-11). Better knee extension ROM in the operated knee was related to better functional performance and self-report (Table 4), explaining 5.7%

of SCT 6 months after TKA (Table 6) and 19.0% of operated KOS score 2 years after TKA (Table 10). Non-operated extension ROM was not a predictor of performance-based or self-reported function. Better bilateral quadriceps strength was related to better functional performance at all time points. The operated limb strength explained more of the functional performance 1 year after TKA compared to 6 months and 2 years after surgery, while non-operated limb strength accounted for similar amounts of the variability for TUG and SCT at all three time points, and explained more of the variability of 6MW test 6 months after TKA compared to 1 year and 2 years after surgery in all three TKA groups (Table 6-11). Quadriceps strength in the operated limb was also related to better self-reported function, accounting for 5.3% of opKOS score 2 years after surgery (Table 10).

Table 4 Pearson Correlations between operated limb clinical impairments and functional outcomes 6 months, 1 year, and 2 years after TKA (*p<0.05, significant correlations between each variable)

		(op) KOS	**TUG**	**SCT**	**6MW**
6 mo	**Age**	0.021	0.442*	0.439*	-0.282*
	BMI	-0.118	-0.008	-0.065	-0.200*
	Op Extension ROM	-0.224*	0.262*	0.349*	0.158
	Op Quad Strength	0.215*	-0.446*	-0.523*	0.532*
1 yr	**Age**	0.125	0.313*	0.363*	-0.355*
	BMI	-0.233*	0.162	0.285*	-0.345*
	Op Extension ROM	-0.019	0.104	0.055	-0.086
	Op Quad Strength	0.150	-0.486*	-0.623*	0.541*
2 yr	**Age**	-0.072	0.508*	0.527*	-0.502*
	BMI	-0.114	0.015	0.049	-0.250*
	Op Extension ROM	-0.450*	0.258*	0.327*	-0.231*
	Op Quad Strength	0.293*	-0.399*	-0.517*	0.545*

Table 5 Pearson Correlations between non-operated limb clinical impairments and functional outcomes 6 months, 1 year, and 2 years after TKA (*p<0.05, significant correlations between each variable)

		(op) KOS	TUG	SCT	6MW
6 mo	**Age**	0.021	0.442*	0.439*	-0.282*
	BMI	-0.118	-0.008	-0.065	-0.200*
	Non Extension ROM	0.053	0.008	-0.022	0.107
	Non Quad Strength	0.089	-0.493*	-0.582*	0.660*
1yr	**Age**	0.125	0.313*	0.363*	-0.355*
	BMI	-0.233*	0.162	0.285*	-0.345*
	Non Extension ROM	-0.009	0.232*	0.237*	-0.255*
	Non Quad Strength	-0.011	-0.471*	-0.545*	0.517*
2 yr	**Age**	-0.072	0.508*	0.527*	-0.502*
	BMI	-0.114	0.015	0.049	-0.250*
	Non Extension ROM	-0.168	0.046	0.144	-0.244*
	Non Quad Strength	0.247*	-0.472*	-0.627*	0.603*

Table 6 Hierarchical Regression Models with Age, BMI, and Operated Limb Clinical Impairments as Independent Variables and Functional Outcomes as Dependent Variables 6 months after TKA.

6mo after TKA	**R**	**R^2**	**ΔR^2**	**ΔF**	**p-value**
TUG					
Age, BMI	0.495	0.245	0.245	11.013	<0.001
Age, BMI + Op Extension ROM	0.512	0.263	0.018	1.633	0.206
Age, BMI + Op Extension ROM + Op Quad Strength	0.622	0.387	0.124	13.387	0.001
SCT					
Age, BMI	0.466	0.217	0.217	9.416	<0.001
Age, BMI + Op Extension ROM	0.523	0.273	0.057	5.220	0.026
Age, BMI + Op Extension ROM + Op Quad Strength	0.680	0.462	0.189	23.132	<0.001
6MW					
Age, BMI	0.467	0.218	0.218	9.502	<0.001
Age, BMI + Op Extension ROM	0.468	0.219	0.001	0.074	0.786
Age, BMI + Op Extension ROM + Op Quad Strength	0.638	0.407	0.188	20.901	<0.001
Operated Limb KOS					
Age, BMI	0.124	0.015	0.015	0.530	0.591
Age, BMI + Op Extension ROM	0.247	0.061	0.046	3.264	0.075
Age, BMI + Op Extension ROM + Op Quad Strength	0.296	0.088	0.027	1.935	0.169

Table 7 Hierarchical Regression Models with Age, BMI, and Non-Operated Limb Clinical Impairments as Independent Variables and Functional Outcomes as Dependent Variables 6 months after TKA.

6mo after TKA	**R**	**R^2**	**ΔR^2**	**ΔF**	**p-value**
TUG					
Age, BMI	0.495	0.245	0.245	11.013	<0.001
Age, BMI + Non-op Extension ROM	0.495	0.245	0.000	0.002	0.969
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.603	0.364	0.119	12.361	<0.001
SCT					
Age, BMI	0.466	0.217	0.217	9.416	<0.001
Age, BMI + Non-op Extension ROM	0.466	0.217	0.001	0.050	0.824
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.662	0.438	0.221	25.901	<0.001
6MW					
Age, BMI	0.467	0.218	0.218	9.502	<0.001
Age, BMI + Non-op Extension ROM	0.492	0.242	0.024	2.103	0.152
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.703	0.494	0.251	32.756	<0.001
Operated Limb KOS					
Age, BMI	0.124	0.015	0.015	0.530	0.591
Age, BMI + Non-op Extension ROM	0.145	0.021	0.006	0.383	0.538
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.153	0.024	0.003	0.174	0.678

Table 8 Hierarchical Regression Models with Age, BMI, and Operated Limb Clinical Impairments as Independent Variables and Functional Outcomes as Dependent Variables 1 year after TKA.

At 1yr	**R**	**R^2**	**ΔR^2**	**ΔF**	**p-value**
TUG					
Age, BMI	0.367	0.135	0.135	5.464	0.006
Age, BMI + Op Extension ROM	0.370	0.137	0.002	0.170	0.681
Age, BMI + Op Extension ROM + Op Quad Strength	0.534	0.285	0.148	14.107	<0.001
SCT					
Age, BMI	0.484	0.234	0.234	10.713	<0.001
Age, BMI + Op Extension ROM	0.485	0.235	0.001	0.057	0.813
Age, BMI + Op Extension ROM + Op Quad Strength	0.684	0.468	0.233	29.747	<0.001
6MW					
Age, BMI	0.520	0.270	0.270	12.960	<0.001
Age, BMI + Op Extension ROM	0.520	0.270	0.000	0.000	0.998
Age, BMI + Op Extension ROM + Op Quad Strength	0.646	0.418	0.147	17.220	<0.001
Operated Limb KOS					
Age, BMI	0.255	0.065	0.065	2.430	0.095
Age, BMI + Op Extension ROM	0.255	0.065	0.000	0.002	0.967
Age, BMI + Op Extension ROM + Op Quad Strength	0.292	0.085	0.020	1.501	0.225

Table 9 Hierarchical Regression Models with Age, BMI, and Non-Operated Limb Clinical Impairments as Independent Variables and Functional Outcomes as Dependent Variables 1 year after TKA.

At 1yr	**R**	**R^2**	**ΔR^2**	**ΔF**	**p-value**
TUG					
Age, BMI	0.367	0.135	0.135	5.464	0.006
Age, BMI + Non-op Extension ROM	0.378	0.143	0.008	0.624	0.432
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.518	0.268	0.126	11.679	0.001
SCT					
Age, BMI	0.484	0.234	0.234	10.713	<0.001
Age, BMI + Non-op Extension ROM	0.487	0.237	0.003	0.237	0.628
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.627	0.394	0.157	17.554	<0.001
6MW					
Age, BMI	0.520	0.270	0.270	12.960	<0.001
Age, BMI + Non-op Extension ROM	0.524	0.274	0.004	0.405	0.527
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.634	0.403	0.128	14.579	<0.001
Operated Limb KOS					
Age, BMI	0.255	0.065	0.065	2.430	0.095
Age, BMI + Non-op Extension ROM	0.256	0.066	0.001	0.064	0.801
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.256	0.066	0.000	0.000	0.990

Table 10 Hierarchical Regression Models with Age, BMI, and Operated Limb Clinical Impairments as Independent Variables and Functional Outcomes as Dependent Variables 2 year after TKA.

At 2yrs	**R**	**R^2**	**ΔR^2**	**ΔF**	**p-value**
TUG					
Age, BMI	0.511	0.261	0.261	12.705	<0.001
Age, BMI + Op Extension ROM	0.523	0.274	0.013	1.236	0.270
Age, BMI + Op Extension ROM + Op Quad Strength	0.582	0.338	0.065	6.848	0.011
SCT					
Age, BMI	0.534	0.285	0.285	14.358	<0.001
Age, BMI + Op Extension ROM	0.562	0.315	0.030	3.148	0.080
Age, BMI + Op Extension ROM + Op Quad Strength	0.669	0.447	0.131	16.637	<0.001
6MW					
Age, BMI	0.578	0.334	0.334	18.017	<0.001
Age, BMI + Op Extension ROM	0.580	0.336	0.003	0.292	0.590
Age, BMI + Op Extension ROM + Op Quad Strength	0.676	0.458	0.121	15.650	<0.001
Operated Limb KOS					
Age, BMI	0.140	0.019	0.019	0.716	0.492
Age, BMI + Op Extension ROM	0.458	0.209	0.190	17.044	<0.001
Age, BMI + Op Extension ROM + Op Quad Strength	0.512	0.262	0.053	4.994	0.029

Table 11 Hierarchical Regression Models with Age, BMI, and Non-Operated Limb Clinical Impairments as Independent Variables and Functional Outcomes as Dependent Variables 2 year after TKA.

At 2 years	**R**	**R^2**	**ΔR^2**	**ΔF**	**p-value**
TUG					
Age, BMI	0.511	0.261	0.261	12.705	<0.001
Age, BMI + Non-op Extension ROM	0.512	0.263	0.002	0.171	0.681
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.610	0.372	0.110	12.235	0.001
SCT					
Age, BMI	0.534	0.285	0.285	14.358	<0.001
Age, BMI + Non-op Extension ROM	0.537	0.288	0.003	0.329	0.568
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.714	0.509	0.221	31.508	<0.001
6MW					
Age, BMI	0.578	0.334	0.334	18.017	<0.001
Age, BMI + Non-op Extension ROM	0.604	0.365	0.031	3.497	0.066
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.719	0.517	0.153	22.149	<0.001
Operated Limb KOS					
Age, BMI	0.140	0.019	0.019	0.716	0.492
Age, BMI + Non-op Extension ROM	0.217	0.047	0.028	2.072	0.154
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.290	0.084	0.037	2.804	0.099

Clinical Impairments Predicting Biomechanical Measures

Younger age and lower BMI were related to larger bilateral knee angles, excursions, and moments in all three TKA groups (Tables 12, 13). Regression analysis demonstrated that age and BMI were significant predictors of bilateral knee mechanics 1 and 2 years after surgery and non-operated knee mechanics 6 months after TKA (Tables 14-19). Greater knee extension ROM and stronger quadriceps were related to larger bilateral knee angles, excursions, and moments, with bilateral knee extension ROM and strength being stronger predictors of bilateral mechanics 6 months after TKA compared to the other surgical time points (Table 14-19).

Table 12 Pearson Correlations between operated limb clinical impairments and operated knee biomechanics 6 months, 1 year, and 2 years after TKA (*p<0.05, significant correlations between each variable)

		KA at IC	**KA at PKF**	**KA at PKE**	**KE at WA**	**KE at MS**	**KM at PKF**	**KM at PKE**
6 mo	**Age**	-0.251*	-0.132	-0.099	-0.167	0.031	-0.008	-0.091
	BMI	0.155	0.097	-0.037	0.080	-0.175	-0.054	0.273*
	Op Extension ROM	-0.400*	-0.360*	-0.496*	-0.049	-0.231*	0.176	0.312*
	Op Quad Strength	0.186	-0.146	0.097	0.477*	0.321*	0.346*	-0.156
1yr	**Age**	-0.060	-0.152	-0.033	0.161	0.172	0.171	-0.038
	BMI	-0.042	0.076	-0.111	-0.176	-0.263*	-0.223*	0.216*
	Op Extension ROM	-0.214*	-0.084	-0.171	-0.151	-0.117	-0.008	0.053
	Op Quad Strength	0.090	-0.094	0.007	0.269*	0.145	0.013	-0.191
2 yr	**Age**	-0.350*	-0.164	-0.290*	-0.267*	-0.166	0.092	0.336*
	BMI	0.190	0.167	-0.069	0.043	-0.258*	-0.314*	-0.026
	Op Extension ROM	-0.459*	-0.257*	-0.420*	-0.294*	-0.220*	0.090	0.274*
	Op Quad Strength	0.196*	-0.099	0.222*	0.403*	0.366*	0.175	-0.233*

Table 13 Pearson Correlations between non-operated limb clinical impairments and non-operated knee biomechanics 6 months, 1 year, and 2 years after TKA (*p<0.05, significant correlations between each variable)

		KA at IC	KA at PKF	KA at PKE	KE at WA	KE at MS	KM at PKF	KM at PKE
6 mo	**Age**	-0.124	0.002	-0.116	-0.148	-0.134	-0.120	-0.047
	BMI	0.298*	0.277*	0.171	-0.012	-0.146	-0.199*	0.032
	Non Extension ROM	-0.313*	-0.186	-0.471*	-0.124	-0.306*	0.059	0.319*
	Non Quad Strength	-0.072	-0.360*	-0.121	0.384*	0.303*	0.388*	0.040
1yr	**Age**	-0.275*	-0.107	-0.255*	-0.209*	-0.230*	-0.057	0.081
	BMI	0.071	0.174	-0.052	-0.179	-0.285*	-0.235*	0.095
	Non Extension ROM	-0.231*	0.084	-0.223*	-0.454*	-0.418*	-0.228*	0.147
	Non Quad Strength	0.298*	-0.014	0.290*	0.436*	0.427*	0.075	-0.375*
2 yr	**Age**	-0.242*	-0.074	-0.271*	-0.156	-0.169	-0.081	0.298*
	BMI	0.269*	0.228*	0.098	-0.013	-0.147	-0.227*	-0.182
	Non Extension ROM	-0.523*	-0.245*	-0.409*	-0.219*	-0.118	0.033	0.294*
	Non Quad Strength	0.208*	-0.192*	0.168	0.429*	0.351*	0.302*	-0.181

Table 14 Hierarchical Regression Models with Age, BMI, and Operated Limb Clinical Impairments as Independent Variables and Operated Knee Biomechanics as Dependent Variables 6 months after TKA.

6mo after TKA	**R**	**R^2**	**ΔR^2**	**ΔF**	**p-value**
KA at IC					
Age, BMI	0.255	0.065	0.065	2.368	0.101
Age, BMI + Op Extension ROM	0.451	0.204	0.139	11.654	0.001
Age, BMI + Op Extension ROM + Op Quad Strength	0.469	0.220	0.016	1.385	0.243
KA at PKF					
Age, BMI	0.138	0.019	0.019	0.661	0.519
Age, BMI + Op Extension ROM	0.381	0.145	0.126	9.854	0.003
Age, BMI + Op Extension ROM + Op Quad Strength	0.433	0.188	0.043	3.484	0.066
KA at PKE					
Age, BMI	0.136	0.018	0.018	0.640	0.530
Age, BMI + Op Extension ROM	0.496	0.246	0.228	20.247	<0.001
Age, BMI + Op Extension ROM + Op Quad Strength	0.496	0.246	0.000	0.000	0.984
KE at WA					
Age, BMI	0.167	0.028	0.028	0.976	0.382
Age, BMI + Op Extension ROM	0.168	0.028	0.000	0.018	0.893
Age, BMI + Op Extension ROM + Op Quad Strength	0.511	0.261	0.233	20.788	<0.001
KE at MS					
Age, BMI	0.184	0.034	0.034	1.194	0.309
Age, BMI + Op Extension ROM	0.280	0.078	0.044	3.231	0.077

Table 14 continued

Age, BMI + Op Extension ROM + Op Quad Strength	0.383	0.147	0.068	5.270	0.025
KM at PKF					
Age, BMI	0.065	0.004	0.004	0.146	0.864
Age, BMI + Op Extension ROM	0.208	0.043	0.039	2.737	0.103
Age, BMI + Op Extension ROM + Op Quad Strength	0.429	0.184	0.140	11.343	0.001
KM at PKE					
Age, BMI	0.276	0.076	0.076	2.798	0.068
Age, BMI + Op Extension ROM	0.402	0.162	0.086	6.833	0.011
Age, BMI + Op Extension ROM + Op Quad Strength	0.407	0.165	0.004	0.298	0.587

Table 15 Hierarchical Regression Models with Age, BMI, and Non-Operated Limb Clinical Impairments as Independent Variables and Non-Operated Knee Biomechanics as Dependent Variables 6 months after TKA.

6mo after TKA	R	R^2	ΔR^2	ΔF	p-value
KA at IC					
Age, BMI	0.298	0.089	0.089	3.319	0.042
Age, BMI + Non-op Extension ROM	0.474	0.225	0.136	11.730	0.001
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.474	0.225	0.000	0.036	0.850
KA at PKF					
Age, BMI	0.314	0.099	0.099	3.717	0.029
Age, BMI + Non-op Extension ROM	0.395	0.156	0.058	4.571	0.036
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.472	0.223	0.066	5.641	0.020
KA at PKE					
Age, BMI	0.176	0.031	0.031	1.089	0.342
Age, BMI + Non-op Extension ROM	0.536	0.287	0.256	24.079	<0.001
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.542	0.293	0.006	0.583	0.448
KE at WA					
Age, BMI	0.173	0.030	0.030	1.051	0.355
Age, BMI + Non-op Extension ROM	0.210	0.044	0.014	1.002	0.320
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.417	0.174	0.130	10.346	0.002
KE at MS					
Age, BMI	0.270	0.073	0.073	2.676	0.076
Age, BMI + Non-op Extension ROM	0.389	0.151	0.078	6.183	0.015

Table 15 continued

Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.450	0.203	0.051	4.238	0.043
KM at PKF					
Age, BMI	0.311	0.097	0.097	3.650	0.031
Age, BMI + Non-op Extension ROM	0.327	0.107	0.010	0.753	0.389
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.430	0.185	0.078	6.297	0.015
KM at PKE					
Age, BMI	0.077	0.006	0.006	0.203	0.816
Age, BMI + Non-op Extension ROM	0.340	0.115	0.109	8.284	0.005
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.340	0.115	0.000	0.012	0.912

Table 16 Hierarchical Regression Models with Age, BMI, and Operated Limb Clinical Impairments as Independent Variables and Operated Knee Biomechanics as Dependent Variables 1 year after TKA.

1yr after TKA	**R**	**R^2**	**ΔR^2**	**ΔF**	**p-value**
KA at IC					
Age, BMI	0.077	0.006	0.006	0.207	0.813
Age, BMI + Op Extension ROM	0.218	0.048	0.042	3.015	0.087
Age, BMI + Op Extension ROM + Op Quad Strength	0.231	0.053	0.006	0.420	0.519
KA at PKF					
Age, BMI	0.164	0.027	0.027	0.968	0.385
Age, BMI + Op Extension ROM	0.181	0.033	0.006	0.414	0.522
Age, BMI + Op Extension ROM + Op Quad Strength	0.220	0.049	0.016	1.130	0.291
KA at PKE					
Age, BMI	0.119	0.014	0.014	0.503	0.607
Age, BMI + Op Extension ROM	0.195	0.038	0.024	1.714	0.195
Age, BMI + Op Extension ROM + Op Quad Strength	0.197	0.039	0.001	0.040	0.843
KE at WA					
Age, BMI	0.228	0.052	0.052	1.918	0.155
Age, BMI + Op Extension ROM	0.273	0.074	0.022	1.677	0.200
Age, BMI + Op Extension ROM + Op Quad Strength	0.406	0.165	0.090	7.367	0.008
KE at MS					
Age, BMI	0.302	0.091	0.091	3.504	0.035
Age, BMI + Op Extension ROM	0.320	0.102	0.011	0.861	0.357

Table 16 continued

Age, BMI + Op Extension ROM + Op Quad Strength	0.352	0.124	0.022	1.696	0.197
KM at PKF					
Age, BMI	0.269	0.072	0.072	2.726	0.072
Age, BMI + Op Extension ROM	0.269	0.072	0.000	0.000	0.998
Age, BMI + Op Extension ROM + Op Quad Strength	0.269	0.072	0.000	0.009	0.924
KM at PKE					
Age, BMI	0.217	0.047	0.047	1.728	0.185
Age, BMI + Op Extension ROM	0.219	0.048	0.001	0.068	0.795
Age, BMI + Op Extension ROM + Op Quad Strength	0.274	0.075	0.027	1.972	0.165

Table 17 Hierarchical Regression Models with Age, BMI, and Non-Operated Limb Clinical Impairments as Independent Variables and Non-Operated Knee Biomechanics as Dependent Variables 1 year after TKA.

1yr after TKA	**R**	**R^2**	**ΔR^2**	**ΔF**	**p-value**
KA at IC					
Age, BMI	0.279	0.078	0.078	2.945	0.059
Age, BMI + Non-op Extension ROM	0.313	0.098	0.020	1.534	0.220
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.382	0.146	0.048	3.822	0.055
KA at PKF					
Age, BMI	0.196	0.039	0.039	1.405	0.252
Age, BMI + Non-op Extension ROM	0.227	0.051	0.013	0.936	0.337
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.229	0.052	0.001	0.058	0.810
KA at PKE					
Age, BMI	0.266	0.071	0.071	2.670	0.076
Age, BMI + Non-op Extension ROM	0.293	0.086	0.015	1.131	0.291
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.354	0.125	0.039	3.066	0.084
KE at WA					
Age, BMI	0.289	0.084	0.084	3.197	0.047
Age, BMI + Non-op Extension ROM	0.475	0.226	0.142	12.675	0.001
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.590	0.348	0.122	12.675	0.001
KE at MS					
Age, BMI	0.385	0.148	0.148	6.082	0.004
Age, BMI + Non-op Extension ROM	0.495	0.245	0.097	8.832	0.004

Table 17 continued

Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.587	0.344	0.099	10.317	0.002
KM at PKF					
Age, BMI	0.248	0.062	0.062	2.301	0.108
Age, BMI + Non-op Extension ROM	0.311	0.097	0.035	2.685	0.106
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.312	0.097	0.000	0.071	0.897
KM at PKE					
Age, BMI	0.131	0.017	0.017	0.615	0.544
Age, BMI + Non-op Extension ROM	0.172	0.029	0.012	0.869	0.354
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.396	0.156	0.127	10.239	0.002

Table 18 Hierarchical Regression Models with Age, BMI, and Operated Limb Clinical Impairments as Independent Variables and Operated Knee Biomechanics as Dependent Variables 2 years after TKA.

2 years after TKA	**R**	**R^2**	**ΔR^2**	**ΔF**	**p-value**
KA at IC					
Age, BMI	0.388	0.150	0.150*	6.367	0.003
Age, BMI + Op Extension ROM	0.560	0.313	0.163*	16.850	<0.001
Age, BMI + Op Extension ROM + Op Quad Strength	0.574	0.329	0.016	1.686	0.198
KA at PKF					
Age, BMI	0.226	0.051	0.051	1.938	0.151
Age, BMI + Op Extension ROM	0.333	0.111	0.060	4.792	0.032
Age, BMI + Op Extension ROM + Op Quad Strength	0.358	0.128	0.017	1.355	0.248
KA at PKE					
Age, BMI	0.303	0.092	0.092	3.651	0.031
Age, BMI + Op Extension ROM	0.458	0.210	0.118	10.598	0.002
Age, BMI + Op Extension ROM + Op Quad Strength	0.469	0.220	0.010	0.896	0.347
KE at WA					
Age, BMI	0.268	0.072	0.072	2.781	0.069
Age, BMI + Op Extension ROM	0.355	0.126	0.055	4.433	0.039
Age, BMI + Op Extension ROM + Op Quad Strength	0.497	0.247	0.121	11.239	0.001
KE at MS					
Age, BMI	0.317	0.100	0.100	4.017	0.022
Age, BMI + Op Extension ROM	0.347	0.121	0.020	1.640	0.205

Table 18 continued

Age, BMI + Op Extension ROM + Op Quad Strength	0.431	0.186	0.065	5.604	0.021
KM at PKF					
Age, BMI	0.321	0.103	0.103	4.145	0.020
Age, BMI + Op Extension ROM	0.340	0.116	0.013	1.015	0.317
Age, BMI + Op Extension ROM + Op Quad Strength	0.366	0.134	0.018	1.446	0.233
KM at PKE					
Age, BMI	0.336	0.113	0.113	4.580	0.013
Age, BMI + Op Extension ROM	0.386	0.149	0.036	2.982	0.089
Age, BMI + Op Extension ROM + Op Quad Strength	0.409	0.167	0.019	1.574	0.214

Table 19 Hierarchical Regression Models with Age, BMI, and Non-Operated Limb Clinical Impairments as Independent Variables and Non-Operated Knee Biomechanics as Dependent Variables 2 years after TKA.

2 years after TKA	**R**	**R^2**	**ΔR^2**	**ΔF**	**p-value**
KA at IC					
Age, BMI	0.350	0.122	0.122	5.024	0.009
Age, BMI + Non-op Extension ROM	0.587	0.344	0.222	24.005	<0.001
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.597	0.357	0.013	1.392	0.242
KA at PKF					
Age, BMI	0.235	0.055	0.055	2.111	0.129
Age, BMI + Non-op Extension ROM	0.323	0.104	0.049	3.862	0.053
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.395	0.156	0.052	4.326	0.041
KA at PKE					
Age, BMI	0.282	0.080	0.080	3.117	0.050
Age, BMI + Non-op Extension ROM	0.459	0.211	0.131	11.815	0.001
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.461	0.213	0.002	0.153	0.697
KE at WA					
Age, BMI	0.158	0.025	0.025	0.922	0.403
Age, BMI + Non-op Extension ROM	0.252	0.064	0.039	2.937	0.091
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.453	0.205	0.141	12.430	0.001
KE at MS					
Age, BMI	0.232	0.054	0.054	2.054	0.136
Age, BMI + Non-op Extension ROM	0.253	0.064	0.010	0.766	0.385

Table 19 continued

Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.373	0.139	0.075	6.101	0.016
KM at PKF					
Age, BMI	0.247	0.061	0.061	2.339	0.104
Age, BMI + Non-op Extension ROM	0.249	0.062	0.001	0.077	0.782
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.359	0.129	0.067	5.379	0.023
KM at PKE					
Age, BMI	0.339	0.115	0.115	4.664	0.012
Age, BMI + Non-op Extension ROM	0.412	0.170	0.055	4.705	0.033
Age, BMI + Non-op Extension ROM + Non-op Quad Strength	0.421	0.177	0.007	0.610	0.437

Biomechanical Measures Predicting Functional Outcomes

Better functional outcomes were related to larger bilateral knee angles, excursions, and moments in all three TKA groups (Tables 20, 21). Beyond the influence of age, BMI, extension ROM, and quadriceps strength, bilateral flexion excursion accounted for 5.7-6.2% of opKOS score 6mo after TKA (Tables 22, 23). Non-operated knee flexion excursion accounted for 5.5% of opKOS score 1 year after TKA. Operated knee extension excursion accounted for 4.9% of opKOS score, while peak flexion moment accounted for 7.4% of opKOS score 2 years after TKA. Bilateral biomechanics were not predictive of TUG beyond the influence of age, BMI, and bilateral extension ROM and strength in any of the surgical groups (Tables 24-25). Non-operated knee mechanics were not predictive of SCT (Table 27). However, better peak operated knee extension moment contributes 5.6% to the prediction of improved SCT performance 1 year after surgery (Table 26). Operated knee extension mechanics explained 4.2-5.3% of the variance of 6MW 1 year after TKA (Table 28), while non-operated limb mechanics predicted 6MW 6 months and 2 years after TKA, with more predictive ability at the 2 year time point (Table 29).

Table 20 Pearson Correlations between operated knee biomechanics and functional outcomes 6 months, 1 year, and 2 years after TKA (*p<0.05, significant correlations between each variable)

		KA at IC	KA at PKF	KA at PKE	KE at WA	KE at MS	KM at PKF	KM at PKE
6mo	**(op) KOS**	-0.025	0.063	0.043	-0.126	-0.021	-0.043	-0.099
	TUG	-0.210*	-0.057	-0.174	-0.216*	-0.168	-0.107	0.166
	SCT	-0.359*	-0.070	-0.241*	-0.409*	-0.245*	-0.171	0.195
	6MW	0.114	-0.134	0.075	0.356*	0.274*	0.312*	-0.072
1yr	**(op) KOS**	-0.039	-0.204*	-0.106	0.271*	0.145	0.195*	-0.117
	TUG	-0.101	0.004	-0.054	-0.140	-0.081	-0.090	0.214*
	SCT	-0.167	0.001	-0.135	-0.222*	-0.190	-0.038	0.360*
	6MW	0.293*	0.130	0.266*	0.183	0.184	0.026	-0.326*
2yr	**(op) KOS**	0.118	-0.110	0.212*	0.308*	0.365*	0.266*	-0.205*
	TUG	-0.262*	-0.005	-0.208*	-0.356*	-0.239*	-0.090	0.314*
	SCT	-0.272*	0.044	-0.272*	-0.434*	-0.366*	-0.156	0.349*
	6MW	0.226*	-0.040	0.256*	0.366*	0.343*	0.230*	-0.256*

Table 21 Pearson Correlations between non-operated knee biomechanics and functional outcomes 6 months, 1 year, and 2 years after TKA (*p<0.05, significant correlations between each variable)

		KA at IC	KA at PKF	KA at PKE	KE at WA	KE at MS	KM at PKF	KM at PKE
6mo	**(op) KOS**	-0.243*	-0.058	-0.187	-0.209*	-0.141	-0.023	0.161
	TUG	0.080	0.190	0.054	-0.154	-0.172	-0.183	-0.080
	SCT	-0.034	0.218*	0.028	-0.324*	-0.235*	-0.307*	-0.046
	6MW	-0.168	-0.396*	-0.130	0.319*	0.337*	0.468*	0.123
1yr	**(op) KOS**	-0.108	-0.231*	-0.085	0.218*	0.159	0.255*	0.110
	TUG	-0.220*	0.011	-0.262*	-0.322*	-0.384*	-0.277*	0.167
	SCT	-0.239*	0.008	-0.283*	-0.344*	-0.409*	-0.270*	0.190
	6MW	0.315*	0.105	0.353*	0.267*	0.371*	0.210*	-0.239*
2yr	**(op) KOS**	0.032	-0.029	0.149	0.072	0.166	0.219*	-0.086
	TUG	-0.274*	0.042	-0.248*	-0.322*	-0.269*	-0.255*	0.289*
	SCT	-0.275*	0.084	-0.284*	-0.367*	-0.344*	-0.294*	0.279*
	6MW	0.272*	-0.156	0.357*	0.443*	0.485*	0.369*	-0.319*

Table 22 Hierarchical Regression Models with Age, BMI, Operated Limb Clinical Impairments, and Operated Knee Biomechanics as Independent Variables and KOS score as the Dependent Variable 6 months, 1 year, and 2 years after TKA.

KOS, 6mo after TKA	**R**	**R^2**	**ΔR^2**	**ΔF**	**p-value**
Age, BMI	0.124	0.015	0.015	0.530	0.591
Age, BMI + Op Extension ROM, Op Quad Strength	0.296	0.088	0.072	2.622	0.080
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at IC**	0.324	0.105	0.017	1.227	0.272
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at PKF**	0.298	0.089	0.001	0.072	0.790
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at PKE**	0.307	0.094	0.006	0.443	0.508
Age, BMI + Op Extension ROM, Op Quad Strength + **KE at WA**	0.380	0.145	0.057	4.325	0.041
Age, BMI + Op Extension ROM, Op Quad Strength + **KE at MS**	0.329	0.108	0.020	1.471	0.230
Age, BMI + Op Extension ROM, Op Quad Strength + **KM at PKF**	0.306	0.094	0.006	0.426	0.516
Age, BMI + Op Extension ROM, Op Quad Strength + **KM at PKE**	0.296	0.008	0.000	0.004	0.950
KOS, 1yr after TKA					
Age, BMI	0.255	0.065	0.065	2.430	0.095
Age, BMI + Op Extension ROM, Op Quad Strength	0.292	0.085	0.020	0.751	0.476
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at IC**	0.297	0.088	0.003	0.229	0.634
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at PKF**	0.332	0.110	0.025	1.865	0.177
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at PKE**	0.318	0.101	0.016	1.205	0.276

Table 22 continued

Age, BMI + Op Extension ROM, Op Quad Strength + **KE at WA**	0.347	0.120	0.035	2.672	0.107
Age, BMI + Op Extension ROM, Op Quad Strength + **KE at MS**	0.296	0.088	0.003	0.185	0.668
Age, BMI + Op Extension ROM, Op Quad Strength + **KM at PKF**	0.320	0.102	0.017	1.283	0.261
Age, BMI + Op Extension ROM, Op Quad Strength + **KM at PKE**	0.295	0.087	0.002	0.136	0.714
KOS, 2yr after TKA					
Age, BMI	0.140	0.019	0.019	0.716	0.492
Age, BMI + Op Extension ROM, Op Quad Strength	0.512	0.262	0.242	11.498	<0.001
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at IC**	0.524	0.275	0.013	1.219	0.273
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at PKF**	0.547	0.299	0.037	3.646	0.060
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at PKE**	0.512	0.262	0.000	0.007	0.936
Age, BMI + Op Extension ROM, Op Quad Strength + **KE at WA**	0.527	0.278	0.016	1.533	0.220
Age, BMI + Op Extension ROM, Op Quad Strength + **KE at MS**	0.558	0.311	0.049	4.904	0.030
Age, BMI + Op Extension ROM, Op Quad Strength + **KM at PKF**	0.580	0.336	0.074	7.719	0.007
Age, BMI + Op Extension ROM, Op Quad Strength + **KM at PKE**	0.517	0.267	0.005	0.515	0.475

Table 23 Hierarchical Regression Models with Age, BMI, Non-Operated Limb Clinical Impairments, and Non-Operated Knee Biomechanics as Independent Variables and KOS score as the Dependent Variable 6 months, 1 year, and 2 years after TKA.

KOS, 6mo after TKA	**R**	**R^2**	**ΔR^2**	**ΔF**	**p-value**
Age, BMI	0.124	0.015	0.015	0.530	0.591
Age, BMI + Non-op Extension ROM, Non-op Quad Strength	0.153	0.024	0.008	0.276	0.760
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at IC**	0.256	0.066	0.042	2.937	0.091
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at PKF**	0.154	0.024	0.000	0.010	0.919
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at PKE**	0.215	0.046	0.023	1.549	0.218
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KE at WA**	0.293	0.086	0.062	4.411	0.040
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KE at MS**	0.233	0.054	0.031	2.129	0.149
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KM at PKF**	0.175	0.031	0.007	0.488	0.487
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KFM at PKE**	0.207	0.043	0.019	1.310	0.257
KOS, 1yr after TKA					
Age, BMI	0.255	0.065	0.065	2.430	0.095
Age, BMI + Non-op Extension ROM, Non-op Quad Strength	0.256	0.066	0.001	0.032	0.969
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at IC**	0.267	0.071	0.005	0.390	0.535
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at PKF**	0.315	0.099	0.033	2.463	0.121
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at PKE**	0.268	0.072	0.006	0.454	0.503

Table 23 continued

Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KE at WA**	0.347	0.120	0.055	4.157	0.045
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KE at MS**	0.290	0.084	0.019	1.360	0.248
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KM at PKF**	0.334	0.111	0.046	3.446	0.068
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KM at PKE**	0.291	0.085	0.019	1.397	0.241
KOS, 2yr after TKA					
Age, BMI	0.140	0.019	0.019	0.716	0.492
Age, BMI + Non-op Extension ROM, Non-op Quad Strength	0.290	0.084	0.064	2.464	0.092
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at IC**	0.298	0.089	0.005	0.367	0.547
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at PKF**	0.290	0.084	0.000	0.000	0.992
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at PKE**	0.301	0.090	0.006	0.484	0.489
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KE at WA**	0.294	0.087	0.003	0.205	0.652
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KE at MS**	0.298	0.089	0.005	0.376	0.542
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KM at PKF**	0.327	0.107	0.023	1.752	0.190
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KM at PKE**	0.292	0.085	0.001	0.076	0.784

Table 24 Hierarchical Regression Models with Age, BMI, Operated Limb Clinical Impairments, and Operated Knee Biomechanics as Independent Variables and TUG time as the Dependent Variable 6 months, 1 year, and 2 years after TKA.

TUG, 6mo after TKA	**R**	**R^2**	**ΔR^2**	**ΔF**	**p-value**
Age, BMI	0.495	0.245	0.245	11.013	<0.001
Age, BMI + Op Extension ROM, Op Quad Strength	0.622	0.387	0.142	7.661	0.001
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at IC**	0.622	0.387	0.000	0.024	0.878
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at PKF**	0.623	0.388	0.001	0.147	0.702
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at PKE**	0.624	0.390	0.003	0.301	0.585
Age, BMI + Op Extension ROM, Op Quad Strength + **KE at WA**	0.623	0.388	0.001	0.127	0.723
Age, BMI + Op Extension ROM, Op Quad Strength + **KE at MS**	0.623	0.388	0.001	0.057	0.813
Age, BMI + Op Extension ROM, Op Quad Strength + **KM at PKF**	0.622	0.387	0.000	0.034	0.854
Age, BMI + Op Extension ROM, Op Quad Strength + **KM at PKE**	0.629	0.396	0.009	0.983	0.325
TUG, 1yr after TKA					
Age, BMI	0.367	0.135	0.135	5.464	0.006
Age, BMI + Op Extension ROM, Op Quad Strength	0.534	0.285	0.150	7.155	0.002
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at IC**	0.535	0.287	0.001	0.116	0.735
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at PKF**	0.534	0.285	0.000	0.003	0.959
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at PKE**	0.535	0.286	0.001	0.054	0.817

Table 24 continued

Age, BMI + Op Extension ROM, Op Quad Strength + **KE at WA**	0.536	0.287	0.002	0.155	0.695
Age, BMI + Op Extension ROM, Op Quad Strength + **KE at MS**	0.535	0.286	0.001	0.068	0.794
Age, BMI + Op Extension ROM, Op Quad Strength + **KM at PKF**	0.544	0.296	0.011	1.008	0.319
Age, BMI + Op Extension ROM, Op Quad Strength + **KM at PKE**	0.549	0.301	0.016	1.505	0.224
TUG, 2yr after TKA					
Age, BMI	0.511	0.261	0.261	12.705	<0.001
Age, BMI + Op Extension ROM, Op Quad Strength	0.582	0.338	0.077	4.093	0.021
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at IC**	0.582	0.339	0.000	0.033	0.857
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at PKF**	0.586	0.343	0.005	0.515	0.475
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at PKE**	0.582	0.338	0.000	0.009	0.927
Age, BMI + Op Extension ROM, Op Quad Strength + **KE at WA**	0.594	0.353	0.015	1.612	0.208
Age, BMI + Op Extension ROM, Op Quad Strength + **KE at MS**	0.585	0.343	0.004	0.466	0.497
Age, BMI + Op Extension ROM, Op Quad Strength + **KM at PKF**	0.591	0.350	0.011	1.205	0.276
Age, BMI + Op Extension ROM, Op Quad Strength + **KM at PKE**	0.589	0.347	0.009	0.976	0.327

Table 25 Hierarchical Regression Models with Age, BMI, Non-Operated Limb Clinical Impairments, and Non-Operated Knee Biomechanics as Independent Variables and TUG time score as the Dependent Variable 6 months, 1 year, and 2 years after TKA.

TUG, 6mo after TKA	**R**	**R^2**	**ΔR^2**	**ΔF**	**p-value**
Age, BMI	0.495	0.245	0.245	11.013	<0.001
Age, BMI + Non-op Extension ROM, Non-op Quad Strength	0.603	0.364	0.119	6.182	0.003
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at IC**	0.610	0.372	0.008	0.855	0.358
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at PKF**	0.604	0.365	0.001	0.117	0.733
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at PKE**	0.606	0.367	0.003	0.318	0.575
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KE at WA**	0.606	0.367	0.004	0.376	0.542
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KE at MS**	0.603	0.364	0.000	0.035	0.853
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KM at PKF**	0.604	0.365	0.001	0.118	0.732
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KM at PKE**	0.605	0.367	0.003	0.227	0.601
TUG, 1yr after TKA					
Age, BMI	0.367	0.135	0.135	5.464	0.006
Age, BMI + Non-op Extension ROM, Non-op Quad Strength	0.518	0.268	0.133	6.200	0.003
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at IC**	0.521	0.272	0.003	0.300	0.586
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at PKF**	0.518	0.268	0.000	0.005	0.942
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at PKE**	0.526	0.277	0.009	0.796	0.375

Table 25 continued

Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KE at WA**	0.524	0.274	0.006	0.530	0.469
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KE at MS**	0.537	0.288	0.020	1.850	0.178
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KM at PKF**	0.556	0.309	0.040	3.897	0.053
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KM at PKE**	0.518	0.269	0.000	0.023	0.880
TUG, 2yr after TKA					
Age, BMI	0.511	0.261	0.261	12.705	<0.001
Age, BMI + Non-op Extension ROM, Non-op Quad Strength	0.610	0.372	0.111	6.216	0.003
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at IC**	0.637	0.406	0.033	3.883	0.053
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at PKF**	0.610	0.373	0.000	0.034	0.854
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at PKE**	0.624	0.389	0.017	1.923	0.170
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KE at WA**	0.626	0.392	0.020	2.241	0.139
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KE at MS**	0.618	0.381	0.009	1.011	0.318
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KM at PKF**	0.623	0.388	0.015	1.716	0.195
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KM at PKE**	0.626	0.392	0.020	2.243	0.139

Table 26 Hierarchical Regression Models with Age, BMI, Operated Limb Clinical Impairments, and Operated Knee Biomechanics as Independent Variables and SCT time as the Dependent Variable 6 months, 1 year, and 2 years after TKA.

SCT, 6mo after TKA	**R**	**R^2**	**ΔR^2**	**ΔF**	**p-value**
Age, BMI	0.466	0.217	0.217	9.416	<0.001
Age, BMI + Op Extension ROM, Op Quad Strength	0.680	0.462	0.245	15.038	<0.001
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at IC**	0.691	0.478	0.016	1.966	0.166
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at PKF**	0.680	0.463	0.001	0.087	0.769
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at PKE**	0.685	0.469	0.007	0.801	0.374
Age, BMI + Op Extension ROM, Op Quad Strength + **KE at WA**	0.695	0.483	0.021	2.575	0.113
Age, BMI + Op Extension ROM, Op Quad Strength + **KE at MS**	0.684	0.467	0.005	0.637	0.428
Age, BMI + Op Extension ROM, Op Quad Strength + **KM at PKF**	0.681	0.464	0.002	0.258	0.613
Age, BMI + Op Extension ROM, Op Quad Strength + **KM at PKE**	0.688	0.474	0.012	1.422	0.237
SCT, 1yr after TKA					
Age, BMI	0.484	0.234	0.234	10.713	<0.001
Age, BMI + Op Extension ROM, Op Quad Strength	0.684	0.468	0.233	14.914	<0.001
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at IC**	0.691	0.478	0.010	1.296	0.259
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at PKF**	0.684	0.469	0.001	0.094	0.761
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at PKE**	0.692	0.479	0.011	1.389	0.243

Table 26 continued

Age, BMI + Op Extension ROM, Op Quad Strength + **KE at WA**	0.691	0.477	0.009	1.179	0.282
Age, BMI + Op Extension ROM, Op Quad Strength + **KE at MS**	0.693	0.480	0.012	1.586	0.212
Age, BMI + Op Extension ROM, Op Quad Strength + **KM at PKF**	0.685	0.469	0.001	0.106	0.745
Age, BMI + Op Extension ROM, Op Quad Strength + **KM at PKE**	0.724	0.524	0.056	7.872	0.007
SCT, 2yr after TKA					
Age, BMI	0.534	0.285	0.285	14.358	<0.001
Age, BMI + Op Extension ROM, Op Quad Strength	0.669	0.447	0.162	10.239	<0.001
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at IC**	0.669	0.447	0.000	0.042	0.838
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at PKF**	0.679	0.461	0.015	1.865	0.177
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at PKE**	0.669	0.447	0.000	0.039	0.843
Age, BMI + Op Extension ROM, Op Quad Strength + **KE at WA**	0.685	0.469	0.022	2.847	0.096
Age, BMI + Op Extension ROM, Op Quad Strength + **KE at MS**	0.686	0.470	0.023	3.054	0.085
Age, BMI + Op Extension ROM, Op Quad Strength + **KM at PKF**	0.687	0.472	0.026	3.337	0.072
Age, BMI + Op Extension ROM, Op Quad Strength + **KM at PKE**	0.676	0.457	0.010	1.223	0.273

Table 27 Hierarchical Regression Models with Age, BMI, Non-Operated Limb Clinical Impairments, and Non-Operated Knee Biomechanics as Independent Variables and SCT time as the Dependent Variable 6 months, 1 year, and 2 years after TKA.

SCT, 6mo after TKA	**R**	**R^2**	**ΔR^2**	**ΔF**	**p-value**
Age, BMI	0.466	0.217	0.217	9.416	<0.001
Age, BMI + Non-op Extension ROM, Non-op Quad Strength	0.662	0.438	0.221	12.985	<0.001
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at IC**	0.662	0.439	0.001	0.069	0.793
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at PKF**	0.663	0.440	0.002	0.251	0.618
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at PKE**	0.662	0.438	0.000	0.012	0.912
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KE at WA**	0.667	0.446	0.007	0.879	0.352
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KE at MS**	0.663	0.440	0.002	0.237	0.628
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KM at PKF**	0.667	0.445	0.007	0.839	0.363
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KM at PKE**	0.662	0.438	0.000	0.026	0.872
SCT, 1yr after TKA					
Age, BMI	0.484	0.234	0.234	10.713	<0.001
Age, BMI + Non-op Extension ROM, Non-op Quad Strength	0.627	0.394	0.159	8.924	<0.001
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at IC**	0.631	0.398	0.004	0.463	0.499
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at PKF**	0.628	0.394	0.001	0.060	0.808
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at PKE**	0.633	0.401	0.007	0.830	0.365

Table 27 continued

Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KE at WA**	0.630	0.397	0.003	0.367	0.546
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KE at MS**	0.636	0.405	0.011	1.284	0.261
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KM at PKF**	0.649	0.421	0.027	3.142	0.081
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KM at PKE**	0.628	0.394	0.000	0.049	0.825
SCT, 2yr after TKA					
Age, BMI	0.534	0.285	0.285	14.358	<0.001
Age, BMI + Non-op Extension ROM, Non-op Quad Strength	0.714	0.509	0.224	15.989	<0.001
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at IC**	0.722	0.522	0.012	1.789	0.185
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at PKF**	0.714	0.509	0.000	0.014	0.906
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at PKE**	0.724	0.524	0.015	2.125	0.149
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KE at WA**	0.721	0.521	0.011	1.614	0.208
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KE at MS**	0.723	0.523	0.013	1.922	0.170
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KM at PKF**	0.724	0.524	0.014	2.064	0.155
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KM at PKE**	0.719	0.518	0.008	1.193	0.278

Table 28 Hierarchical Regression Models with Age, BMI, Operated Limb Clinical Impairments, and Operated Knee Biomechanics as Independent Variables and 6MW time as the Dependent Variable 6 months, 1 year, and 2 years after TKA.

6MW, 6mo after TKA	**R**	**R^2**	**ΔR^2**	**ΔF**	**p-value**
Age, BMI	0.467	0.218	0.218	9.502	<0.001
Age, BMI + Op Extension ROM, Op Quad Strength	0.638	0.407	0.189	10.498	<0.001
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at IC**	0.638	0.407	0.000	0.007	0.934
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at PKF**	0.644	0.414	0.007	0.794	0.376
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at PKE**	0.638	0.407	0.000	0.000	0.988
Age, BMI + Op Extension ROM, Op Quad Strength + **KE at WA**	0.649	0.421	0.014	1.535	0.220
Age, BMI + Op Extension ROM, Op Quad Strength + **KE at MS**	0.646	0.418	0.011	1.194	0.279
Age, BMI + Op Extension ROM, Op Quad Strength + **KM at PKF**	0.654	0.427	0.020	2.312	0.133
Age, BMI + Op Extension ROM, Op Quad Strength + **KM at PKE**	0.639	0.408	0.001	0.156	0.694
6MW, 1yr after TKA					
Age, BMI	0.520	0.270	0.270	12.960	<0.001
Age, BMI + Op Extension ROM, Op Quad Strength	0.646	0.418	0.147	8.610	<0.001
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at IC**	0.686	0.471	0.053	6.744	0.012
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at PKF**	0.664	0.441	0.023	2.748	0.102
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at PKE**	0.684	0.468	0.050	6.328	0.014

Table 28 continued

Age, BMI + Op Extension ROM, Op Quad Strength + **KE at WA**	0.650	0.423	0.005	0.566	0.454
Age, BMI + Op Extension ROM, Op Quad Strength + **KE at MS**	0.654	0.428	0.010	1.179	0.281
Age, BMI + Op Extension ROM, Op Quad Strength + **KM at PKF**	0.646	0.418	0.000	0.001	0.973
Age, BMI + Op Extension ROM, Op Quad Strength + **KM at PKE**	0.678	0.459	0.042	5.147	0.027
6MW, 2yr after TKA					
Age, BMI	0.578	0.334	0.334	18.017	<0.001
Age, BMI + Op Extension ROM, Op Quad Strength	0.676	0.458	0.124	8.001	0.001
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at IC**	0.678	0.459	0.002	0.203	0.654
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at PKF**	0.678	0.460	0.002	0.305	0.582
Age, BMI + Op Extension ROM, Op Quad Strength + **KA at PKE**	0.677	0.459	0.001	0.168	0.683
Age, BMI + Op Extension ROM, Op Quad Strength + **KE at WA**	0.687	0.472	0.015	1.936	0.169
Age, BMI + Op Extension ROM, Op Quad Strength + **KE at MS**	0.683	0.467	0.009	1.179	0.281
Age, BMI + Op Extension ROM, Op Quad Strength + **KM at PKF**	0.695	0.483	0.025	3.330	0.072
Age, BMI + Op Extension ROM, Op Quad Strength + **KM at PKE**	0.677	0.459	0.001	0.139	0.711

Table 29 Hierarchical Regression Models with Age, BMI, Non-Operated Limb Clinical Impairments, and Non-Operated Knee Biomechanics as Independent Variables and 6MW time as the Dependent Variable 6 months, 1 year, and 2 years after TKA.

6MW, 6mo after TKA	**R**	**R^2**	**ΔR^2**	**ΔF**	**p-value**
Age, BMI	0.467	0.218	0.218	9.502	<0.001
Age, BMI + Non-op Extension ROM, Non-op Quad Strength	0.703	0.494	0.275	17.928	<0.001
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at IC**	0.705	0.497	0.004	0.503	0.481
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at PKF**	0.714	0.510	0.016	2.142	0.148
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at PKE**	0.703	0.494	0.000	0.003	0.958
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KE at WA**	0.708	0.502	0.008	1.050	0.309
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KE at MS**	0.720	0.519	0.025	3.404	0.070
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KM at PKF**	0.728	0.530	0.036	4.988	0.029
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KM at PKE**	0.704	0.496	0.002	0.256	0.615
6MW, 1yr after TKA					
Age, BMI	0.520	0.270	0.270	12.960	<0.001
Age, BMI + Non-op Extension ROM, Non-op Quad Strength	0.634	0.403	0.132	7.532	0.001
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at IC**	0.654	0.428	0.025	2.944	0.091
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at PKF**	0.652	0.425	0.023	2.671	0.107
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at PKE**	0.656	0.430	0.027	3.200	0.078

Table 29 continued

Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KE at WA**	0.636	0.404	0.002	0.178	0.674
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KE at MS**	0.636	0.405	0.002	0.265	0.609
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KM at PKF**	0.640	0.410	0.007	0.818	0.369
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KM at PKE**	0.636	0.404	0.002	0.172	0.679
6MW, 2yr after TKA					
Age, BMI	0.578	0.334	0.334	18.017	<0.001
Age, BMI + Non-op Extension ROM, Non-op Quad Strength	0.719	0.517	0.184	13.344	<0.001
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at IC**	0.729	0.532	0.014	2.093	0.152
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at PKF**	0.724	0.525	0.007	1.063	0.306
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KA at PKE**	0.742	0.551	0.034	5.197	0.026
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KE at WA**	0.746	0.557	0.039	6.074	0.016
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KE at MS**	0.761	0.579	0.061	10.008	0.002
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KM at PKF**	0.741	0.549	0.032	4.834	0.031
Age, BMI + Non-op Extension ROM, Non-op Quad Strength + **KM at PKE**	0.736	0.542	0.024	3.617	0.061

Discussion

The results of this study partially support our hypotheses. Bilateral clinical impairments were predictors of functional outcomes 6 months, 1 year, and 2 years after unilateral TKA. In particular, bilateral limb strength plays a critical role in functional performance, regardless of time after surgery. Our results agree with findings reported by Mizner et al[24]that greater bilateral quadriceps strength is correlated to better functional performance 6 months after TKA. With less functional performance deficit compared to the other two post-surgical time points, it appears that 1 year after TKA, slightly better operated limb strength (though not significant) may yield better functional performance, which agrees with previous findings at this time point[16,22]. Reliance on non-operated limb strength 6 months and 2 years after TKA may be due to operated limb weakness at 6 months and possibly reduced limb function at 2 years. As Farquhar & Snyder-Mackler[22] illustrated, the non-operated limb weakens from 1 year to 3 years post-TKA and non-operated limb strength and pain predicts functional performance 3 years after TKA. Therefore, the present data further indicates not only the need to strengthen already weakened quadriceps of the operated limb, but also retain strength on the non-operated side to maintain functional ability. Operated limb quadriceps strength also predicts 5.3% of the operated KOS score variance only in the 2 year group. With an operated limb strength deficit of 23%, perhaps long-term strength deficits influence long term self-perceived joint function.

Although bilateral quadriceps strength was most predictive of performance-based function, operated knee extension ROM was only predictive of self-reported function 2 years after surgery. The relationship between post-operative knee extension deficits and self-reported function has been reported by Ritter et al[30], who found that knees with post-operative flexion contracture of 6° or more are more likely to have poorer post-operative self-reported function than those with normal extension ROM (5-9° of extension). Although present data show that the mean operated knee extension ROM in the present study was within normal range of extension ROM at all three time points, its relationship with self-reported function shows that even small changes in joint ROM may result in poor functional outcomes. Therefore, maintenance of extension ROM after surgery is imperative to patients' perception of long-term joint function.

The second hypothesis, bilateral clinical impairments will be predictors of bilateral biomechanics 6 months, 1 year, and 2 years after unilateral TKA surgery, was also partially supported by our results. Bilateral strength and extension ROM are related to a variety of biomechanical measures at all three post-operative time points. However, the influence of physical impairments on these measures appears to be time dependent. Six months after surgery, bilateral extension ROM is predictive of knee joint kinematics, which is expected, due to the inherent relationship between dynamic joint movement and available joint ROM. At the same time point, bilateral strength is predictive of knee joint kinetics, which is also expected, due to the quadriceps role of providing an internal moment to oppose the external moments imposed by ground reaction forces. Similar trends were found 1 and 2 years after surgery, but the relationships were not as strong. Such outcomes may indicate that factors related to TKA other than physical impairments may be predictive of joint biomechanics as time increases from surgery.

Finally, the third hypothesis, bilateral biomechanics will be predictors of functional outcomes after accounting for clinical impairments 6 months, 1 year, and 2 years after unilateral TKA surgery, was also partially supported by our results. Knee biomechanics were predictive of operated KOS score beyond the influence of clinical impairments, with bilateral flexion excursion explaining similar amounts of KOS score variance 6 months after TKA, non-operated flexion excursion explaining KOS score 1 year after TKA, and operated knee extension excursion and peak flexion moment explaining similar amounts of KOS score variance 2 years after TKA. These results show that biomechanics during weight acceptance influence self-reported function shortly after TKA surgery and that long-term self-reported function is reliant on operated limb biomechanics. Therefore, clinicians should consider not only resolving strength and ROM deficits, but should also aim to restore knee joint biomechanics.

In addition, joint excursions, peak extension angle, and peak flexion moment on the non-operated limb were predictive of 6MW 2 years after TKA. The relationship between joint movement and function is of particular interest in the non-operated limb, as abnormal post-operative joint movement seems to drive poor functional performance 2 years after TKA. Clinicians should strive to not only resolve operated limb strength deficits, improve joint ROM, and normalize joint mechanics to improve self-reported function, they should also work to maintain non-operated limb strength, joint ROM, and knee mechanics to improve and retain functional performance gains and improve functional ability 2 years after TKA.

There are several limitations to this study. The cross sectional nature of this study does not allow for the determination of changes in prediction of functional outcomes over time. However, this study was able to establish the influence of bilateral impairments and joint mechanics on function after TKA surgery. In addition, this study did not include a pre-surgical group, preventing the ability to determine how surgical and rehabilitation intervention may have affected how impairments and joint movement influences function. Future studies should include pre-surgical and post-surgical data to determine bilateral limb predictors of function longitudinally, as well as the evaluation of a rehabilitation protocol that incorporates non-operated limb maintenance to improve functional outcomes.

In summary, clinicians should not only resolve strength deficits to improve post-operative function, but should also seek to restore knee joint ROM and normalize joint biomechanics to improve and maintain long-term functional outcomes. Traditional rehabilitative protocols following TKA surgery focus on reducing pain and swelling and utilize exercises to increase joint ROM, and improve mobility. Several studies from this research group have already shown the importance of implementing progressive quadriceps strengthening to further improve post-operative functional outcomes[31–33]. However, it is possible that clinicians are missing a vital component in maintaining long-lasting function by not including a focus on normalizing asymmetrical movement patterns. Few studies have begun to explore symmetry retraining as a viable rehabilitative option after arthroplasty[34–36]. However, the present study offers strong evidence to the influence of knee joint biomechanics on functional outcomes after TKA.

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Chapter 4

PRE-OPERATIVE PREDICTORS OF CONTRALATERAL TOTAL KNEE ARTHROPLASTY FOLLOWING UNILATERAL TOTAL KNEE ARTHROPLASTY

Abstract

Objective: Dynamic loading patterns and unresolved impairments following unilateral TKA may be contributing factors that could lead to contralateral TKA. Therefore, the purpose of this study was to identify biomechanical and clinical predictors of contralateral TKA use in a unilateral TKA population. We hypothesized that operated and non-operated limb clinical impairments and biomechanics would be predictive of contralateral TKA. Identifying the factors associated with contralateral TKA may help clinicians develop targeted rehabilitation protocols designed to improve limb coordination and reduce contralateral joint loading.

Methods: This cross-sectional retrospective study evaluated 117 subjects 6 months, 1 year, or 2 years after unilateral TKA surgery. All subjects underwent three dimensional gait analysis, isometric quadriceps strength testing, active extension range of motion, and completed Knee Outcome Survey-Activities of Daily Living Scale (KOS-ADLS) survey. Knee pain score was also analyzed from the KOS-ADLS. Relationships between contralateral TKA and activity level and socioeconomic status were also determined.

Results: The prevalence of contralateral TKA after primary unilateral TKA for this study sample was 19.7%. The operated limb was not predictive of contralateral TKA. Non-operated knee pain and peak adduction moment were determined to be the primary predictors of contralateral TKA. For every 1 point increase in pain, the risk for contralateral TKA surgery increased by 67% and for every 0.1 N·m/kg·m increase in adduction moment, the risk for contralateral TKA surgery increased 5.75 times.

Conclusion: This study provides further evidence of the importance of maintaining non-operated limb function following unilateral TKA. Clinicians should develop treatments that focus on bilateral function, improving deficits on the operated limb while preserving non-operated limb function.

Introduction

Total knee arthroplasty is a successful procedure to reduce the pain and symptoms associated with end-stage knee OA. Over the past 20 years, the number of primary TKA surgeries has increased by 161.5% and the incidence is expected to grow to a projected 3.48 million procedures by 2030, with a disproportionate increase in patients under the age of 45[1–3]. What is most concerning are the recent studies that have revealed a large number of individuals require an additional arthroplasty on a different joint after the index surgery. Of those that underwent unilateral TKA, 49.5% required a second arthroplasty procedure and the median time to this surgery was only 3.1 years[4]. Nearly 25% of individuals underwent contralateral TKA within 2 years of the initial TKA[4].

Within one year of TKA, most patients experience improvements in self-perceived knee function, functional performance, and clinical metrics compared to pre-operative status[5,6]. However, outcomes after TKA are variable and many have persistent physical impairments and movement asymmetries when compared to healthy control subjects[7–10]. After TKA, patients demonstrate less knee flexion and extension excursion during gait, which requires compensatory movement strategies in the non-operated limb to maintain forward progression during gait[11]. Subjects also demonstrate increased external knee adduction moments on the non-operated limb[12]. Increased adduction moment is correlated with greater medial compartment joint loads[13] and greater adduction moments are predictive of radiographic OA progression[14]. For every 1 unit increase in adduction moment, the risk for knee OA progression increases 6.46 times[14]. Therefore, it is possible that the persistent sagittal and frontal plane asymmetries after TKA put the contralateral knee at risk for developing OA, and possibly at risk for future TKA surgery. The pattern of joint loading after TKA supports observational studies that have found that the evolution of OA after the initial procedures occurs in a non-random pattern. After the initial TKA, the contralateral joint is most likely to be replaced next[15].

After TKA, factors other than frontal plane joint kinetics may also predict or contribute to OA progression on the contralateral joints. Improved quadriceps strength may have a chondroprotective effect. After quadriceps strength training, incidence of progressive joint space narrowing decreased[16]. While the mechanisms underlying this relationship have not been fully elucidated, some studies have shown that restoring and maintaining normal quadriceps strength on the operated limb after TKA may reduce the magnitude of movement asymmetries that overload the non-operated joint[7]. Ensuring normal range of motion on the operated and non-operated knee may also help prevent future contralateral OA progression. In a study of 120 subjects with moderate knee OA, lower knee extension range of motion was found to be a primary predictor of the need for a future TKA[17].

By three years after unilateral TKA, the status of the non-operated knee is the primary driver of functional limitations[18]. Therefore, preserving the integrity of the non-operated knee is essential to preventing long-term disability in patients who undergo unilateral TKA. Identifying potentially modifiable risk factors of contralateral TKA may help shape interventions and rehabilitation paradigms that mitigate contralateral OA progression. Therefore, the purpose of this study was to identify biomechanical and clinical predictors of future contralateral TKA in subjects with primarily unilateral disease at baseline. We hypothesized that clinical impairments and knee biomechanics in the operated and non-operated limbs would predict the need for contralateral TKA at least 2.5 years after the initial surgery.

Methods

Study design

This study was designed as a retrospective cohort study (Figure 6). Subjects participated in two testing sessions several days apart. The first testing session was conducted in the University of Delaware Physical Therapy Clinic. The second testing session was conducted in the University of Delaware Department of Physical Therapy Motion Analysis Laboratory. Subjects were then contacted with a one-time follow-up via telephone interview two or more years after initial testing to determine if they had additional contralateral TKA surgery. Those that were lost to follow-up were excluded from this study.

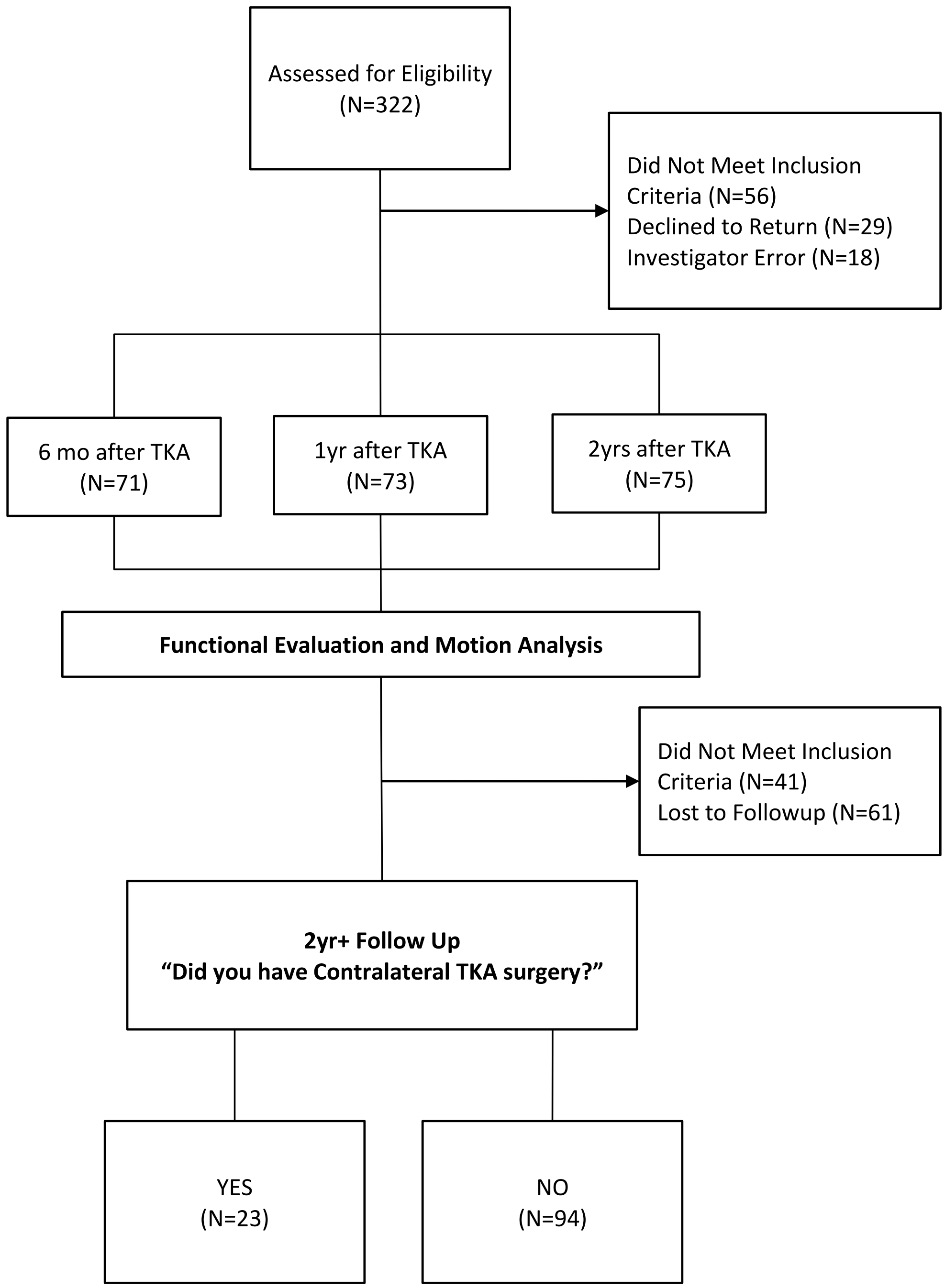

Figure 6 Study Flow Diagram

Subjects

Individuals between the ages of 50 and 85 years who underwent unilateral TKA due to end-stage knee OA six months previously were recruited for this study. Subjects were excluded if they had a known history of uncontrolled or insulin controlled diabetes; neurological, vascular, or cardiac problems that limit function; greater than mild osteoarthritis or other orthopedic conditions affecting the non-operated lower extremity that may limit function; >4/10 pain on the non-operated knee; planned staged TKA, orthopedic problems of the operated lower extremity, other than the TKA, that may limit function; or a Body Mass Index (BMI) of 40 or greater. All subjects signed informed consent forms approved by the Human Subjects Review Board at the University of Delaware prior to participation.

Functional Testing

Functional Performance: Functional performance based testing included Timed-Up-And-Go (TUG), Stair Climbing Test (SCT), and Six-Minute Walk (6MW). TUG is a test of mobility, strength, and balance that measures the amount of time it takes to rise from a standard height chair (46 cm), walk 3 m, and return to a seated position in the same chair. One practice trial was performed, followed by two recorded trials. This test is used to assess mobility, strength, and balance and has been commonly used in the OA and TKA populations[19]. SCT is a test that measures the time it takes to ascend and descend 12 7in high steps. A hand rail was available for subjects to use during testing. One practice trial was performed, followed by two recorded trials. During 6MW, subjects walk at a self-selected pace for as long of a distance they can walk, on level ground, for 6 min. This is a test of endurance and mobility over long distances. All tests are commonly used in the OA and TKA populations[19]. Subjects were instructed to walk as quickly and as safely as possible for all tests.

Self-reported function: Self-reported function was assessed using the Knee Outcomes Survey-Activities of Daily Living (KOS-ADLS). The KOS-ADLS is a knee specific self-reported outcome measure that determines functional limitation in individuals with a variety of pathological disorders of the knee. The survey has 14 items with scores from 0 to 5. A percentage score is totaled, with a higher score indicating greater self-perceived functional ability. KOS-ADLS is a valid, reliable, and responsive measure of functional performance after TKA[20,21]. Knee pain was also assessed on a scale from 0 to 5 using a question from the KOS-ADLS questionnaire. Zero indicates no pain while 5 indicates pain that prevents the subject from all daily activities. KOS-ADLS is a valid, reliable, and responsive measure of functional performance after TKA[20,21].

Clinical Impairment Measures

Weight and height were measured and BMI were recorded for each subject. A questionnaire of activity level and socioeconomic status was given to obtain information about pre-operative and present day activity level, employment status, marital status, income level, and education level. Quadriceps strength was measured during a maximal voluntary isometric contraction (MVIC). Patients were seated on an isokinetic dynamometer (Kincom, Chattecx Corp, Harrison, TN), with a measuring arm secured to the ankle, the hip was fixed at 90° flexion, and the knee was fixed at 75° flexion. The peak volitional force was used to quantify quadriceps strength, and normalized to BMI to allow for between subject comparisons. Active knee extension range of motion (AROMe) was measured using a long arm goniometer. Subjects were placed in a supine position with the distal arm aligned with the lateral malleolus and the proximal arm aligned with the greater trochanter. Subjects were instructed to actively extend their knee. The maximal extension angle was recorded, with positive values indicating flexion, zero indicating full extension, and negative values indicating hyperextension.

Motion Analysis

Joint kinetics during walking were measured using an 8 camera infrared motion capture system (VICON, Oxford Metrics, London, England) synchronized with force plates (Bertec Corp., Worthington, OH). Sixteen 16 mm-millimeter spherical retro-reflective markers were placed bilaterally on the acromion, iliac crest, greater trochanter, medial and lateral femoral condyle, medial and lateral malleolus, and head of the 5th metatarsal to identify joint centers. Segments were defined using marker clusters fixed on rigid thermoplastic shells and will be secured on the lower leg and thigh bilaterally, and on the trunk and pelvis. Two additional retro-reflective markers were placed bilaterally on the heel. Marker data were sampled at 120 Hz, while data from the force platforms data were collected at 1,080 Hz. Standing calibration was performed prior to walking trials to identify joint centers with respect to the coordinate system of each segment. Following the standing calibration, subjects were asked to walk over a 13m walkway at a self-selected speed (±5%) across force platforms embedded in the walkway, with clear contact of only one foot on each force plate. Subjects were allowed several practice walks until reaching a consistent self-selected speed prior to data collection. Five trials were collected for each subject.

Marker trajectories and force plate data were low pass filtered at 6 Hz and 40 Hz, respectively, using a second-order phase-corrected Butterworth filter. Joint angles were calculated using Euler XYZ sequence corresponding to a flexion/extension, abduction/adduction, and internal/external rotation sequence. Gait events (initial contact, toe-off) were identified using a 20N vertical ground reaction force threshold. External joint moments were calculated using inverse dynamics and were normalized to body mass and height (N·m/kg·m). Ensemble averaged trials were time normalized to 100% stance for each kinetic variable using a custom LabView program (National Instruments, Austin, TX) and Visual 3D 4.91.0 software (C-motion Inc., Rockville, MD). Comparisons between groups were based on the averaged normalized trials. External knee moment at peak knee flexion (KM at PKF) and peak knee adduction moment (PKAM) were calculated for both limbs.

Statistical Analysis

Groups were created based on whether or not subjects underwent contralateral TKA within the study period (YES group vs NO group). Receiver operating characteristic (ROC) curve analysis was used to determine optimum cutoff values for each clinical and biomechanical variable in relation to contralateral TKA. Cutoff values were selected as the value that maximized the sensitivity, or the rate of correctly identified subjects in the YES group, and minimized 1-specificity, or the rate of incorrectly identified subjects in the NO group. Contingency tables were formed to display the frequency distribution of the predicted outcome compared to the actual outcome, as a function of the dichotomized test variables. Sensitivity and specificity were also calculated to determine the ability of the variable to classify subjects according to contralateral TKA status. Sensitivity was determined based on the ratio of people who were correctly identified as having contralateral TKA to the number of people who actually had contralateral TKA. Specificity was determined based on the ratio of people who were correctly identified as not having contralateral TKA to the number of people who actually did not have contralateral TKA. Likelihood ratios were calculated to assess the value of a particular variable as a diagnostic test. Positive likelihood ratio was determined as the probability of an individual correctly identified as having contralateral TKA divided by the probability of an individual falsely identified as having contralateral TKA. Negative likelihood ratio was determined as the probability of an individual falsely identified as not having contralateral TKA divided by the probability of an individual correctly identified as not having contralateral TKA. Univariate logistic regression models were used to examine the association between age, BMI, quadriceps strength, AROMe, KM at PKF, PKAM, and knee pain, with the incidence of contralateral TKA. All independent variables entered into the regression models were continuous. Regression models were tested for linearity, normality, homoscedasticity and multicollinarity. Differences between limbs across groups were assessed using a 2x2 (limb x group) mixed design ANOVA. Independent t-test or paired t-test was used to for post hoc testing when the interaction effect was significant. Mann-Whitney U Test was used to determine group differences in KOS-pain score. Wilcoxon Signed Ranks Test was used to determine between limb differences. Anthropometric and functional variables that were not limb specific were analyzed using independent t-test to determine differences between the two surgical groups. Chi-squared tests were conducted to determine differences in frequencies of subjects for each activity level and socioeconomic factor based on contralateral TKA status. All analyses were performed with SPSS 21. Significance level was set at 0.05.

Results

Of the 219 subjects accessed for eligibility, 41 were ineligible due to having less than 2 years between initial study and follow-up. Therefore, 198 subjects were included in this study. Sixty-one were lost to follow-up (did not respond, change of address/phone number, etc.), leaving a total of 117 to be assessed for analysis. Differences between those included in the study and those that were lost to follow-up were assessed and the only significant differences were age (Included = 68.89 yrs, Lost to follow-up = 66.39 yrs, p=0.042), SCT (Included = 13.85s, Lost to follow-up = 12.45s, p=0.029), and time from surgery, with a greater proportion of people who were tested 1yr after TKA being lost to follow-up compared to those tested at 6 months after surgery (50.9% vs 20.0%, p<0.001, two-tailed Fisher's exact test, φ=0.317) or 2 years after surgery(50.9% vs 27.7%, p=0.013, two-tailed Fisher's exact test, φ=0.229). Of the 117 assessed for analysis, twenty-three subjects underwent contralateral TKA within the follow-up period (YES), 94 subjects did not (NO). Of the subjects in the YES group, 9 were tested 6mo after TKA, 9 were tested 1yr after TKA, and 5 were tested 2yrs after TKA. Of the subjects in the NO group, 39 were tested 6mo after TKA, 26 were tested 1yr after TKA, and 29 were tested 2yrs after TKA. There were no significant differences in the time from surgery for either group (χ^2 (2, N=117) =1.366, p=0.505, φ=0.108). No significant differences were detected between the two groups in age (p=0.337), height (p=0.388), BMI (p=0.173) , speed (p=0.884), TUG (p=0.820), SCT (p=0.551), and 6MW (p=0.469). However, the YES group weighed 10.63kg more than the NO group (p=0.032) (Table 4.1).

Table 30 Anthropometric, Clinical, and Biomechanical Outcomes. Negative Extension Range of Motion indicates hyperextension. (†Significant difference from NO group (p<0.05), *Significant difference from non-operated limb)

Variable	YES Contralateral TKA (N=23, 9M/14F)		NO Contralateral TKA (N=94, 50M/44F)	
Age (yrs)	67.52±7.16		69.22±7.68	
Height (m)	1.68±0.11		1.70±0.09	
Weight (kg)	80.60±29.48†		91.24±18.47	
BMI (kg/m²)	29.84±5.74		31.65±5.65	
Speed (m/s)	1.27±0.15		1.27±0.17	
TUG (s)	8.52±1.65		8.42±1.96	
SCT (s)	13.38±3.18		13.97±4.43	
6MW (m)	526.62±74.08		541.03±87.58	
	Operated	**Non-Operated**	**Operated**	**Non-Operated**
KOS (%)*	83.39±13.58	87.73±10.91	84.09±13.81	90.83±12.46
KOS-pain	1 (0,2)	1 (0,2) †	1 (0,1)	0 (0,1)
Quad Strength (N/BMI)*	17.54±7.24	19.53±6.90	17.86±6.70	20.84±7.46
AROMe (°)*	-0.26±3.89	-0.65±3.89	0.47±4.22	-1.69±3.67
KM at PKF (N·m/kg·m)*	0.31±0.16	0.28±0.17	0.35±0.14	0.34±0.18
PKAM (N·m/kg·m)*	0.31±0.09	0.44±0.13	0.26±0.23	0.37±0.14

For quadriceps strength, there was no significant interaction effect (F(1,115) =0.814, p=0.369) or main effect of group (F(1,115) =0.273, p=0.602) (Table 30). However, there was a main effect of limb (F(1,115) =20.643, p<0.001), with the operated limb having 2.49 N/BMI less quadriceps strength than the non-operated limb. There was no interaction effect for AROMe (F(1,115) =2.694; p=0.103) or main effect of group (F(1,115) =0.044; p=0.835) (Table 30). However, there was a significant main effect of limb (F(1,115) =5.607; p=0.020), with the operated knee having 1.28° less extension ROM than the non-operated knee. There was no interaction effect for

KOS score (F(1,115) =0.703; p=0.403) or main effect of group (F(1,115) =0.509; p=0.477) (Table 30). However there was a significant main effect of limb (F(1,115) =14.924; p<0.001), with the operated limb having 0.06 less percentage points than the non-operated limb There was a significant difference in non-operated knee pain between the two groups, with the YES group having significantly more pain than the NO group (U=742.00, p=0.009). There were no significant differences in operated knee pain between groups, nor were there significant differences between limbs in either group (YES: Z=-0.319, p=0.750; NO: Z=-1.907, p=0.056).

For KM at PKF, there was no interaction effect (F(1,115) =1.216; p=0.273) or main effect of group (F(1,115)=0.003; p=0.955),. However, there was a main effect of limb (F(1,115)=10.378; p=0.002), with the operated knee having 0.18 N·m/kg·m more knee flexion moment than the non-operated knee. For PKAM, there was no interaction effect (F(1,115) =0.197; p=0.658) or main effect of group (F(1,115)=3.647; p=0.059). However, there was a main effect of limb (F(1,115)=19.401; p<0.001), with the operated knee having 0.12 N·m/kg·m less knee adduction moment than the non-operated knee.

A two-way contingency table analysis was conducted to evaluate whether those who had contralateral TKA had different socioeconomic levels than those that did not have contralateral surgery (Table 31). There was no significant relationship between prevalence of contralateral TKA and present day activity level (χ^2 (3, N=71)=7.382, p=0.0.061, φ=0.322), pre-operative spare time activity level (χ^2 (3, N=77)=2.467, p=0.481, φ=0.179), present day spare time activity level (χ^2 (3, N=80)=0.778, p=0.855, φ=0.099), education (χ^2 (5, N=79)=5.977, p=0.308, φ=0.275), employment (χ^2 (5, N=82)=5.707, p=0.222, φ=0.264), marital status (χ^2 (4, N=86)=8.827, p=0.066, φ=0.066), or annual income (χ^2 (4, N=49)=7.544, p=0.110, φ=0.392). Contralateral TKA and pre-operative activity level were found to be significantly related, (χ^2 (3, N=75) =8.681, p=0.034, φ=0.034). The proportions of people who had contralateral surgery that had preoperative activity levels of sedentary, sitting, walking, and heavy manual labor were 23.1%, 15.4%, 46.2%, and 15.4%, respectively. Post hoc analysis revealed there were significant differences between heavy labor and walking (p=0.022, two-tailed Fisher's exact test, φ=0.342). More patients who engaged in heavy manual labor underwent contralateral TKA (66.7%) when compared to those who walked (14.3%). There were also significant differences between heavy labor and sitting (p=0.011, two-tailed Fisher's exact test, φ=0.510). More patients who engaged in heavy manual labor underwent contralateral TKA (66.7%) when compared to those who sat (9.7%).

Table 31 Activity Level and Socioeconomic Information

	YES	NO
Pre-operative/Present Activity Level		
Response Rate (%)	*56.5/47.8*	*66.0/63.8*
Sedentary (%)	8.1/23.1	11.1/6.7
Sitting, some standing (%)	32.3/15.4	32.1/38.3
Walking (%)	58.1/46.2	51.9/55.0
Heavy manual labor (%)	1.6/15.4	4.9/0.0
Pre-operative/Present Spare-time Activity Level		
Response Rate (%)	*65.2/65.2*	*66.0/69.1*
Inactive (%)	20.0/13.3	8.1/10.8
Mildly active (%)	46.7/60.0	54.8/50.8
Moderately active (%)	26.7/20.0	22.6/30.8
Very active (%)	6.7/6.7	14.5/7.7
Education		
Response Rate (%)	*65.2*	*68.1*
Less than high school (%)	0.0	1.6
Graduated high school (%)	46.7	21.9
Some college (%)	20.0	17.2
Graduated college (%)	20.0	31.3
Some post-grad (%)	13.3	12.5
Graduated post-grad (%)	0.0	15.6
Employment		
Response Rate (%)	*65.2*	*71.3*
Regular duty full time (%)	20.0	17.9
Part time (%)	0.0	4.5
Light Duty (%)	0.0	0.0
Retired (%)	53.3	70.1
Unemployed (%)	20.0	4.5
Homemaker (%)	6.7	3.0
Disabled (%)	0.0	0.0
Student (%)	0.0	0.0
Marital Status		
Response Rate (%)	*65.2*	*75.5*
Single (%)	13.3	1.4
Married (%)	53.3	80.3
Living with Significant Other (%)	0.0	1.4
Divorced/Separated (%)	20.0	7.0
Widowed (%)	13.3	9.9

Table 31 continued

Annual Income		
Response Rate (%)	*52.2*	*39.4*
<$20,000 (%)	8.3	10.8
$20-35,000 (%)	16.7	16.2
$35-50,000 (%)	50.0	13.5
$50-70,000 (%)	8.3	21.6
>$70,000 (%)	16.7	37.8

Utilizing the ROC curve analysis (Figure 7), cutoff values were determined for age (67.5 yrs), BMI (27.22 kg/m^2), quadriceps strength (op=14.85 N/BMI; non=18.12 N/BMI), AROMe (op=0.5°; non=-1.5°), KOS-pain (op=0.5; non=0.5), KM at PKF (op=0.35 N·m/kg·m; non=0.22 N·m/kg·m) and PKAM (op=0.28 N·m/kg·m; non=0.45 N·m/kg·m). The relationships between each variable according to their cutoff values and contralateral TKA can be found in Table 32. The variable with the strongest sensitivity was non-operated knee flexion moment (0.783). The variable with the strongest specificity was non-operated PKAM (0.745). The variables with the strongest positive likelihood ratios were non-operated knee pain (LR+=1.982) and non-operated PKAM (LR+=2.043). The variable with the strongest negative likelihood ratio was KOS-pain (LR-=0.469) (Table 33).

Univariate logistic regressions analysis revealed non-operated knee pain (p=0.036) and non-operated knee PKAM (p=0.023) were the only variables that were significantly predictive of contralateral TKA. The risk of contralateral TKA increased 1.666 times for every 1 point increase in pain and 57.469 times for every 1 N·m/kg·m increase in PKAM (Table 34).

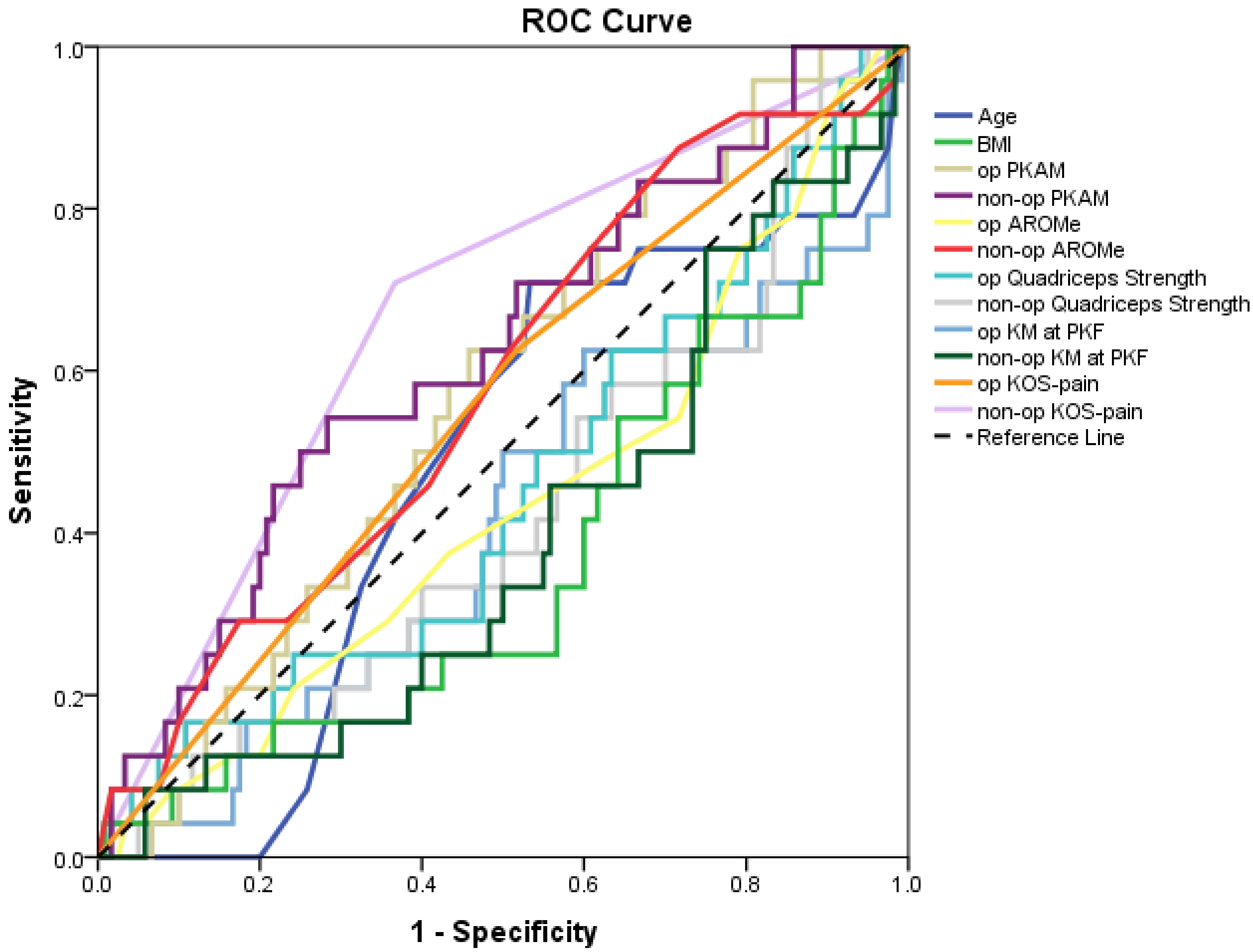

Figure 7 Receiver operating characteristic curves of age, BMI, KOS-pain, quadriceps strength, AROMe, KM at PKF, and PKAM, for discriminating incidence of contralateral TKA surgery.

Table 32 Relationships between Contralateral TKA status and Predictor Variables

	YES	**NO**	Total
Age (yrs)			
≥67.5	16	51	67
<67.5	7	43	50
Total	23	94	117
BMI (kg/m²)			
≥27.22	16	71	87
<27.22	7	23	30
Total	23	94	117
Op KOS-pain			
≥0.5	14	50	64
<0.5	9	44	53
Total	23	94	117
Non KOS-pain			
≥0.5	16	33	49
<0.5	7	61	68
Total	23	94	117
Op Quad Strength (N/BMI)			
≥14.85	14	60	74
<14.85	9	34	43
Total	23	94	117
Non-op Quad Strength (N/BMI)			
≥18.12	12	56	68
<18.12	11	38	49
Total	23	94	117
Op AROMe (°)			
≥0.5	8	40	48
<0.5	15	54	69
Total	23	94	117
Non-op AROMe (°)			
≥-1.5	14	48	62
<-1.5	9	46	55
Total	23	94	117
Op KM at PKF (N·m/kg·m)			
≥0.35	12	43	55
<0.35	11	51	62

Table 32 continued

Total	23	94	117
Non-op KM at PKF (N·m/kg·m)			
≥0.22	18	68	86
<0.22	5	26	31
Total	23	94	117
PKAM (N·m/kg·m)			
≥0.28	14	39	53
<0.28	9	55	64
Total	23	94	117
Non-op PKAM (N·m/kg·m)			
≥0.45	12	24	36
<0.45	11	70	81
Total	23	94	117

Table 33 Cutoff value, sensitivity, specificity, and positive & negative likelihood ratios for each predictor variable

	Cutoff Value	**Sensitivity**	**Specificity**	**Positive Likelihood Ratio**	**Negative Likelihood Ratio**
Age	67.50 yrs	0.696	0.457	1.282	0.665
BMI	27.22 kg/m^2	0.696	0.245	0.921	1.244
Op KOS-pain	0.5	0.609	0.468	1.144	0.836
Non-op KOS-pain	0.5	0.696	0.649	1.982	0.469
Op Quad Strength	14.85 N/BMI	0.609	0.362	0.954	1.082
Non-op Quad Strength	18.12 N/BMI	0.522	0.404	0.876	1.183
Op AROMe	0.5°	0.348	0.574	0.817	1.135
Non-op AROMe	-1.5°	0.609	0.489	1.192	0.800
Op KM at PKF	0.35 N·m/kg·m	0.522	0.543	1.141	0.882
Non-op KM at PKF	0.22 N·m/kg·m	0.783	0.277	1.082	0.786

Op PKAM	0.28 N·m/kg·m	0.609	0.585	1.467	0.669
Non-op PKAM	0.45 N·m/kg·m	0.522	0.745	2.043	0.642

Table 34 Univariate odds ratios (OR) and 95% confidence interval (CI) for factors associated with contralateral TKA. Analysis by logistic regression model.

	p value	OR	95% CI
Age (yrs)	0.332	0.971	0.914 to 1.031
BMI (kg/m^2)	0.161	0.942	0.863 to 1.027
Op KOS-pain	0.437	1.209	0.753 to 1.940
Non KOS-pain	0.036	1.666	1.039 to 2.671
Op Quad Strength (N/BMI)	0.839	0.993	0.928 to 1.063
Non Quad Strength (N/BMI)	0.439	0.975	0.915 to 1.040
Op AROMe (°)	0.445	0.957	0.855 to 1.072
Non AROMe (°)	0.227	1.079	0.953 to 1.223
Op KM at PKF	0.580	1.294	0.519 to 3.225
Non-op KM at PKF	0.174	0.429	0.012 to 2.317
Op PKAM (N·m/kg·m)	0.215	9.892	0.164 to 597.890
Non PKAM (N·m/kg·m)	0.023	57.469	1.497 to 2206.272

Discussion

The rate of contralateral TKA for the study population was 19.7%. This is high given that subjects were excluded from testing if they reported substantial pain or symptoms (pain greater than 4/10) at the time of testing. The 19.7% prevalence of contralateral TKA in this study exceeds the rates reported by Ritter and colleagues[22] who found 12.4% of individuals required contralateral TKA within 5 yrs of initial surgery. And in those that had healthy contralateral knees at baseline, the rate of contralateral TKA was 4.7% (2/43) within 7 yrs of initial surgery. However, greater rates have been reported, with Shao and colleagues[4] reporting 46% of people requiring contralateral TKA within 3 yrs of initial surgery.

The results of the current study support our hypothesis that non-operated limb biomechanical and clinical outcomes predict future contralateral TKA surgery. The presence of knee pain and the magnitude of PKAM were significant predictors of future TKA use. For every 1 point increase in pain in the non-operated knee, the risk for contralateral TKA increased by 67%. While this seems intuitive, there is little evidence to support the predictive relationship between knee pain and TKA use, although pain is a common prerequisite for TKA[23]. For every 0.1 N·m/kg·m increase in adduction moment in the non-operated knee, the risk for contralateral TKA increases 5.75 times. This supports previous work that looked at predictors of OA progression in individuals with knee pathology at baseline[14]. For every 1% increase in adduction moment, the risk for knee OA progression increases more than 6 times[14]. However, this study was conducted in individuals without previous TKA, looked at radiographic OA changes, and evaluated subjects at a longer term follow-up. The results from our study suggest that a threshold of 0.45 N·m/kg·m seems to best determine the incidence of contralateral TKA. The results from our study also indicate that while non-operated knee pain and adduction moment are the best predictors of the presence of contralateral TKA, pain is also capable of predicting the absence of contralateral TKA. Pain was dichotomized into two categories: no pain and the presence of pain. Therefore, the presence of pain alone can be highly influential on the future need for surgical intervention.

Prevalence of contralateral TKA cannot be attributed to education, employment status, annual income, marital status, spare-time activity level, or present day activity level, as there were no significant differences between surgical groups. However, pre-operative activity level was significantly related to contralateral TKA, with 66.7% of those who engaged in heavy manual labor eventually requiring contralateral surgery. However, this outcome is based on just 2 out of 3 people who reported heavy manual labor as their pre-operative activity level, so it is unclear whether high activity level is actually related to future contralateral TKA use. Nevertheless, the accumulation of high levels of physical activity may have sufficiently contributed to the need for contralateral TKA. Although physical activity is may not be a risk factor for TKA revision surgery[24], heavy physical activity and long-term exposure to heavy manual labor are risk factors for knee OA development[25,26]. It is possible that the long-term exposure to heavy physical activity may be related to for the need for future contralateral surgery, but the current findings are not yet conclusive.

There are several limitations to this study. There is an inherent time component in the progression of knee OA that was not considered in this study. Shao and colleagues[4] reported an average time to second knee replacement at 3.1±3.5yrs, which was within the present study's follow-up time of 2.5 or more years after initial TKA. However, determining the amount of time between initial and subsequent surgeries may have been helpful in understanding the relationship between clinical and biomechanical predictors and time to subsequent surgery. In addition, we did not have access to radiographs of the contralateral knee at initial testing to determine K-L grade. Such information would have also helped us to determine the likelihood of future contralateral surgery. In a seminal study by McMahon & Block[27], K-L grade was determined to be a significant predictor of contralateral knee OA progression. Tracking subjects for up to 14 years, researchers were able to determine that those with a contralateral knee K-L grade of 4 had a mean survival time of 80.45 months, those with K-L grades of 2-3 had a mean survival time of 131.7-127.6 months, and those with K-L grades of 0-1 did not progress to TKA[27]. Therefore, the risk of contralateral TKA is dependent on OA severity at the time of initial surgery. Riddle et al[28] also determined that OA severity, along with functional ability, was the strongest predictor for knee arthroplasty. Sayeed et al[29] reported that contralateral knee OA severity strongly correlates with risk of future contralateral TKA after primary TKA surgery. Additionally, we limited our study to prevalence of contralateral TKA. However, after the contralateral knee, the second more likely joint to be replaced after initial TKA is the hip, although there is debate over whether it is ipsilateral[4] or contralateral[15]. Future studies should include more complete information about the prevalence and location of future joint replacement. Furthermore, although we recruited subjects at three different time points after initial TKA surgery (6mo, 1yr, and 2yrs), we did not discriminate our outcomes based on time after initial surgery. Future studies should consider such separate analyses to further determine the influence of time on future prevalence of contralateral TKA. Finally, although we did not determine our socioeconomic factors to be influential on prevalence of contralateral surgery, there may have been additional factors to consider, such as race, healthy insurance, and willingness to undergo surgery that could have influenced post-operative outcomes.

In summary, 19.7% of the study population reported prevalence of contralateral TKA after primary unilateral TKA. Non-operated knee pain and adduction moment were found to be the primary predictors of contralateral TKA. These results provide further evidence of the importance of maintaining non-operated limb function following unilateral TKA. Clinicians should develop treatments that focus on bilateral function, improving deficits on the operated limb while preserving non-operated limb function.

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Chapter 5

INTERLIMB MOVEMENT ASYMMETRIES IN SUBJECTS WITH UNILATERAL TOTAL KNEE ARTHROPLASTY AND IDENTIFYING BIOMECHANICAL AND CLINICAL IMPAIRMENT PREDICTORS OF FUNCTION AND CONTRALATERAL TOTAL KNEE ARTHROPLASTY

Persistent Asymmetrical Movement after TKA Surgery

Sagittal plane asymmetries throughout midstance and frontal plane asymmetries throughout stance remain up to 2 years after unilateral TKA surgery. Reductions in operated knee movement in the sagittal plane and reduced joint loading in the frontal plane compared to healthy controls contribute to long-standing movement asymmetries of the knee. Unresolved truncated movement of the operated limb may reflect lingering unilateral quadriceps weakness and extension range of motion deficits driving compensatory movement strategies that favor the non-operated limb during gait. Although this work confirmed previously reported findings of asymmetrical knee movement during weight acceptance phase of gait, this work has shown that asymmetrical movement is most prevalent during the midstance phase of gait. It is during this phase that full knee extension is required to stabilize the knee during single limb support. Therefore, those with unilateral TKA may require additional post-operative rehabilitation with a particular focus on improving extension deficits, muscle strengthening, and correcting movement strategies that likely developed prior to surgery and without intervention, will persist. Failure to improve asymmetrical movement might result in long-term dysfunction and could put patients at risk for future surgery.

Bilateral Knee Biomechanics Influences Long-Term Function Beyond the Effect of Clinical Impairments

Bilateral quadriceps strength is primarily predictive of performance-based function while operated limb extension ROM is primarily predictive of self-reported function. Bilateral quadriceps strength and extension ROM were predictive of bilateral knee mechanics throughout stance. Self-reported function is most influenced by quadriceps strength and extension range of motion, particularly in the operated limb. Clearly, muscle weakness and range of motion deficits can result in patient perceptions of dysfunction, making such impairments critical targets for clinicians to resolve through post-operative rehabilitation in order to best improve patient quality of life. However, operated knee biomechanics, primarily during weight acceptance phase of gait, also influences self-reported function, particularly 2 years after TKA. Therefore, maintenance of long-term patient perceived function is not only prohibited by residual weakness and unresolved extension deficits, it is also affected by abnormal and truncated operated knee biomechanics. Such abnormal joint movement is a hallmark of the unilateral TKA population, and without intervention, it can also drive long-term functional deficits and declines. In addition, the non-operated limb is predictive of, primarily, long-term performance-based functional outcomes. Beyond the influence of non-operated limb quadriceps strength, non-operated knee biomechanics drive functional performance 2 years after TKA. Although long-term perceptions of ability are driven by operated limb function, it is the non-operated limb that is most determinative of long-term disability. Therefore, during post-operative rehabilitation, attention should be paid not only to the restoring deficits and normalizing joint movement in the operated limb, but clinicians should also work to maintain non-operated limb function to best improve long-term quality of life and ability.

Predictors of Contralateral TKA Surgery

Non-operated knee pain and joint loading are two primary influencers on the need for contralateral TKA. Although pain is a common prerequisite for TKA surgery and is often implicated in the need for surgery, few studies have quantified the effect of pain on the need for surgical intervention. However, this work demonstrates that small increases in knee pain can greatly increase the risk for contralateral TKA. Moreover, the mere presence of knee pain can make one more likely to require future contralateral surgery. However, peak knee adduction moment has the largest effect on need for contralateral surgery. This finding agrees with previous studies that have linked adduction moment to OA development and progression and TKA surgery use. This work provides further evidence of the importance of maintaining non-operated limb function following unilateral TKA. Clinicians should develop treatments that focus on bilateral function, improving deficits on the operated limb while preserving non-operated limb function.

Summary of Significance

This work has led to several important findings for the treatment of the unilateral TKA population. Persistence of operated limb movement deficits and impairments are responsible for long-term asymmetrical joint movement patterns after initial surgery. While clinicians should pay attention to strength and extension ROM deficits during treatment, restoration of knee biomechanics is also important for the improvement and maintenance of long-term functional outcomes. In addition, bilateral limb function is critical to lasting ability. Therefore, post-operative rehabilitation should not only focus on improving the operated limb, but it should also work to maintain non-operated limb function as well. Ultimately, maintenance of non-operated limb function is a fundamental component to post-operative functional ability and prevention of additional joint replacement surgery.

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Appendix A

INFORMED CONSENT FORM

Project title: Impairments and Altered Movement Patterns 6 months, 1 year and 2 to 4 years following Total Knee Arthroplasty

Part 1: Self Report of Function Questionnaires
Part 2: Functional testing
Part 3: Strength testing
Part 4: Motion analysis

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You are being asked to participate in a research study that will help describe differences in how people move their legs after having knee replacement surgery. These patterns may lead to arthritis changes in other joints of the legs. Participation is voluntary and you may withdraw at any time without consequence. A total of 360 subjects will participate in this study: 120 subjects each at 6 months, 1 year, and at 2 to 4 years following knee replacement surgery will be recruited. All testing will be performed once on each subject who enrolls in the study.

<u>Testing Procedures</u>

First, we ask you to complete questionnaires regarding what you think about your ability to perform activities of daily living. Strength testing and testing of tasks you do every day provides information on your abilities during your daily life. This information will help to determine patterns in walking, stair climbing, and getting out of a chair, which may lead to problems in other joints of the legs after knee replacement. It will teach us about the strength differences between your two legs, particularly the muscles on the front of your thigh. If you choose to participate, you will be asked to participate in one functional and strength testing session that lasts about 2 hours, and one motion analysis session that lasts about 3 hours.

<u>Part 1: Self Report of Function Questionnaires</u>

You will complete two questionnaires (one for each knee) about how your knees are working. You will also complete a standard questionnaire called the Short-Form 36 (SF-36) that includes questions about your overall physical and emotional health. You will also complete a standard health history.

Part 2: Functional testing

How far you can bend and straighten both knees will be measured. If you have diabetes, we will test sensation on the bottom of your feet. Diabetes causes changes in your body, which may affect some of the data we collect. Therefore, if sensation is absent, you may not participate in the study.

Functional testing will include four parts: a timed walking test, a timed stair-climbing test, balance when standing on each leg, and a six minute walk test. The timed walking test times how long it takes you to stand up from a chair, walk three meters, turn around and return a seated position in the chair. The balance test assesses how you can stand on one leg; both legs are tested. The stair-climbing test times how long it takes you to walk up and down one flight of stairs. The six minute walk test assesses how far you can walk in 6 minutes.

Part 3: Strength testing

The strength of the muscles of your calf and on the outside of your thigh are tested with a hand held device. You will be positioned on a padded table and asked to push into the device as hard as you can for each group of muscles tested.

A second strength test will be performed to assess the strength of the muscles on the front of your thigh. You will be seated and stabilized in a device that will measure the amount of force you are able to produce. Two self-adhesive 3" x 5" electrodes will be placed on your thigh. You will be asked to kick as hard as you can, during which a brief burst of electrical pulses will be given to your thigh to determine if you are maximally contracting your muscle. Depending on the results, we may ask you to repeat this procedure as many as three times. If at any time, discomfort becomes more than you care to tolerate, let us know and we will stop further testing.

Part 3b: Power testing

You will be asked to volunteer to participate in a third set of strength testing of the muscles on the front of your thigh. During this test, you will remain seated in the device described above and asked to straighten your knee as quickly and forcefully as possible. However, this time, the device attached to your leg will move as you contract your muscles and straighten your leg. The machine will still provide resistance against your movement and the speed at which the arm of the machine moves will be determined by how much force you can generate or by a pre-programmed speed. You will be asked to complete up to 20 contractions (10 at a pre-programmed speed and 10 at a speed determined by how hard you are kicking). The purpose of this test is to determine the power that your thigh muscles can generate. You are not obligated to participate in this portion of the testing and are free to withdrawal at anytime for any reason.

Part 4: Motion Analysis and Muscle Activity

Motion analysis provides information about how you walk, ascend and descend a single step, and stand from and sit down into a chair. Four-inch wide elastic bands will be wrapped around your thighs, calves, and pelvis to which small, reflective markers will be attached. Additional reflective markers will be taped to your sneakers, and skin of your ankles, knees and hips with adhesive skin tape. You will be asked to perform 10 trials arising from a chair and returning to sitting and 10 walking trials. While you are performing these activities, a computer records the motion of your head, trunk, pelvis and legs.

We also use special sensors that record muscle activity, that are attached to your skin with adhesive skin tape over the muscles of your hips, thighs and calves. Cables from each of the sensors will be plugged into a small transmitter box (6" x 4" x 3"). You will wear a small backpack that the transmitter box will be placed in. The sensors will record your muscle activity. These measurements are taken at the same time as the motion analysis testing. The transmitter box sends the signals to a computer to determine when the muscles are active.

Risks

The procedures to which you will be exposed are safe, but you may experience some muscle soreness a day or two following strength testing. This soreness is similar to the muscle soreness that you may feel if you lift weights or vigorously exercise, and is often a sign that you are increasing your muscle strength. Although the force levels to be used in this study pose very little risk for injury, it is possible that a muscle strain could occur. The potential for equipment malfunction also exists, which may result in skin burns; however, the equipment used is well cared for, and this is unlikely. The prolonged exposure necessary to cause serious skin damage is very unlikely, but there is a risk of minor skin irritation (small areas of skin redness).

The risks associated with the motion analysis testing are minimal. Minor skin irritation may occur from the adhesive tape used to place reflective markers, and sensors on the skin. Hypoallergenic tape is used; however, if you have known allergy to adhesive materials, you may choose not to participate. Because the testing period is relatively short, this is highly unlikely. The muscle activity recordings pose little risk. There may be some minor irritation of the skin around the site of the sensors following the experiment, which is likely due to the tape adhesive and how the sensors work. There is a risk of tripping on stair ascent and descent; however, you will be screened to ensure you can safely step up and down the stair.

Compensation

You will be paid an honorarium of $50 upon completion of both the motion analysis session and the functional and strength testing sessions to compensate you for travel expenses and the time involved in the testing procedure.

Benefits:

The benefits of this study include comprehensive analyses by a licensed physical therapist that provides you with detailed information concerning your legs and how you perform the tasks we are testing. The information that we obtain with our testing will be used to guide future physical therapy treatments and will help us learn how what you do, and how it might lead to changes in your legs following knee replacement surgery.

Confidentiality

Data will be entered from the record to a computerized data base where all patients will be identified by a case number. Neither your name nor any identifying information will be used in any publication or presentation resulting from this study. Only you and the investigators will have access to the data. Data will be stored indefinitely. You may reach the investigator at any time, if you have questions or problems associated with the study. The telephone numbers are listed at the end of this form.

Subject Statement

By signing this informed consent, I signify that I choose to participate in this study. The investigators have explained the purposes of this study, described the risks and benefits associated with my participation, and have defined what is expected of me as a subject. The investigators have answered all of my questions about the procedures to my satisfaction.

The functional and strength testing session will last about 2 hours. Motion analysis testing will last approximately 3 hours. I am between the ages of 50-85 and have never had:

Blood vessel disease involving either my arteries or veins
Hypertension (high blood pressure) that is not controlled by medication
Neurologic impairments (for example, stroke, or head injury)
Neurologic impairments that affect the sensation in my feet (such as diabetes)
I am not currently receiving treatment for active cancer
I am able to go up and down a single stair without assistance

In the event of physical injury resulting from these research procedures, the investigators will provide emergency first aid. If I require additional medical treatment, it is my responsibility to seek additional medical care and to pay for all expenses for any medical treatment received.

Subject′s Signature Date Witness (Signature)

Subject′s Name (Printed)

If you have any questions concerning your consent to be a participant, you may contact the head of the Human Subjects Review Board, University of Delaware, (302-831-2136). Further questions regarding the study may be addressed to: Lynn Snyder-Mackler, Sc.D., PT; Physical Therapy Department, 302-831-3613

Appendix B

INSTITUTIONAL REVIEW BOARD APPROVAL

UNIVERSITY OF DELAWARE

RESEARCH OFFICE

210 Hullihen Hall
University of Delaware
Newark, Delaware 19716-1551
Ph: 302/831-2136
Fax: 302/831-2828

DATE:	February 27, 2014
TO:	Lynn Snyder-Mackler
FROM:	University of Delaware IRB
STUDY TITLE:	[143664-9] Impairments and Altered Movement Patterns 6 months, 1 year and 2 years following Total Knee Arthroplasty
SUBMISSION TYPE:	Continuing Review/Progress Report
ACTION:	APPROVED
APPROVAL DATE:	February 24, 2014
EXPIRATION DATE:	February 24, 2015
REVIEW TYPE:	Expedited Review
REVIEW CATEGORY:	Expedited review category # 9

Thank you for your submission of Continuing Review/Progress Report materials for this research study. The University of Delaware IRB has APPROVED your submission. This approval is based on an appropriate risk/benefit ratio and a study design wherein the risks have been minimized. All research must be conducted in accordance with this approved submission.

This submission has received Expedited Review based on the applicable federal regulation.

Please remember that informed consent is a process beginning with a description of the study and insurance of participant understanding followed by a signed consent form. Informed consent must continue throughout the study via a dialogue between the researcher and research participant. Federal regulations require each participant receive a copy of the signed consent document.

Please note that any revision to previously approved materials must be approved by this office prior to initiation. Please use the appropriate revision forms for this procedure.

All SERIOUS and UNEXPECTED adverse events must be reported to this office. Please use the appropriate adverse event forms for this procedure. All sponsor reporting requirements should also be followed.

Please report all NON-COMPLIANCE issues or COMPLAINTS regarding this study to this office.

Please note that all research records must be retained for a minimum of three years.

Based on the risks, this project requires Continuing Review by this office on an annual basis. Please use the appropriate renewal forms for this procedure.

If you have any questions, please contact Nicole Farnese-McFarlane at (302) 831-1119 or nicolefm@udel.edu. Please include your study title and reference number in all correspondence with this office.