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Neuromuscular factors related to varus thrust during walking in knee osteoarthritis

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NEUROMUSCULAR FACTORS RELATED TO VARUS THRUST DURING WALKING IN KNEE OSTEOARTHRITIS

by

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NEUROMUSCULAR FACTORS RELATED TO VARUS THRUST DURING WALKING IN KNEE OSTEOARTHRITIS

SOFIA ESPINOSA MARAZITA

ABSTRACT

Background: Up to 37% of people with knee osteoarthritis (OA) present with varus thrust, an abrupt and dynamic worsening of varus alignment during the load-bearing stages of gait. Varus thrust is associated with up to 4-fold increased odds of medial knee OA progression as well as worsening clinical outcomes. While the implications of varus thrust have been well studied, the neuromuscular factors related to varus thrust are still not well understood and many studies report contradictory findings. Additionally, many potential factors remain unstudied. This warrants further efforts to determine associations between neuromuscular factors and varus thrust. The purpose of this study is to investigate knee muscle strength and muscle activation during walking in relation to biomechanical measures of varus thrust.

Methods: Analyses of existing data from participants with and without knee OA recruited at three institutions were used for this study. All participants underwent gait analyses at their self-selected pace while kinematics, kinetics, and surface EMG data were collected. Quadriceps and hamstrings strength was measured using isokinetic dynamometry. Gait data were used to calculate adduction excursion and peak knee adduction velocity as measures of varus thrust. A custom MATLAB code was used to calculate the rate of force development of the quadriceps, and a muscular co-contraction equation was used to calculate co-contraction values for four antagonist muscle pairs (VL-LH, VM-MH, VL-LG, and VM-MG) from surface EMG data during walking. Correlational analyses were performed to assess associations of strength, rate of force development, and muscle co-contraction variables with measures of varus thrust.

Results: A total of 183 participants were enrolled, however, a varying number of participants were used for different analyses based on available data. Peak isokinetic quadriceps strength at 60 degrees/second and peak hamstrings strength at both 60 and 120 degrees/second were negatively correlated with knee adduction velocity in people with knee OA. This association was not observed for people without knee OA. VLLH and VMMH co-contraction indices during preactivation were positively correlated with knee adduction excursion. VLLG co-contraction during midstance was positively correlated with peak knee adduction velocity. Association between rate of force development and varus thrust variables was not significant.

Conclusions: Lower isokinetic thigh muscle strength and greater preactivation during walking are related to greater magnitude of varus thrust measured using motion capture. These results advance our understanding of neuromuscular factors related to varus thrust and could inform future interventions to reduce thrust and prevent further progression of OA.

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LIST OF ABBREVIATIONS

BU	Boston University
BMI	Body Mass Index
BML	Bone Marrow Lesions
EMG	Electromyography
GRF	Ground Reaction Force
HKA	Hip-Knee-Ankle Angle
JSW	Joint Space Width
KAM	Knee Adduction Moment
KLG	Kellgren-Lawrence Grade
KOOS	Knee Injury and Osteoarthritis Outcomes Score
KOOS-ADL	KOOS-Activities of daily living
KOOS-QOL	KOOS-Quality of Life
KOOS-SR	KOOS-Sports and Recreation
LG	Lateral Gastrocnemius
LH	Lateral Hamstrings
MA	Mechanical Axis
MG	Medial Gastrocnemius
MH	Medial Hamstrings
MOST	Multicenter Osteoarthritis Study
MVC	Maximum Voluntary Contraction
MVIC	Maximum Voluntary Isometric Contraction

OA	Osteoarthritis
OAI	Osteoarthritis Initiative
QH	Quadriceps-Hamstrings
RFD	Rate of Force Development
SD	Standard deviation
TKA/TKR	Total Knee Arthroplasty/Replacement
UD	University of Delaware
US	United States
UCSF	University of California San Francisco
VL	Vastus Lateralis
VM	Vastus Medialis
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index

INTRODUCTION

Knee Osteoarthritis

Osteoarthritis (OA) is the most common joint disease and is the leading cause of disability in the United States (Bessho, Honda, Kondo, & Negi, 2011). It affects up to 37% of adults over the age of 60 in the US with increased prevalence in women and in older age groups (Lawrence et al., 2008). The disease also has substantial economic impact contributing an estimated $185.5 billion increase in aggregate annual medical care expenditure in 2007 (Kotlarz, Gunnarsson, Fang, & Rizzo, 2009). With rising rates of obesity and a growing elderly population in the US, the prevalence and associated cost of OA is expected to increase further. By 2030, 25% of the adult population is projected to have arthritis (Hootman & Helmick, 2006), of which OA is the most common (Lawrence et al., 2008). While adults over the age of 65 will account for 50% of these cases, working adults between the ages of 45 and 64 will account for almost one third of cases, suggesting that OA will start to become more prominent earlier in life (Hootman & Helmick, 2006).

Osteoarthritis is characterized by the degeneration of joint tissue, including articular cartilage, bone, meniscus, muscle, etc. Though the development of OA can occur in any joint, the most affected weight-bearing joint of the body is the knee. The medial compartment of the knee joint is disproportionally affected compared to the lateral compartment due to both anatomical and mechanical factors. For example, the medial compartment of the knee has thinner articular cartilage and takes on greater loads during functional activities such as walking and stair climbing than its lateral counterpart making it more susceptible to the development of OA (Lewek, Rudolph, & Snyder-Mackler, 2004). Risk factors for OA include age, race, ethnicity, sex, hormone levels, genetics, nutrition, bone mineral density, history of knee injury or surgery, and obesity (Zhang & Jordan, 2010). Presently, there is no cure available for knee OA, and the end stage treatment is a highly invasive and expensive total knee arthroplasty (TKA), also known as total knee replacement (TKR). In fact, knee OA is the most common reason for TKAs (Defrances, Lucas, Buie, & Golosinskiy, 2008). Hence, there is an urgent need to develop non-surgical treatments aimed at slowing the disease and preventing the need for TKA surgeries.

Radiographic Assessment of Knee OA

Weight-bearing, i.e. standing, radiographs are used to identify signs of knee OA. The joint space width (JSW), or the minimum distance between the femur and tibia, is an indirect measurement of OA severity and is a widely accepted outcome measure for the structural progression of medial knee OA (Peterfy et al., 2003). The Kellgren-Lawrence Grading (KLG) is also widely used to determine the severity of radiographic knee OA (Kellgren & Lawrence, 1957). Based on key radiographic features such as osteophyte formation, narrowing of joint cartilage, and bone deformity, KLG can range from 0 to 4 as shown in *Table I*. KLG greater than 1 is used to define radiographic knee OA. Standing radiograph of the legs that includes hip, knee, and ankle joints can reveal a static frontal plane malalignment through a measure of the mechanical axis (MA), also called the hip-knee-ankle (HKA) angle. As seen in *Figure 1*, HKA is the angle created by

Table 1. *Kellgren-Lawrence Grading (KLG) for knee osteoarthritis*

KL Grade	Description
0	No radiographic features of osteoarthritis
1	Doubtful joint space narrowing and possible osteophyte lipping
2	Definite osteophytes and possible joint space narrowing
3	Multiple osteophytes, definite joint space narrowing, sclerosis, possible bony deformation
4	Large osteophytes, marked narrowing of joint space, severe sclerosis, and definite deformity of bone ends

the intersection of two lines, one from the center of the femoral head to the center of the tibial spines and one from the center of the tibial spines to the center of the talus. An existing static varus, or "bow-legged", malalignment has been strongly identified as a risk factor for the development and progression of knee OA (Brouwer et al., 2007; Felson et al., 2013).

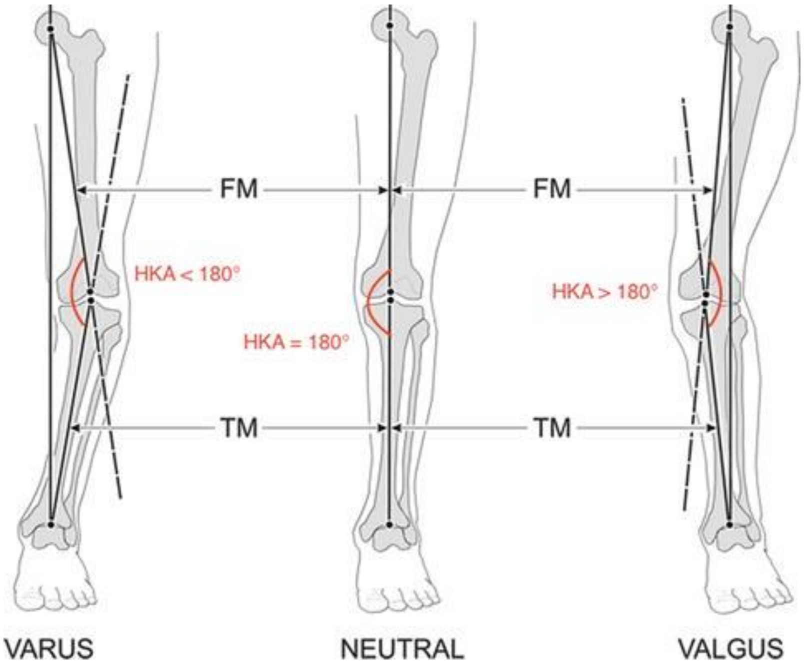

Figure 1. Mechanical axis (HKA) of the lower limb
FM, femoral mechanical axis; TM, tibial mechanical axis
Courtesy of Total Knee Arthroplasty: A Comprehensive Guide (Carlos Rodriguez-Merchan & Oussedik, 2015)

Patient-Reported Outcomes in Knee OA

Knee pain is often the first clinical indicator that will lead a person with undiagnosed knee OA to seek the help of a clinician and discover they have the disease. Furthermore, a person may experience functional changes as their OA progresses including decreased mobility and increased difficulty performing tasks of daily living. Because the characteristics of OA present themselves differently between individuals with OA, standard measures of clinical symptoms have been developed.

The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scale is a widely used and verified health status measure that assesses three subscales of OA symptoms - pain, stiffness and function - with a recall period of 48 hours (Collins, Misra, Felson, Crossley, & Roos, 2011). WOMAC can be used to assess both hip and knee OA independently and focuses primarily on long-term consequences of the disease, such as functional decline. The Knee Injury and Osteoarthritis Outcomes Score (KOOS) was developed as a knee-specific extension of WOMAC and evaluates both short term and long term consequences of knee OA and knee injury (Roos & Lohmander, 2003). It has five subscales including pain (KOOS-Pain), function during activities of daily living (KOOS-ADL), function in sports and recreation (KOOS-SR), knee related quality of life (KOOS-QOL), and other symptoms (KOOS-Symptoms).

The use of self-administered questionnaires such as WOMAC and KOOS gives clinicians an idea as to how symptoms are being manifested and are affecting the lives of people living with knee OA. Additionally, these measures have been used as clinical outcome measures to follow the changes in symptoms following treatments or interventions.

Biomechanics of Gait in People With Knee OA

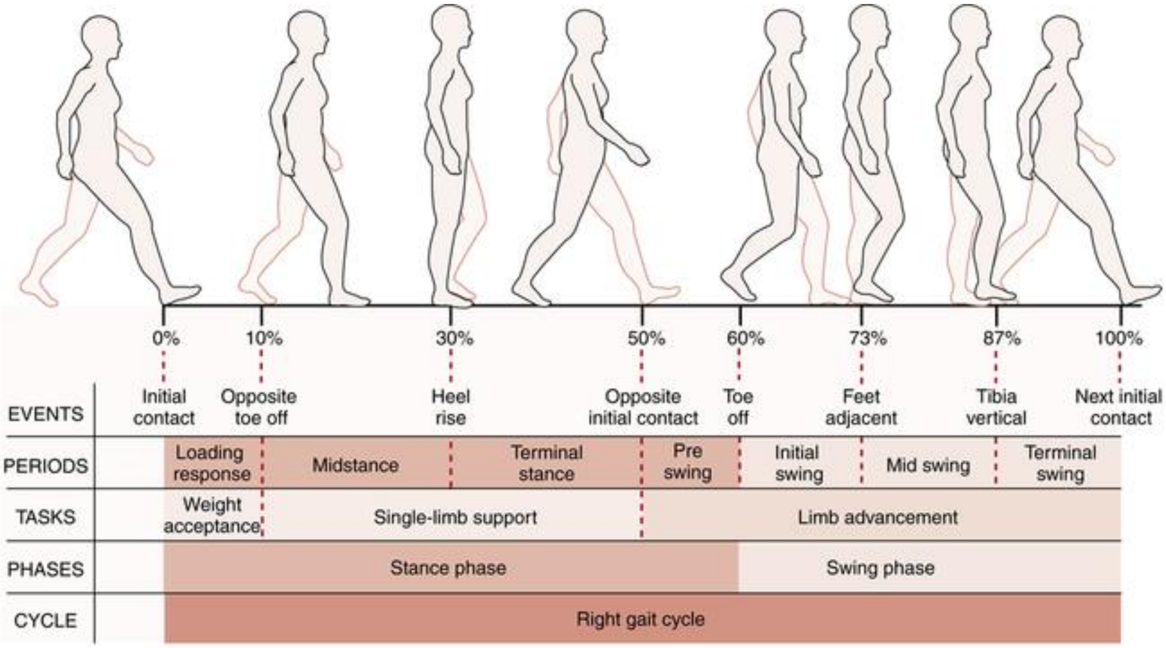

Figure 2. The gait cycle
Courtesy of Kinesiology of the Musculoskeletal System: Foundations for Physical Rehabilitation (Neumann, n.d.)

One of the major functional changes that occur in people with knee OA is a change in gait pattern. The normal gait cycle, seen in *Figure 2*, uses different phases to describe the cyclical pattern of walking from the initial contact of one foot to the next initial contact of the same foot. As the limb accepts the body’s weight, a load, or mechanical force, is placed on the articular surfaces of the tibiofemoral joint. Tissue studies have shown that damage to articular cartilage tissue may be mechanically induced (Cooke, Lawless, Jones, & Grover, 2018), suggesting that mechanical loading may be implicated in the development and progression of knee OA. However, it is very difficult to measure mechanical loading *in vivo* without invasive approaches. Therefore, gait analysis can be used to examine mechanical loading.

In people with medial knee OA, there are identifiable differences in biomechanical parameters during the stance or load bearing stages of gait compared to those of healthy individuals. A key biomechanical parameter of interest is the external knee adduction moment (KAM), which is used as a surrogate biomechanical measure to describe the loading over the medial tibiofemoral compartment (A. H. Chang et al., 2015). The external KAM represents the angular forces that cause the joint to adduct, or become more varus, along the joint axis. Simplistically, it is calculated using the ground reaction force (GRF) and its lever arm, or the perpendicular distance from the GRF vector to the point of rotation in the knee, as shown in *Figure 3*.

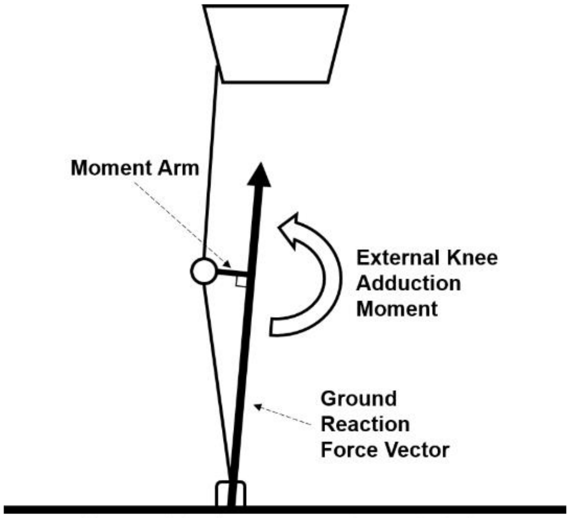

Figure 3. The external knee adduction moment (KAM)
Reprinted from Alexandra E Wink, 2018

KAM usually exhibits a bimodal pattern with peaks in early and late stance phase, referred to as the first and second peak KAM, respectively.

In people with medial knee OA, the external KAM is elevated compared to the external KAM in knees without knee OA. For this reason, KAM is also an important outcome measure in many studies investigating conservative treatments for knee OA such as gait modifications and knee or foot orthoses (Arnold, Wong, Jones, Hill, & Thewlis, 2016; Tokuda et al., 2018). One study in people with knee OA, KAM was found to be inversely proportional with cartilage thickness demonstrating the importance of biomechanics in cartilage degradation (Maly et al., 2015). Furthermore, one study quantified a 6.46 increased risk of radiographic knee OA progression for every 1% increase in KAM (Miyazaki et al., 2002). Studying gait biomechanics in people with and without knee OA provides a greater understanding of the mechanical differences that exists in the two populations, and biomechanical risk factors can even be used to assess a person's risk for OA progression.

Varus thrust in Knee OA

Varus knee thrust is a dynamic frontal-plane motion of the knee characterized by an increase in varus alignment during the weight acceptance phase of gait followed by a return to less varus alignment during the lift-off and swing phases as seen in *Figure 4*. This abnormal gait pattern is present in up to 36.7% of persons with radiographic knee OA (A. Chang et al., 2010). A study done in 2004 showed that people with varus thrust have a 3.96 greater odds of medial knee OA progression over 18 months making it a highly relevant risk factor in the OA population (A. Chang et al., 2004). Furthermore, varus thrust can be visualized in the clinic, which presents an opportunity for early identification of increased risk of developing knee OA.

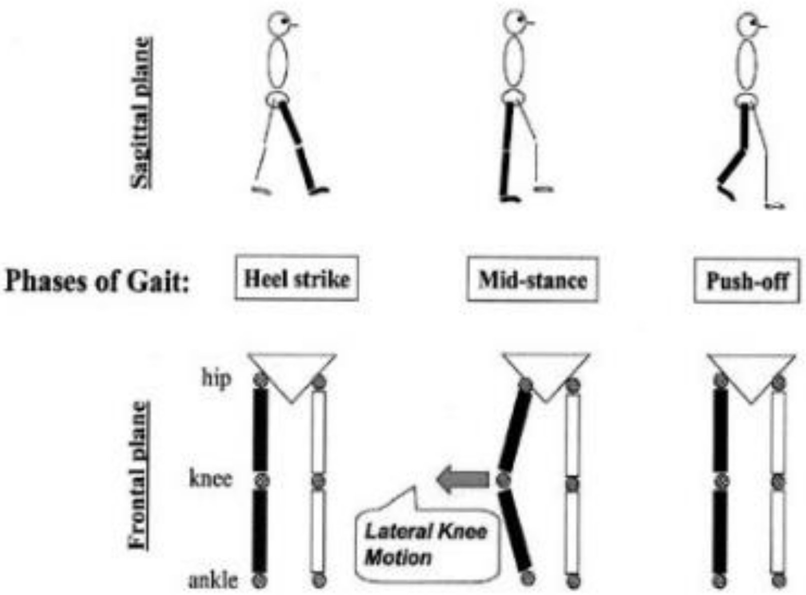

Figure 4. Visualization of varus thrust during gait
Reprinted from A. Chang et al., 2004

Biomechanical Relevance of Varus Thrust

The most likely mechanism by which varus thrust contributes to the progression of medial knee OA is through an increase in medial knee loading, which places repetitive excessive stress on the articular cartilage of the femur and tibia leading to pain and degenerative changes (Mahmoudian et al., 2016). This assumption is supported by studies that show a correlation between the magnitude of varus thrust and the increase in external KAM (A. Chang et al., 2004; Kuroyanagi et al., 2012; Mahmoudian et al., 2016). In people with knee OA, knees with varus thrust were reported to have greater external

KAM (3.63 %BW*Ht) than knees without thrust (2.60 %BW*Ht) (A. Chang et al., 2004). Furthermore, varus thrust occurs during the highest weight bearing stages of the gait cycle, where the knee is already vulnerable to malalignment allowing the joint to become more susceptible to the effects of improper mechanical loading (Sharma et al., 2017).

Biomechanical parameters that have been investigated in an attempt to quantify varus thrust include peak knee adduction angle, knee adduction angle excursion from initial contact to midstance, and peak knee adduction velocity during the same period. The knee adduction angle quantifies the maximum varus position of the knee in stance phase, but provides little information about the dynamic movement of the knee joint (A H Chang et al., 2013). The adduction excursion is defined as the difference in knee adduction angle at initial contact and the maximum knee adduction angle between initial contact and the end of mid stance. Knees with thrust generally have a higher knee excursion (Dixon, Gomes, Preuss, & Robbins, 2018). The knee adduction velocity represents the change in adduction angle over time and characterizes both the direction and speed of movement of the knee along the frontal plane (A H Chang et al., 2013; Foroughi, Smith, & Vanwanseele, 2009). In the knee OA population, knees with varus thrust have a higher knee adduction angle throughout gait and a higher knee adduction velocity in the first 10% of the gait cycle compared to knees without varus thrust as shown in *Figure 5*. Measuring these parameters through motion capture gait analysis quantifies the frontal plane motion of the knee during gait.

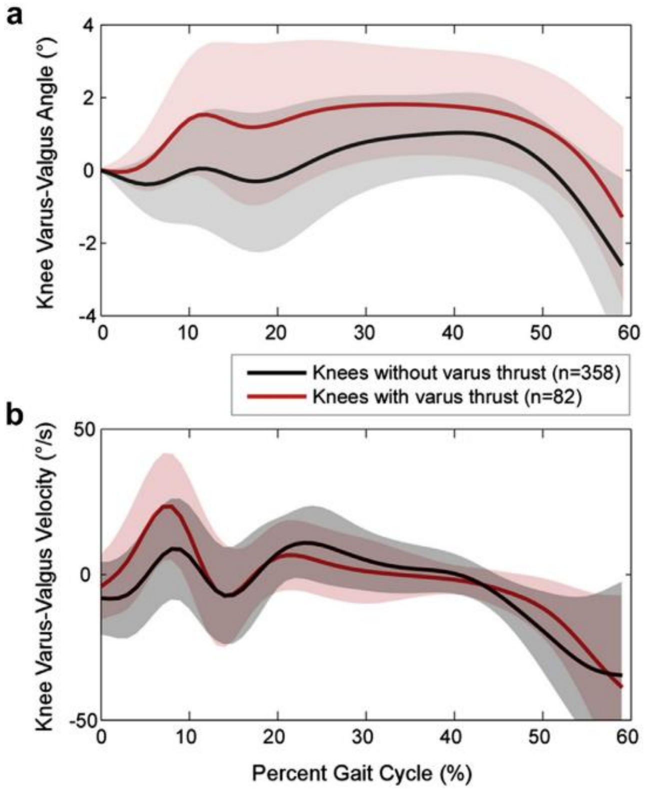

Figure 5. Knee varus angle and knee varus velocity in osteoarthritic knees with and without varus thrust throughout the gait cycle. Reprinted from A H Chang et al., 2013

Clinical Relevance – Association with OA Outcomes

The presence of varus thrust has implications for clinical outcomes in people with knee OA in addition to the associated biomechanical changes in their gait. Using data from the Multicenter Osteoarthritis Study (MOST), it was reported that the presence of varus thrust is associated with the increased odds of incident (OR = 2.17, 95% CI: 1.51, 3.11) and worsening (OR = 2.51, 95% CI: 1.85, 3.40) medial tibiofemoral bone marrow lesions (BMLs) as well as increased odds of worsening medial cartilage loss (OR = 1.85, 95% CI: 1.35, 2.55) over two years (A.E. Wink et al., 2017). The odds for worsening BML and cartilage loss were even greater in knees with varus alignment (A.E. Wink et al., 2017). Another study using MOST data reported that the presence of varus thrust was associated with increased odds of incident (OR = 1.78, CI: 1.33, 2.39) and worsening (OR = 1.43, CI: 1.20, 1.70) WOMAC knee pain as well as incident WOMAC pain in joints distal (OR = 1.34, 95% CI: 1.05, 1.68) and proximal (OR = 1.26, 95% CI: 1.01, 1.58) to the knee (Alexandra E Wink, 2018; Alexandra E Wink et al., 2018).

Factors Related to Varus Thrust

Due to its prevalence and implications in the progression of knee OA and worsening outcomes, there have been many studies conducted to determine risk factors for varus thrust. Using data from MOST, it was seen that varus thrust is more prevalent in limbs with static varus malalignment (OR = 2.39, CI: 1.96, 2.92) and supinated feet during gait (OR = 1.24, CI: 1.04, 1.45) (Alexandra E Wink, 2018). Varus knee laxity, or ligament weakness, and leg length discrepancy were not found to be related to presence of varus thrust in MOST (Alexandra E Wink, 2018).

A greater magnitude of varus thrust suggests a decreased level of control in the frontal plane of the knee that may be associated with decreased proprioceptive acuity, and reduced muscular strength (A. Chang et al., 2010; Alison H. Chang, Lee, Zhao, Ren, & Zhang, 2014). However, knee joint proprioception and knee vibratory perception were not found to be related to the presence of varus thrust in MOST (Alexandra E Wink, 2018). There was also no significant relationship between varus thrust and isokinetic quadriceps strength at 60 degrees/second, though a trend was seen for decreased quadriceps strength being protective against varus thrust [p for trend = 0.07] (Alexandra

E Wink, 2018). In contrast, another study using data from the Osteoarthritis Initiative (OAI) reported that greater knee extensor isometric strength was associated with a reduced odds of varus thrust in knees without radiographic knee OA (OR = 0.96, 95% CI: 0.94, 0.99) (A. Chang et al., 2010). However, this association was not significant in knees with radiographic knee OA (OR = 0.99, 95% CI: 0.97, 1.00) (A. Chang et al., 2010). It is still unclear how quadriceps strength may be related to varus thrust due to these contradictory findings, and association of hamstring strength with varus thrust has not been investigated. While quadriceps muscle is an important stabilizer of the knee, the hamstring muscles have a larger mechanical lever arm to counter forces tending to cause varus thrust during walking.

Muscle activation patterns are another neuromuscular factor that might be implicated in varus thrust. A recent study in a relatively small sample explored the correlations between knee muscle co-contraction, or the simultaneous activation of an antagonist muscle group during muscle action, during walking and varus thrust. It was reported that, in people with knee OA, varus thrust was associated with higher vastus lateralis–lateral hamstring ($R^2 = 0.35$, $p < 0.001$) and vastus medialis–medial hamstring ($R^2 = 0.17$, $p = 0.028$) co-contraction during walking, while the correlations between quadriceps-gastrocnemius co-contraction and varus thrust were not significant (Dixon et al., 2018).

A neuromuscular factor that has not been considered in relation to varus thrust in the knee OA population is the rate of force development (RFD) of the quadriceps, or how quickly the quadriceps generate a force. The argument to use RFD as an alternate outcome measure to maximum voluntary contractions (MVC) has been made, because a leg muscle's ability to generate a force quickly is integral in many daily activities characterized by a limited time frame to develop that force, such as fast walking and descending stairs. Furthermore, RFD may have a role in the stability of the knee joint along the frontal as well as the sagittal plane during early stance phase, during which mechanical loading has already been determined as a mechanism of OA progression (Winters & Rudolph, 2014). Past studies have shown that differences in RFD do exist in populations with OA compared to those without OA, however the presence of varus thrust was not considered in these studies.

Varus thrust can be assessed visually by a trained and certified examiner or quantitatively through gait analysis. Most studies mentioned above used visual determination of thrust. However, by describing the degree of varus thrust through the use of surrogate biomechanical parameters, such as the adduction velocity, more accurate associations may be drawn.

Aims

Varus thrust is a known risk factor in the progression of medial knee OA and has clinical implications not only in the knee but also in neighboring joints of the lower limb and back. While these implications of varus thrust have been well described, the neuromuscular factors related to varus thrust are still not well understood and many studies report contradictory findings. Additionally, many potential modifiable factors remain unstudied. Considering the increased clinical risks and implications compounded by the growing prevalence of knee OA, more research is needed to identify possible neuromuscular factors that may be associated with the presence of varus thrust. This greater understanding of what may contribute to varus thrust may lead to the development of more effective interventions to minimize the presence of varus thrust and its effects on medial knee OA. Therefore, the overall objective of this thesis is to quantify the association of neuromuscular factors with varus thrust. This will be accomplished by addressing two specific aims:

1) To investigate the relationship between isokinetic quadriceps and hamstring strength and quadriceps RFD with biomechanical measures of varus thrust.
2) To determine the relationship between knee muscle co-contraction and biomechanical measures of varus thrust during walking.

METHODS

Participant Population/Study Sample

The data reported for this thesis are secondary analyses from participants in studies conducted at three different research institutions: Boston University (BU), University of Delaware (UD), and University of California, San Francisco (UCSF). These studies were approved by the Institutional Review Boards of each participating intuition and all study participants provided written consent.

At BU, adults between the ages of 45 and 80 and experiencing pain and stiffness upon waking up in the morning in one or both knees were recruited from the local community using advertisements and flyers. They were eligible for the study if they had a body mass index (BMI) of greater or less than 35 kg/m^2, KLG ≥ 2, and medial JSW less than lateral JSW in one or both knees. Participants were excluded if they required the use of a walking aid or self-reported inflammatory arthritis, TKA in both knees, neurological conditions, muscular disease, and painful injuries or conditions of the back or legs (excluding the knees) that could affect walking.

At UD, adults with and without medial knee OA were recruited from the community. Participants were referred from local physicians and recruited from communities in northern Delaware through newspaper advertisements. Standing semi-flexed, posterior-anterior radiographs were used to determine the KLG. Participants with OA had KLG ≥ 2 and greater medial involvement than lateral. Participants without OA had KLG < 2 and were included in the control group. If a participant had bilateral knee OA that fit the criteria, the more symptomatic knee was identified by the individual and used in the analysis. Participants were excluded if they had a history of other orthopedic injuries in the lower extremities (e.g., knee ligament injuries) or spine, used an assistive device, had a history of neurological injury, had a history of rheumatoid arthritis, were pregnant, or had undergone a joint replacement or skeletal realignment procedure in either lower extremity.

At UCSF, adults with and without knee OA were recruited from the community for an observational cross-sectional study. Participants were included in the OA cohort if they were older than 35 years, had OA-consistent knee symptoms such as pain, aching, stiffness or use of medication for knee pain on most days per month during the past year, and had radiographic evidence of knee OA (KLG ≥ 2). The control group consisted of individuals without knee OA that were pain free and had KLG < 2. The exclusion criteria included the concurrent use of an investigational drug, history of intraarticular fracture or surgical intervention in the knee being used in the study, conditions other than knee OA that could that could affect walking or would confound the evaluation of function, and contraindication to MRIs.

Radiographic and Functional Measures

At all three institutions, a bilateral weight-bearing, flexed, posterior-anterior radiograph were acquired for assessment of medial JSW and KLG. Standing full limb radiograph were used to measure HKA. HKA less than 180 degrees was defined as varus while an HKA greater than 180 degrees was defined as valgus as shown in *Figure 1*. KOOS scores were obtained at all three institutions.

Strength Testing

Strength testing protocols were different across the three institutions. Only isometric strength data were acquired at UD and were, therefore, not used in the analyses. Isokinetic strength data were acquired at BU and UCSF using different devices. Since the number of participants at BU was much smaller than at UCSF, only data from UCSF were used for analyses of strength and varus thrust. RFD was only available from BU and these data were used for analyses of RFD and varus thrust.

At UCSF, isokinetic strength testing was performed using a Primus RS instrumented dynamometer (BTE, Hanover, MD, USA). Quadriceps and hamstrings strength data were acquired during isokinetic contractions at 60 degrees/second and 120 degrees/second between 20 and 90 degrees of knee flexion. For each condition, participants performed three warm up trials at progressive effort levels before they completed three maximal effort trials separated by one-minute rest periods. The maximal isokinetic torque normalized to body mass (Nm/kg) during the two conditions was used in the analyses.

At BU, strength testing was performed using a dynamometer (System3, Biodex, Shirley, NY). The knee was placed at 70 degree flexion, and participants were told to push against the device with their leg for 5 seconds. Participants completed three practice trails at submaximal effort, and then performed 2 to 3 - 5 second maximum effort trials with a 60 second rest period for both the quadriceps (extension) and the hamstrings (flexion). These tests were then repeated under isokinetic conditions at 60 degrees/second and 120 degrees/second between 20 and 90 of flexion.

Gait Analysis

At all three institutions participants underwent gait analysis while walking at their self-selected comfortable pace for 4-10 trials. At BU, kinematic data was collected at 250 Hz using a passive 15 camera Qualisys system (QTM, Sweden). Kinetic data was collected at 2000 Hz from floor-embedded force platforms (AMTI, Watertown, MA, USA). At UD, kinematic data was collected at 120 Hz using a passive 8 camera VICON system (Oxford Metrics, UK) and kinetic data was collected at 1080 Hz from a floor-imbedded force platform (Bertec Corp, Worthington, OH, USA). At UCSF, kinematic data was collected at 250 Hz using a passive 10-camera VICON system (Oxford Metrics, UK), while kinetic data was collected at 1000 Hz from floor-imbedded force platforms (AMTI, Watertown, MA, USA). At all three sites, fourteen millimeter spherical retroreflective markers were adhered to bony landmarks of the pelvis, trunk, and lower extremities to identify joint centers. Rigid clusters were placed on the lateral side of the subjects' thighs and legs. Criteria for an acceptable trial included a clean foot strike on any of the embedded force platforms and consistent speed within +/- 5% of the first good trial. All data was processed in Visual 3D (C-motion, Georgetown, MD, USA) to calculate kinetic and kinematic data. Net joint moments were normalized to body weight and height (%BW*Ht) and reported as external moments, and all angles were expressed in degrees. For each participants the average of all trials was computed for stance phase variables. Key variables included the peak KAM and KAM impulse (area under the curve) during first half of stance, adduction excursion from initial contact to midstance, and peak adduction velocity between initial contact and midstance. The adduction excursion and peak adduction velocity variable were used as measures of varus thrust.

EMG

At all three institutions, surface electromyography (EMG) data was recorded concurrently with gait data for the following muscles: vastus lateralis (VL) and vastus medialis (VM) of the quadriceps, the medial (MH) and lateral (LH) heads of the hamstrings, or the biceps femoris, and the medial (MG) and lateral (LG) heads of the gastrocnemii. The electrodes were placed on the mid-bellies of each muscle and parallel to the orientation of the muscle fibers. The skin above each muscle belly was prepared with an alcohol rub, abrading, and shaving before the surface electrodes were applied. At UCSF and BU, muscle activity was recorded at 1000 Hz using a 16-channel wireless EMG system (Trigno Wireless, Delsys Inc., Natick, MA, USA) and preamplified surface electrodes (Baseline noise $< 4.5\ \mu V$, Bandiwidth = 20 – 450 Hz ± 10%, $|CMRR| > 80$ dB, Range = 16 bits, Electrode contact area = 50 mm^2). At UD, muscle activity was recorded at 1080 Hz using a 16-channel EMG system (Motion Lab Systems, Baton Rouge, LA, USA), and preamplified surface electrodes (20 mm inter-electrode distance, 12 mm disk diameter, input impedance 108 U, common-mode rejection ratio (CMRR) > 10 dB) were used. For normalization purposes, EMG data was also collected at rest and at maximal voluntary isometric contraction (MVIC) for each muscle group. The EMG data were analyzed in Visual3D. A high pass filter was applied to the raw data using a recursive 4th order Butterworth filter with a 20 Hz cutoff. Then, a full wave rectified linear envelope was created and a low pass 4th order recursive Butterworth filter with a cut-off of 20 Hz was applied. The processed EMG data taken at rest was subtracted from the processed data from the active trials and then normalized to peak activity from the MVIC. Muscle co-contraction was calculated between four opposing muscle groups: Lateral quadriceps and the lateral hamstrings (VL-LH), the lateral quadriceps and the lateral gastrocnemius (VL-LG), the medial quadriceps and the medial hamstrings (VM-MH), and the medial quadriceps and the medial gastrocnemius (VM-MG). Calculations were done with the previously published equation below, where *i* is the sample number and *n* is the number of data samples in the interval (Rudolph, Scholz, Snyder-Mackler, Axe, & Buchanan, 2002).

$$co - contraction\ value = \frac{\sum_{i=1}^{n} \frac{lower\ EMG_i}{higher\ EMG_i} (lower\ EMG_i + higher\ EMG_i)}{n}$$

Calculating the co-contraction value with this methods accounts for both the timing and magnitude of muscle activity throughout the interval. An average value was calculated for each opposing muscle pair during preactivation (100 ms prior to initial contact), loading response (initial contact to peak knee flexion), and midstance (peak knee flexion to peak knee extension) intervals. *Figure 6* illustrates these intervals of stance phase.

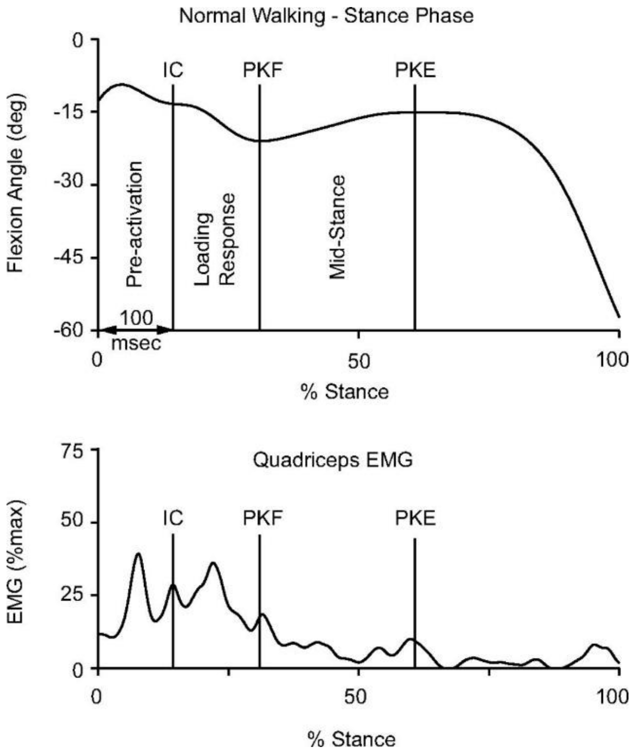

Figure 6. Intervals of stance phase used in the analysis
Knee flexion angle (top) and quadriceps EMG activity (bottom)
IC, initial contact; PKF, peak knee flexion; PKE, peak knee extension
Reprinted from Kumar et al., 2014

Calculations – Rate of Force Development

Calculations for RFD were done using a custom code written in MATLAB R2018b software (MathWorks, Natick, MA). The data was filtered using a 2 Hz Butterworth filter, determined through a fast Fourier transform. The data for each participant was separated into three individual trials and a maximum function was used to calculate T_{max}, the maximum torque generated by the quadriceps and hamstrings in each trial. The trial with the greatest maximum strength for each muscle group was used for the remaining calculations.

$$RFD = \frac{\Delta Torque}{\Delta Time}$$

As seen in the equation above, RFD describes a change in force/torque (T) over a change in time (t). The threshold for all calculations was set at 12 Nm, and the time at which this threshold was reached was considered the time of onset, or t = 0.There are several ways to determine RFD. Three ways were utilized with the BU data and are described below:

1. From the time of onset, $t_{onset} = 0$, to a time of interest such as the first 50, 100, or 200 milliseconds of a muscle contraction. T_{time}, the torque generated by each muscle at t_{time} was extrapolated with the MATLAB code for t_{time} = 50, 100, or 200 milliseconds, and RFD_{50}, RFD_{100}, and RFD_{200} were calculated using the equation below. Because the threshold cutoff was set at 12 Nm, T_{onset} = 12 Nm (Aagaard, Simonsen, Andersen, Magnusson, & Dyhre-Poulsen, 2002; Maffiuletti, Bizzini, Widler, & Munzinger, 2010).

$$RFD_{time} = \frac{T_{time} - T_{onset}}{t_{time} - t_{onset}}$$

2. From different percentages of T_{max} generated over the trial and the time at which these values occurred before T_{max} was reached. $T_{\%}$ was calculated for 10%, 20%, 30%, 80%, and 90% of T_{max}, and the times at which these torque values occur in the trial, $t_{\%}$, were extrapolated in the code. $\text{RFD}_{10\text{-}90\%}$, $\text{RFD}_{30\text{-}90\%}$, and $\text{RFD}_{20\text{-}80\%}$, were calculated using the equation below (Blackburn, Pietrosimone, Harkey, Luc, & Pamukoff, 2016; Hu et al., 2018).

$$RFD_{x-y\%} = \frac{T_{y\%} - T_{x\%}}{t_{y\%} - t_{x\%}}$$

3. Maximum instantaneous RFD was found using a built in MATLAB calculus function. The rate of force development is the first derivative of the force curve, or the slope of the tangent line to the curve. RFD_{peak} is where that slope is the steepest. (Winters & Rudolph, 2014).

For the analyses, $RFD_{20-80\%}$ and peak instantaneous RFD were used as these were found to be the most reliable.

Statistical analysis

The knee adduction excursion and knee adduction velocity obtained from gait analysis data were used as varus thrust variables for all analyses. Descriptive statistics were used to report demographic, radiographic, and KOOS data in people with and without knee OA. For Aim 1, Pearson's correlations were assessed between isokinetic strength and varus thrust variables, separately in people with and without knee OA using data from UCSF. Correlations were assessed between RFD and varus thrust measures using data from BU. For Aim 2, Pearson's correlations were assessed between muscle co-contraction indices and varus thrust variables across all participants. Additionally, measures of knee joint loading and varus thrust were compared between people with and without knee OA using independent t-tests. Varus thrust measures were also compared between various KLG using one-way ANOVA and post-hoc Bonferroni tests were used for pair-wise comparisons. Finally, correlations were assessed between varus thrust measures and demographic, radiographic, and KOOS scores. All analyses were performed using IBM SPSS. Significance was set at $p < 0.05$.

RESULTS

There were a total of 183 participants between the three sites, each contributing one knee each to analysis. *Table 2* shows the demographics of the participants at all three sites, as well as the distribution of medial KLG for the whole sample.

Table 2. Demographic and other characteristics of study participants.

		BU (n = 15)	**UD** (n = 63)	**UCSF** (n = 105)	**Whole Sample** (N = 183)
Sex, Female/Male		10/5	36/27	64/41	110/73
Age, years		66.7 ± 7.6	65.5 ± 9.07	52.8 ± 10.5	58.3 ± 11.9
Weight, kg		78.3 ± 17.2	84.1 ± 18.1	66.5 ± 10.6	73.5 ± 16.4
BMI, kg/m^2		28.4 ± 3.83	28.9 ± 5.04	24.5 ± 3.23	26.3 ± 4.51
KLG, %	**0**	0	37	21	29
	1	7	31	15	24
	2	20	12	27	18
	3	47	15	19	19
	4	27	4	18	10
HKA angle, degrees		175.87 ± 3.1	175.97 ± 3.9	178.82 ± 3.0	177.59 ± 3.6
Medial JSW, mm		2.28 ± 1.79	2.11 ± 2.08	3.70 ± 0.89	3.00 ± 1.69
Notes: Age, weight, BMI, HKA, and JSW reported as mean ± standard deviation (SD); BMI = Body Mass Index, HKA = Hip-Knee-Ankle angle, JSW = Joint Space Width					

Clinically, KLG ≥ 2 are used to define radiographic knee OA. This value was also used to define the OA and non-OA control group for this thesis. Demographic and KOOS score differences between the OA and control groups are shown in *Table 3* and *Figure 7*, respectively. Compared to the control group, the OA group was older and had a higher BMI. Although there were more female participants in the overall sample set, the OA and control groups had comparable numbers of male and female participants. The OA group had more pronounced varus static alignment and less medial joint space width, traits consistent with progressed radiographic OA.

Table 3. Demographic differences between OA and control groups

	Age	**Sex**	**BMI**	**HKA**	**Medial JSW**
Control	52.73 ± 11.03	58/38	25.08 ± 4.11	178.91 ± 2.77	4.01 ± 0.83
OA	64.40 ± 9.58	38/35	27.65 ± 4.57	176.15 ± 3.92	1.92 ± 1.71
p-value	< 0.001	0.929	< 0.001	< 0.001	< 0.001
Notes: Age (years), BMI (kg/m^2), HKA (degrees), and Medial JSW (mm) reported as mean ± standard deviation (SD); Sex reported as Female/Male BMI = Body Mass Index, HKA = Hip-Knee-Ankle angle, JSW = Joint Space Width					

The OA group also had lower KOOS scores corresponding to worse symptomatic and functional outcomes compared to the control group. The p-values for between group differences in KOOS scores were all < 0.001.

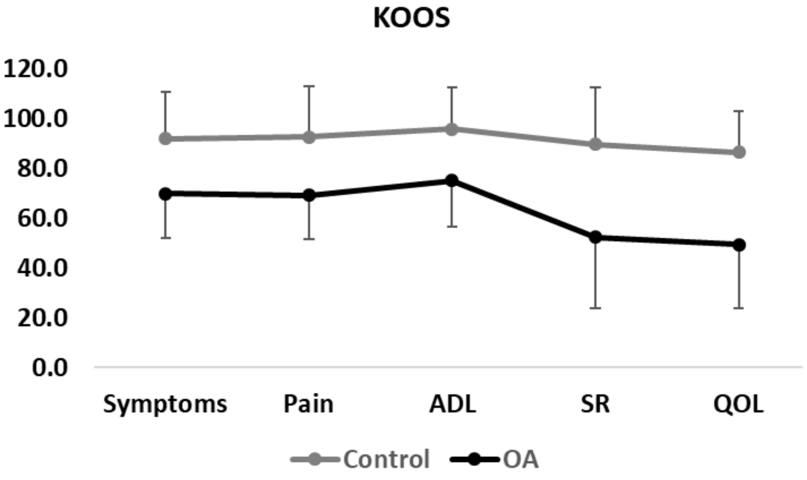

Figure 7. Group Differences in KOOS scores

Figure 8 shows the differences between the OA and control groups for peak KAM and KAM impulse. Numerically, peak KAM and KAM impulse were greater in the OA group, but only KAM impulse was statistically significant (p = 0.003) while peak KAM was not (p = 0.591).

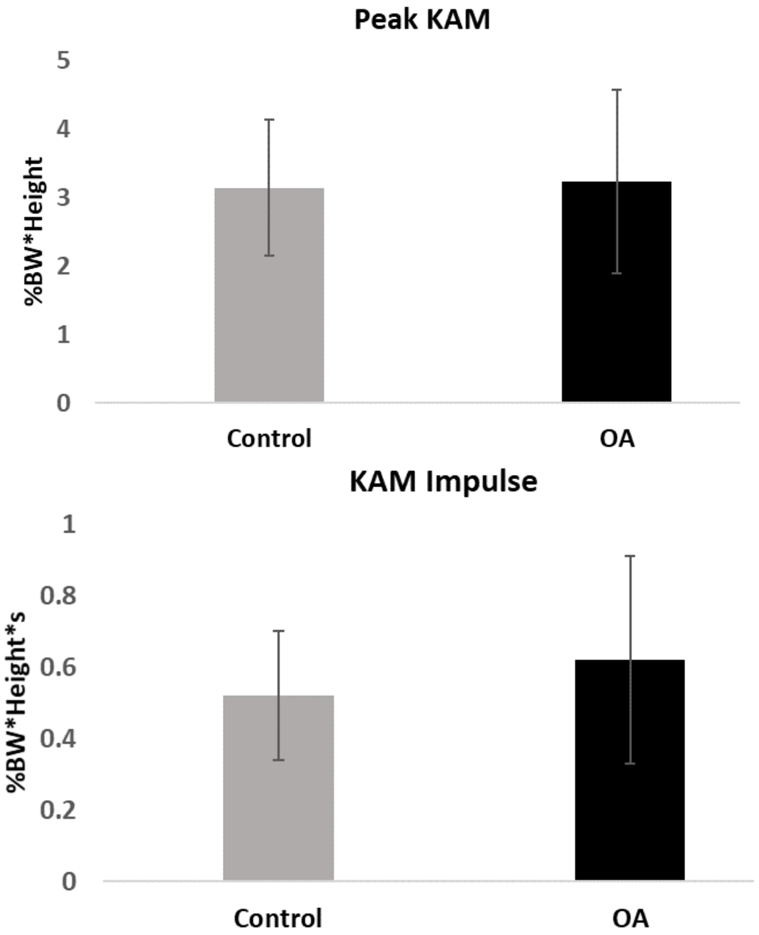

Figure 8. Group differences in peak KAM and KAM impulse between OA and control group

Figure 9 shows the between group differences in varus thrust metrics used in analysis. The knee adduction excursion and knee adduction velocity were both numerically higher in the OA group compared to the control group. However, only peak adduction velocity was statistically significant (p = 0.024) while adduction excursion was not (p = 0.629).

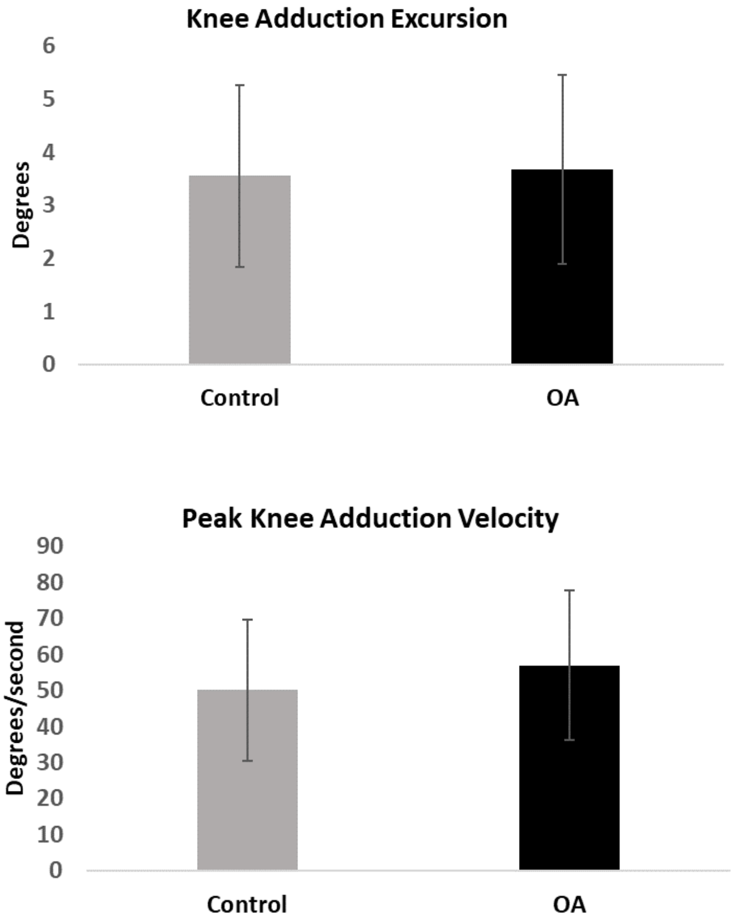

Figure 9. Group differences in varus thrust variables between OA and control group

When adduction excursion and peak adduction velocity were compared between KLG, we observed that overall there were significant differences between groups (p = 0.017 for adduction excursion and p = 0.001 for peak adduction velocity). These results are shown in *Figure 10*. Post-hoc analyses using Bonferroni tests shows that people with KLG = 4 walked with greater adduction excursion compared to those with KLG = 1 (p = 0.022) and those with KLG = 3 (p = 0.014). For peak adduction velocity, post-hoc tests showed that individuals with KLG = 4 walked with greater velocity compared to those with KLG

= 0 ($p < 0.001$), KLG = 1 ($p = 0.001$), KLG = 2 ($p = 0.003$), and KLG = 3 ($p = 0.047$). We also observed a significant correlation between peak knee adduction velocity and KLG (Spearman’s $\rho = 0.246$, $p = 0.001$) and close to significant relationship with adduction excursion (Spearman’s $\rho = 0.142$, $p = 0.055$). These results show worsening varus thrust with increasing severity of knee OA.

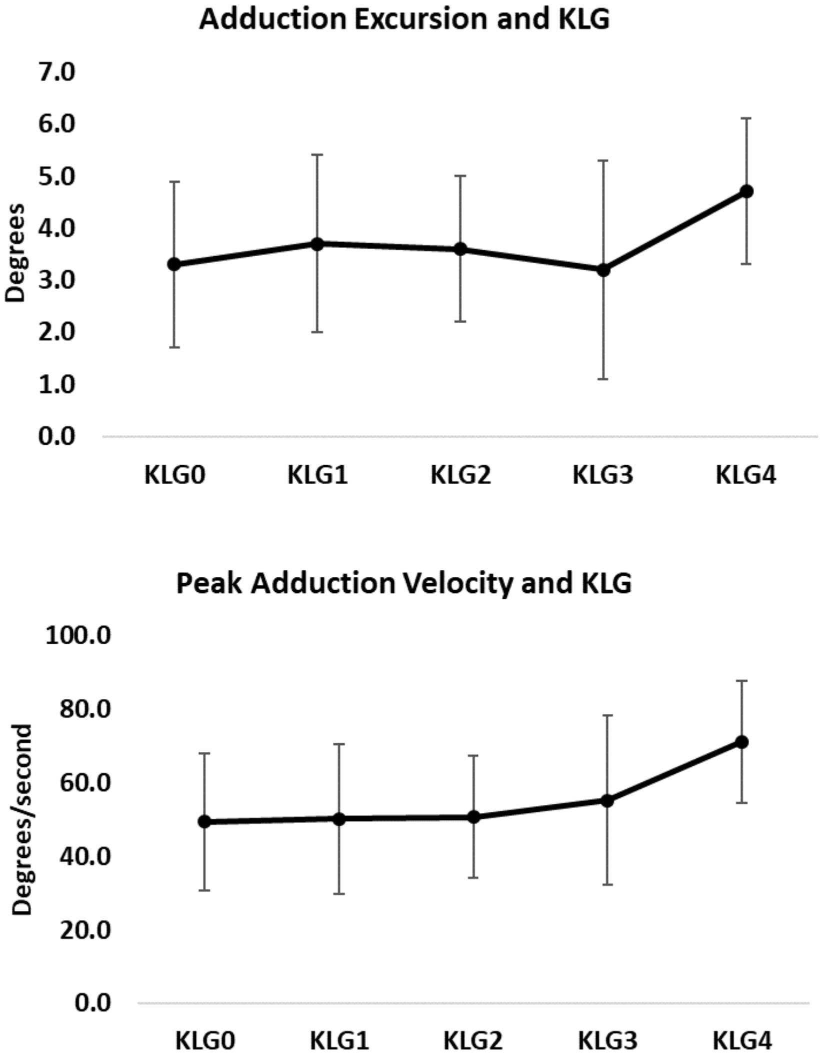

Figure 10. Varus thrust variables correlated with KLG

Correlations between varus thrust variables and demographic factors are shown in *Table 4* for both the OA and control groups. In the control group, greater BMI and smaller medial JSW were associated with greater adduction excursion. In the OA group, greater varus static alignment and less medial JSW were correlated with greater adduction excursion and peak adduction velocity. The relationship between BMI and adduction excursion was not seen in the OA group. The association between walking speed and biomechanical measures of varus thrust was not significant in control (p = 0.339 for adduction excursion and p = 0.453 for adduction velocity) or OA groups (p = 0.901 for adduction excursion and p = 0.324 for adduction velocity).

Table 4. Correlations between varus thrust variables and demographics

		Age	**BMI**	**HKA**	**MJSW**	**KOOS pain**
Control Group						
Excursion	**r**	0.072	**0.376***	0.018	**-0.219***	-0.116
	p-value	0.484	<0.001	0.862	0.040	0.265
Velocity	**r**	0.028	0.126	0.077	-0.120	-0.038
	p-value	0.785	0.223	0.459	0.266	0.714
OA Group						
Excursion	**r**	0.072	0.074	**-0.365***	**-0.452***	-0.105
	p-value	0.510	0.495	0.001	<0.001	0.337
Velocity	**r**	0.078	0.046	**-0.336***	**-0.352***	-0.191
	p-value	0.474	0.675	0.002	0.001	0.077

Notes: Excursion = knee adduction excursion, Velocity = knee adduction velocity Smaller HKA angle corresponds to more varus static alignment, and a lower KOOS pain score corresponds to more pain; Statistically significant values (*p < 0.05) are bolded

Aim 1 Results

Correlations between muscle strength and varus thrust variables were only performed for data from UCSF site. *Table 5* shows the correlations between peak isokinetic quadriceps and hamstrings strength and the varus thrust variables in the control and OA groups.

There were no significant correlations between strength and varus thrust measures in the control group. In the OA group, peak isokinetic quadriceps and hamstrings strength at 60 degrees/second and hamstrings strength at 120 degrees/second were all negatively correlated with knee adduction velocity. These results are shown in *Figure 11* and *Figure 12*. None of the strength measures had significant associations with adduction excursion in the OA group.

Table 5. Correlations between peak isokinetic strength and varus thrust variables in OA and control groups

		Peak Q 60	**Peak H 60**	**Peak Q 120**	**Peak H 120**
Control Group					
Excursion	**r**	0.147	-0.218	-0.049	-0.221
	p-value	0.230	0.076	0.695	0.073
Velocity	**r**	0.138	-0.047	-0.056	-0.052
	p-value	0.260	0.703	0.650	0.679
OA Group					
Excursion	**r**	-0.250	-0.154	-0.103	-0.173
	p-value	0.199	0.434	0.603	0.379
Velocity	**r**	**-0.497***	**-0.514***	-0.288	**-0.389***
	p-value	0.007	0.005	0.137	0.041

Notes: Excursion = knee adduction excursion, Velocity = knee adduction velocity,
Q = Quadriceps, H = Hamstrings, 60 = 60 degrees/second, 120 = 120 degrees/second
Statistically significant values (*p < 0.05) are bolded

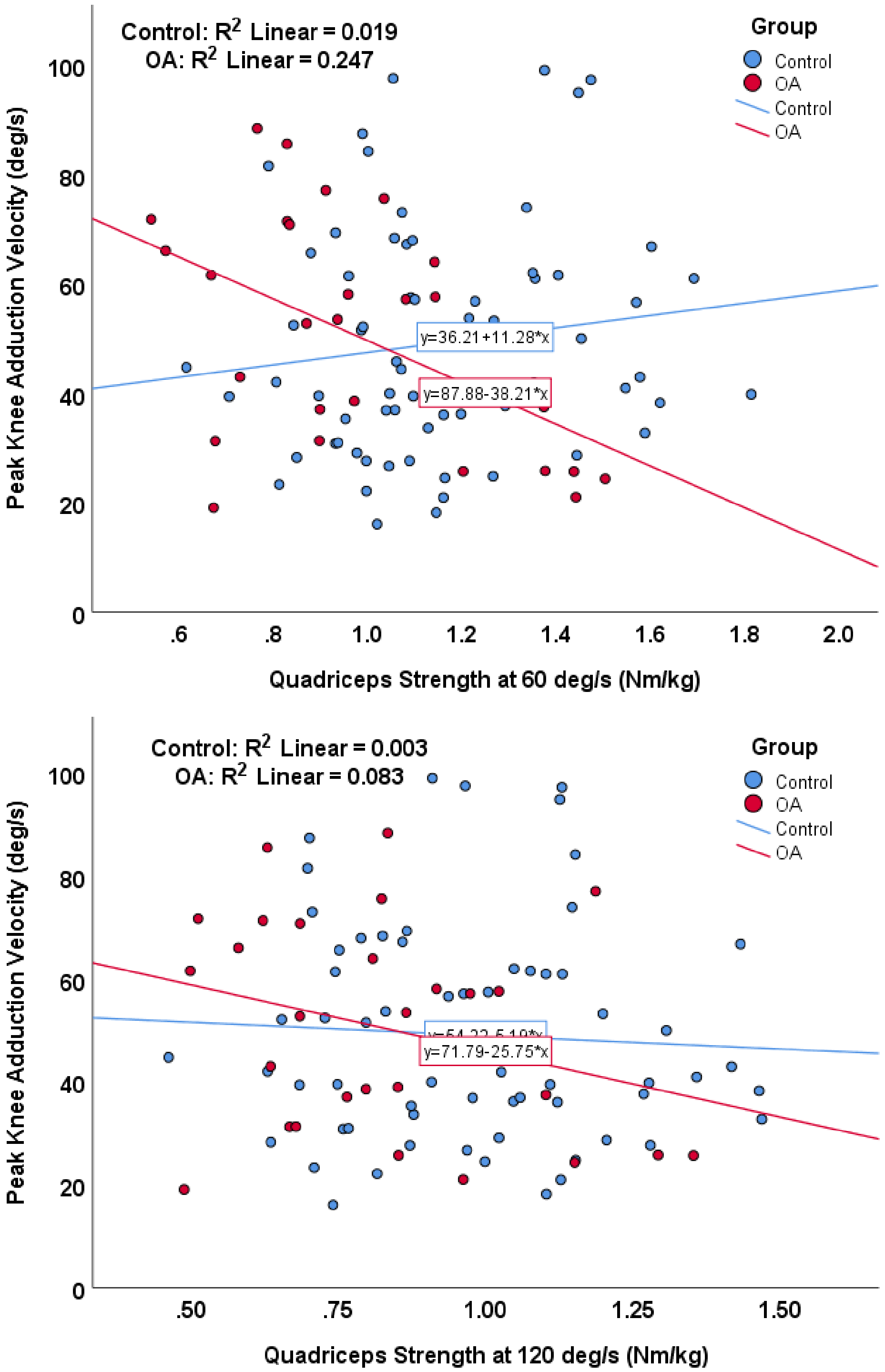

Figure 11. Peak isokinetic quadriceps strength and peak knee adduction velocity in 60 degree/second (top) and 120 degree/second (bottom) conditions in both OA and control groups

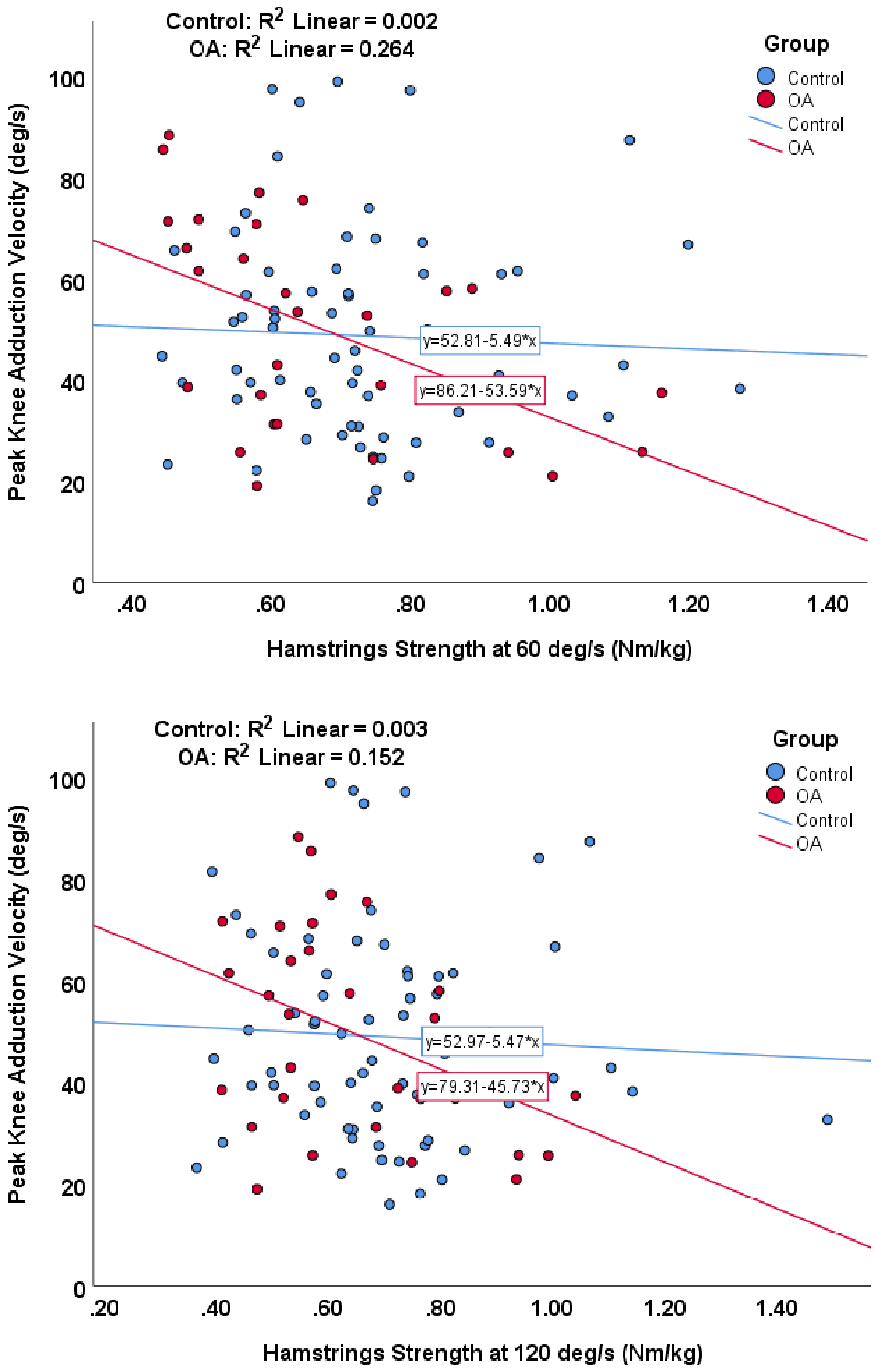

Figure 12. Peak isokinetic hamstring strength and peak knee adduction velocity in 60 degree/second (top) and 120 degree/second (bottom) conditions in both OA and control groups

The correlations between RFD and varus thurst measures were not significant in the participants from BU (n=14). These results are shown in *Table 6.*

Table 6. Correlations between quadriceps RFD and varus thrust variables

		RFD$_{20-80\%}$	**Peak Instantaneous RFD**
Peak Adduction Excursion	**r**	-0.104	-0.087
	p-value	0.725	0.767
Peak Adduction Velocity	**r**	-0.098	-0.121
	p-value	0.739	0.680
Notes: RFD = rate of force development; 20-80% = between 20% and 80% of maximum torque generated			

Aim 2 Results

Using data from participants from all three sites, *Table 7* shows the correlations between the calculated co-contraction values for each muscle pairing at each of the three predetermined stages of stance phase and the varus thrust variables. During preactivation (100 ms prior to initial contact), greater VLLH and VMMH co-contraction was associated with greater adduction excursion and similar trends were seen for association with peak adduction velocity but not reaching significance. During loading response (initial contact to peak knee flexion), the correlations between muscle co-contraction and adduction excursion were not significant. There were trends for greater VLLG and VMMH co-contraction during loading response being related with greater peak knee adduction velocity. During midstance (peak knee flexion to peak knee extension), greater VLLG co-contraction was associated with greater peak knee adduction velocity and there was a trend for greater VMMH co-contraction being associated with greater adduction excursion.

Table 7. Correlations between muscle co-contraction values and varus thrust variables

		VLLG	**VLLH**	**VMMG**	**VMMH**
Preactivation					
Adduction Excursion	**r**	0.088	**0.188***	0.015	**0.210***
	p-value	0.269	0.023	0.853	0.009
Peak Adduction Velocity	**r**	0.132	0.155	0.111	0.153
	p-value	0.096	0.061	0.169	0.059
Loading Response					
Adduction Excursion	**r**	0.106	0.081	0.026	-0.001
	p-value	0.183	0.334	0.746	0.989
Peak Adduction Velocity	**r**	0.152	0.113	0.124	0.151
	p-value	0.055	0.174	0.123	0.061
Midstance					
Adduction Excursion	**r**	0.054	0.052	-0.046	-0.150
	p-value	0.502	0.533	0.573	0.064
Peak Adduction Velocity	**r**	**0.178***	0.049	0.117	0.001
	p-value	0.025	0.557	0.148	0.991
Notes: Statistically significant values (*p < 0.05) are bolded					

DISCUSSION

The objectives of this study were (1) to investigate the relationship between isokinetic quadriceps and hamstring strength, and quadriceps and hamstrings RFD, with biomechanical measures of varus thrust, and (2) to determine the relationship between knee muscle co-contraction and biomechanical measures of varus thrust during walking. We observed that lower quadriceps and hamstrings isokinetic strength was associated with greater varus thrust measured as knee adduction velocity in people with knee OA but not in people without knee OA. We also observed that greater muscle co-contraction prior to initial contact is associated with greater varus thrust. Overall, these results improve our understanding of potentially modifiable neuromuscular factors that may be related to varus thrust and could be used to develop rehabilitation interventions to prevent varus thrust in people with knee OA.

We observed that lower quadriceps isokinetic strength at 60 degrees/second and lower hamstring isokinetic strength at 60 and 120 degrees/second were associated with greater peak knee adduction velocity during walking in people with knee OA. This association was not seen in the control group. There have been previous studies that have investigated the association of quadriceps strength in relation to varus thrust. However, these studies have inconclusive and inconsistent findings. One study reported a trend for decreased isokinetic quadriceps strength at 60 degrees/second being protective against varus thrust [p for trend = 0.07], but the overall relationship was not significant (Alexandra E Wink, 2018). Another study reported that knees with varus thrust had lower isometric quadriceps strength compared to knees without varus thrust (A. Chang et al., 2010). Both of these studies used visual assessment of thrust that might have limited the ability to discern magnitude of varus thrust. We used objective biomechanical measures that allowed us to detect associations between strength and thrust. Furthermore, the use of isokinetic measures may more closely represent the dynamic control of knee that is required during walking vs. isometric measures of strength.

This is the first known study to investigate the peak isokinetic strength of the hamstring in relation to varus thrust. We observed that lower hamstring isokinetic strength at both 60 and 120 degrees/second was associated with greater peak knee adduction velocity in people with knee OA. These findings implicate the hamstrings as an important muscle group in knee joint stabilization in gait and suggest that overall knee muscle weakness is strongly associated with varus thrust in walking in people with knee OA. The results from our study could be used to guide muscle strengthening and training programs for people with varus thrust. Future studies should be conducted to determine whether such rehabilitation programs can reduce varus thrust and prevent progression of knee OA among people who exhibit varus thrust. This is also the first known study to investigate the relationship between the RFD of the quadriceps muscles in people with varus thrust. Our findings did not show a significant relationship between RFD and varus thrust measures. However, this analysis was limited to a small sample set (n = 14), and future studies in a larger cohort are recommended.

Muscle co-contraction has been thought to stiffen and stabilize the knee joint during gait. For this reason, previous studies discuss muscle co-contraction as a potential mechanism to limit varus thrust during walking in people with knee OA. However, these studies do not report co-contraction values at different time periods during stance phase. One study shows that greater quadriceps-hamstrings co-contraction is associated with a greater degree of varus thrust in people with knee OA (Dixon et al., 2018). These findings were replicated in the analysis of this thesis as VLLH and VMMH were positively correlated with knee adduction excursion during the preactivation period of stance phase. Additionally, VLLG was positively correlated with knee adduction velocity during the midstance period. It should be noted that overall, the observed association were weak even though they were statistically significant.

Distinguishing muscle activity patterns in different stages of stance phase provides a greater picture of muscle activity in the moments before and during varus thrust. A greater degree of varus thrust is associated with greater medial and lateral QH co-contraction in the 100 milliseconds preceding heel strike during walking while a greater lateral quadriceps-gastrocnemius co-contraction during midstance. These results may suggest the presence of a compensatory muscle activation mechanism to stabilize the knee joint and reduce the degree of varus thrust before a load is placed on the knee joint and a lateral muscle group tightening after the load is placed to correct the lateral displacement caused by thrust. However, while there were trends, the lack of significant findings for the co-contraction of any muscle pair during loading response is interesting since this is the first instance where the knee adduction angle would begin to increase.

The participant population was comprised of data obtained from three different research institutions across the US. There were more female participants enrolled in the study, though this difference was not statistically significant, and the OA and control groups had comparable number of female and male participants. Compared to the control group, the OA group was older, had a higher BMI, more pronounced varus static alignment, and lower KOOS scores compared to the control group. Though the peak KAM values between the OA and control groups were not statistically significant, the OA group did have a statistically significant higher peak KAM impulse value. The OA group also had less medial joint space width indicative of more progressed radiographic knee OA.

Significant differences were found when the varus trust variables were compared between KLG groups, revealing a positive correlation between worsening varus thrust and knee OA severity. These findings are consistent with previous research (A H Chang et al., 2013; Dixon et al., 2018; Foroughi et al., 2009). Post hoc analyses revealed that this difference is especially pronounced in participants with KLG = 4, the most progressed stage of radiographic knee OA. While our whole sample set (n = 183) is not as large compared to the MOST or OAI databases, we feel that our demographics were still representative of the OA population.

One limitation for this thesis is that data was collected at three different sites, which adds a level of variability in the methodology of data collection such as the functional tests performed, the demographic data collected, and the varying sets of equipment that were used. One specific example where this had an effect was the Primus RS instrumented dynamometer which was used to collect strength data at UCSF. While this dynamometer recorded the peak strength a participant generated, it did not record strength data at a consistent sampling rate over the course of the trial. Therefore, this data was not usable in calculating the RFD of the quadriceps and hamstrings. This discrepancy limited the sample size for this analysis to the BU data (n = 15) and reduced the power of this part of the study. A second limitation for this thesis is the quantitative way in which thrust was assessed. Many studies on varus thrust use visual assessment of varus thrust due to its lower associated time and financial cost compared to that of gait analysis technology. Furthermore, varus thrust is standardly assessed in the clinic visually. For this thesis, an objective measure of varus thrust was used. This difference in thrust classification makes it more difficult to compare the findings of this thesis to previous studies where visual assessment of varus thrust was used. However, quantifying varus thrust through surrogate biomechanical measures allows us to objectively determine associations between neuromuscular factors and the degree of varus thrust rather than relying on the subjective measure of a trained rater. The findings in this thesis are also limited in that the study design was cross-sectional. Future studies should include repeated data collections at follow up visits in order to determine how these factors impact the degree of varus thrust long term, especially if interventions to minimize varus thrust are implemented.

These findings should also be taken into consideration when investigating and developing potential interventions to minimize the degree of varus thrust present in walking. Current varus thrust interventions are limited in addressing biomechanical features through foot orthoses. For example, there have been several studies investigating the effectiveness of valgus knee braces and lateral wedge insoles in reducing peak KAM in people with varus thrust and knee OA (Arnold et al., 2016; Jafarnezhadgero, Oliveira, Mousavi, & Madadi-Shad, 2018).

However, because neuromuscular factors such as muscle strength and muscle activation can be modified through physical therapy and training interventions, the information gained from these analyses can be used to develop more effective interventions in reducing varus thrust.

CONCLUSION

Knee OA is a progressive joint disease that leaves many people disabled every year. With the growing elderly population and rise in obesity rates, OA is projected to increase in prevalence dramatically in the coming years. Varus thrust is a known risk factor in the progression of medial knee OA and is present in up to 37% of people with knee OA. Due to its well-studied clinical implications and easy clinical identification, varus thrust is a potentially modifiable risk factor that can be addressed to slow the progression of knee OA.

In this thesis, knee muscle strength metrics and activation during walking in relation to biomechanical measures of varus thrust were investigated. Gait analysis, EMG, and quadriceps and hamstrings strength testing were completed at three research institutions and correlations were drawn between select neuromuscular factors and biomechanical measures of varus thrust. The finding of this thesis show that a greater degree of thrust is associated with lower isokinetic quadriceps and hamstring strength in people with knee OA. Future studies should investigate whether this knee muscle weakness is protective against varus thrust or failing to compensate for a lack of joint stability. The results also show that a greater degree of varus thrust is associated with greater medial and lateral QH co-contraction in the 100 milliseconds preceding heel strike during walking as well as greater lateral quadriceps-gastrocnemius co-contraction during midstance. These results may suggest a compensatory muscle activation mechanism to stabilize the knee joint and reduce the degree of varus thrust before a load is placed on the knee joint and a lateral muscle group tightening after the load is placed to correct the lateral displacement caused by thrust.

These findings can be used to lead the direction of future research into these neuromuscular factors in relation to varus thrust in the OA population as well as the development of potential interventions to modify these neuromuscular factors in a way that minimizes varus thrust and prevents the further progression of OA.

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