DETERMINING THE ASSOCIATION BETWEEN KNEE MUSCLE STRENGTH AND VARUS THRUST IN KNEE OA

by

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This thesis is dedicated
To my parents, Prasad and Anjali Kamat, for their unconditional love and support
And also in loving memory of my beloved Shona.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABSTRACT

Varus thrust (VT), a biomechanical feature reported in knee OA is identified visually, quantified using frontal kinematics and associated with OA progression. Objectives: To determine the association between i) two objective measures of VT, ii) knee muscle strength and objective measure of VT, and iii) biomechanical variables and objective measure of VT. 87 ASYM and 135 MOD OA participants underwent gait assessment. Frontal and sagittal plane knee angles (KFA range) and frontal plane moments (KAM: peak and impulse) were calculated. Participants completed MVICs of knee extensors, flexors and plantarflexors on a Cybex™ Dynamometer. Correlation and multivariate regression indicated no significant association between two objective measures of VT as well as strength, KAM impulse, KFA range and the objective measure of VT ($p>0.05$). Significant associations were found between peak KAM and objective measure of VT ($p<0.05$). Factors other than muscle strength are related to objective measure of VT including biomechanical variables.

LIST OF ABBREVIATIONS USED

ASIS	Anterior Superior Iliac Spine
AMTI	Advanced Mechanical Technology Incorporation
ASYM	Asymptomatic
BW	Body Weight
BMI	Body Mass Index
CNS	Central Nervous System
Deg	Degrees
DOHM	Dynamics Of Human Motion
GCS	Global Co-ordinate System
Hz	Hertz
HT	Height
IRED	Infrared
ISB	International Society Of Biomechanics
JSN	Joint Space Narrowing
ICC	Intraclass Correlation Coefficients
KAM	Knee Adduction Moment
KFA	Knee flexion angle
KL	Kellgren and Lawrence
Kg	Kilograms
k	Cohen's Kappa Coefficient
KVAV	Knee Varus Angular Velocity
KAA	Knee Adduction Angle
KE	Knee Extension
KF	Knee Flexion
m	Meter
MVIC	Maximum Voluntary Isometric Contraction
MOD	Moderate
N	Newton
OA	Osteoarthritis

OR	Odds Ratio
pKVAV	Peak Knee Varus Angular Velocity
PNS	Peripheral Nervous System
PF	Plantarflexion
S/Sec	Second
TKA	Total Knee Arthroplasty
WOMAC	Western Ontario and McMasters Universities Osteoarthritis Index
WHO	World Health Organisation

GLOSSARY

VARUS THRUST

Varus thrust is defined as a rapid change in the knee varus angle (frontal plane) during early stance with a return to a less varus and more neutral alignment during toe-off (Chang et al., 2004; Lo et al., 2012). In this thesis "Varus thrust" indicates a non-visually assessed varus thrust and the possibility of quantifying a varus thrust by the objective measures used in this thesis.

Clinical VARUS THRUST

Commonly observed visually the visual appearance of this rapid change in knee varus angle will be defined as a clinical varus thrust.

INSTABILITY

Three sub-systems (active, passive and neural) are theorized to work in cohesion with each other in order to maintain joint stability i.e. reduce motion within a pain free range (Panjabi, 1992). A failure in one or more of the sub-systems compromises the ability of the joint to stay within the control limits after the application of forces and results into an instability.

An instability when observed during a dynamic activity like walking is termed as dynamic instability in this thesis.

LAXITY

Laxity is a state where there is a lack of tautness in the ligamentous structures which results into an increase in the joint freedom of movement (Medical Dictionary for the Health Professions and Nursing, 2012). In this thesis, laxity occurs as a result of over stretching of ligamentous structures and "Pseudo-laxity" occurs as a result of slacking of ligamentous structures.

ASYMPTOMATIC

Participants over the age of 35 years with no previous history of injuries to the lower extremity or knee surgery. No symptoms of any degenerative joint disorder such as knee pain, morning stiffness or crepitus.

MODERATE KNEE OSTEOARTHRITIS

Participants were diagnosed with knee osteoarthritis based on radiographic and clinical criteria according to the American College of Rheumatology guidelines (Altman, 1995). Participants were categorized into the moderate knee OA group if they had a Kellgren Lawrence (KL) (Kellgren & Lawrence, 1952) score ranging from KL score I to KL score IV and self-reported that they were able to perform functional activities such as walk one city block, reciprocally ascend and descend a flight of stairs and jog five meters. These participants were also not scheduled for a total knee arthroplasty (Hubley-Kozey et al., 2006).

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CHAPTER 1: INTRODUCTION

1.1 Overview

Osteoarthritis (OA) is a progressive degenerative joint disorder affecting the articular cartilage, subchondral bone and peri-articular tissue resulting in symptoms such as pain, stiffness, and swelling (Buckwalter & Martin, 2006). It is the most prevalent form of arthritis affecting millions worldwide (Lawrence et al., 2008) being the eleventh highest contributor to global disability (Cross et al., 2014). The focus of this study was the knee joint which is commonly affected (Oliveria et al., 1995). Knee OA is a chronic condition with no known cure and total knee arthroplasty (TKA) is the end-stage treatment for knee OA. Researchers have attempted to look at the various biomechanical (Astephen et al., 2008; Andriacchi et al., 2006), biochemical (Stannus et al., 2010) and psychological (Wise et al., 2010) factors associated with the onset and progression of knee OA with a view to impede the progressive nature of this disease.

There are a number of risk factors such as aging (Anderson & Loeser,2010), abnormal joint mechanics (OR 3.5) (Sharma et al.2012;Felson et al.,2013;Maly et al.,2008), muscle strength deficits (OR 1.66) (Segal et al.,2010; Van der Esch et al.,2007; Hurley et al.,1999;Baert et al.,2013), obesity (RR 1.7 to 2.4) (Niu et al.,2009; Gelber et al.,1999;Felson et al.,2000) and previous injury (RR 2.95) (Martin et al.,2004; Gelber et al.,2000; Saxon et al.,1999;) associated with the OA disease process. Of these, joint mechanics has been found to be associated with the severity (Mundermann et al.,2004; Astephen et al.,2008) and progression (Miyazaki et al.,2002; Bennell et al.,2011; Hatfield et al.,2014) of knee OA (Felson et al.,2013) and thus, has been gaining

importance in recent years. Joint level biomechanics reflects the intrinsic environment within the joint during activities like walking, stair climbing etc. An abnormality in this environment such as a disturbance in the load distribution within the joint can affect the normal functionality of the joint structures (Andriacchi et al., 2004). Once affected these structures respond negatively to the abnormal joint loads, disturbing the normal process of cartilage synthesis and degeneration which may eventually contribute to disease progression (Andriacchi et al., 2004 & 2009). The study of these abnormal joint mechanics is central to this thesis.

Among the knee OA studies, gait is a common model used to analyze the joint mechanics (Andriacchi, 1994; Al-Zaharani et al., 2002; Baliunas et al., 2002). Gait represents the natural cyclic loading during daily activities (Andriacchi & Mundermann, 2006) and is a common activity in weight-bearing. Gait analysis can capture the joint motion, joint moments and muscle activity patterns of an individual. These motions and moments can be examined in three planes namely, sagittal, frontal and transverse plane. The most common variable dominating the knee OA literature is the external knee adduction moment (KAM) captured in the frontal plane. KAM features (peak and impulse) have been predictive of knee OA progression (Chehab et al., 2014; Miyazaki et al., 2002; Hatfield et al.,2014; Chang et al.,2015; Bennell et al.,2011). The KAM is reported to be a proxy measure that represents the relative medial- lateral force distribution rather than the actual force on the medial compartment (Kutzner et al., 2013). However, these moments can be examined only with complex gait analysis techniques, which may be difficult in a clinical setting. Gait analysis in a clinical setting is usually visual where abnormal motions about the joint can be observed. One such

abnormal motion is the rapid change in the knee varus angle (frontal plane) during early stance with a return to a less varus and more neutral alignment during toe-off clinically termed as varus thrust (Chang et al.,2004; Lo et al.,2012). Varus thrust was found to increase the odds of knee OA progression (Chang et al., 2004) and has been directly associated with the peak KAM magnitudes (Chang at al., 2004; Hunt et al., 2011; Kuroyanagi et al., 2012). Collectively, this work provides the rationale for examining frontal plane mechanics and more specifically frontal plane angular motion (varus thrust) given its potential clinical relevance.

A second clinical feature associated with knee OA are knee muscle strength deficits, specifically of the quadriceps muscle (Baert et al., 2013; Slemenda et al., 1998; Segal et al., 2009; Hubley-Kozey et al., 2014). These deficits have been found to become more pronounced as the disease progresses (Palmieri-Smith et al., 2010). Maintaining muscle function is important as muscle forces are key components of the active joint stability system (Panjabi,1992) and are thought to counteract external joint moments and absorb limb loading (Bennell et al.,2013). Unlike the structural changes that occur within the joint which may not be modifiable conservatively, muscle strength deficits can be rehabilitated. Since these deficits can be modified, studies have attempted to determine if strength training exercises can reduce biomechanical variables such as the peak KAM magnitudes. However, in spite of an overall improvement in knee muscle strength no significant changes were found in the peak KAM measures (Lim et al.,2008;Thornstensson et al.,2007; Foroughi et al.,2011). The primary focus of most of these studies was on strengthening the quadriceps muscle. The lack of significant findings may in part be due to the exclusive focus on the quadriceps muscle despite

strength deficits found in the hamstrings and plantarflexors in knee OA (Hubley-Kozey et al., 2014; Baert et al., 2013).

Unlike the peak KAM, varus thrust can be assessed visually and as mentioned earlier, both have been associated with each other. To our knowledge the role of strength of the three knee muscles with varus thrust has not been evaluated directly and knowing this association may have direct clinical relevance compared to the peak KAM as a recent study indicated that the presence of varus thrust has an influence on the type of quadriceps strengthening protocol for those with knee OA (Bennell et al., 2015). Understanding this relationship can provide further insight on the control of a varus thrust and in turn the peak KAM or KAM impulse for which emerging evidence shows predictive value for OA progression. The overall goal of this thesis is to better understand the association between varus thrust and knee joint muscle strength and joint biomechanics during walking. To achieve this goal there are three objectives stated below with a brief rationale for each. Concisely, objective 1 determined the association between two methods used to quantify varus thrust in the literature that used frontal plane kinematics, objective 2 looked at the association between an objective measure of "varus thrust" and knee joint muscle strength and objective 3 looked at the association between an objective measure of "varus thrust" and knee joint biomechanical variables. Objective 2 and 3 are the main focus of this study.

1.2 Objectives And Study Rationale

Motion data in the frontal plane can be used to determine the frontal plane angular displacement or knee adduction angle (KAA) which has been examined in

studies of medial compartment knee OA (Duffell et al.,2014; Yang et al.,2010; Thorp et al.,2006). The rapid dynamic change in this angle, defined earlier as a varus thrust (Chang et al,2010; Lo et al.,2012), is commonly assessed visually and this subjective approach relies on the clinician's proficiency to identify the thrust. The reported prevalence of varus thrust varies from 17% to 40% among several studies (Chang et al.,2004 & 2010; Harvey et al.,2009; Bennell et al.,2015) and is predominant in Caucasians, medial knee OA, older age group, high BMI (Chang et al., 2010) and men (Lo et al.,2012). Varus thrust may cause a repetitive stress on the medial aspect of the knee joint. With visual identification of varus thrust being previously associated with radiographic disease progression (Chang et al., 2004), both visual identification (Chang et al., 2004; Hunt et al., 2011) and quantitative measure (Kuroyanagi et al., 2012) of varus thrust has been associated with the peak KAM and thus, make it an interesting variable that if better understood could open up the potential for its use as a valuable screening metric in knee OA management. Different methods exist in the literature to quantify "varus thrust" and they have different degrees of technical and computational complexity but include frontal plane knee angular motions (Kuroyanagi et al.,2012) and velocity measures (Chang et al.,2013; Takigami et al.,2000).

Objective 1: Determine the association between two methods that utilize frontal plane knee varus angular velocity measures as an objective measure of varus thrust.

Rationale for objective 1

Researchers including Chang et al., 2013, Takigami et al., 2000 and Kuroyanagi et al., 2012 have developed methods to quantify varus thrust based on the change in KAA early in the stance phase of the gait cycle. The methods proposed to quantify varus thrust by these investigators are different and there is no consensus on a gold standard. Chang et al., 2013 quantified varus thrust by calculating peak angular velocity from the time derivative of the knee angle in the frontal plane (peak knee varus angular velocity (pKVAV)), whereas Takigami et al, 2000 calculated the absolute angular velocity as a change in the angle formed by lower limb markers from heel strike to foot flat with respect to time. In contrast, Kuroyanagi et al, 2012 calculated the varus thrust as a change in the lower limb markers from heel strike to first peak varus. However, among the three methods mentioned above, the Chang and Takigami methods quantify varus thrust by calculating an angular velocity measure, but whether they are comparable is not known. While the method proposed by Chang et al, 2013, is the only method found to be validated against a visually observed varus thrust in those with knee OA, the Takigami method is easier to implement, does not require complex mathematical calculations and expertise. Therefore, this method has the potential to be used by clinicians to quantify varus thrust and this can help improve objectivity in determining a varus thrust. Thus, the current thesis examined the association between the Chang and Takigami methods in an attempt to determine if these two measures can be used interchangeably as a measure of varus thrust.

Objective 2: To determine the relationship between an objective measure of "varus thrust" and knee muscle strength (quadriceps, hamstrings and plantarflexors).

2 a).Determine if this relationship is affected by OA severity, as determined by KL scores, within the moderate knee OA group.

Rationale for objective 2

The proposed research aims to examine factors related to varus thrust. One such factor is knee muscle strength as deficits have been observed in the knee OA population compared to controls. Defined as an ability to generate maximal force by a muscle group (Knuttgen and Kraemer, 1987), strength of the muscles around the knee measured by a net external torque were lower in those with knee OA and the reduction was dependent on the degree of knee OA severity (Hubley-Kozey et al., 2014), sex (Baert et al., 2013; Hubley-Kozey et al., 2014; Segal et al., 2010) and age (Frontera et al., 2008). Among the knee muscles, quadriceps muscle strength is typically measured and found to be reduced more so in women and with an increase in OA disease severity (Slemenda et al.,1998; Brandt et al.,1999; Segal et al.,2009). However, it has been reported that the hamstrings and plantarflexors also have strength deficits (Hubley-Kozey et al., 2014; Baert et al., 2013) in those with established knee OA.

Measuring muscle strength gives an idea about the functioning of the muscle. Muscles function during activities like walking and help in the appropriate load distribution and absorption within the joint (Bennell et al., 2013). But in conditions like knee OA, these muscles may not be mechanically efficient causing them to work at a higher capacity and by using compensatory strategies such as co-contraction to enhance stability (Schmitt & Rudolph, 2008; Lewek et al., 2004). Additionally, the voluntary and reflex control of strength deficient muscles is slower than well-conditioned muscles

thereby compromising the neuromuscular protective mechanisms leading to excessive instability (Hurley, 1999). Varus thrust understood to be a dynamic instability is related to reduced knee extensor strength which is a potent risk factor (Chang et al., 2010) and has been shown to respond positively to neuromuscular strengthening exercises (Bennell et al., 2015). Varus thrust may appear as a result of an inability of the internal soft tissue structures around the joint to balance the high KAM (Andriacchi, 1994; Cooper et al., 2006; Kumar et al., 2010 &2013). Assuming that the strength deficient knee muscles aren't able to counteract the high moments, the stability would then rest on the passive lateral ligaments that would respond only to a stretch. However, small associations have been reported between the strength deficit knee muscles and high KAM magnitudes (Hubley-Kozey et al., 2014; Aaboe et al., 2011). This may indicate that it is not just strength but the inability of these muscles to 'switch on' at the appropriate time during the gait cycle where the dynamic instability occurs. Andriachhi (1994) suggested that active contraction of the hamstrings and the lever arm between the line of action of the quadriceps muscle and medial point of contact of the joint reaction force, can provide dynamic stabilization and thus reduce varus thrust. So a first step in understanding the relationship of muscle function with varus thrust, we examined muscle strength of the major muscle groups around the knee joint that can contribute to the active component of joint stability.

Objective 3: To determine the relationship between an objective measure of "varus thrust" and the frontal plane moment (KAM peak and impulse) and sagittal plane angular displacement (KFA range).

Rationale for objective 3

Initiation and progression of knee OA has been related to the mechanics of gait (Andriacchi, 2004). As mentioned earlier the most frequently measured gait variable used as an indicator of the ratio between medial and lateral compartment loading, and thus examined in medial knee OA, is the peak and more recently, the impulse of the KAM (Bennell et al.,2011; Kutzner et al.,2013). Varus thrust being a distinct occurrence has been associated with higher peak KAM magnitudes (Chang et al., 2004; Hunt et al., 2011; Kuroyanagi et al., 2012). The KAM variables have been important predictors in OA progression models as mentioned earlier (Miyazaki, et al.2002;Bennell,et al.,2011;Chehab,et al.,2014;Hatfield,et al.,2013;Chang,et al.,2015) and knowing their association with varus thrust, which is an observable or more easily measured variable clinically could have clinical relevance. However, the KAM impulse that accounts for both magnitude and duration of loading throughout the stance phase (Maly et al., 2013) has not been previously associated with a visual or an objective varus thrust measure. The proposed study will look at both the peak KAM and the KAM impulse and its association with an objective quantitative measure of frontal plane motion "varus thrust".

Finally this study will also look at the relation between the sagittal plane knee angular displacement and varus thrust. Varus thrust is observed at the beginning of mid-stance when the knee is near extension (Kuroyanagi et al., 2012). In knee OA the overall knee flexion excursion during early stance is reduced (Kaufman et al., 2001;Astephen et al.,2008;Zeni et al.,2009;McCarthy et al.,2013; Childs et al.,2004; Lewek et al 2004) and the magnitude of reduction is influenced by OA severity (Astephen et al.,2008).

Varus thrust has also been associated with knee OA severity (Takigami et al., 2000; Kuroyanagi et al., 2012; Chang et al., 2013) and thus, the early stance sagittal plane knee angle may have an influence on the varus thrust presence. While knee extension is otherwise considered as a stable position (close-packed) due to adequate bone congruency and ligament tautness, OA structural changes (genu varum and medial joint space narrowing (JSN) greater than lateral) can compromise bone congruency and lead to imbalances between medial and lateral forces as reflected by a high KAM. This may result in the chronic stretching of the postero-lateral structures inducing laxity (Andriacchi,1994) reported in the knee OA literature (Lewek et al.,2004; Sharma et al.,1999 & 2003;Wada et al.,1996) and thereby contribute to a varus thrust (Cooper et al.,2006). Knee flexion is assumed as a stable position among this group (Brown & Neumann, 2004) and thus, used as a strategy to reduce the appearance of varus thrust (Noyes et al., 1996). However, while this strategy may appear to reduce varus thrust, it can not only increase the overall joint loading but also compromise stability as the muscle co-contraction required to maintain this position may not be as efficient owing to strength deficits. Thus, associations between varus thrust and the sagittal plane knee angular displacement may shed light on strategies to manage varus thrust.

In summary varus thrust has been found to be prevalent among men, varus aligned knees, medial knee OA and high BMI. It has been associated with knee OA progression and the biomechanical marker of progression, peak KAM. This study examined factors associated with its occurrence and in particular factors that can be altered and hence included in conservative management such as muscle strengthening or gait re-training for medial compartment knee OA. Conservative treatments such as

lateral wedge insoles (Ogata et al., 1997), orthotics, gait modifications like toe-out and lateral trunk lean (Hunt et al., 2011) and invasive approaches such as high tibial osteotomies (Takigami et al., 2000) aim to alter the frontal plane dynamics and thus help to reduce the varus thrust. But whether the role of other factors such as deficits in knee muscle strength can have greater or equal impact on this dynamic feature may offer more insight into optimal OA management.

1.3 Hypothesis

1) There will be a strong positive association ($R^2 \geq 90\%$) between two methods (Chang et al.,2013 and Takigami et al.,2000 method) that utilize frontal plane knee varus angular velocity measures as an objective measures of varus thrust indicating that the two can be used interchangeably.
2) There will be a negative relationship between the quadriceps, hamstring and plantarflexor strength and an objective measure of "varus thrust" indicating that higher muscle strength is associated with less varus thrust.

   Sub hypothesis: the above relationship in the moderate knee OA group, will be affected by disease severity as measured by KL grades. This could indicate that those with a lower KL scores (I-II) will have a higher muscle strength and less varus thrust as opposed to those with higher KL scores (III-IV).

3) a) The objective measure of "varus thrust" will explain significant variance in the KAM magnitude measures, but more variance will be explained in the peak KAM compared to the KAM impulse, as the peak normally occurs early to mid-stance.

b) There will be a negative relationship between an objective measure of "varus thrust" and the KFA range, indicative that greater "varus thrust" will be related to a smaller KFA range and a more extended knee.

This thesis is divided into 6 chapters. The first chapter included a brief introduction, rational for the study objectives and hypothesis. Chapter 2 provides an insight into the background and literature review, Chapter 3 describes the methods employed to fulfil the study objectives. The results of this study are presented in Chapter 4 and Chapter 5 provides a discussion and interpretation of the results. Finally, the concluding remarks of this study are included in Chapter 6.

CHAPTER 2: BACKGROUND AND RATIONALE

2.1 Osteoarthritis

Arthritis (*Arthron*- 'joint', *-itis* - 'inflammation') is a joint disorder characterized by tissue degeneration, inflammation, stiffness and pain that affects both the small and large joints. Arthritis has existed since the times of the pre-historic Amerindians (Bridges et al., 1992, Panush et al., 2012) and continues to affect the human body even today. There are different forms of arthritis which can be distinguished on the basis of signs, symptoms and clinical laboratory tests. The most common form of arthritis is Osteoarthritis (*Osteo* – 'bone') and this will be the focus of the thesis.

Osteoarthritis (OA), also known as a degenerative joint disorder, includes progressive loss of the articular cartilage accompanied by an attempted repair of the articular cartilage, remodeling and sclerosis of the subchondral bone and osteophyte formation (Buckwalter & Martin, 2006). The meaning of the word is somewhat misleading as osteoarthritis is not a disease of just the bones but also the articular cartilage, capsule, and surrounding periarticular structures making it a disease of the whole joint (Brandt, 1986). OA is commonly seen in the joints of hip, knee, hand and spine. Among the weight bearing joints the knee joint is most commonly affected (Oliveria et al., 1995; Arthritis Alliance of Canada, 2010) and hence the focus of this thesis. Most often the exact cause of knee OA is unknown or idiopathic and this is commonly known as primary OA. However if knee OA occurs as a result of a previous

injury, trauma or surgery, as in the case of an ACL injury or fractures , then it is known as secondary OA. These terms are not universally accepted however it is clear that it is not one disease and that there are various phenotypes (Castaneda et al., 2013; Knoop et al.,2011) making the study of knee OA mechanisms sometimes difficult. Risk factors for knee OA include aging (Anderson&Loeser,2010), obesity (Zhou et al.,2014; Lee et al.,2012;Oliveria et al.,1999), abnormal joint mechanics (Maly,2008), muscle strength (van der Esch et al. 2007; Hurley, 1999), joint overuse and trauma/injury (Martin et al.,2004; Gelber et al.,2000; Saxon et al.,1999). Risk factors vary depending on the sex, for example reduced muscle strength is a factor in women (Slemenda et al., 1999) whereas knee varus misalignments is a factor in men (Wise et al., 2012).

2.1.1 Epidemiology Of Knee Osteoarthritis

Arthritis Alliance of Canada, 2010 has reported that OA affects 1 in 8 (13%) of Canadians and has a significant impact on long-term disability. Further, it is expected that by 2040, 10.4 million Canadians will suffer from OA compared to the 4.4 million osteoarthritic people in 2010. The prevalence of knee OA is higher in women than men with an average ratio of women to men being 1.46:1 over the next 30 years. The difference between women and men is greater post 50 years, with men being affected more frequently below 45 years and women above 50 years (Petersson et al., 2002). Knee OA is likely to become the fourth most important cause of disability in women. It has also been estimated that the total economic burden of OA will increase from $2.7 billion in 2010 to $1455.5 billion in 2040 (Arthritis Alliance of Canada, 2010).

According to WHO, 80% of those affected by knee OA have limitations in movement and 25% cannot perform major activities of daily living. While this is only in Canada, 33 % of the United Kingdom population over the age of 45 years has OA of which 18 % is knee OA (Arthritis research, UK, 2013). In 2005, 27 million Americans had OA and according to the Framingham study the prevalence of knee OA above the age of 45 years is 19.2 % (Lawrence et al., 2008). According to the COPCORD studies, 27 % of the East Asian population has knee OA (Fransen et al., 2011). Thus, knee OA is a global burden affecting both developed and developing countries. Considering this exponential rise in the number of people living with osteoarthritis, that there is no known cure, with total joint replacement as an end-stage OA treatment, it is necessary to implement appropriate intervention strategies in order to slow down the disease process.

2.1.2 Pathophysiology Of Knee Osteoarthritis

The mechanisms responsible for the degeneration and loss of articular cartilage with changes in the periarticular structures in knee OA are not well understood (Buckwalter & Martin, 2006). It has been postulated that an interplay between biochemical and biomechanical factors can potentially cause the disease (Felson et al., 2000). Biomechanical insults like high-impact, torsional loads in conjunction with abnormal joint anatomy, joint instability, or inadequate muscle strength potentially increase the risk of degeneration of normal joints (Buckwalter et al, 1998; Vincent et al., 2012) by initiating proteoglycan depletion and collagen destruction (Oliverio et al., 2010). Consequently this results into the release of pro-inflammatory markers that may cause joint synovitis which is further suggested to cause cartilage degradation (Sellam

& Berenbaum et al., 2010; Egloff et al., 2012; Kapoor et al., 2011). Studies have shown that during normal activities of daily living like walking, stair climbing etc. certain aspects of the articular cartilage adapt to the repetitive loading and respond by thickening in healthy cartilage (Andriachhi & Mundermann,2006; Seedhom,2006; Andriachhi,2009). This type of mechanical loading is favorable as it regulates the structure and function of the articular cartilage and maintains cartilage homeostasis (Bader et al., 2011). Thus a healthy cartilage with no sudden change in the loading patterns during daily activities like walking can adapt to the loads it is subjected to and maintain cartilage homeostasis. This may explain why not all athletes or runners develop knee osteoarthritis in spite of the high impact forces acting on the knee joint. While moderate mechanical loading may be favorable for the cartilage, overuse (excessive loading) or disuse (reduced loading) both have catabolic effects on the articular cartilage (Bader et al., 2011; Vanwanseele et al., 2002). Overuse can cause damage to the extracellular matrix in the cartilage whereas disuse or immobility may lead to thinning of the articular cartilage and decrease in the proteoglycan content as it is now not subjected to loads (Sun, 2010). Additionally, comprehensive research conducted by Andriachhi et al. (2004), looked at the in vivo pathomechanics of OA, indicating that the way the articular cartilage responds to loads depends on the health of the cartilage.

This leads us to believe that changes to the 'normal patterns of loading' have the potential to initiate knee OA. According to Andriacchi et al. (2009), the initiation of OA is associated with changes in the kinematic patterns of walking which could be a result of injury, joint laxity, neuromuscular changes, aging or increased obesity. This basically

interferes with the normal balance between the mechanics of walking and the cartilage biology and structure. Furthermore they hypothesize that once the cartilage starts to degrade, it responds negatively to load and the rate of progression of osteoarthritis increases with further loading as shown in Figure 2.1. Thus, joint mechanics during gait plays a role in the disease process and thus gait is used a as a model to study the initiation and progression of the disease.

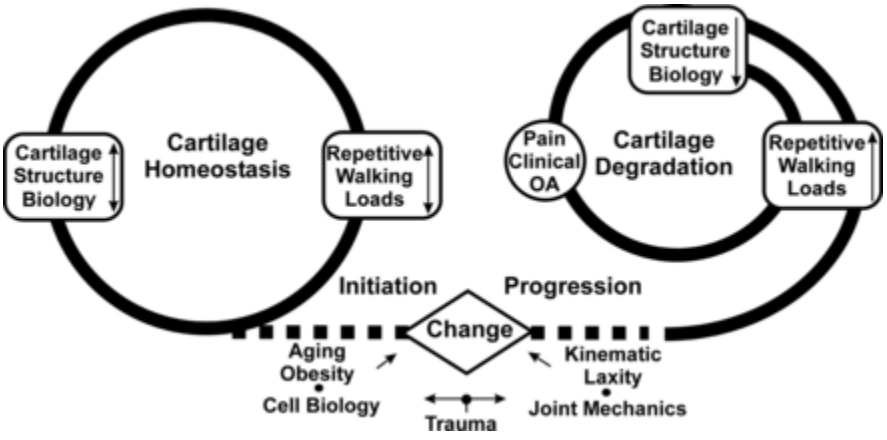


Figure 2.1: Healthy cartilage homeostasis. OA process initiated by factors like aging, obesity which changes the cartilage homeostasis resulting into cartilage degradation. (Adopted from original published by Andriacchi et al, 2009, Journal of Bone and Joint Surgery, with permission Appendix 3).

2.2 Knee Osteoarthritis, Kinetics And Muscle Strength

Kinetics refers to forces and moments of force acting on the system and in human studies it includes the external (gravitational and ground reaction force) and internal (muscle, ligaments) torques generated as a result of activity. The lower limb joint moments during an activity like walking can be determined by the ground reaction force obtained from force plates. The magnitude of the ground reaction force is equal and opposite to the magnitude of the force exerted when the foot strikes the ground during heel strike of the gait cycle. The external torques are generated on the joints depending on the position and direction of the ground reaction force with respect to the joint's axis of rotation. To counteract this external torque, the muscles produce an internal torque which helps to prevent collapse of the lower limb. Joint moments can provide an indication of the knee joint loads. Link segment modelling is a process by which the reaction forces and joint moments are calculated making use of the available kinematic, anthropometric and external forces measures (Winter, 2009; Vaughan, 1992; Neumann, 2002). The unit of the torque/moment is in newton*meters (Nm) which may be normalized to body mass (Nm/Kg) (Rudolph et al.,2007; Astephen et al.,2008; Kaufmann et al.,2001) or percent body mass times height (% BW*HT) (Baliunas et al.,2002;Thorp et al.,2006; Bennell et al.,2011). Another approach of representing the moment is by determining the impulse which is the positive area under the moment - time curve and is denoted by Nm.s/Bw*Ht (if normalized by body mass times height). Normalization makes it a relative measure, minimizing the influence of demographic

features such as body mass and height and thus allows for comparison since body mass and height varies between participants (Bazett-Jones et al., 2011).

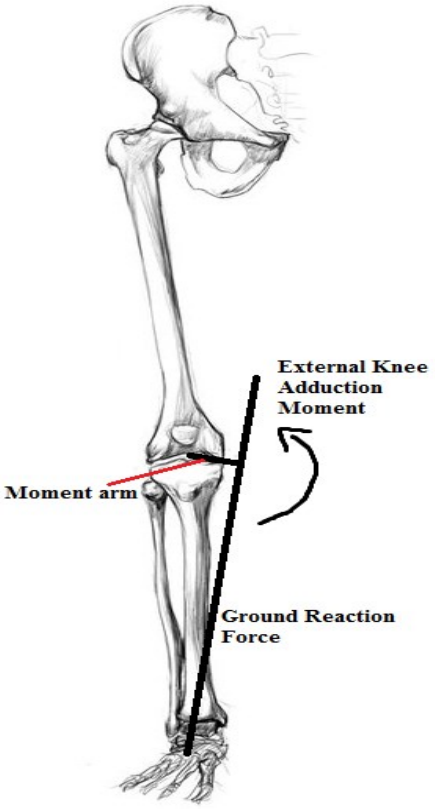


Figure 2.2: Knee adduction moment, gross depiction of the ground reaction force and moment arm.

Initiation and progression of knee OA has been related to the mechanics of ambulation (Andriacchi et al, 2004). The KAM has become an ambulatory biomechanical marker for the risk of progression of the medial compartment of the knee (Andriacchi et al, 2006). The KAM represents the relative medial-lateral force distribution rather than the actual force on the medial compartment (Kutzner et al, 2013). It is a common gait variable analyzed in the study of medial knee OA. KAM magnitudes are reported to be predictive of knee OA progression (Miyazaki et al.,2002; Bennell et

al.,2011; Hatfield et al.,2013; Chehab et al,2014; Chang et al.,2015). For instance, in a 6 year follow up study conducted on medial knee OA participants, it was found that those who progressed radiographically, as measured by KL scores and joint space narrowing, had higher baseline peak KAM scores (Miyazaki et al., 2002). However, a more recent follow up study looked at structural progression by measuring the medial cartilage volume loss. This group found a high KAM impulse among those who progressed but no significant findings with the peak KAM (Bennell et al., 2011). Thus there is a likelihood that the KAM impulse provides better understanding of the knee loading as it represents both magnitude and duration of loading during the stance phase of the gait cycle (Bennell et al., 2011; Thorp et al., 2006) and not just the early stance where the peak KAM usually appears. Compared to asymptomatic controls, the KAM magnitude was found to be higher in knee OA during mid-stance and it increased with an increase in disease severity (Figure 2.3). This finding was suggested to be indicative of a decreased ability to unload the joint throughout the stance phase resulting in a more persistent joint loading (Astephen et al., 2008) (Figure 2.3).

Most studies report the KAM as peak values and the magnitude of this peak which occurs approximately between 10-20% of the stance phase depends on characteristics like body mass and walking velocity. It has been found among healthy participants that those who walk faster than their self-selected walking velocity have higher peak KAM magnitudes (Robbins & Maly, 2009). However as mentioned earlier higher peak KAM measures have been associated with severe knee OA and on the contrary they walk at relatively slower walking velocities (Mundermann et al.,2005). Primarily to look at if reduced walking speed is a strategy used by those with knee OA

to reduce the peak KAM, Mundermann et al. (2004) conducted a study on 44 asymptomatic and knee osteoarthritic participants and found that this strategy was applicable only in those with less severe knee OA (KL≤II) as compared to controls. This could indicate that less severe knee OA is still devoid of number of morphological changes such as decreased muscle strength, mal-alignment and joint space narrowing and thus reducing walking speed alone can reduce the peak KAM. However, these changes are apparent in the later stages of the disease and may contribute to the abnormal joint loading despite slower walking velocities. Furthermore slower walking speeds among severe OA contributes to greater duration of loading as reflected by the KAM.

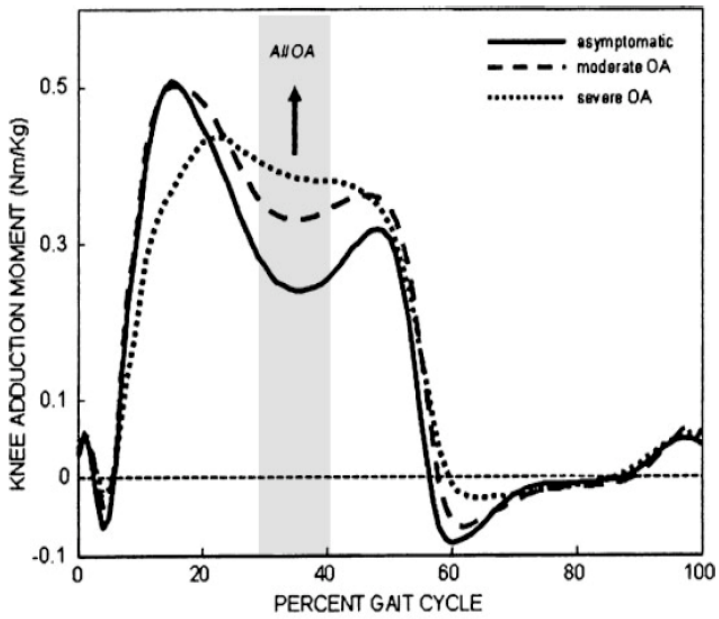


Figure 2.3: Knee adduction moment waveform during gait of asymptomatic, moderate and severe knee OA participants. There seems to be a sustained increase in the waveform for those with severe knee OA during the stance phase of the gait cycle, indicative of inability to unload. (As obtained from Astephen et al., 2008, Journal of Orthopaedic Research, with permission Appendix 3)

2.2.1 Kinetics And Muscle Strength

Muscles function to counteract the external moments acting on the joint thereby maintain a balance of force distribution within the joint. According to a muscle model study conducted by Shelbourne et al (2006), the main muscles counteracting the KAM were the quadriceps and gastrocnemius with primary resistance from the posterolateral ligaments. Hence if strength deficits exist in the knee joint muscles it may not be able to counter balance the high KAM. Conversely this was not found in a study conducted

on 12 established knee OA participants by Baert et al (2013). They found no correlation between the increased peak KAM and the strength deficit in quadriceps and hamstring muscles (Baert et al., 2013; Lim et al., 2008). Also a study conducted by Hubley-Kozey et al. (2014) on 187 knee OA participants found small correlations between the peak KAM and quadriceps ($r=0.17$, $p<0.05$) and hamstring ($r=0.16$, $p<0.05$) strength. Furthermore, a three month progressive lower limb muscle strength training program found no changes in the peak KAM measures among 18 knee OA participants despite improvements in muscle strength (Foroughi et al.,2011). Similar results were found in studies conducted by Lim et al. (2008) and Thornstensson et al. (2007). Interestingly, Aaboe et al. (2011) examined 136 medial knee OA participants reporting a positive correlation between isometric hamstrings strength and peak KAM and suggested that this might be a strategy to reduce the lateral knee joint opening by generating a higher hamstring moment (principally by the lateral hamstrings) to overcome the large peak KAM.

In summary the KAM magnitude is a common gait variable analyzed and reported to be an important indicator predicting medial knee OA progression (Andriacchi et al., 2006; Miyazaki et al, 2002; Hatfield et al., 2013). A higher magnitude as measured by the KAM during mid-stance found in the severe group is indicative of an inability to unload the joint during gait, reflective of persistent loading (Astephen et al., 2008). Internal torques generated by the muscles and ligaments counteract the external joint moments, with the quadriceps, gastrocnemius and posterolateral ligaments found to be the main muscles resisting the KAM (Shelbourne et al.,2006). Knee muscle strength deficits reported in knee OA may reduce the ability of the muscles to generate

sufficient amount of torque to overcome the large external KAM magnitude. However, while small associations have been reported between the strength deficit in the knee joint muscles and KAM magnitudes (Hubley-Kozey et al.,2014;Aaboe et al.,2011), muscle strengthening programs have no effect on peak KAM measures (Foroughi et al.,2011; Lim et al.,2008; Thornstensson et al.,2007). Thus the strength of the muscles may be important but this has not been explicitly examined although muscle strength, in particular quadriceps strengthening is a cornerstone of knee OA therapeutic interventions. This study will examine this relationship although other muscle features such as the inability of these muscles to activate at the appropriate time to counteract the high KAM, may explain the appearance of a biomechanical alteration, known as a varus thrust, during gait.

2.3 Varus Thrust And Its Impact On The Osteoarthritic Knee

As mentioned in the previous section, KAM is found to be an important biomechanical marker predicting medial knee OA progression. However, this gait variable cannot be observed visually and can be determined only by complex computing methods. Motion of the joints can be observed visually making it possible to identify abnormal kinematic patterns during gait. One such abnormal motion is the sudden lateral movement of the knee joint during the stance phase of the gait cycle in knee OA participants that has been observed in few studies (Chang et al. 2004, 2010 &2013). This sudden lateral movement is known as a varus thrust which is defined as the dynamic increase or abrupt onset of a varus alignment during early stance phase, with a return to a less varus and more neutral alignment during toe-off and the non-weight

bearing (swing) phase of gait (Chang et al., 2004; Lo et al.,2012). Varus thrust in knee OA has been inadequately represented in the literature owing to the difficulty in visually identifying and quantifying it. However, this doesn't deny the fact that it exists and is a problem. The reported prevalence of varus thrust varies from 17% to 40% among several studies (Chang, et al, 2004 & 2010; Harvey et al, 2009; Bennell et al, 2015). Varus thrust when observed visually was found to be dominant in Caucasians, medial knee OA, older age group and high BMI (Chang et al., 2010). It was also found that the odds of varus thrust were reduced in those who had a greater quadriceps strength (OR: 0.96) (Chang et al., 2010) but only in asymptomatic controls. Greater prevalence was found in varus aligned knees (Chang et al., 2004; Lo et al., 2012). With respect to sex, percentage of women (36%) with a definite varus thrust was found to be lower than men (Lo et al., 2012). Varus thrust has been associated with pain as measured by WOMAC scores (Lo et al., 2012) and Visual Analogue Scales (Bennell et al., 2015; Iijima et al., 2015).

Using visual observation methods Chang et al (2004) observed the varus thrust during gait in 401 osteoarthritic knees, reporting that 67 knees had varus thrust. They concluded based on radiographic alterations that a varus thrust observed at baseline was associated with a four-fold increase in the likelihood of medial knee OA post 18 months. They also found that knees with a varus thrust had a higher peak KAM. Chang et al. conducted another study in 2013 to determine if quantitative kinematic data relates to a visually observed varus thrust. The peak knee varus (frontal plane/adduction) angular velocity (pKVAV) was used as an objective measure to quantify varus thrust in this study and was calculated as the time derivative of the varus angle in the stance phase

(0-60% of the gait cycle). They found that OA knees with a varus thrust had a greater pKVAV and peak knee varus angle during the beginning of mid-stance (17-30%) phase of the gait cycle. To our knowledge this is the only study that has validated their quantitative measure to a visually observed varus thrust.

Prior to the Chang et al. (2013) method of quantifying varus thrust, Takigami et al., 2000 quantified varus thrust in knee OA during gait by determining the absolute angular velocity, which was the change in the angle constituted by the markers on the ASIS, tibial tuberosity and lateral malleolus and the elapsed time from heel strike to foot flat at the beginning of the stance phase. This method was not validated against a visually observed thrust. They calculated the thrust for all their participants under the pretext that majority of the medial knee OA patients demonstrate some degree of varus thrust during the stance phase. They found a higher angular velocity in those with severe knee OA (as graded by Koshino grading, 1993) as compared to those with less severe knee OA.

The two studies (Chang et al., 2013 and Takigami et al., 2000) described above used different angular velocity calculation methods and knee OA grading scores. The method suggested by Takigami et al. (2000) may determine the knee angular velocity but its ability to quantify a 'clinically observed' varus thrust is unknown. However, it is easier to implement in a clinical setting and does not require complex mathematical calculations. Nonetheless, both studies showed that there was a range in varus angular velocity measures during early stance across participants with knee OA suggesting that some participants have and some do not have this dynamic instability.

While the above two studies quantified varus thrust by calculating the angular velocity, Kuroyanagi et al. (2012) quantified it by determining the difference in the hip-knee-ankle angle marker positions at heel strike and first varus peak angle (10-20% of stance). They also found that with increase in the knee OA severity, the peak knee adduction moment and the varus thrust amount increased. These investigators also found a significant correlation of the quantified varus thrust with the peak KAM (R = 0.73) and the tibio-femoral angle (R = 0.47) (Kuroyanagi et al., 2012) which is similar to the findings of Chang et al. (2004) and Hunt et al. (2011). Again like the study conducted by Takigami et al., 2000, this study also did not visually observe the varus thrust and computed the thrust in all their participants.

Based on the above studies varus thrust appears to be a factor worth examining among the OA population and may be valuable to understanding OA phenotypes to help address therapies. As the definition suggests varus thrust is "a dynamic worsening of an existing varus alignment", indicating that it is a subset of varus alignment. Both, varus thrust and static varus alignment, have been identified as clinical OA phenotypes (Iijima et al.,2015) with a greater prevalence as the disease severity increases (Chang et al.,2004 & 2010; Takigami et al.,2000; Kuroyanagi et al.,2012; Iijima et al.,2015). Varus thrust in an already varus mal-aligned knee (static varus alignment) has been found to be associated with more pain (Lo et al.,2012;Iijima et al.,2015) and greater odds for progression (OR 3.17) (Chang et al.,2004) as opposed to varus thrust or static mal-alignment alone. This makes sense as varus thrust adds stress to an already compromised medial compartment thereby contributing to progression.

There are few methods to quantify varus thrust as mentioned in the studies above. Although the intrarater and interrater reliability of visually observing varus thrust was found to be excellent (k=0.81-0.92) (Chang et al., 2004; Iijima et al., 2015) and good (k=0.73) (Iijima et al., 2015) respectively, visual observation does require an expert to identify it and it appears to be related to the severity of the thrust i.e. possible only when it is apparent during gait. There could be a possibility where the presence of this thrust has been missed due to the lack of expertise and the subjectivity associated with it and thus we need to devise and/or validate an objective measure which would establish an assurance in the presence of a varus thrust. The method suggested by Chang et al. (2013) is the only one validated against a visually observed varus thrust, however the Takigami method is probably easier to implement in a clinical setting. The current study compared the Chang and Takigami methods, as they both are an objective measure of "varus thrust" and use frontal plane angular velocity measures.

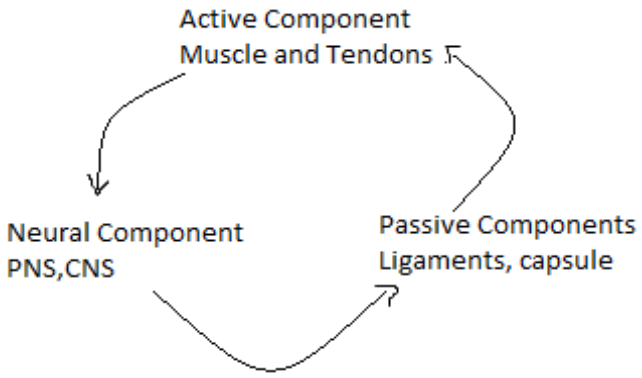


Figure 2.4: Interaction between the three components that maintain a balance between mobility and stability and if optimum it maintains homeostasis within the joint.

Like any other joint the knee joint also strives to maintain a balance between stability and mobility and in order to do so there needs to be a balance between three subsystems i) active component (muscles and tendons) ii) passive component (ligaments and capsule), iii) neural component (Panjabi,1992) (Figure 2.4). Dysfunction in any one of the components may result in compensation by the other components and if they are unable to react efficiently then it may lead to an injury or adjustment in the movement patterns. In medial knee OA, there may be laxity in both medial and lateral ligamentous structures. Laxity in the lateral structures may be due to the over stretching as a result of the high KAM and varus malalignment whereas in the medial structures it may be due to the medial cartilage loss, greater medial JSN than lateral JSN or bony erosions leading to pseudo-laxity (Andriacchi et al.,1994; Lewek et al.,2004)(Figure 2.5).

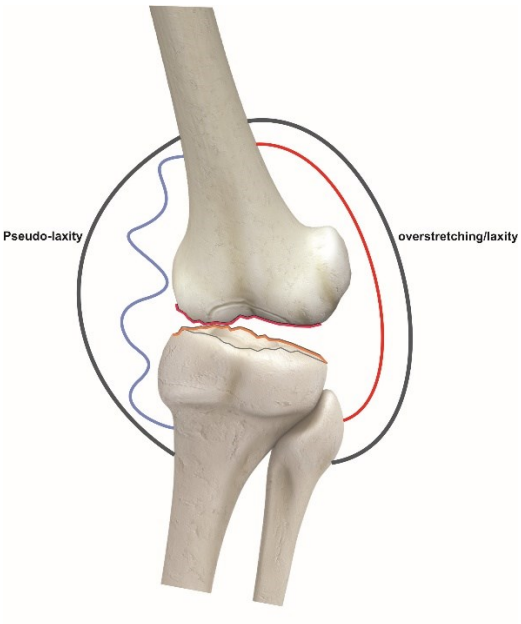


Figure 2.5: Diagram indicating both lateral laxity and medial pseudo-laxity which may be responsible for varus thrust in knee OA. This will increase the medial compartment compression and thereby lead to disease progression.

Kumar et al. suggested that lateral femoral condylar lift-off during mid-stance found in half of their medial OA participants may be due to an inability to generate sufficient muscular forces to resist the high KAM or a failure in the neuro muscular system (Kumar et al., 2013 & 2010). They stated that varus thrust could be the visual indication of this lateral condylar lift-off. However, a clinically observed varus thrust was not tested in this study. It has been suggested that injuries to the postero-lateral complex of the knee may result in the lateral opening of the knee and varus subluxation resulting into a varus thrust (Cooper et al., 2006). Thus, the passive ligamentous structures also play a role in preventing the occurrence of varus thrust. This brings us to the explanation provided by Andriacchi in 1994 that the knee joint is dependent on soft

tissue structures for medio-lateral stability and the large KAM during gait must be balanced by soft tissues (both passive and active) to reduce the lateral opening of the joint during walking. Assuming that the active structures aren't able to generate sufficient amount of force to balance the moment, the stability of the knee joint then completely rests on the passive structures which responds only when stretched. Stability is also achieved with bone on bone approximation, for example those with lax knees tend to lock their knees at extreme ranges to achieve stabilization. While this may improve stability among non-OA individuals, structural changes in knee OA compromise the bone congruency and in conjunction with laxity observed in knee OA (Sharma et al., 1999) it would hamper the ability of the lateral structures to combat the KAM during gait, thus resulting in a varus thrust. In the presence of a varus thrust, the reaction forces would be directed on the medial compartment leading to an imbalance in the medial-lateral force distribution thereby a further increase in the medial compartmental loads leading to further articular degeneration (Andriachhi, 1994).

On observing muscle activation patterns it was found that that the lateral muscle sites are more active during gait in knee OA and also in order to improve the joint stability these muscle sites co-contract (Childs et al.,2004; Hubley-Kozey et al.,2006; Rutherford et al.,2013). To counteract a varus thrust muscles need to create a valgus moment. It was found in a study conducted by Zhang et al. (2001) that the primary muscles responsible for generating a valgus moment are biceps femoris and lateral gastrocnemius. This would imply that the lateral muscle sites would be able to prevent the lateral opening of the knee joint and it has been contemplated that the greater response of the lateral muscle sites during the stance phase of the gait cycle is probably

a strategy to reduce the medial joint loading which is known to be high in those with medial knee OA (Thorp et al., 2006). However, a recent study conducted by Brandon et al (2014) on 8 participants with medial knee OA in order to determine if selective lateral site muscle activation patterns could unload the medial tibial condyle. It was found that this type of activation neither reduced the medial joint load nor increased it and may in fact only be a strategy to increase the overall joint stiffness. Subsequently in the EMG driven model devised by Kumar et al (2012) to determine the loading in knee OA, low activation in the biceps femoris and lateral gastrocnemius muscle was found during the unloading of the tibial lateral condyle of the knee joint occurring approximately around 40 % of the stance phase, that is between 20-30 % of the gait cycle. This may indicate that these two muscle sites are unable to overcome the high peak KAM and thus, prevent the occurrence of a varus thrust. However, if not all, at least a few OA knees are still affected by varus thrust which means that there is an inadequacy in the active subsystem where lateral muscles are not able to activate themselves sufficiently due to compromised strength and laxity in the passive subsystem, thereby unable to counteract the KAM and thus prevent a varus thrust.

2.3.1 Sagittal Plane Knee Angle, Varus Thrust And Knee OA

Varus thrust, as mentioned earlier occurs between 10-30% of the gait cycle during early mid-stance, a phase during which the knee is close to extension (Kuroyanagi et al., 2012). As found in the study conducted by Astephen et al. (2008) on 120 knee OA participants, the overall knee flexion excursion in the stance phase was reduced in the OA group as compared to the controls. The magnitude of this reduction

was influenced by knee OA severity with a greater decrease in severe OA compared to the moderate OA group. These findings are supported by other knee OA studies indicating a pattern seen in this group (Kaufmann et al.,2001; Zeni et al.,2009; McCarthy et al.,2013; Childs et al.,2004; Lewek et al 2004). Attenuation of the bimodal knee flexion-extension pattern would indicate that the knee remains in a more extended position. Varus thrust accounts for a dynamic instability and one may argue that knee extension is a stable position due to adequate bone on bone contact or congruency and sufficient ligament tautness, and thus an instability would not be expected. However, as mentioned earlier the occurrence of varus thrust may be due to an injury or laxity in the postero-lateral complex (Cooper et al., 2006) which includes the posterior cruciate and lateral co-lateral ligament with the primary function to resist knee hyperextension, varus angulation and tibial external rotation (LaPrade et al., 2007; Kozanek et al., 2009; Malone et al., 2006) and this may occur as a result of knee joint structural changes observed in OA. OA structural changes are directly proportional to the severity of the disease and changes like genu varum and greater medial JSN than lateral JSN observed in medial knee OA can compromise bone congruency and may result into chronic stretching of the lateral structures reflecting laxity and instability in this knee position leading to varus thrust as indicated in the earlier section (Figure 2.5).

In summary, varus thrust reflects a dynamic instability within the joint defined as an abrupt worsening of knee alignment in the varus direction during early mid-stance. Researchers have devised methods to quantify this thrust with only Chang's (2013) method being validated against a visually observed varus thrust. Despite good to excellent reliability in visual observation techniques, it is subjective and requires

expertise. Thus, the need of a valid objective measure. Varus thrust may occur due to the structural changes that occur in the knee joint associated with the disease process. Structural changes compromising bone congruency and imbalances between the medial and lateral joint forces reflected as a high peak KAM, may lead to laxity in the postero-lateral structures and thus hamper their ability to balance the high medial moments during early mid-stance when the knee is near extension resulting into a varus thrust. With varus thrust being associated with high peak KAM magnitudes and disease progression and based on the summary above the current study will explore its association with peak KAM and two biomechanical gait features i) the KAM impulse and ii) sagittal plane KFA.

2.4 Muscle Strength

Muscle strength is a physiological concept used to refer to one of the output capabilities of the motor system. Strength has been defined in a number of ways by different researchers, one of them being the ability to develop force against an unyielding resistance in a single contraction of unrestricted duration (Atha et al., 1981). Knuttgen and Kraemer (1987) defined strength as the maximal force a muscle group or a muscle can generate at a specific velocity. However, the most precise definition of skeletal muscle strength would be the one defined by Harman in 1993 which is the ability to exert force under a given set of conditions defined by body position, body movement by which force is applied, movement type (concentric, eccentric, isometric and plyometric) and movement speed. Thus, muscle strength does not only depend on the amount of force generated but also the pattern of movement, the position of the body

and the type of muscle contraction. In summary muscle strength is the ability to generate maximal force, stressing on the term maximal.

There are a few factors that influence the strength production which are as follows:

1. Muscle Size: a direct relationship exists between the force of contraction and the number of cross-links between the actin and myosin chains (Aagaard, 1998; Fitts, 1991). Actin and myosin are contractile proteins and its availability depends on the number of muscle fibers and thus the muscle size. A measure used to approximate the number of muscle fibers of a whole muscle is by its physiological cross-sectional area (Oatis, 2004).
2. Moment Arm: it is the perpendicular distance from the line of action of the muscle to the point of rotation and larger the moment arm greater the moment generated by the muscle contraction (Rassier, 1999).
3. Motor unit and muscle fiber type: A motor unit consists of a single alpha motor neuron and the muscle fibers it innervates. The ability of a muscle to produce high force or maintain prolonged durations of muscle contractions, thus avoiding early fatigue, depends on the muscle physiology and the type of motor units proportions of which differ in the different skeletal muscles.

2.4.1. Muscle Strength Deficits And Association With The OA Process

A decrease in the lower limb muscle strength could be a factor for disease initiation as well as progression. It has been reported in a recent paper that quadriceps strength reduction was observed in early as well as established knee OA suggesting that

it plays a role in both the disease onset and progression (Baert et al., 2013). For instance in a longitudinal study conducted by Slemenda et al (1998) on 342 older adults, it was seen that those who developed knee OA over a period of 30 months had decreased knee extensor strength by 18 % at baseline when compared to controls which indicates that diminished quadriceps strength (relative to body weight) may be a risk factor for knee OA. This finding was significant in women only. However it has been reported in a longitudinal MOST study conducted by Segal et al (2009), which had a similar follow-up of 30 months like Slemenda et al., (1998), that knee extensor strength may be a predictor for incident symptomatic knee OA but not incident radiographic knee OA. This means that having a good quadriceps strength at baseline with no radiographic changes will not prevent radiographic knee OA changes post 30 months but can protect against symptomatic changes (more so in women). Thus the role of muscle strength, more specifically quadriceps strength, in the incidence of knee OA is still not clear.

Decrease in knee muscle strength, and specifically quadriceps, can be a risk factor for knee OA progression. It has been reported that there is a negative correlation between radiographic disease severity and quadriceps muscle strength, which decreases as the severity increases (Palmieri-Smith et al., 2010). In fact it was found in the Multicenter osteoarthritis study conducted by Segal et al (2010), that decreased quadriceps strength at baseline in knee OA was associated with worsening knee joint space over 30 months in women and not men. Women with a quadriceps strength below 60Nm (OR 1.66) were at a significant risk compared to those greater than 80Nm (OR 1.0) ($p<0.01$). This could indicate that significantly lower quadriceps muscle strength can be associated with progression of the disease. However in a study conducted by

Brandt et al. (1999), looking at the relationship between lower extremity strength deficits and progressive knee OA as determined by established radiographic changes in 79 participants, it was found that mean knee extensor strength was not significantly different between those who progressed radiographically and those who were radiographically stable over a period of 2.5 years. Additionally a longitudinal study indicated that decreased quadriceps strength at baseline was not associated with tibio-femoral cartilage loss post 30 months with the inclusion of mal-aligned knees (Amin et al., 2009). However, the study did indicate that those with strength deficient quadriceps had greater knee joint pain. The controversy around the effect of quadriceps strength and knee OA progression indicates that this may not be the only factor contributing to knee OA and factors such as abnormal joint loading, instability, malalignment and pain may influence the effect of muscle strength during gait. Additionally decreased quadriceps strength may contribute more towards symptomatic OA progression as compared to radiographic OA progression. Thus, there still isn't a clear picture indicating the role of muscle strength in the progression of knee OA.

This unclear picture may possibly be because the literature mainly focuses on the quadriceps strength and that there are multiple other risk factors associated with OA progression. The quadriceps is not the only muscle involved in the disease process with Baert et al (2013), showing a significant reduction in the hamstrings strength in women with established knee OA as compared to controls . Similarly a recent study (Hubley-Kozey, 2014) conducted in Dynamics of Human motion lab on 136 moderate knee OA and 51 severe OA participants, found that along with the quadriceps muscle, strength deficits, there were deficits observed in both the hamstrings and plantar flexors as well.

However, women exhibited a greater strength deficits in the hamstrings and plantarflexors compared to men and these strength deficits were more evident in those with severe OA. Thus, muscle strength in knee OA depends on the mechanical environment of the lower limb, disease severity and sex with women being more affected than men.

Adequate muscle strength works as a natural brace supporting the knee joint during dynamic activities. However, adequate muscle strength in an unstable environment can also contribute to OA progression (Sharma et al., 2003). With some dispute, reduced muscle strength is found to be a factor for knee OA initiation and progression. However, reduced muscle strength accompanied with factors like disease severity, joint alignment, normalizing techniques and sex may have a better effect in predicting the course of the disease.

Gait as a functional activity requires the adequate functioning of not just the quadriceps muscle but also the hamstrings and plantarflexors, but as mentioned earlier the literature mainly focuses on the quadriceps muscle. The current study would focus on the strength of all the three knee muscles, namely the quadriceps, hamstrings and plantarflexors. With respect to varus thrust, it has been postulated that the postero-lateral structures play a role in controlling the thrust. However, despite greater muscle activity observed in these structures in knee OA, they are unable to reduce and control the lateral opening of the knee joint resulting into a varus thrust. This does reflect that strength influences the efficiency of muscle activity and hence, compromised by strength deficits. It has also been indicated that reduced quadriceps strength is a risk factor for varus thrust (Chang et al., 2010) in asymptomatics. The functioning of the muscles

specific to varus thrust has been poorly represented. Only one recent study indicated the positive effect of neuromuscular exercises on their 85 Knee OA varus thrust participants (Bennell et al., 2015). Thus it identifies the need to determine the role of the knee muscles. However, since the literature is limited in providing information specific to knee muscle strength and varus thrust in knee OA it would be a stepping stone to look at this association. In order to devise muscle strengthening exercises to modulate varus thrust during gait in knee OA it is necessary to determine the association between the two, if at all it exists.

2.5 Summary

To summarize, knee OA is chronic morbid condition which is highly prevalent and a great burden on the society due to the disability associated with the disease. It is progressive in nature with no known cure with end stage treatment being total knee replacement surgery. Total knee replacement lasts only for a definite and relatively short period of time making it unsuitable for younger patients. Physiotherapists attempt to manage patients with conservative treatment strategies in order to provide temporary symptomatic relief and delay the chances of surgery. To develop conservative strategies it is necessary to identify the factors that may be responsible for disease progression.

Factors like KAM features have been reported to be associated with the disease progression. However, in a typical clinical practice it is not easy and at this time feasible to measure moments in knee OA patients. Unlike moments, it is possible to visualize joint motion, an example being varus thrust. Varus thrust is a clinical criterion that has been linked to KAM and to both pain and structural progression in knee OA. It can be

identified in a clinical setting with good interrater reliability however requires expertise and is subjective. Prevalence rate of varus thrust varies from 17 to 40% among various studies. Varus thrust is found to be prevalent among Caucasians, those with a high BMI and more so in men than women. It has been related to reduced quadriceps muscle strength with respect to greater odds of a varus thrust. Methods have been developed to quantify varus thrust, however only the method proposed by Chang et al. (2013) has been validated against a visually observed varus thrust. While this method quantifies varus thrust by calculating the peak knee varus angular velocity another considerably simpler measure to quantify varus thrust has been suggested by Takigami et al. (2000) that also calculates varus thrust by an angular velocity measure. The proposed study will examine both of these angular velocity calculations with the later more easily applied to examine varus thrust in asymptomatic and moderate knee OA participants.

Furthermore, if varus thrust is a factor contributing to disease progression, conservative strategies must be developed that aim to reduce its occurrence. A commonly used management strategy is muscle strengthening. In order to determine if strengthening is an appropriate strategy to reduce varus thrust, one needs to determine the relation between muscle strength and varus thrust. Knee muscle strength, that is the quadriceps, hamstrings and plantarflexors, is found to be reduced in knee OA but is modified by sex and disease severity. Varus thrust reflecting a dynamic instability may occur due to insufficiencies in the postero-lateral active and passive structures of the knee joint to counterbalance the high medial moments. It has been suggested that prompt dynamic stabilization can be achieved by active muscle contraction. The quadriceps, hamstrings and gastrocnemius are postulated to play a role in reducing the varus thrust

appearance and thus their association with varus thrust will be explored in this study. Finally, owing to its distinct appearance, varus thrust has been associated with high peak KAM magnitudes across various studies. It has been identified as a factor in disease progression being more prevalent as the disease progresses. Along with peak KAM the current study will also explore the association of varus thrust with KAM impulse measures which has also been identified as a biomechanical marker for disease progression.

Varus thrust is apparent during early mid-stance when the knee is near extension. While this position is otherwise considered to be stable, knee OA structural changes can compromise its stability. Moreover, the overall knee flexion excursion is reduced in knee OA and thus, along with the other factors the sagittal plane knee angle may influence varus thrust. Consequently, knee flexion has been observed to be a more stable position among these individuals and used as a treatment strategy. However, it has been well established that adopting a knee flexion gait pattern can increase the loads on the joint, which can further exacerbate the disease process. Hence, better strategies must be employed that will enhance stability without compromising the disease state among varus thrust individuals. Thus, the need to determine the association of varus thrust with the sagittal plane knee angles.

CHAPTER 3: METHODS

3.1 Participants And Study Design

Gait waveforms and muscle strength from participants in a larger study (conducted by Drs. Cheryl Kozey and Janie Astephen Wilson) were examined to address the three objectives of this thesis with my contribution to data collections beginning in 2014. The knee OA participants were recruited from the Orthopedic and Sports Medicine Clinic of Nova Scotia, Capital District Health Authority and the asymptomatic participants from the general community between 2003and 2014. The participants were categorized into groups of asymptomatic and moderate knee OA. The asymptomatic group includes participants that had no known lower extremity pathology and no lower extremity injuries within the past 6 months. The Knee OA groups were diagnosed based on radiographic and clinical criteria according to the American College of Rheumatology guidelines (Altman, 1995). They were classified as moderate knee OA based on a functional and clinical management criteria (Landry et al., 2007; Hubley-Kozey et al., 2006). Participants were categorized into the moderate knee OA group if they had a Kellgren Lawrence (KL) (Kellgren & Lawrence,1952) score (Appendix 1) between I-IV and self-reported that they were able to perform functional activities such as walk one city block, reciprocally ascend and descend a flight of stairs and jog five meters. They were classified as medial knee OA if their medial joint space narrowing scores (medial JSN) were greater than the lateral joint space narrowing scores (lateral JSN) (Appendix 1).

The Inclusion and exclusion Criteria for those involved in this study are as follows:

Inclusion criteria:

1. Moderate medial knee OA as per the criteria indicated above.

2. Body Mass Index of less than 35 kg/m^2 : to minimize error from recording skin motion rather than the underlying joint motion.

3. Age > 35 years

Exclusion Criteria

1. Lateral JSN scores > medial JSN scores

2. Severe knee OA: Those who were on waitlist for total knee arthroplasty and self-reported that they were unable to perform functional activities such as walk one city block, reciprocally ascend and descend a flight of stairs and jog 5 m.

3. A greater change in the valgus direction than varus in the frontal plane knee angle that may denote a valgus thrust. This criteria was selected as per the definition of varus thrust.

4. Presence of any neuro-muscular and cardiovascular impairment, total knee replacement in the tested knee and any recent surgery (within past 6 months).

3.2 Procedure

Participants were introduced to lab settings, the basic procedure was explained and an appropriate ethical and informed consent documentation was obtained as per Dalhousie University Health Science Human Research and Capital Health District Authority ethics review board. Participants were asked to walk across a 6 m walkway approximately 5-7 times at their self-selected walking velocity. The self-selected walking velocity was considered consistent if it was within the ± 10 % range. Two photo-electric gait

measurement timers set apart at a known distance were used to calculate the walking velocity. A trial with consistent self-selected walking velocity and with complete foot contact (heel strike to toe off) of the testing leg with the force plate was considered as successful.

3.3 Data Acquisition And Processing

3.3.1 Muscle Torque

Maximum voluntary isometric contraction (MVIC) of the quadriceps, hamstrings and plantarflexor muscles was determined using the torque data measured from the Cybex^{TM} Dynamometer (Lumex NY, USA). The standardized exercises (Hubley-Kozey et al., 2006) consisted of a) knee extension with the knee at 45° and participant seated (KE45), b) knee flexion with the knee at 55° and participant seated (KF55), c) plantar flexion with participant seated, the knee as close as possible to full extension and the ankle in neutral (PF) (Figure 3.1). Each exercise was performed twice along with one trial for gravity. Each MVIC was held for 3 seconds with a 90second rest between trials. Participants were given one practice trial along with verbal and visual encouragement. Maximum torque generated against the Dynamometer for KE45, KF55, and PF for a 0.5 second steady state window was used as a measure for the quadriceps, hamstrings and plantar flexors strength respectively (Hubley-Kozey et al. 2006). The maximum of the two trials was considered as an MVIC. The MVIC for each muscle group will then be used for further analysis.

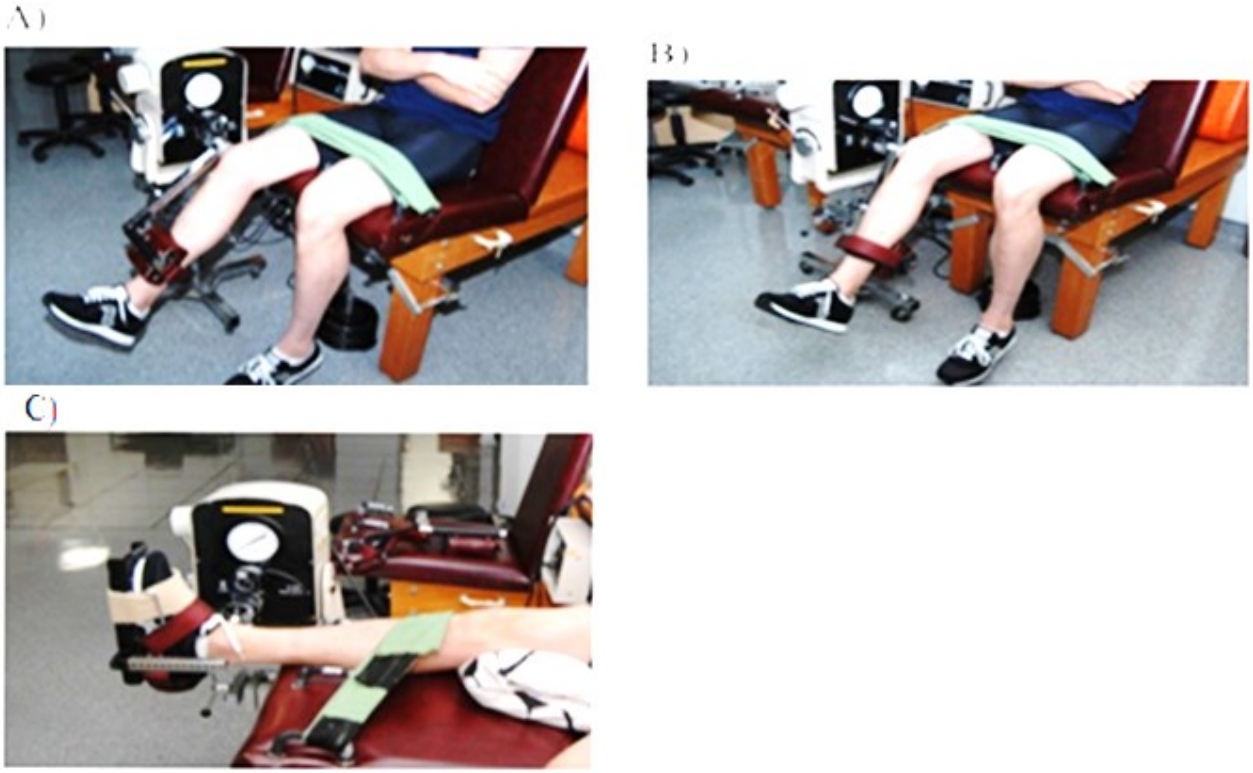
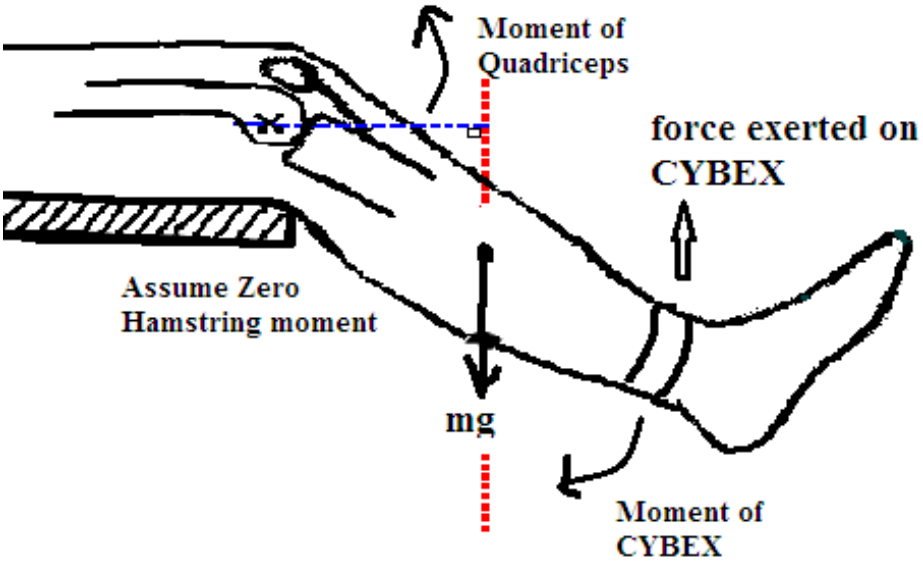


Figure 3.1: MVIC exercises on the Cybex™ Dynamometer. A) Knee extension 45 in sitting (KE45), B) Knee flexion 55 in sitting (KF55), C). Plantarflexion in neutral ankle (PF). (As obtained from Rutherford et al., 2011, Journal of Electromyography and Kinesiology, with permission Appendix 3)

In order to obtain the torque produced by the MVIC, the measure was corrected for gravitational force due to the weight of the limb and of the lever arm which aids or opposes the movement depending on the direction of the movement (Knutsson, 1979; Knutsson & Martesson, 1980). For example, while performing KE45 the gravitational moment is added to the moment generated by the quadriceps muscle (Figure 3.2). It has to be noted that during these exercises the antagonist muscle moment is assumed to be zero. That is the antagonist muscle is in a completely relaxed state indicating no antagonist co-activation.



1).Moment of force (torque) of quadriceps (Nm) =

Moment of the CYBEX + Moment mass (mg)

2).Moment of force (torque) of hamstrings (Nm) =

Moment of the CYBEX - Moment mass (mg) [assume zero quadriceps moment]

3) Moment of force (torque) of plantarflexors (Nm) =

Moment of the CYBEX - Moment mass (mg)

Figure 3.2: A sketch of the MVIC of the quadriceps muscle during knee extension. The curved arrow indicate the direction of the moments. Equations 1), 2) and 3) indicate how the moments for quadriceps, hamstrings and plantarflexors were calculated.

The unit for the moment of force is Nm (force in Newtons x moment arm length in meters), which is divided by body mass in kilograms. The moment data is represented in

Nm/Kg. Normalizing the moment by body mass eliminates the influence of body mass making it an absolute value and allowing for comparisons between different body mass participants (Bazett-Jones, 2011).

3.3.2 Kinematic Data Acquisition

Participants walked through a calibrated space within two optoelectric motion analysis sensors (Optotrak™, Northern Digital Inc, Waterloo, ON). The sensors defined the location of the IRED (infra-red emitting diodes) skin markers in space. There were 16 IRED markers affixed to the anatomical bony landmarks to define the lower limb position and movement. There were four sets of triads attached on the pelvis, mid-thigh, mid shank and lateral border of the foot, five individual markers on the lateral malleolus, lateral femoral epicondyle, greater trochanter and acromion process of the shoulder (Landry et al.,2007). The markers were secured with the help of micro-pore and adhesives. Along with these, 8 virtual points were determined for the other anatomical landmarks, i.e right and left ASIS, medial femoral epicondyle, fibular head, tibial tuberosity, medial malleolus, second metatarsal head and heel during the standing calibration (Cappozzo et al., 1997). The virtual points locate the anatomical co-ordinate system in the pelvis, thigh, shank and foot. The skin markers were attached on the knee OA limb side for the OA participants and any random limb with no known injury or impairment for the asymptomatic participants.

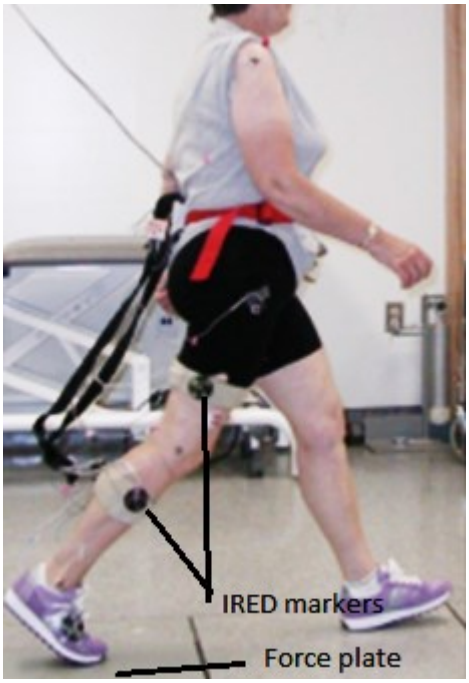


Figure 3.3: Participant walking on the force plate with the 16 IRED markers attached on the right leg.

Three dimensional motion capture makes use of the X, Y, Z Cartesian co-ordinate system. The space calibrated within the 2 optoelectric motion analysis sensors has its own fixed co-ordinate system known as the global co-ordinate system (GCS). During the standing calibration, the positions of the markers in the GCS would be transformed to the anatomical co-ordinate system of the segments of the limb analyzed during gait. The anatomical co-ordinate system is defined at the center of mass of the limb segment. Once the calibration is done, the axes of the markers would remain fixed relative to the defined anatomical axes. That is, the anatomical co-ordinate system of the tibia (T) is described in relation to the anatomical co-ordinate system of the femur (F). The International Society of Biomechanics (ISB) suggests that lower extremity angular kinematics can be calculated using an XYZ sequence of rotations called as Euler

angles, where X is the flexion/extension, Y is the abduction/adduction, and Z is the axial (internal/external) rotation (Cole et al., 1993; Wu & Cavanagh, 1995; Wu et al., 2002). Taking this into consideration, the orientation of the axis of the DOHM laboratory is with the X axis is in the antero-posterior direction, Y axis in the medio-lateral direction and Z axis is along the length of the bone (Figure 3.5). The mid-point between the medial and lateral femoral epicondyles will determine the knee joint center.

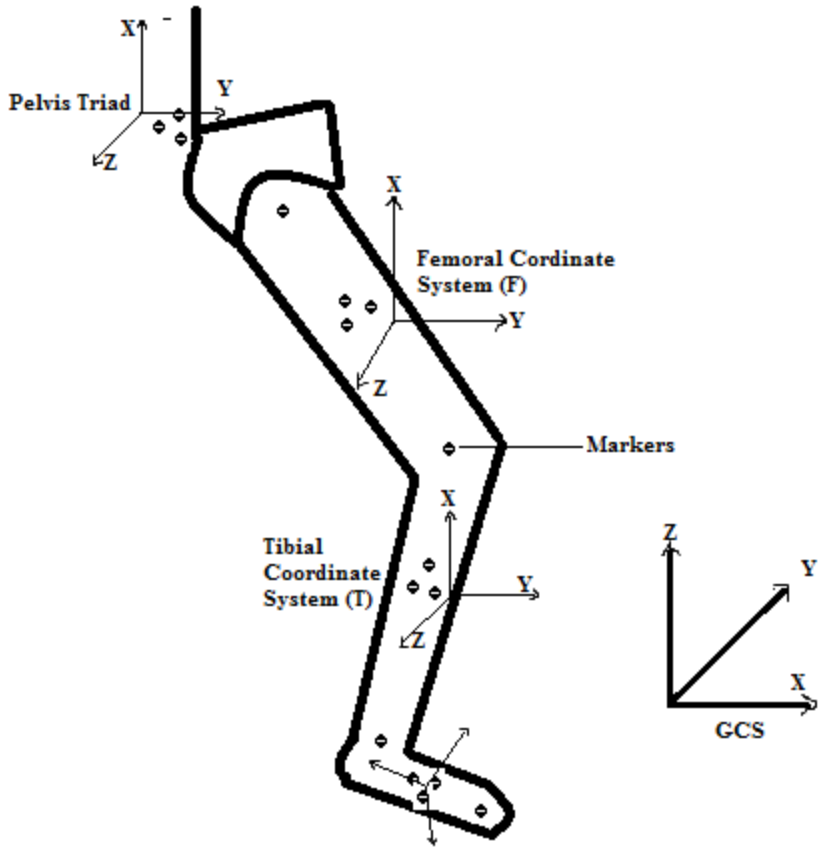


Figure 3.4: Anatomical co-ordinate system for the femur and tibia of the rigid lower limb segments along with the triad markers and individual markers.

Once the marker positions are defined the next step is to calculate the 3D joint angles during gait. These are calculated for one gait cycle which is from heel strike to

ipsilateral heel strike (100% gait cycle). The femoral and tibial anatomical co-ordinate systems described earlier will be used in a 3x3 matrix to calculate the three dimensional knee joint angles by using the Euler angle principles. According to these principles flexion-extension is calculated about the medio-lateral axis, internal- external rotation about the vertical axis and adduction-abduction about a floating axis perpendicular to the above axes. The unit vectors (i,j,k) of the femoral and tibial co-ordinate system were used to calculate the joint angles as per equations 1.1 and 1.2. The angles in the positive direction would be flexion, adduction and internal rotation. By differentiating the angles with respect to time, the angular velocities and accelerations will be determined. This study will mainly focus on the angles in the frontal and sagittal plane.

Knee joint angle (flexion /extension) = $\sin^{-1}$(I knee . i thigh)------(1.1)

Knee joint angle (abduction/adduction) = $\sin^{-1}$(k thigh . i calf)-----(1.2)

Where, i is the vertical axis; j is the adduction-abduction axis; k is the medio-lateral axis. Equations are according to those indicated in Vaughan et al., 1992.

3.3.3 Kinetic Data Acquisition

An AMTI™ force plate (Advanced Mechanical Technology Incorporation, Newton, MA, USA) captured the 3D ground reaction forces and moments. The force plate co-ordinate system was aligned with the global co-ordinate system prior to collecting trials. To determine the moments of force about the joint center, the kinematic segmental angular and linear accelerations, anthropometrics and inertial properties were used. The reaction forces were calculated by multiplying mass (kg) by the segment

linear acceleration whereas the moments were calculated by multiplying the moment of inertia by the segment angular acceleration. The process used to determine joint moments is called Inverse dynamics which makes use of a link-segment model. In case of the lower limb, the calculation was started at the foot with a known ground reaction force and moment as determined by the force plate (which is according to Netwons Third Law of Motion: every action has an equal magnitude and is in opposite direction), segment anthropometrics and the angular acceleration determined from kinematics (Winter, 2009; Neumann, 2002). This calculates the forces and moments of force around the ankle joint and following the same procedure the model calculated the forces and moments about the knee joint.

The free body diagram in Figure 3.6 shows the required components in order to calculate the net joint forces and moments about the joint.

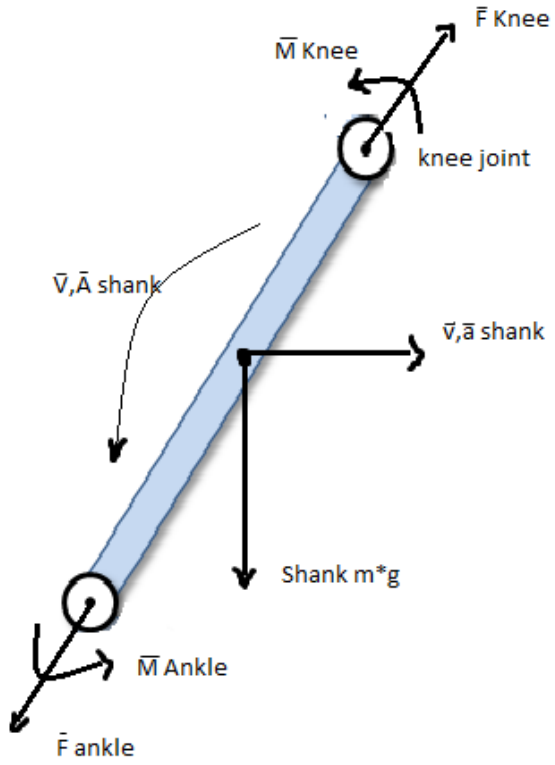


Figure 3.5: A free body diagram with the Forces (F) and Moments (M) acting at the ankle and knee joint. Shank m*g= mass* acceleration due to gravity of the shank, v=linear velocity and a= linear acceleration, V= angular velocity and A= angular acceleration. The arrows show the direction of the vectors.

3.3.4 Data Processing For Motion And Force Data

A standard procedure acquiring and processing motion capture and force plate data were used in this study consistent with our published work (Landry et al., 2007; Robbins

et al., 2013). Briefly the IRED markers were captured at a frequency of 100 Hz by the Optotrak™ system and the force data were collected at a frequency of 2000Hz (Robbins et al., 2013). This procedure has been found to be highly reliable between days to determine both discrete and waveform kinematics and kinetics motion and moment of force data with intra class coefficients greater than 0.70 (Robbins et al., 2013). The motion and force data were low pass filtered at 8Hz and 60Hz respectively by using a Butterworth filter (4^{th} order recursive) and processed using custom made programs in MatLab™ version 7.12 (The Mathworks Inc., Natick, Massachusetts, USA). The motion and force data were time normalized to 100% of the gait cycle and amplitude normalized to % MVIC. The amplitude of the net external moment (KAM) was normalized by body mass to eliminate the influence of body mass making it an absolute value and allowing for comparisons between different body mass participants (Bazett-Jones et al., 2011). The maximum magnitude of the KAM during early stance, between 0-30% of the gait cycle was considered as the peak. The KAM impulse was determined by calculating the time integral of the non-time normalized KAM during the stance phase of the gait cycle. Also the non-time normalized knee adduction angle was used to determine the knee varus angular velocity that is used an objective measure of varus thrust (Details in section 3.3.5). Along with the knee adduction angle, the sagittal plane knee flexion angle from heel strike to maximum within 30% of the gait cycle was also looked at to determine if decreased knee flexion is associated with varus thrust. The between day reliability of these gait variables was found to be high with an intra-class coefficient for the knee flexion angle being greater than 0.75, knee adduction angle being 0.60 and knee adduction moment being greater than 0.90 (Robbins et al., 2013). This thesis will mainly focus on the motion and moments in the frontal plane.

$F_{ANKLE\_x} + F_{GROUND\_x} = m_{foot}\, a_{foot\_x}$

$F_{ANKLE\_y} + F_{GROUND\_y} - m_{foot}\, g = m_{foot}\, a_{foot\_y}$

$M_{ANKLE} + r_{ANKLE}\, F_{ANKLE} + r_{GROUND}\, F_{GROUND} = I_{foot}\, \alpha_{foot}$ ----------(1.3)

Where; m= mass; a = foot linear acceleration I= moment of inertia vector; α= foot angular acceleration; r_{ANKLE} = distance between the ankle joint center and foot center of mass; r_{GROUND} = distance between the center of pressure and foot center of mass; F_{ANKLE} = Force acting on the ankle; F_{GROUND} = Ground reaction force; M_{ANKLE} = moment at the ankle joint.

3.3.5 Quantifying Varus Thrust

The method proposed by Chang et al., 2013, was used to determine the knee varus angular velocity (KVAV) during the entire stance phase (0-60%) of the gait cycle in the asymptomatic and moderate knee OA group. According to this method the KVAV was calculated as the time derivative of the knee abduction adduction angle during the above mentioned phase of the gait cycle (Details on the motion data acquisition and processing that will determine the frontal plane angles are provided in section 3.3.4). The first peak in the varus direction within 30% of the gait cycle was considered as the peak knee varus angular velocity (pKVAV). Participants who had a first peak in the valgus direction (greater than the varus peak) were excluded considering them to have a valgus thrust.

Another method used to quantify varus thrust suggested by Takigami et al., 2000 was compared to the method used by Chang et al., 2013 to satisfy the goals of objective 1. The method suggested by Takigami et al., 2000 calculates the absolute angular velocity as

a change in the angle constituted by the three markers (the ASIS, tibial tuberosity and lateral malleolus) and elapsed time from heel strike to foot flat during the beginning of the stance phase of the gait cycle. Foot flat occurs during the loading response phase, between 10-20% of the gait cycle. The three markers were used to form two vectors as indicated in equation 2.2. The current study calculated the angle formed by the above lower limb markers at every time frame to provide a visual feedback of the angle waveform throughout the stance phase of the gait cycle. To calculate the velocity by this method, the angle at footflat and heel strike was extracted (Footflat occurs at approximately around 16.6% of the stance phase) and the time between the two phases was determined. All calculations were programmed in MatLab™ version 7.12 (The Mathworks Inc., Natick, Massachusetts, USA) and manually verified. All waveforms were plotted against the smallest stance time (seconds) recorded among the participants in both groups. The two methods, Chang and Takigami method, were compared to determine if the two objective measures can be used interchangeably to calculate varus thrust in asymptomatic and moderate knee OA participants.

Chang et al., 2013 method

$$\text{Knee varus angular velocity} = \frac{d\,(knee\ angle(n+1) - knee\ angle(n-1))}{2 * deltaT} \quad (2.1)$$

Where; d: derivative; knee angle: knee abduction-adduction angle; n refers to the knee abduction-adduction angle at each time frame; deltaT: change in time.

Takigami et al., 2000 method

Absolute angular velocity = $\theta_2 - \theta_1$ / elapsed time---------- (2.2)

Where; θ_1 and θ_2 are the angles formed between the vectors joining the lateral malleolus & ASIS and lateral malleolus and Tibial tuberosity at heel strike and foot flat respectively; elapsed time: time from heel strike to footflat.

3.5 Statistical Analysis

The statistical procedures were completed using Minitab™ ver. 17 (Minitab.Inc, State College, PA, USA), SPSS Statistics v.22.0 (IBM, USA) and G*Power v3.1.9.2 (Universität Kiel, Germany).

An Anderson-Darling normality test was conducted to determine the distribution of the pKVAV in both groups. Box plots were used to determine the presence of outliers in both the asymptomatic and moderate OA group. A power analysis was performed in cases where the p value was close to the level of significance (0.05) to determine if lack of sufficient sample size was responsible for non-significant results.

Objective 1

To determine the association between two methods (Chang and Takigami methods) that utilize frontal plane knee varus angular velocity measures as an objective measure of varus thrust and if the two measures can be used interchangeably in some sense, a Pearson Product Correlation and simple linear regression analysis was performed. A high variance (R^2>90%) explained by the association would indicate a strong relationship between the two quantifying measures. Students' t-test was used to

determine significant differences (at alpha =0.05) between the pKVAV (Chang et al., 2013) and absolute angular velocity (Takigami et al., 2000) values in the asymptomatic and moderate OA groups. One way ANOVA was used to determine differences in the pKVAV measures between KL scores in the moderate OA group.

Objective 2

A) Students' t-test were used to determine statistical differences in the quadriceps, hamstrings and plantarflexor muscle groups between the asymptomatic and moderate OA groups at alpha=0.05.

B) Pearson product correlation was used to determine the relationship between knee muscle strength (quadriceps, hamstrings and plantarflexor muscle groups) and an objective measure of "varus thrust" in both the asymptomatic and moderate OA groups.

C) Multivariate linear regression analyses were used to determine the association between knee muscle strength (quadriceps, hamstrings and plantarflexors groups) and an objective measure of "varus thrust" in both asymptomatic and moderate OA groups. Regression analysis were both unadjusted and adjusted for walking speed (continuous variable) and sex (categorical variable). The objective measure of "varus thrust" was entered as the dependant variable. Statistical significance was determined at alpha=0.05

D) With the moderate OA group, that is KL score I-II and KL scores III-IV, multivariate linear regression analysis were used to determine the association between knee muscle strength (quadriceps, hamstrings and plantarflexors groups) and an objective measure

of “varus thrust”. Regression analyses were both unadjusted and adjusted for walking speed (continuous variable) and sex (categorical variable). The objective measure of “varus thrust” was entered as the dependant variable. Statistical significance was determined at alpha=0.05.

Objective 3

A) Students’ t-tests were used to determine significant differences in the peak KAM, KAM impulse and KFA range between the two groups. Statistical significance was determined at alpha=0.05.

B) Pearson product correlation was used to determine the relationship between the frontal plane moments (peak KAM, KAM impulse) and sagittal plane angular displacements (KFA range) and an objective measure of “varus thrust” in both the asymptomatic and moderate OA groups.

C) Multivariate linear regression analyses were used to determine the association between the frontal plane moments (peak KAM, KAM impulse) and sagittal plane angular displacements (KFA range) individually, and an objective measure of “varus thrust” in both asymptomatic and moderate OA groups. Regression analyses were both unadjusted and adjusted for walking speed (continuous variable) and sex (categorical variable). The frontal plane moments and sagittal plane angular displacement variables were entered as dependant variables in the analysis.

CHAPTER 4: RESULTS

4.1 Participant Demographics

One hundred and thirty five moderate knee OA participants and eighty seven asymptomatic controls met the inclusion criteria and were included in this study (Figure 4.1).

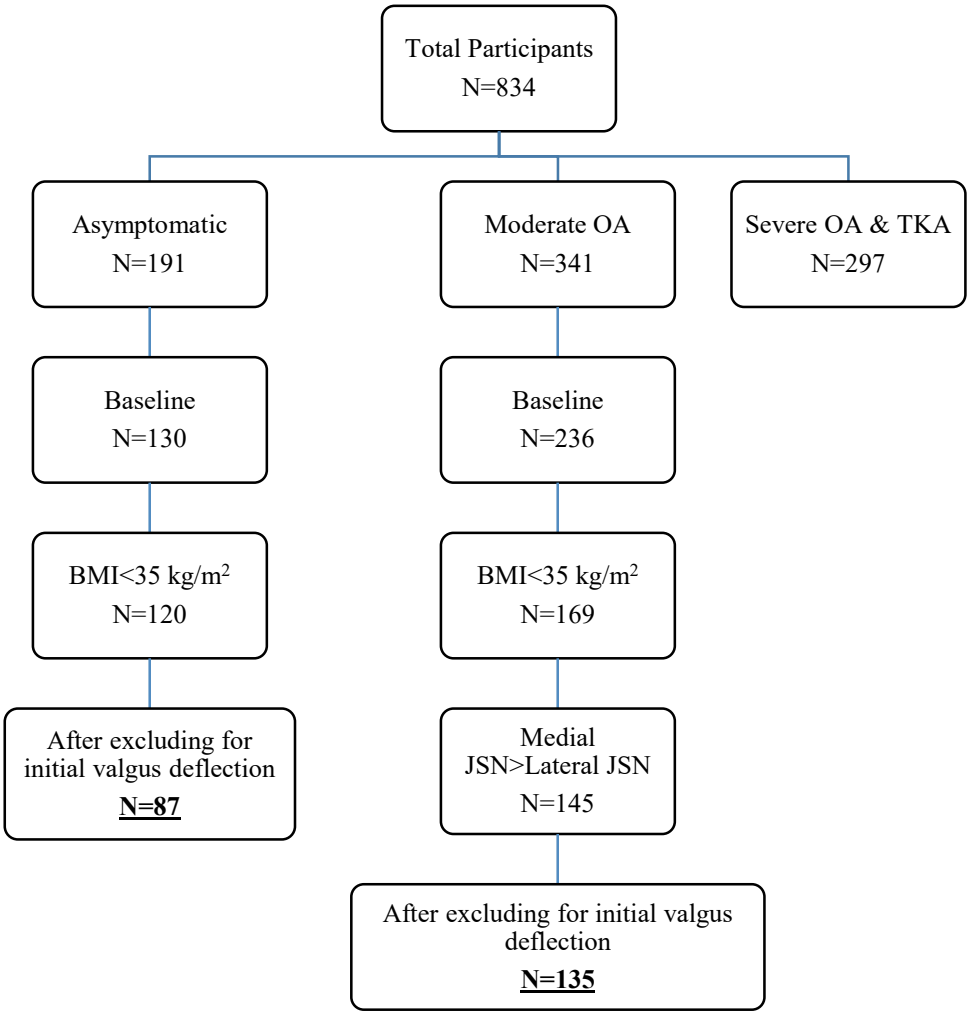


Figure 4.1: Flow diagram indicating the participant inclusion criteria. TKA: Total knee Arthroplasty; BMI: Body mass index in kg/m^2; JSN: Joint space narrowing.

Since there were more women than men in the asymptomatic group compared to the moderate OA group, the data were first analyzed for the whole group (Table 4.1a) and then re-analyzed after categorizing by sex (Table 4.1b). As indicated in Table 4.1a, there were significant differences for age ($p<0.01$), BMI ($p<0.01$) and walking speed ($p<0.01$) between the two groups. The moderate OA group was older, with a larger BMI and walked slower compared to controls (Table 4.1a). The relative (normalised to body mass) isometric torque measures of the quadriceps, hamstrings and plantarflexor muscle groups, represented as KE-45, KF-55 and PF respectively, were lower in the moderate knee OA group. This was significant for the quadriceps ($p<0.01$) and plantarflexors ($p<0.01$) only in the whole group.

As indicated in Table 4.1b, both men and women in the moderate OA group were significantly older with a larger BMI than their sex-matched asymptomatic controls ($p<0.01$) consistent with the total group. However, there were no significant sex differences within each group in age and BMI. Women in the asymptomatic group walked significantly faster than women in the moderate OA group ($p<0.01$) consistent with the total group, whereas men in both groups walked at similar speeds. Significant sex differences within the asymptomatic and moderate OA groups were found for walking speed ($p<0.01$). Interestingly, asymptomatic women walked significantly faster than asymptomatic men. With respect to torque measures, OA men had significantly lower strength in the hamstrings ($p=0.03$) and plantarflexor ($p=0.02$) muscle groups only while OA women were significantly lower in all three relative isometric muscle torque measures compared to asymptomatic controls. These findings differ from the whole group. Additionally, as indicated in Table 4.1b asymptomatic and OA women had significantly

lower strength measures in the quadriceps, hamstrings and plantarflexor muscle groups ($p<0.05$) (Table 4.1b) compared to asymptomatic and OA men respectively.

Table 4.1a: Group characteristics with mean (standard deviation) of the variables

Variable	**Asymptomatic(n=87)**	**Moderate(n=135)**	**p value (between grps)**
Age(years)	50.2(9.3)	58.3(8.6)	**<0.01**
BMI(kg/m^2)	25.7(3.6)	28.8(3.2)	**<0.01**
Speed(m/s)	1.3(0.2)	1.2(0.2)	**<0.01**
KE45(Nm/Kg)	1.48(0.36)	1.35(0.46)	**<0.01**
KF55(Nm/Kg)	0.73(0.30)	0.69(0.28)	0.40
PF(Nm/Kg)	1.19(0.34)	1.07(0.38)	**0.01**

Total number of participants =222; BMI: Body mass index; Speed: self-selected walking velocity; KE45: knee extension at 45 deg; KF55: knee flexion at 55 deg; PF: plantarflexion in neutral; Nm/Kg: Newton meters normalised to body mass in Kgs. P value corresponds to a **Students' t-test** looking at a significant differences between the two groups, the values in bold indicate a significant difference ($p<0.05$).

Table 4.1b: Group characteristics with mean (standard deviation) of the variables categorized by sex

Variable	**Sex**	**Asymptomatic(n=87) Men(30) Women(57)**	**Moderate(n=135) Men(90) Women(45)**	**p value (between grps)**
Age(years)	Men	52.1(9.6)	58.2(8.4)	**<0.01**
	Women	49.1(8.9)	58.6(9.1)	**<0.01**
BMI(kg/m^2)	Men	26.3(3.3)	29.0(3.8)	**<0.01**
	Women	25.4(3.7)	28.3(3.6)	**<0.01**
Speed(m/s)	Men	1.3(0.2)*	1.3(0.2)*	0.52
	Women	1.4(0.2)*	1.2(0.2)*	**<0.01**
KE45(Nm/Kg)	Men	1.64(0.36)*	1.51(0.43)*	0.11
	Women	1.39(0.33)*	1.05(0.40)*	**<0.01**
KF55(Nm/Kg)	Men	0.93(0.34)*	0.79(0.29)*	**0.03**
	Women	0.62(0.21)*	0.50(0.15)*	**<0.01**
PF(Nm/Kg)	Men	1.31(0.32)*	1.15(0.37)*	**0.02**
	Women	1.13(0.34)*	0.91(0.30)*	**<0.01**

Total number of participants =222; BMI: Body mass index; Speed: self-selected walking velocity; KE45: knee extension at 45 deg; KF55: knee flexion at 55 deg; PF: plantarflexion in neutral; Nm/Kg: Newton meters normalised to body mass in Kgs. P value corresponds to a **Students' t-test** looking at a significant differences between the two groups, the values in bold indicate a significant difference ($p<0.05$). * - indicates significant sex differences by a **Students' t-test** in the same group ($p<0.05$).

4.2 Objective Measures Of Varus thrust: pKVAV And Absolute Angular Velocity

4.2.1 Peak Knee Varus Angular Velocity (based on Chang et al., 2013 method)

The ensemble averaged frontal plane knee angle for the asymptomatic and moderate OA group is depicted in Figure 4.2a. To minimize confusion in interpreting the velocity data, the waveforms were averaged over the slowest stance time (0.51 seconds) found in both groups and thus, the x-axis was in seconds. Both groups showed a similar pattern with an initial valgus (negative) followed by a sudden change in the varus direction (positive) between 0.10 to 0.20 seconds. However, qualitatively the asymptomatic group showed a greater overall change from valgus to varus as compared to the moderate OA group. Figure 4.2b depicts the ensemble averaged KVAV for both groups. Again like the frontal plane knee angle, the overall waveform pattern in Figure 4.2b was similar for both groups. Qualitatively, the peak appears to be lower and occurs slightly earlier in the moderate OA group as compared to asymptomatic group. Both Figure 4.2a and 4.2b indicate that a large amount of variability exists in the waveforms.

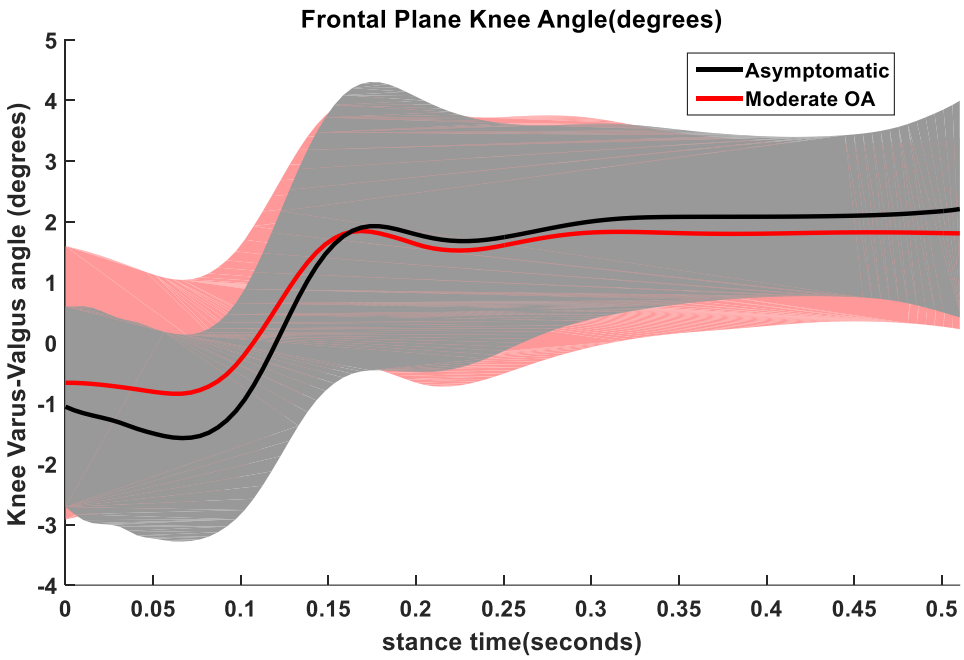


Figure 4.2a: Ensemble average of the frontal plane knee angle with the standard deviation (shaded) for asymptomatic (black line and grey shading) and moderate OA (red line and pink shading) groups during the stance phase of the gait cycle. On the Y axis, valgus is in the negative direction and varus is in the positive direction. Lowest stance time (seconds) in the asymptomatic and moderate OA group on the X axis.

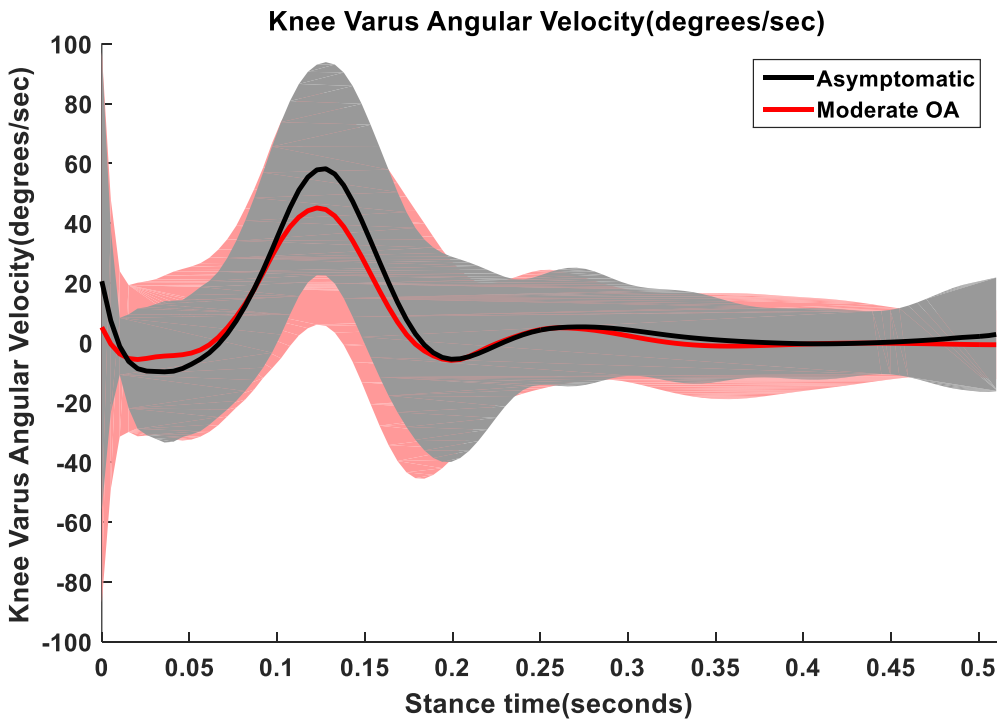


Figure 4.2b: Ensemble average of the knee varus angular velocity with the standard deviation (shaded) for asymptomatic (black line and grey shading) and moderate OA (red line and pink shading) groups during the stance phase of the gait cycle. On the Y axis, valgus is in the negative direction and varus is in the positive direction. Lowest stance time (seconds) in the asymptomatic and moderate OA group on the X axis.

Figure 4.3a shows a histogram with a distribution curve of the pKVAV for all the participants (n=222). An Anderson-Darling normality test found a significantly large difference between the pKVAV distribution and the expected normal distribution ($p<0.01$) indicating that the data was not normally distributed (Figure 4.3b). Both the asymptomatic and moderate OA groups had outliers which tended to skew the data to the right (skewness=2.92). Thus the median pKVAV (52.62 deg/sec) was lower than the mean (64.74 deg/sec). The box plots in Figure 4.3c show the outliers in both the groups. Each

outlier was individually assessed to look for errors in data collection and processing. However, since no obvious errors were observed they were included in the analysis. Considering the lack of normal distribution in the pKVAV measures the data were transformed and reanalysed. However, no differences in the statistical findings were observed in the results post transformation and hence the non-transformed data are presented.

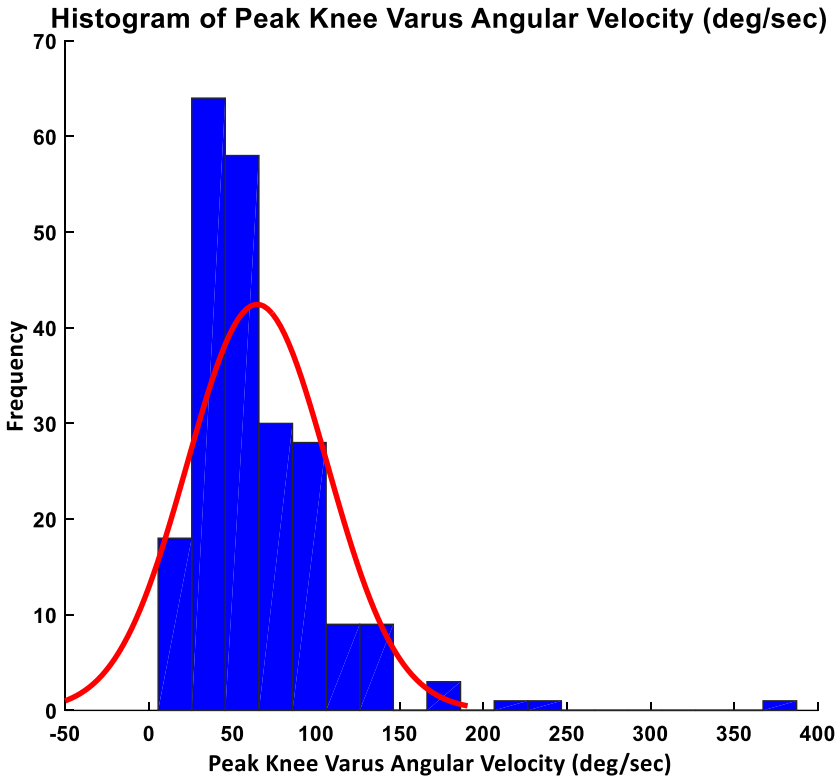


Figure 4.3a: Histogram with distribution curve of the Peak Knee Varus Angular Velocity (deg/sec) for all the participants N=222 (asymptomatic and moderate OA).

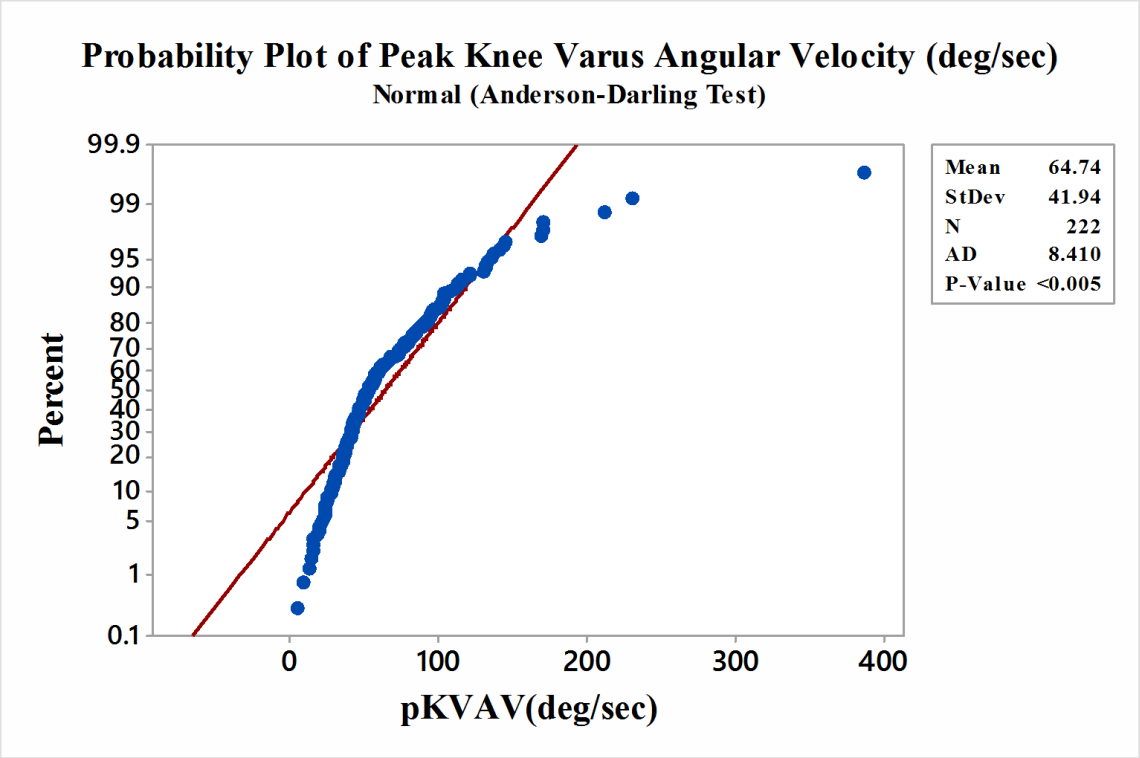


Figure 4.3b: Probability plot of the Peak Knee Varus Angular Velocity (deg/sec) after applying the Anderson-Darling test for all the participants (asymptomatic and moderate OA).

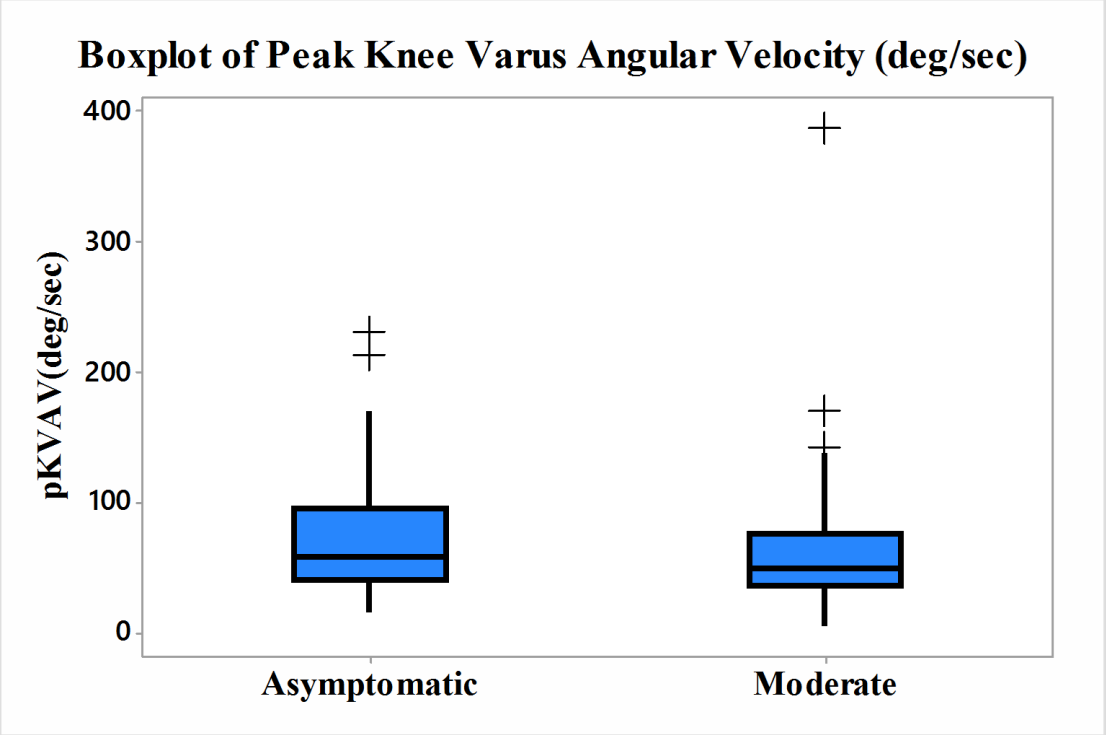


Figure 4.3c: Box plot of the peak knee varus angular velocity for the asymptomatic and moderate OA group. +: indicates outliers in the groups.

As indicated in Table 4.2, the moderate OA group had a lower mean pKVAV compared to asymptomatic controls, but this was not significant (p=0.07). To assess whether the non-significant results was due to the lack of sufficient sample size, a power analysis was conducted which indicated a small Cohen's d effect size (0.25) with a power (at the study's sample size) to be equivalent to 44.9% (G*Power v3.1.9.2, Universität Kiel, Germany).

Categorizing by sex, no significant differences were found in the mean pKVAV measures between the two groups for both men (p=0.76) and women (p=0.08). A power analysis (G*Power v3.1.9.2, Universität Kiel, Germany) for women in both groups indicated a small Cohen's d effect size (0.35) with a power (at the study's sample size) to

be equivalent to 72.7%. Only the asymptomatic women had a significantly higher pKVAV than asymptomatic men ($p<0.01$) (Refer to Appendix 2 for KVAV waveforms categorized by sex).

Additionally, there were no significant differences in the mean pKVAV among the KL scores in the moderate OA group as determined by one way ANOVA (Table 4.2).

4.2.2 Absolute Angular Velocity (based on the Takigami et al., 2000 method)

Figure 4.4a shows a histogram with a distribution curve of the absolute angular velocity for all the participants (n=222). An Anderson-Darling normality test found no significant difference between the absolute angular velocity distribution and the expected normal distribution ($p>0.05$) indicating that the data was normally distributed (Figure 4.4b). Both the asymptomatic and moderate OA groups had outliers which tended to skew the data slightly to the right (skewness=0.35). In contrast to the pKVAV, the median (45.3 deg/sec) and mean (44.6 deg/sec) absolute angular velocities were similar. The box plots in Figure 4.4c show the outliers in both the groups. Each outlier was individually assessed to look for errors in data collection and processing. However, since no obvious errors were observed they were included in the analysis.

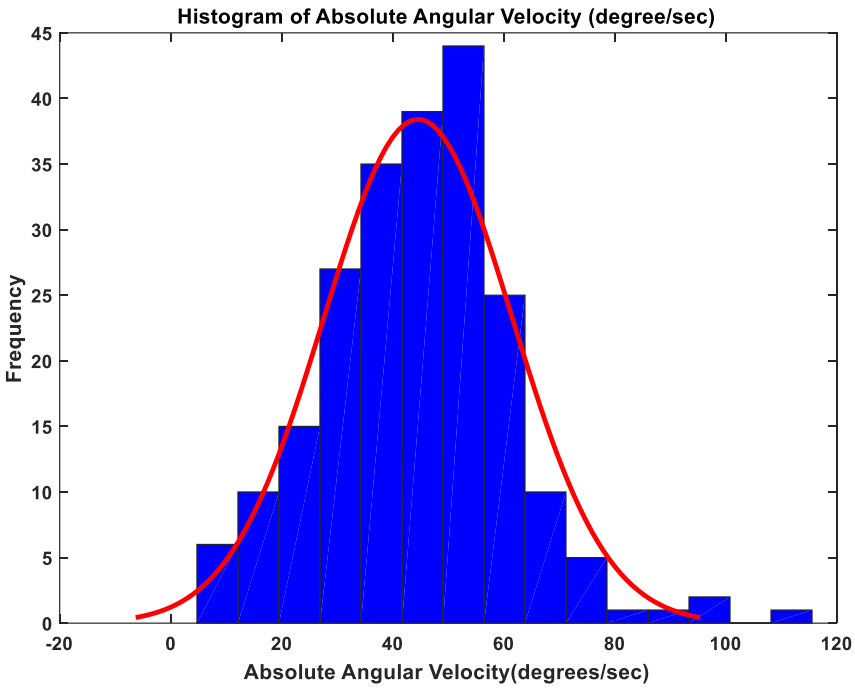


Figure 4.4a: Histogram with distribution curve of the Absolute Angular Velocity (deg/sec) for all the participants N=222 (asymptomatic and moderate OA).

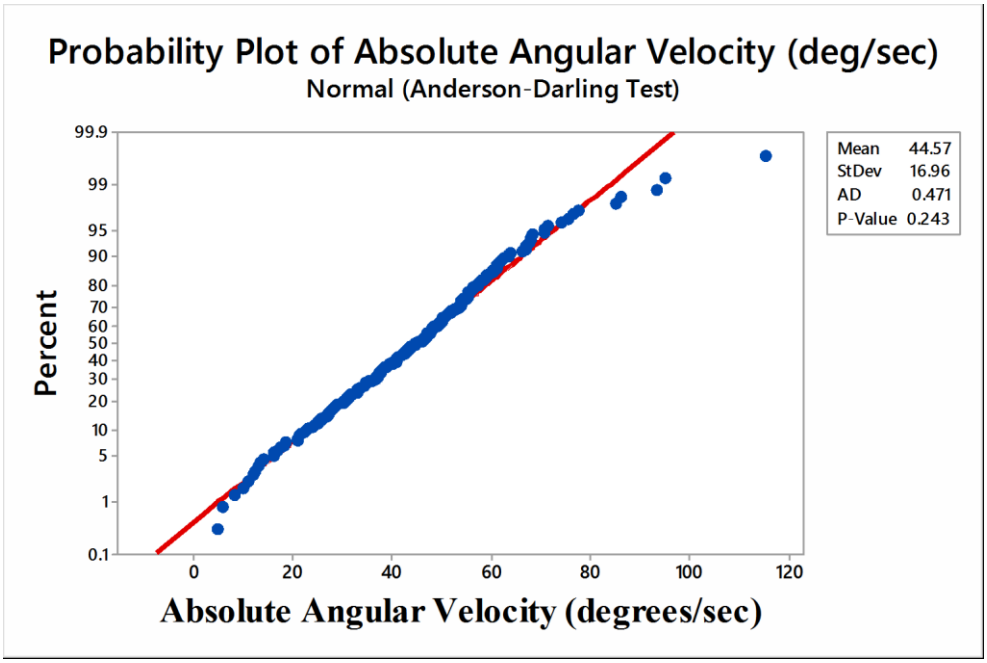


Figure 4.4b: Probability plot of the Absolute Angular Velocity (deg/sec) after applying the Anderson-Darling test for all the participants (asymptomatic and moderate OA).

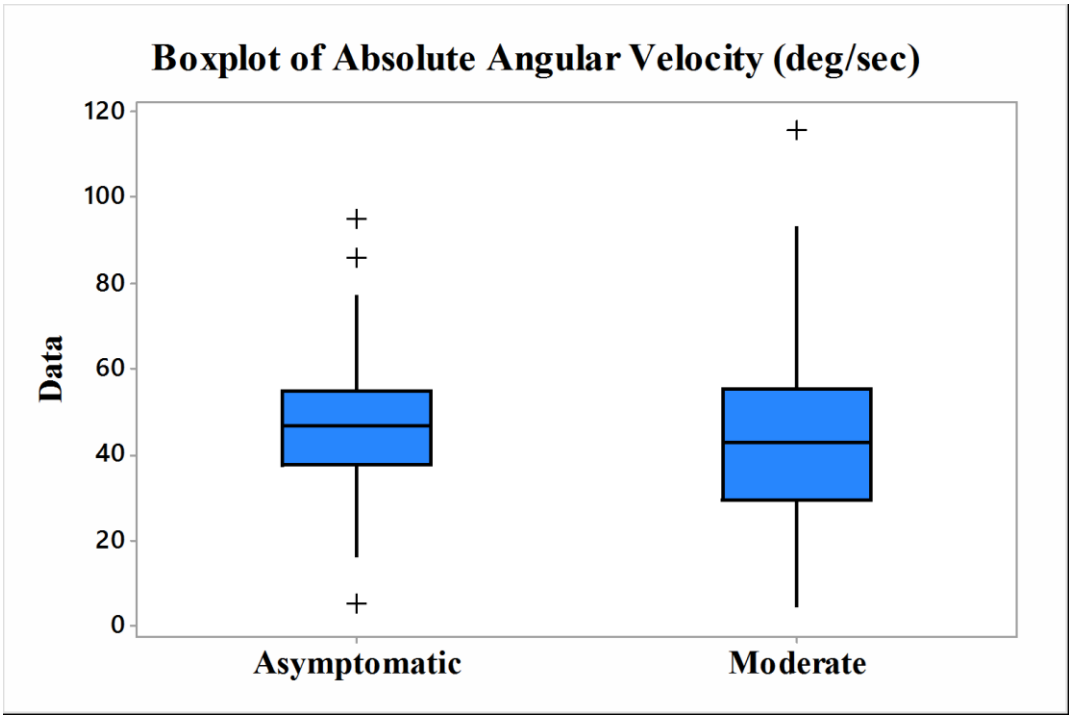


Figure 4.4c: Box plot of the Absolute Angular Velocity for the asymptomatic and moderate OA group. +: indicates outliers in the groups.

As indicated in Figure 4.5, the asymptomatic group depict a slightly greater peak knee angle, as calculated by the Takigami method, between 0.15 to 0.20 seconds of stance time which may denote a deflection towards "varus". The mean absolute angular velocity computed from the knee angles in Figure 4.5 using the Takigami method are in Table 4.2. The moderate OA group had a lower mean absolute angular velocity measure compared to asymptomatic controls ($p=0.07$). Similar to the pKVAV measures, the current sample size had a low statistical power at 57.1% with the Cohen's d effect size equivalent to 0.24 (G*Power v3.1.9.2, Universität Kiel, Germany). The mean absolute angular velocity was approximately 20 deg/sec lower that the pKVAV (Table 4.2).

Categorizing by sex, significant differences in the absolute angular velocity measures were found only between asymptomatic and OA women. OA women were significantly lower than asymptomatic women ($p<0.01$) and OA men ($p<0.01$).

In summary, the comparison of the demographics and descriptive data provide an objective assessment of the samples studied so that they can be compared to other studies and determine terms to adjust the regression analyses.

Table 4.2: Peak knee varus angular velocity measures, categorised by sex and KL scores for asymptomatic controls and moderate OA group.

Variable			**Asymptomatic(n=87) Men(30) Women(57)**	**Moderate (n=135) Men(90) Women(45)**	**P value (between groups)**
pKVAV (deg/sec)			71.1(41.2)	60.6(42.0)	0.07
	Men		56.7(23.7)*	58.7(45.9)	0.76
	Women		78.7(46.4)*	64.6(33.2)	0.08
	KL Scores	1(n=10)		61.4(23.2)	0.98#
		2(n=47)		59.1(33.2)	
		3(n=51)		61.7(56.6)	
		4(n=21)		57.0(25.5)	
Absolute Angular velocity (deg/sec)			47.0(14.3)	42.9(18.3)	0.07
	Men		49.6(13.8)	47.9(18.0)*	0.59
	Women		45.7(14.5)	32.8(14.4)*	**<0.01**

Mean values with standard deviation in parenthesis. pKVAV: peak knee varus angular velocity (deg/sec). KL scores: Kellgren Lawrence scores; Absolute Angular velocity: varus thrust quantification by Takigami et al., 2000 method; P value corresponds to a Students' t test looking at a significant difference between the two groups, the values in bold indicate a significant difference ($p<0.05$). *: indicates significant sex differences within the same group ($p<0.05$). #: p value corresponds to one way ANOVA looking at the significant differences between the KL scores ($p<0.05$).

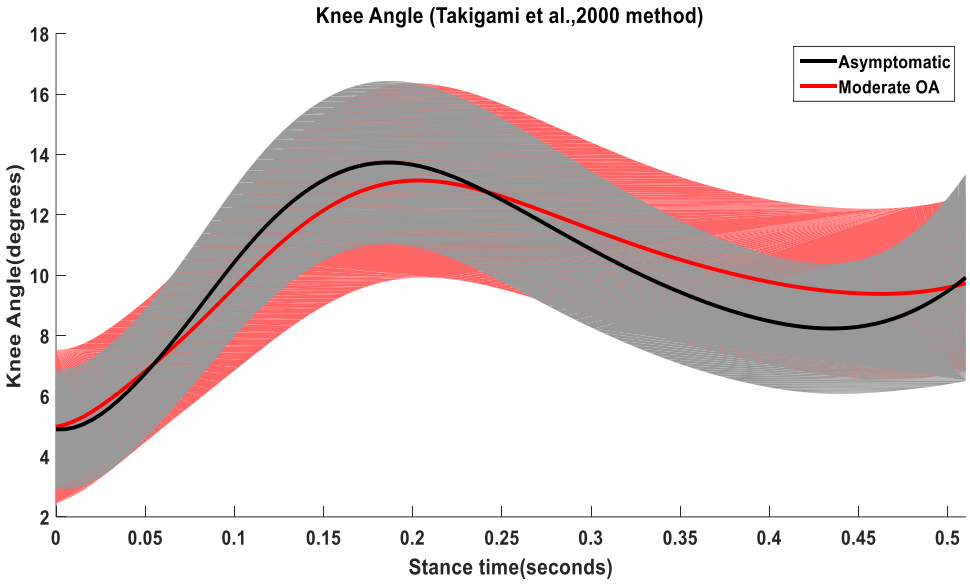


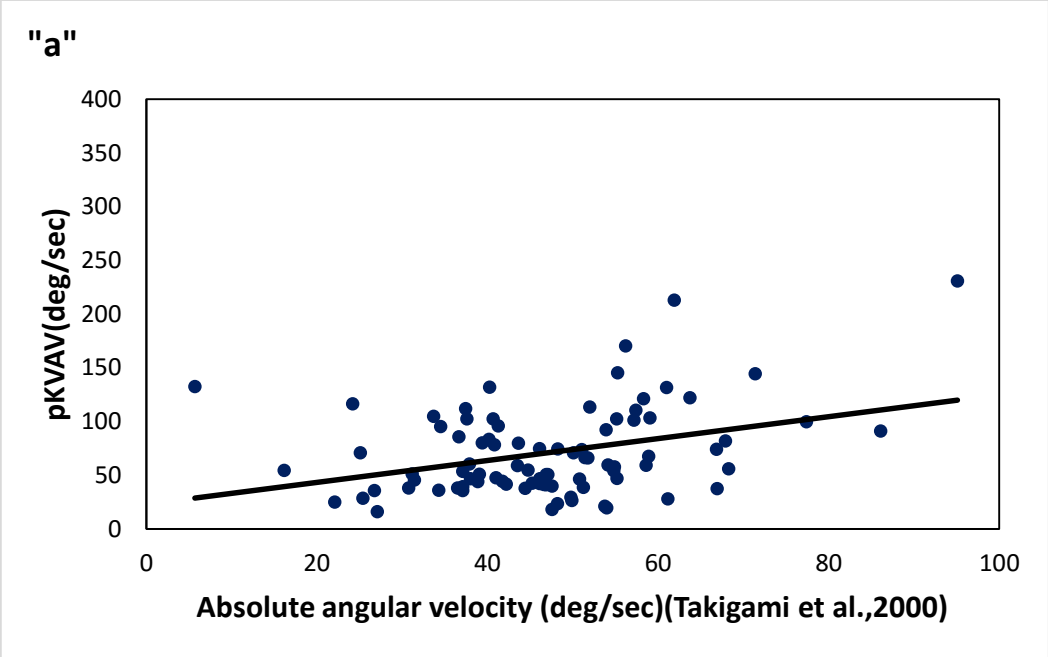
Figure 4.5: Ensemble averaged knee angle in degrees along with the standard deviation (shaded) calculated between the vectors formed by the lower limb markers during the stance phase of the gait cycle for the asymptomatic(black line and grey shading) and moderate OA(red line and pink shading) group. The two vectors were lateral malleolus-ASIS and lateral malleolus-tibial tuberosity. On the Y axis, a positive deflection indicates varus. Lowest stance time for the asymptomatic and moderate OA group on the X axis

4.3 Association Between pKVAV And Absolute Angular Velocity

The first objective of this study was to determine the association between the two objective methods of calculating "varus thrust" using an angular velocity measure by examining the correlation between the pKVAV (Chang et al.,2013) and the absolute angular velocity (Takigami et al., 2000). On linear regression analysis a significant positive but weak association was found between the two varus thrust quantifying

measures (R^2=12.5%, p value <0.01) in the asymptomatic controls (Figure 4.6a). However, the same relation had no association in the moderate OA group (R^2=0.2%, p value=0.60) (Figure 4.6b). The hypothesis stated that there would be a strong positive association (R^2 ≥90%) between two methods (Chang et al.,2013 and Takigami et al.,2000 method) that utilize frontal plane knee varus angular velocity measures as an objective measures of varus thrust indicating that the two can be used interchangeably. However, since the findings were not in support of this hypothesis, it was rejected.

Since, the Chang method has been validated against a visually assessed varus thrust it was used as the objective measure of "varus thrust" to achieve the remaining objectives.



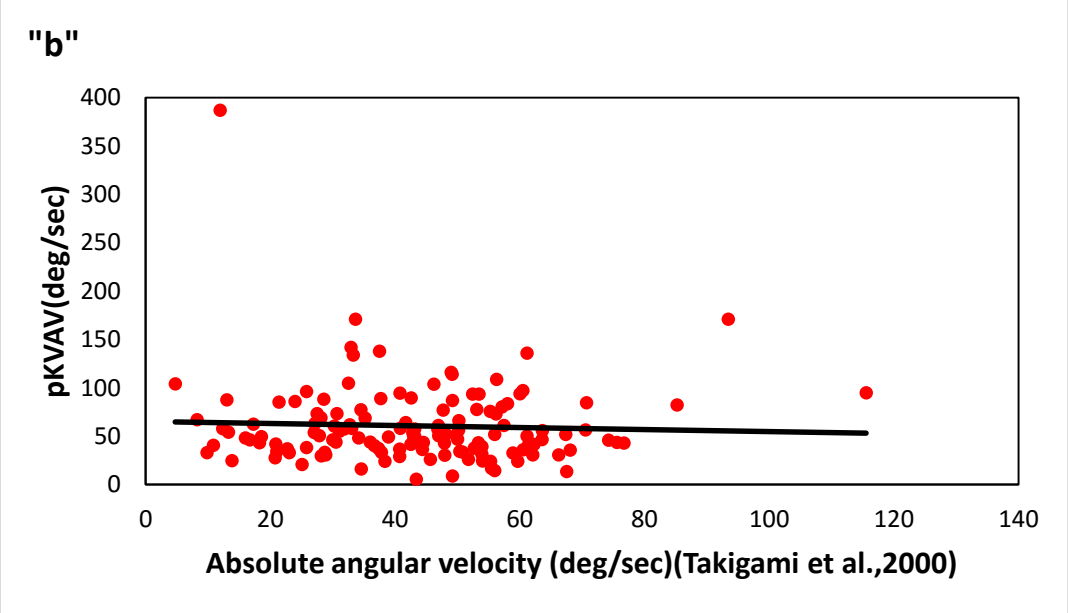
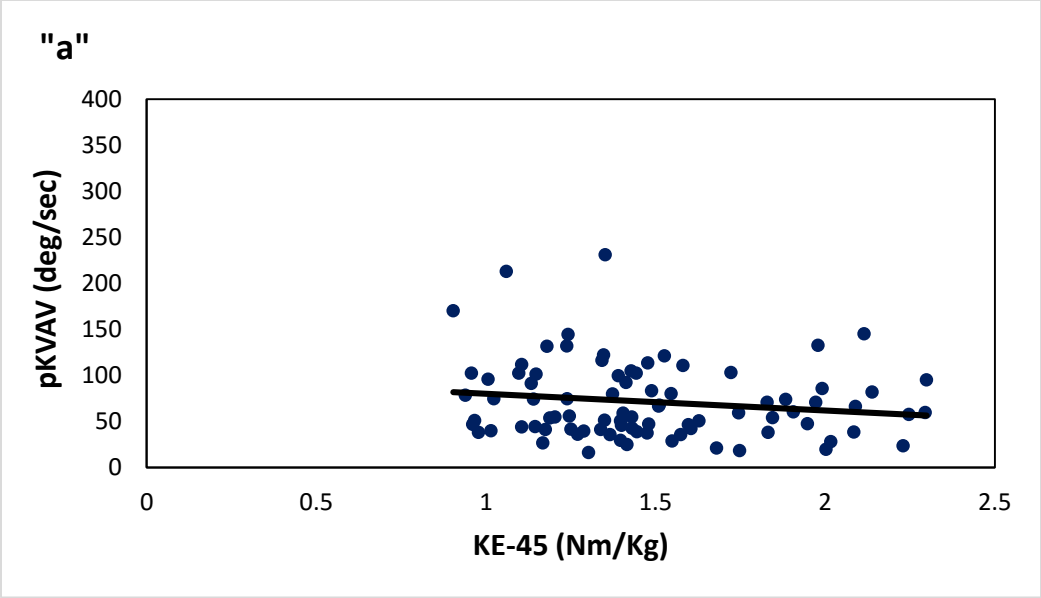


Figure 4.6a &b: Scatter plots with regression line showing the relationship between the peak knee varus angular velocity(pKVAV in deg/sec) and Absolute angular velocity for asymptomatic controls (R^2=12.5%, r = 0.4, p value <0.01) upper panel 'a' and moderate OA (R^2=0.2%, r = -0.04 pvalue=0.60) group lower panel 'b' respectively.

4.4 Peak Knee Varus Angular Velocity And Knee Muscle Strength

The scatter plots for the three knee muscle torque values and pKVAV measures are found in Figures 4.7, 4.8 and 4.9. The Pearson Product correlation coefficient indicates a negative non-significant ($p>0.05$) association between the muscle torque values and pKVAV in all three muscle groups for both study groups (Table 4.3). The correlation coefficient ranged only from -0.2 to -0.1 for the asymptomatic group and -0.04 to -0.1 for the OA group. The results for the linear regression analysis models to determine if the knee muscle strength measures predicted the pKVAV, are found in Table 4.3a. Muscle strength predictors were selected on the basis of best subsets analysis in Minitab® v.17.2.1. All the multiple regression models which included the three muscle groups and adjusted for walking speed and sex did not result in significant associations.



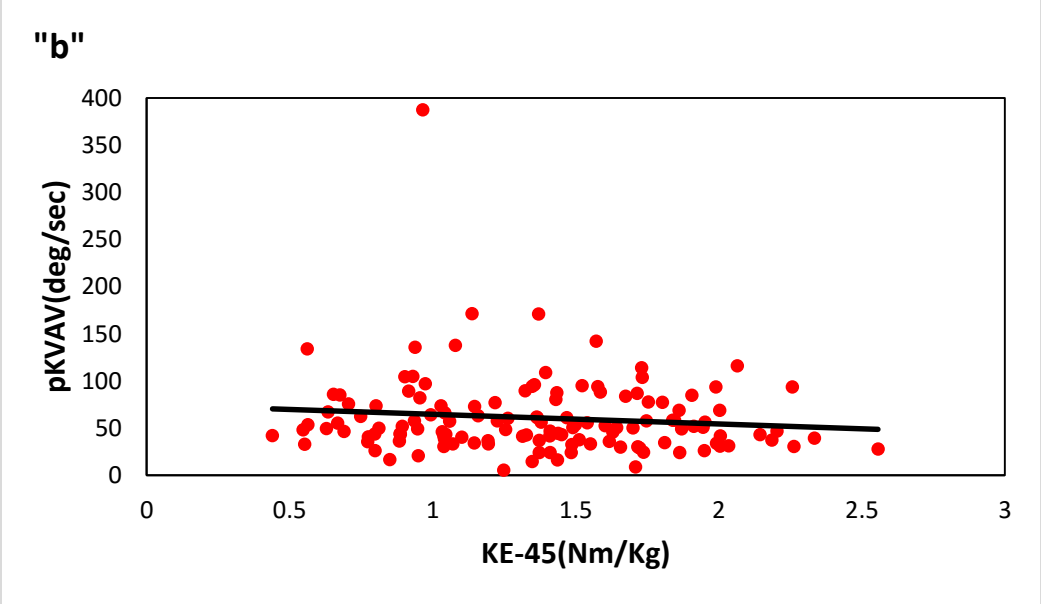
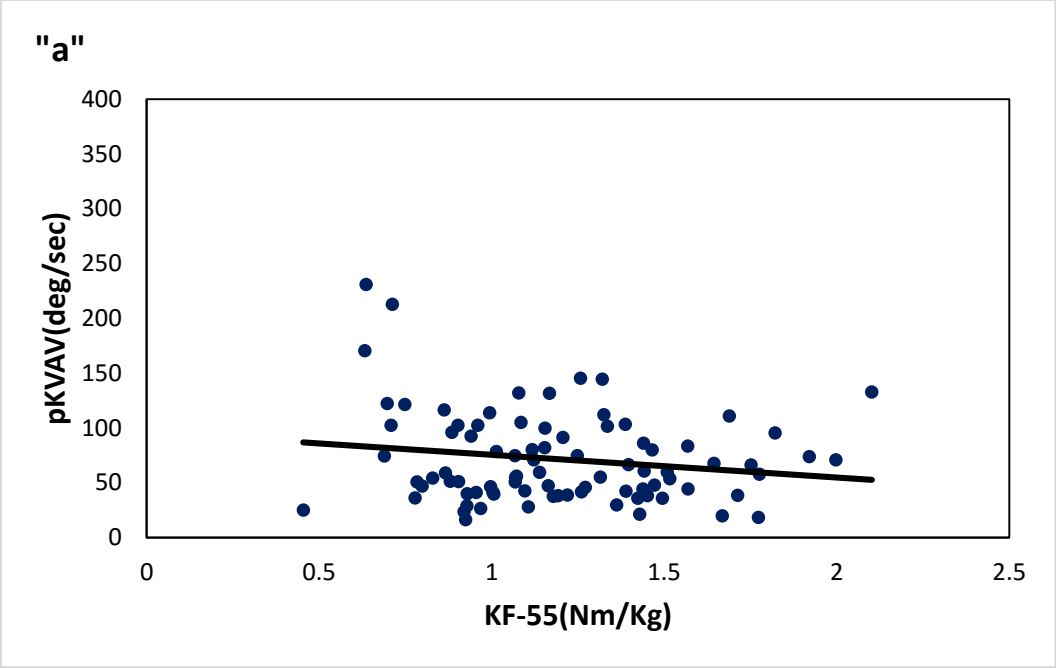


Figure 4.7a &b: Scatter plots with regression line showing the relationship between the peak knee varus angular velocity (pKVAV in deg/sec) and quadriceps torque(normalised to body mass) in asymptomatic (r=-0.2, p value=0.15) upper panel 'a' and moderate OA (r=-0.1, p value=0.20) group lower panel 'b' respectively.



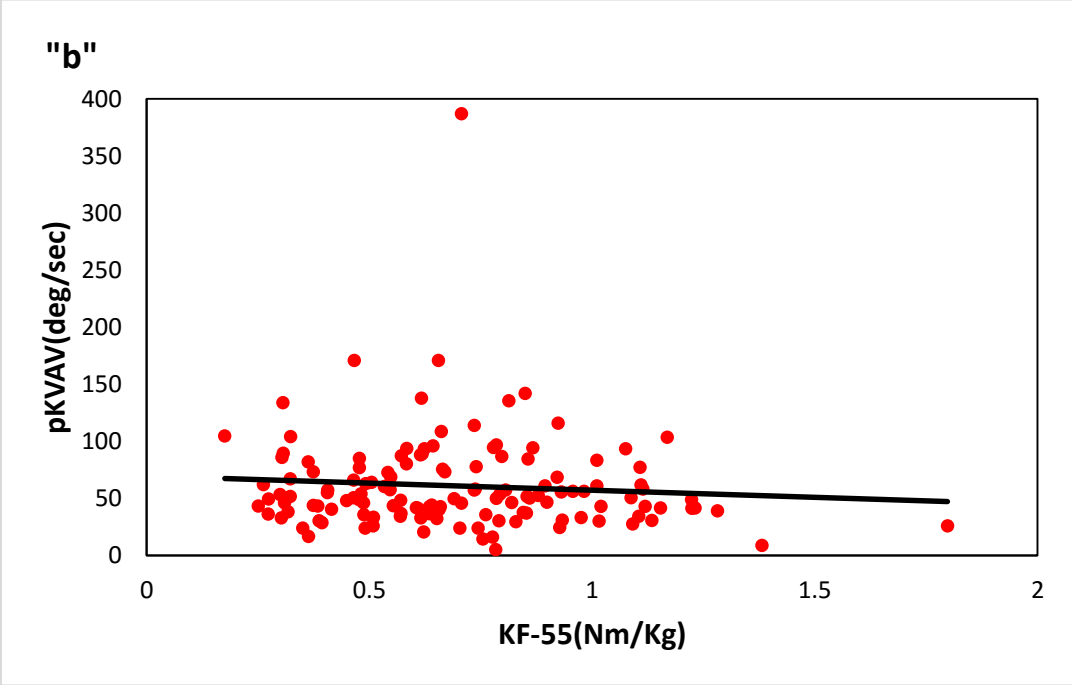


Figure 4.8a &b: Scatter plots with regression line showing the relationship between the peak knee varus angular velocity (pKVAV in deg/sec) and hamstrings torque(normalised to body mass) in asymptomatic (r=-0.1,p value=0.39)upper panel 'a' and moderate OA (r=-0.1, p value=0.33) group lower panel 'b' respectively.

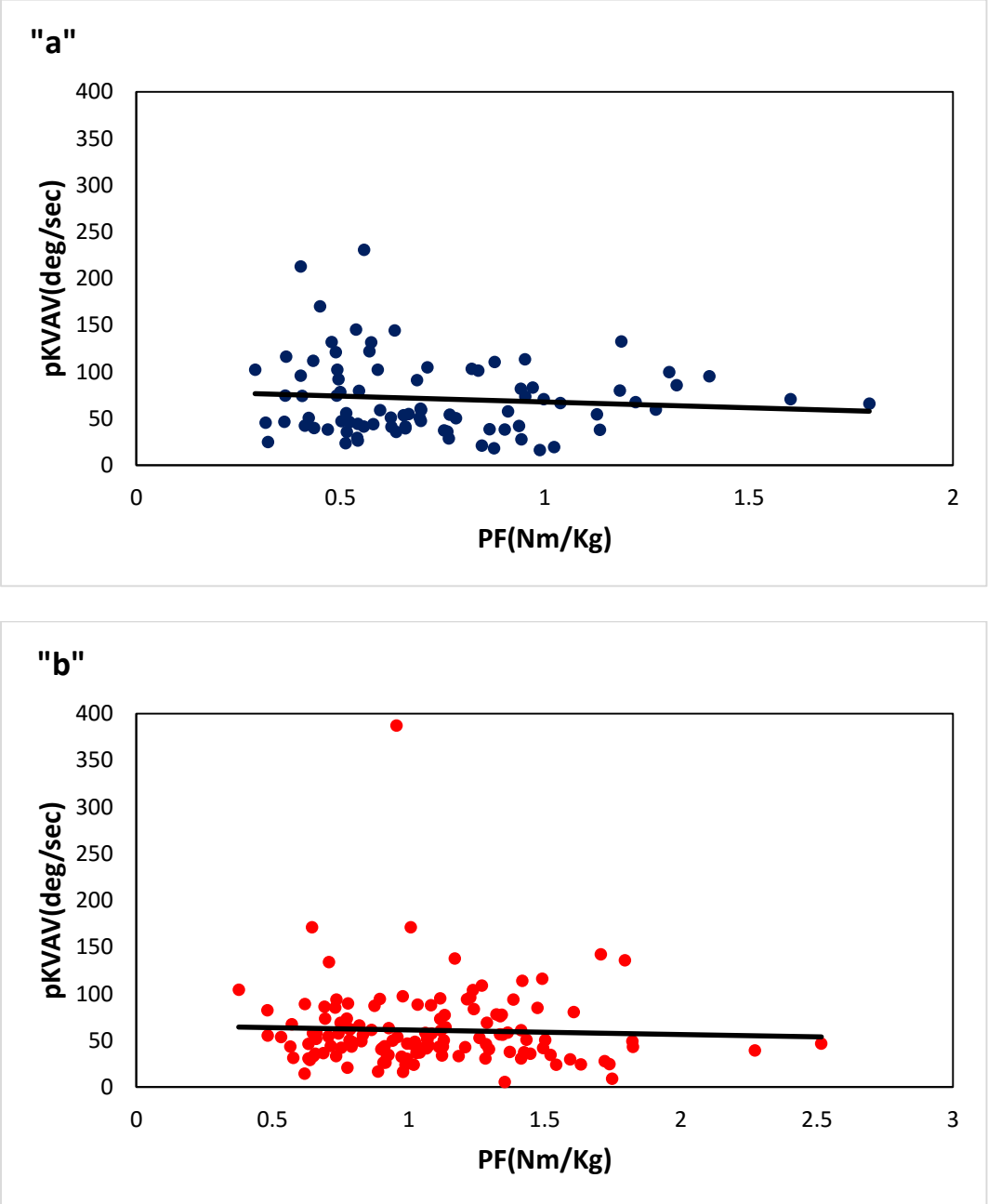


Figure 4.9a &b: Scatter plots with regression line showing the relationship between the peak knee varus angular velocity (pKVAV deg/sec) and plantarflexor torque(normalised to body mass) in asymptomatic (r=-0.2,p value=0.11)upper panel 'a' and moderate OA (r=-0.04, p value=0.63) group lower panel 'b' respectively.

Table 4.3a: Results of the regression models: peak knee varus angular velocity versus Knee Muscle Strength (adjusting for sex and walking speed)

Dependent variable : pKVAV	Asymptomatic Controls					Moderate OA				
	Unadjusted			Adjusted		Unadjusted			Adjusted	
	r	R^2%	p	R^2%	p	r	R^2%	p	R^2%	p
Linear Regression										
KE 45 (Nm/kg)	-0.2	2.5	0.15	7.6	0.09	-0.1	1.2	0.20	1.7	0.54
KF 55 (Nm/kg)	-0.1	0.9	0.39	7.0	0.11	-0.1	0.7	0.33	0.8	0.77
PF (Nm/kg)	-0.2	2.9	0.11	8.2	0.07	-0.04	0.2	0.63	0.4	0.91
KE45 + KF55		2.5	0.34	8.6	0.12		1.3	0.40	1.7	0.71
KE45 + PF		3.6	0.21	8.3	0.13		1.3	0.40	1.6	0.72
KE45 +KF55 +PF		3.9	0.35	10.6	0.10		1.3	0.65	1.6	0.84

Linear regression analysis results with the Peak knee varus angular velocity in deg/sec as the dependent variable. r: Pearson product correlation co-efficient, R^2: co-efficient of determination; p: p value <0.05 is considered as significant; KE45,KF55 and PF: Knee extension at 45^0, knee flexion at 55^0 and plantarflexion in neutral respectively; Adjusted: for walking speed and sex.

Table 4.3b: Results of the regression models: peak knee varus angular velocity versus Knee Muscle Strength on categorizing by KL scores (adjusting for sex and walking speed)

Dependent variable : **pKVAV**	**Moderate OA**				
	Unadjusted			**Adjusted**	
	r	**R^2%**	**p**	**R^2%**	**p**
Linear Regression					
KL Scores I-II					
KE 45 (Nm/kg)	-0.03	0.1	0.27	0.6	0.96
KF 55 (Nm/kg)	0.05	0.2	0.73	0.8	0.93
PF (Nm/kg)	0.10	1.1	0.31	2.2	0.77
KL Scores III-IV					
KE 45 (Nm/kg)	-0.13	1.7	0.27	4.3	0.40
KF 55 (Nm/kg)	-0.13	1.6	0.24	2.6	0.62
PF (Nm/kg)	-0.12	1.5	0.31	3.0	0.56

Linear regression analysis results with the Peak knee varus angular velocity in deg/sec as the dependent variable. r: Pearson product correlation co-efficient, R^2: co-efficient of determination; p: p value <0.05 is considered as significant; KE45, KF55 and PF: Knee extension at 45^0, knee flexion at 55^0 and plantarflexion in neutral respectively; Adjusted: for walking speed and sex; KL scores I-II: those with KL scores I and II; KL scores III-IV: those with KL scores III and IV.

In summary, relative torque measures, both individually and in combination, could not significantly predict the "varus thrust" at the knee as indicated by the pKVAV.

4.5 Peak Knee Varus Angular Velocity And Biomechanical Gait Variables

The biomechanical gait variables examined in this study were the frontal plane moments (KAM: peak and impulse) and sagittal plane angular displacement (KFA range). Figure 4.10 shows the ensemble average KAM waveforms normalised to body mass for the asymptomatic and moderate OA groups. The moderate OA group had a significantly higher (by 16%) 1st peak, approximately between 10-20% of the gait cycle, than the asymptomatic group ($p<0.01$) (Table 4.4a). As indicated in Table 4.4a, the relative KAM impulse was also significantly higher in the moderate OA group as compared to asymptomatic controls ($p<0.01$) approximately by 24%.

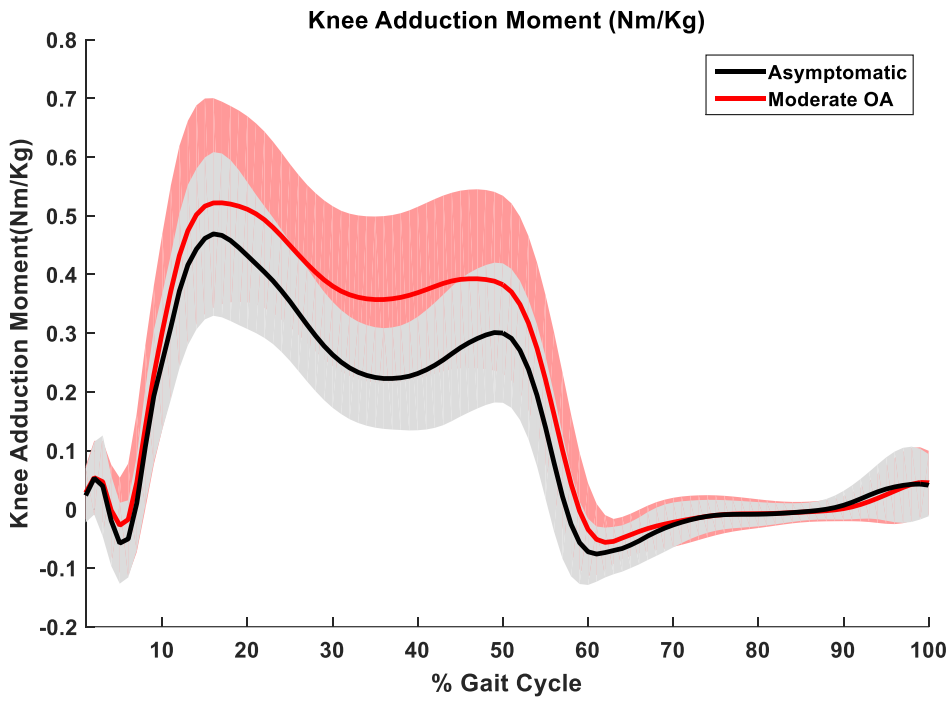


Figure 4.10: Ensemble average of the knee adduction moment (normalised to body mass) with the standard deviation (shaded) for the asymptomatic (black line and grey shading) and moderate OA (red line and pink shading) groups during the gait cycle.

The ensemble average sagittal plane KFA for the asymptomatic and moderate OA group during the gait cycle is shown in Figure 4.11. Qualitatively, the moderate OA group showed an overall lower knee excursion during the gait cycle. Students' t-test indicate that the asymptomatic controls had a significantly higher KFA range from heel strike to maximum within 30% of the gait cycle compared to moderate OA group ($p<0.01$) (Table 4.4a). Approximately a 12% difference in the KFA range between the two groups was found.

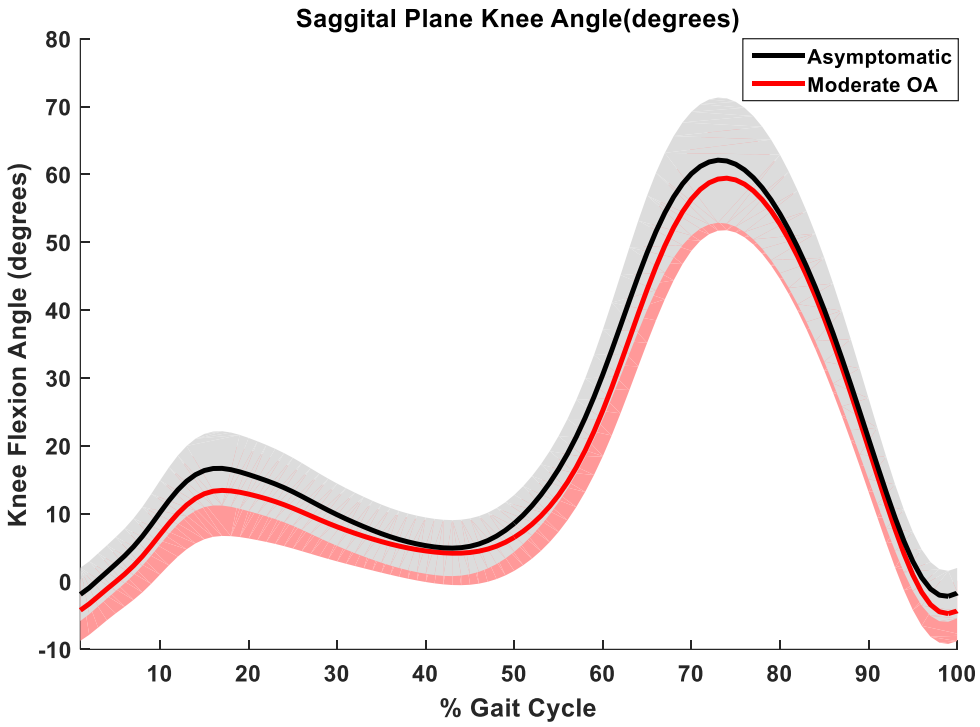


Figure 4.11: Ensemble averaged sagittal plane knee flexion angle in degrees with the standard deviation (shaded) for the asymptomatic (black line and grey shading) and moderate OA (red line and pink shading) group during the gait cycle. KFA range was calculated from heel strike to maximum within 30% of the gait cycle

Table 4.4a: Mean (standard deviation) of the biomechanical gait parameters.

Variable	**Asymptomatic(n=87)** **Men(30)** **Women(57)**	**Moderate(n=135)** **Men(90)** **Women(45)**	**p value (between grps)**
Peak KAM (Nm/Kg)	0.50(0.12)	0.58(0.15)	**<0.01**
KAMimpulse (Nm*s/Kg)	0.21(0.07)	0.26(0.10)	**<0.01**
KFA range (deg)	21.3(4.9)	18.7(6.7)	**<0.01**

KAM: knee adduction moment; KFA range: Knee flexion angle range; Nm/Kg: Newton meters normalised by body mass; Nm*s/kg: Newton meter seconds normalised by body mass; deg: degrees; P value corresponds to a **Students' t test** looking at a significant difference between the two groups, the values in bold indicate a significant difference ($p<0.05$).

As indicated in Table 4.4b, categorizing by sex, the peak KAM was significantly higher in OA men compared to asymptomatic men ($p<0.01$) and OA women ($p<0.01$), consistent with the whole group. Both sexes in the moderate OA had a significantly higher KAM impulse compared to asymptomatic controls ($p<0.01$) and was consistent with the whole group results. Asymptomatic women, had a significantly higher KAM impulse than asymptomatic men ($p<0.01$). No sex differences were found in the moderate OA group ($p>0.05$). Like the whole group findings, the KFA range was significantly lower in OA women compared to asymptomatic women ($p<0.01$) and OA men ($p<0.05$).

Table 4.4b: Mean (standard deviation) of the biomechanical gait parameters, on categorizing by sex.

Variable	Sex	Asymptomatic(n=87) Men(30) Women(57)	Moderate(n=135) Men(90) Women(45)	p value (between grps)
Peak KAM (Nm/Kg)	Men	0.48(0.1)	0.61(0.2)*	**<0.01**
	Women	0.52(0.13)	0.55(0.15)*	0.32
KAMimpulse (Nm*s/Kg)	Men	0.18(0.05)*	0.25(0.09)	**<0.01**
	Women	0.22(0.07)*	0.28(0.09)	**<0.01**
KFA range (deg)	Men	22.5(5.6)	20.6(6.4) *	0.14
	Women	20.6(4.4)	14.9(5.8)*	**<0.01**

KAM: knee adduction moment; KFA range: Knee flexion angle range; Nm/Kg: Newton meters normalised by body mass; Nm*s/kg: Newton meter seconds normalised by body mass; deg: degrees; P value corresponds to a student t test looking at a significant difference between the two groups, the values in bold indicate a significant difference ($p<0.05$).

*: indicates significant sex differences within the same group ($p<0.05$).

Tables 4.4c & d show the correlation between the biomechanical gait variables and walking speed. A significant moderate positive correlation can be seen between peak KAM and walking speed. KAM impulse and walking speed had a significant negative correlation in both groups. This relationship was strongest in asymptomatic women. The correlation between the KFA range and walking speed was significant and positive, being moderately strong in OA men.

Table 4.4c: Pearson product correlation of biomechanical variables versus walking speed

Correlation Coeff / Variable	Asymptomatic(n=87) Men(30) Women(57)	P value	Moderate(n=135) Men(90) Women(45)	P value
	r		r	
Peak KAM(Nm/Kg)	0.33	**<0.01**	0.26	**<0.01**
KAMimpulse(Nm*s/Kg)	-0.26	**0.02**	-0.27	**<0.01**
KFA range(deg)	0.22	**0.04**	0.49	**<0.01**

Table 4.4d: Pearson product correlation of biomechanical variables versus walking speed categorized by sex

Correlation Coeff / Variable	Sex	Asymptomatic (n=87) Men(30) Women(57)	P value	Moderate(n=135) Men(90) Women(45)	P value
		r		r	
Peak KAM(Nm/Kg)	Men	0.44	**0.02**	0.27	**0.01**
	Women	0.27	**0.04**	0.16	0.28
KAMimpulse(Nm*s/Kg)	Men	-0.28	0.14	-0.23	**0.03**
	Women	-0.36	**<0.01**	-0.30	**0.05**
KFA range(deg)	Men	0.25	0.18	0.58	**<0.01**
	Women	0.28	**0.03**	0.21	0.16

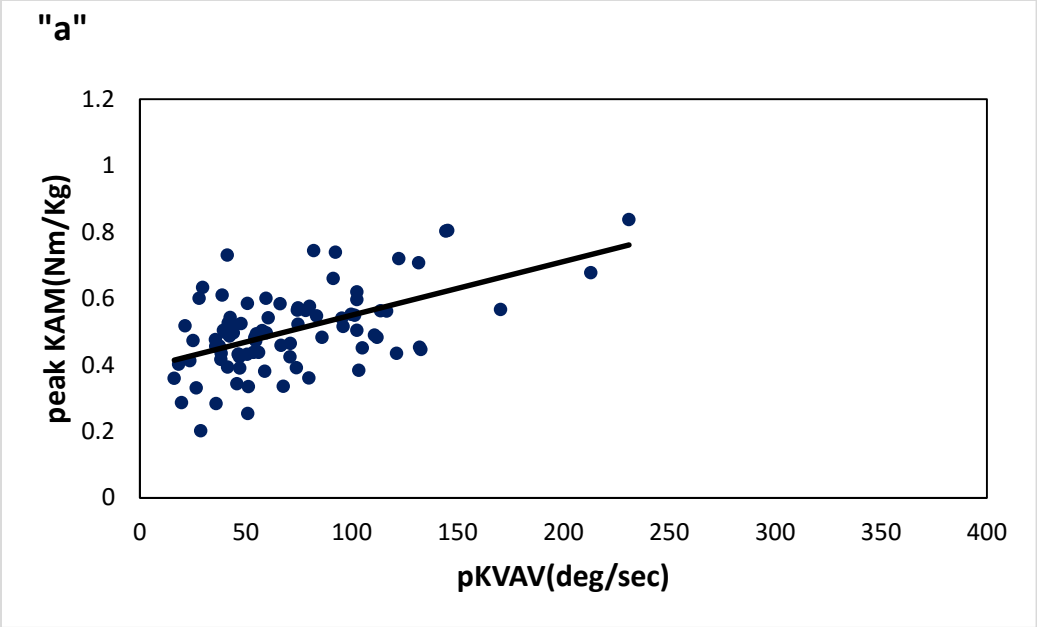
KAM: knee adduction moment; KFA range: Knee flexion angle range; Nm/Kg: Newton meters normalised by body mass; Nm*s/kg: Newton meter seconds normalised by body mass; deg: degrees; r: Pearson product correlation coefficient; P value corresponds to a Pearson product correlation looking at a significant correlation between variables, the values in bold indicate a significant difference ($p<0.05$).

The scatter plots depicting the relationship between pKVAV and peak KAM, KAM impulse and KFA range individually are found in Figures 4.11, 4.12 and 4.13 respectively. A positive relationship exists between pKVAV and all the biomechanical gait variables (Figures 4.12, 4.13a, 4.14) except for Figure 4.13 b, where a weak negative relationship can be seen between the KAM impulse and pKVAV in the moderate OA group. To determine the relationship between the pKVAV and peak KAM, KAM impulse and KFA range individually several regression analysis were performed. Using simple linear regression analysis the pKVAV could significantly predict the peak KAM ($p<0.01$) in both the asymptomatic controls and moderate OA group (Figure 4.12 a&b, Table 4.5). However as indicated in Table 4.5, a stronger variance was explained in the asymptomatic group (R^2=29.6%) compared to the moderate OA (R^2=4.7) group. Using multivariate regression analysis although a significant change in the R squared was observed, cofounders (sex and walking speed) had minimal role to play in explaining the variability in the asymptomatic group. Likewise, a significant increase in the R squared on addition of cofounders was also observed in the moderate OA group however, the majority of contribution was attributed for walking speed (R^2=6.6%). However, this contribution was not different from the pKVAV (R^2=4.7). Overall, pKVAV was the biggest contributor to the model in the asymptomatic group whereas walking speed was the biggest contributor to the model in the moderate OA group.

Using simple linear regression the pKVAV could not significantly predict the KAM impulse in both groups. After adding cofounders a significant change in R squared was

observed in both groups with a stronger variance explained in the asymptomatic group (R^2=18.5%) compared to the moderate OA (R^2=9.7%) group. However, pKVAV had a minimal role in explaining the variability in the model in both groups. Walking speed had a significant effect on the KAM impulse-pKVAV relationship and was approximately similar in both groups. However, the overall greater variance explained in the asymptomatic group compared to the moderate OA group was due to the significant contribution by sex, being about 8.4 % in the asymptomatic group as opposed to 1.1% in the moderate OA group.

As for the KFA range, using simple linear regression there was a significant positive but weak association between the KFA range and pKVAV in the asymptomatic group and no association in the moderate OA group (Figure 4.13a&b). The pKVAV had a minimal effect on the relationship in the moderate OA group. However, like the peak KAM and KAM impulse addition of cofounders significantly changed the R squared in both groups with a stronger variance explained in the moderate OA group (R^2= 35.9%, $p<0.01$) compared to the asymptomatic group (R^2= 19.4%, $p<0.01$). While sex had a similar contribution in explaining the variability in the relationship in both groups, walking speed explained about 24.0% of the variance in the KFA range-pKVAV relationship in the moderate OA group as opposed to 3.8% in the asymptomatic group.



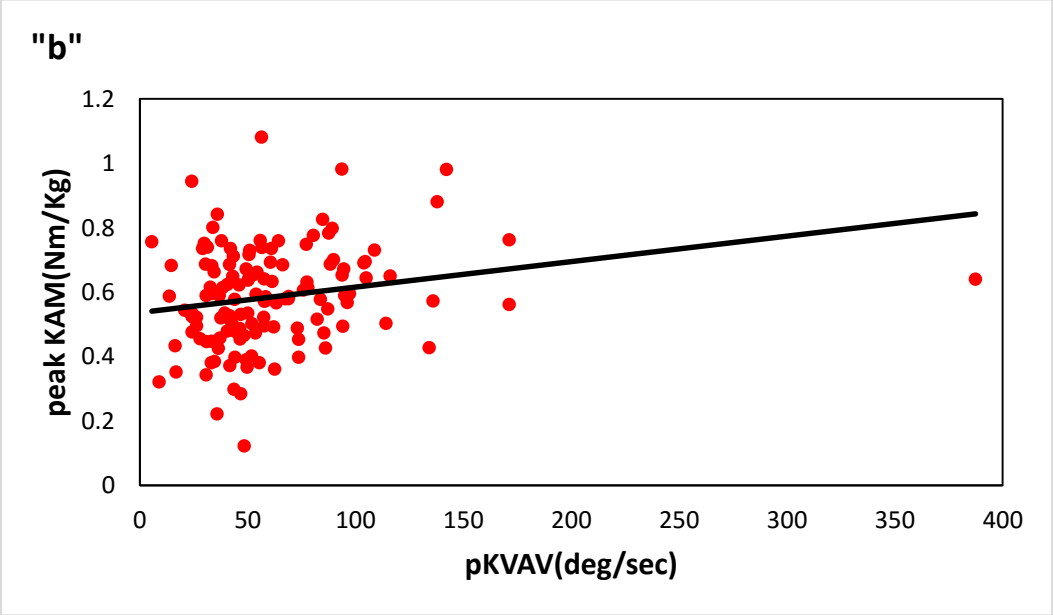


Figure 4.12a &b: Scatter plots with regression line showing the relationship between the peak knee varus angular velocity (deg/sec) and peak KAM(normalised to body mass) in asymptomatic (r=0.54,p value<0.01) upper panel "a" and moderate OA (r=0.22, p value=0.04) group lower panel "b" respectively.

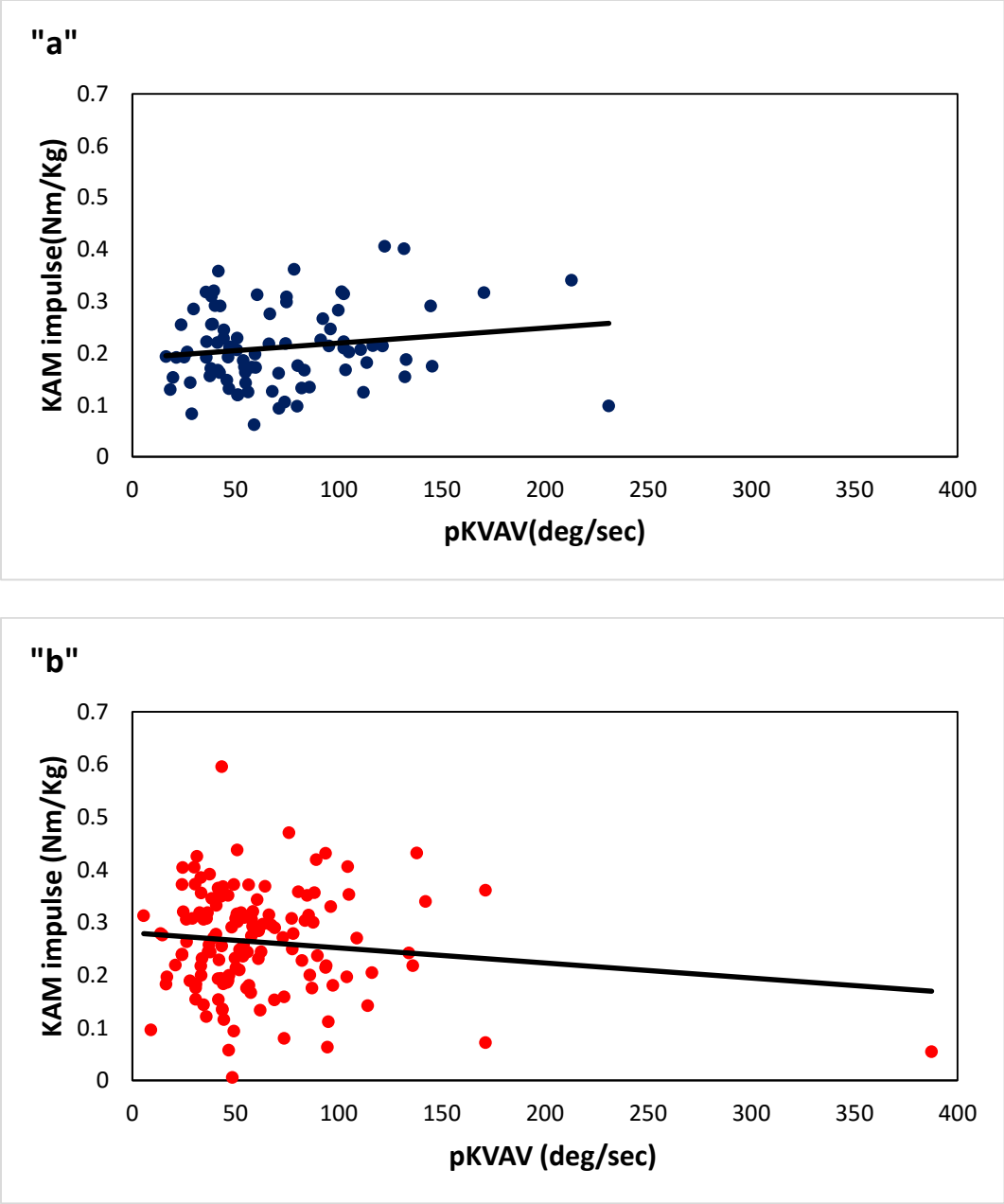
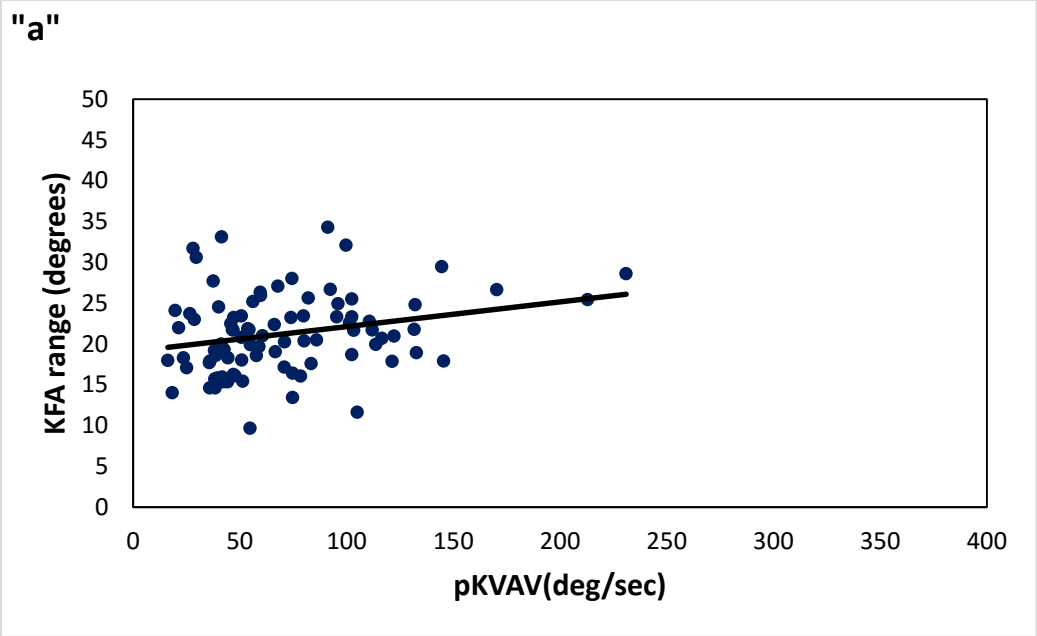


Figure 4.13a &b: Scatter plots with regression line showing the relationship between the peak knee varus angular velocity (deg/sec) and KAM impulse(normalised to body mass) in asymptomatic (r=0.16,p value=0.14) upper panel "a" and moderate OA (r=-0.12, p value=0.15) group lower panel "b" respectively.



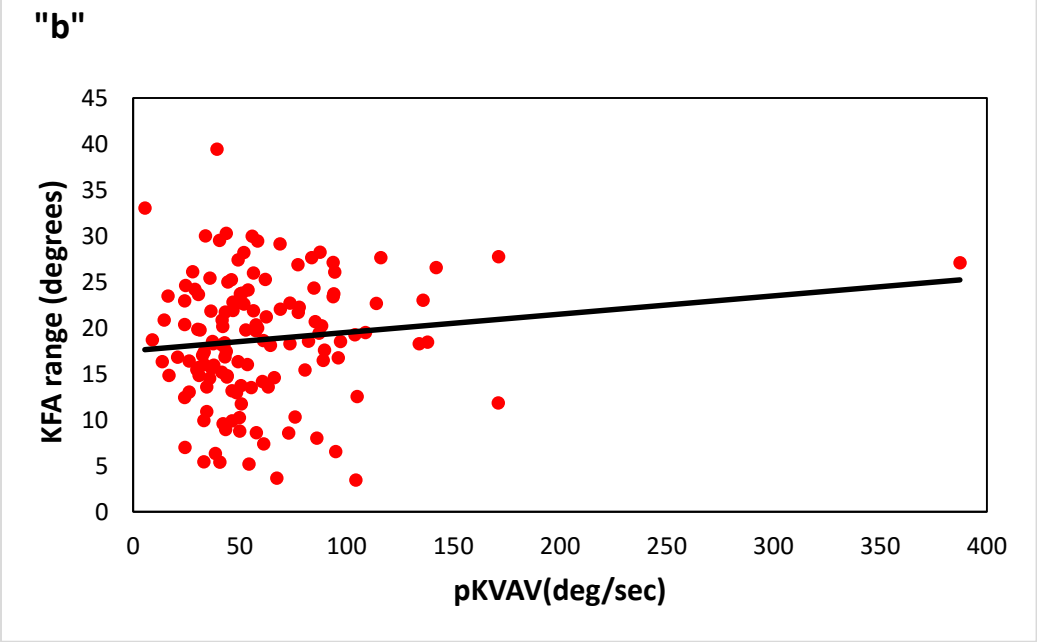


Figure 4.14a &b: Scatter plots regression line showing the relationship between the peak knee varus angular velocity (deg/sec) and KFA range (degrees) in asymptomatic (r=0.26,p value=0.02) upper panel "a" and moderate OA (r=0.12, p value=0.15) group lower panel "b" respectively.

Table 4.5: Results of the regression models: peak knee varus angular velocity versus Biomechanical gait variables (Unadjusted and adjusted: adjusting for walking speed and sex)

Independent variable : Peak knee varus angular velocity	**Asymptomatic Controls**					**Moderate OA**				
	Unadjusted Simple Regression			**Adjusted** Multivariate Regression		**Unadjusted** Simple Regression			**Adjusted** Multivariate Regression	
	r	**R^2%**	**p**	**R^2%**	**p**	**r**	**R^2%**	**p**	**R^2%**	**p**
Dependant variables ⬇										
Peak KAM (Nm/Kg)	0.54	29.6	**<0.01**	38.0	**<0.01**	0.22	4.7	**0.01**	13.7	**<0.01**
				A 29.6	**<0.01**				A 4.7	**<0.01**
				B 8.3	**<0.01**				B 6.6	**<0.01**
				C 0.2	0.63				C 2.4	0.06
KAM impulse (Nm*s/kg)	0.16	2.6	0.14	18.5	**<0.01**	-0.12	1.5	0.15	9.7	**<0.01**
				A 2.6	0.27				A 1.5	0.13
				B 7.5	**<0.01**				B 7.0	**<0.01**
				C 8.4	**<0.01**				C 1.1	0.20
KFA range (deg)	0.26	6.6	**0.02**	19.4	**<0.01**	0.12	1.6	0.15	35.9	**<0.01**
				A 6.6	**<0.01**				A 1.5	0.05
				B 3.8	**0.01**				B 24.0	**<0.01**
				C 9.0	**<0.01**				C 10.4	**<0.01**

- r: Pearson product correlation co-efficient; R^2: co-efficient of determination;
- p value <0.05 is considered as significant, values in bold are significant;
- A, B, C : indicates R^2 contribution in the multivariate regression model by pKVAV, walking speed and sex respectively

In summary, pKVAV, an objective measure of "varus thrust", could successfully predict the peak KAM with a positive association in both the asymptomatic and moderate knee OA group. However, a comparatively stronger relationship was found in the asymptomatic group (r=0.54) as compared to the moderate OA group (r=0.22). While the adjusted regression models improved the overall R squared in both groups, pKVAV was the biggest contributor in the asymptomatic group whereas walking speed was the biggest contributor in the moderate OA group. In the KAM impulse-pKVAV relationship, walking speed explained similar amounts of variance in both groups (about 7.0%). However, the difference in the overall variance between the two groups was explained by sex, where sex was the biggest contributor to the model in the asymptomatic group (R^2= 8.4%). In the KFA range-pKVAV relationship, pKVAV (R^2= 6.6%) and sex (R^2= 9.0%) were the dominating contributors in explaining the model variance in the asymptomatic group whereas walking velocity (R^2= 24.0%) was the biggest contributor in the moderate OA group.

CHAPTER 5: DISCUSSION

The main objective of this study was to determine the association between knee muscle strength and an objective measure of "varus thrust". Two methods, the one by Takigami et al, 2000 (absolute angular velocity) and the other one by Chang et al., 2013 (pKVAV) were examined as they both calculated a frontal plane angular velocity measure. We hypothesized both methods to be highly correlated with a strong association and hence, could be used interchangeably. However, the findings of this study revealed weak to no associations between the two methods and thus, cannot be used interchangeably. Though the Chang method is comparatively more complex it has been previously validated against a visually observed varus thrust, and thus, used as the objective method of "varus thrust" for the two main objectives (objective 2 and 3) of this study.

We expected the moderate knee OA group to have a higher pKVAV compared to the asymptomatic group suggesting a higher prevalence of varus thrust in this population, however the results indicated otherwise. It was hypothesized that a lower knee muscle strength would be associated with a high pKVAV but the findings indicated no significant associations between the two. In addition, the current study aimed at determining the association between frontal plane moment features and sagittal plane angular displacement variable and pKVAV. This analysis found a significant association between peak KAM and pKVAV but no significant association between KAM impulse and pKVAV supporting the hypothesis where greater variance would be explained by the peak KAM-pKVAV relationship. Finally, it was hypothesized that a

lower KFA range would be associated with a high pKVAV but the findings indicated otherwise. Consistent with the literature significant differences were found in the knee muscle strength and biomechanical gait variables between the asymptomatic controls and moderate knee OA group. The following sections provide a discussion of the findings in this study and how they relate to the present literature.

5.1 Participant Demographics

The moderate OA group was significantly older with a higher mean BMI compared to asymptomatic controls. The mean BMI of both groups were within the overweight range. The values for the moderate OA group, at the same age, were consistent with the literature (Hubley-Kozey et al., 2006; Creaby et al., 2013; Zeni et al., 2009; Mundermann et al., 2005). Men and women within each group had similar ages and BMI values. The significant differences found in the walking speed between the two groups indicated that the asymptomatic group ambulated approximately 0.10 m/s faster than the moderate OA group. The asymptomatic group had a mean walking speed close to previous reported values for healthy populations whereas the moderate group walked faster than those reported for knee OA populations (Kaufman et al., 2001; Thorp et al.,2006;Baliunas et al.,2002,Ko et al.,2011;Sims et al.,2009). This latter finding indicates a younger and less severe OA group in this study. Interestingly, when categorized by sex, differences were seen in both groups and especially in women. Healthy adults between ages 50 to 59 years, are reported to ambulate between 1.23m/s to 1.45 m/s for both men and women in various studies (Ble et al.,2005; Bohannon et al.,1996,1997 &2011;Busse et al.,2006;Lord et al.,1996; Mundermann et

al.,2004;Willen et al.,2004). However, a great amount of variability exists in these reported values, which could arise as a result of different methods used for measuring walking speed. With respect to that, both sexes in the asymptomatic group ambulated close to those previously reported, but women walked significantly faster than men. OA men walked at a similar speeds as asymptomatic men and close to the above values reported for healthy adults. This trend has also been found in an older age group (above 70 years) where healthy men walked at similar speeds compared to OA men (Sims et al., 2009). However, OA women walked significantly slower than their healthy counterparts (Sims et al., 2009) which is consistent with the findings of this study. In this study, while both sexes in the moderate OA group had similar characteristics in terms of age and BMI there are differences in their basic walking patterns which is consistent with previous reports that the osteoarthritic gait in women do not follow the same trend as men (McKean et al., 2007). In summary, the demographic characteristics are significantly different between the two groups and consistent with the values reported by similar studies but some of the differences are sex-specific.

5.2 Knee Muscle Strength

Consistent with the literature, the relative isometric quadriceps torque was significantly lower in the OA group compared to controls (Baert et al.,2013; Hubley-Kozey et al.,2014; Palimieri-Smith et al.,2010; Segal et al.,2009;Lim et al.,2008). Likewise, the OA group demonstrated significant strength deficits in the plantarflexors as well (Hubley-Kozey et al., 2014). However, no significant strength deficits were found in the hamstrings between the two groups. This is in accordance with the findings

reported in a few studies, where deficits in the hamstrings are found in the later stages of the disease (Baert et al., 2013). Considering that our OA group was moderate may partially explain the lack of significant findings. However categorizing by sex, women in both groups had a more general muscle strength deficit than men with lower maximum toques in all three muscle groups. Interestingly, this deficit was highest in the quadriceps muscle group (Table 4.1b). Also, OA women had significant strength deficits in the quadriceps, hamstrings and plantarflexor compared to asymptomatic women, whereas OA men had significant strength deficits only in the hamstrings and plantarflexors muscle groups compared to asymptomatic men. Hamstring deficits, which were not seen in the whole group but apparent when groups were categorized by sex could be indicative of the influence of sex. Non-significant findings in the quadriceps strength in between OA and asymptomatic men may indicate that men show substantial strength deficits only in the severe stages of the disease (Hubley-Kozey et al., 2014). This could also indicate that OA men are in general more physically active and thus have a quadriceps strength similar to controls (Pietrosimone et al., 2014). However, on the other hand if that's the case a similar pattern should have been observed in the hamstring and plantarflexor muscle groups as well, which was not the case. However, the strength deficit between OA men and asymptomatic men in all three muscle groups were approximately similar ranging from 8% to 13% (Table 4.1b). The relative torque values for extension and flexion in men and women are similar to those reported in a few studies (Palimieri-Smith et al.,2010; Baert et al.,2013;Segal et al.,2009) and higher than others (Amin et al.,2009;Slemenda et al.,1999). A younger and less severe OA group may explain the higher torque values in this study.

In summary the literature has consistently shown a strength difference in the quadriceps muscles in OA when compared to controls and the present findings partially supports the literature but only in women. These deficits have been linked to disease initiation and progression and more so in women. However, to date we have no clear picture indicating how the deficits in the quadriceps muscle influence the disease process. While less well studied, deficits have also been previously noted in the hamstrings and plantarflexors and the present results when categorized by sex partially supports the literature. Considering strength deficiency in all the muscles functioning around the knee joint and not just the quadriceps can help to further answer questions regarding disease progression.

5.3 Objective Measures Of Varus Thrust (pKVAV And Absolute Angular Velocity)

Two published methods that quantify the rapid change in the varus angle early in stance that used an angular velocity measure were compared in this study as a part of the first objective. The first method was the pKVAV which was a measure used to quantify varus thrust based on the method devised by Chang et al., 2013. The peak in the varus direction was extracted within the initial 30% of the gait cycle, a phase where varus thrust is usually apparent as indicated in previous literature (Chang et al., 2013; Kuroyanagi et al., 2012; Lo et al., 2010). The second method which is comparatively less complex mathematically was by Takigami et al., 2000 which quantifies varus thrust by using an absolute angular velocity measure. It was expected that since the above measures were suggested to quantify varus thrust, they may be used interchangeably. However, the current findings indicate weak to no associations between the two

methods with only 12.5% of the variance explained in the asymptomatic group and 0.2% of the variance explained in the moderate OA group. These findings were significant only in the asymptomatic group. As a result of the very low variance explained, the first hypothesis of this study was rejected. A potential explanation for the lack of associations between the two measures is the difference in the method of quantifying the frontal plane angular velocity (Figures 4.2 a&b, 4.5). Firstly, Chang et al., 2013 captured the peak angular velocity in the varus direction anywhere between 0-30% of the gait cycle. Whereas, Takigami et al., 2000 considered varus thrust to occur at footflat that is at 10% of the gait cycle indicating that the change in varus angulation occurs earlier in stance. Since this method required extraction at a single point, there is a possibility that a thrust that may have occurred earlier or later may not have been quantified. Subsequently, Figures 4.2a and 4.5 show differences in the representation of the angle data. That is, the initial valgus to varus change and the group differences seen in the Chang method (Figure 4.2a) are not seen in the knee angle computed by the Takigami method (Figure 4.5). Qualitatively, the Takigami method shows group differences only at the peaks. Secondly, the Chang method was validated against a visually observed varus thrust whereas the Takigami method was not. The lack of associations between the two measures suggests that they cannot be used interchangeably and it can be inferred that the Takigami method does not capture a varus thrust. Since the Chang method has been validated against a clinically assessed varus thrust, the current study used this as the objective varus thrust method to address the two main objectives of the study

The present study had a large range of pKVAVs as seen in Figure 4.3b. The mean value for the asymptomatic controls although higher than the moderate OA group

was not significant. However, interestingly Figure 4.2a shows that qualitatively the asymptomatic group had a slightly greater initial valgus motion compared to the moderate OA group with the peak varus angle similar between the two groups at the beginning of mid-stance. Thus the greater valgus to varus change may have influenced the pKVAV measure in the asymptomatic group. Also, the study included only those with medial knee OA with a greater medial JSN than lateral which could explain the lack of an initial valgus motion in the OA group and excluded those who had a greater initial valgus than varus motion from both groups. We expected the OA group to have a higher pKVAV due to its relevance to a varus thrust (Chang et al., 2013 & 2004) and the knee instability (Lewek et al., 2004; Sharma et al., 1999) associated with the OA group. However, similar findings were observed in a recent study conducted on severe OA participants, where the varus thrust magnitude was higher in their control group compared to the OA group (Sosdian et al., ISB 2015). This illustrates that varus thrust is not exclusive to knee OA. However, while the asymptomatic group is known to be free from knee OA symptoms like pain, swelling and limitations in functional activities, it was not known if any underlying OA radiographic changes were present. Structural changes like meniscal degeneration, cartilage lesions and presence of osteophytes have been identified previously in asymptomatic individuals (mean age 41 years) (Beattie et al., 2005) and since our study participants were a decade older, it is possible that these changes may be present. Likewise, joint laxity and hypermobility has also been identified in apparently healthy groups (Sharma et al., 1999). The probability of these changes in our asymptomatic group should be taken into account when interpreting the high varus angular velocities in this group. The mean pKVAVs found in this study were

higher by approximately 30 deg/sec than those reported by Chang et al., 2013. Demographically the current study was not very different from those reported by Chang et al., 2013. However, the method suggested by Chang et al., 2013 was not described in great details that may leave room for misinterpretations and errors.

Within the knee OA group, varus thrust was found to be more prevalent among those with greater radiographic OA severity (Takigami et al., 2000; Chang et al., 2013; Kuroyanagi et al., 2012; Iijima et al., 2015). In the present study there was no effect of the KL scores on the pKVAV, all the KL scores had similar pKVAVs. Our findings were consistent with Lo et al.,2012 where those who had a definite varus thrust (by visual observation) did not show a specific trend within the KL scores, that is the prevalence of varus thrust among KL scores II,III and IV being the same. But these findings are not in agreement with the literature. For instance, the absolute angular velocity used to quantify thrust was significantly higher in the 'more severe' knee OA group as classified by the Koshino grading system, 1993 (Takigami et al., 2000). Similarly, another frontal plane measure quantifying varus thrust found higher thrust measures in those with KL- IV scores (Kuroyanagi et al., 2012). The study conducted by Chang et al., 2013, on which our current methodology is based, also found majority of their visually assessed varus thrust participants with KL scores III and IV. The probable reason for this may be that the moderate OA group in this study was categorized as "moderate" not only based on their KL scores but also on the self-reported functional status of the participants. Also, demographically our moderate OA group was younger with a less severe disease status as compared to the above studies. Furthermore, the different methodologies used to identify varus thrust by the above

studies, either by quantification or visual assessment can add variability among these findings.

While sex was not a factor identified in the main objectives, our sample had a higher percentage of men in the moderate OA group compared to asymptomatic controls and due to the high prevalence of varus thrust among men reported in the literature (Chang et al., 2010; Lo et al., 2012; Harvey et al., 2009), a sub analysis to look at sex was conducted. This study found higher pKVAVs in women in both groups but these differences were significant only in the asymptomatic group. However, they do not support the literature. In a study conducted by Lo et al in 2012, 64 % of those with a visually observed varus thrust were men. Likewise, Chang et al., 2010 found more than half of their visually assessed varus thrust population to be men. While not consistent with these findings there are potential explanations for these inconsistencies and some research that may support the findings. Women in general are found to have greater knee instability than men owing to anatomical variations such as a larger Q angle and pelvic obliquity and the influence of the hormones on the ligament structure (Heitz et al., 1999; Shultz et al., 2005). It was found that women demonstrated an overall greater instability in the knee ligaments, as measured by varus-valgus stress tests, compared to men (prevalence: 16.6% versus 12.9%) (Odding et al., 1996). Additionally, the same study found a higher percentage of women with a valgus deformity and men with a varus deformity. These findings are in accordance with the knee OA literature (Sharma et al., 2010; Wise et al., 2012). Moreover, during dynamic activities like jumping and running, women were found to have greater valgus or abducting torques (Hewett et al., 2006; Olsen et al., 2004). However, in this study qualitatively both sexes had a similar

initial valgus motion (Figures A.2.1a & A.2.2a) but women had a greater peak varus motion than men (Figures A.2.1a & A.2.2a) in both groups. In general, regardless of the disease state, women are found to have a greater varus-valgus laxity (Sharma et al., 1999). In summary, the current study found women especially in the asymptomatic group, to have higher pKVAVs. In contrast, the literature reports a higher prevalence of varus thrust among men and higher incidence of valgus motion among women. This study included those only with medial knee OA and excluded those with a greater initial valgus than varus motion. While this may explain the lack of a greater valgus motion in women it also suggests the need for more work to understand the sex differences in the pKVAV values. As women are found to have lower muscle strength characteristics compared to men with (Hubley-Kozey et al.,2014;Baert et al,2013) or without (Lephart et al.,2002) OA, one factor that is different between sexes in this study and could explain for the high pKVAVs in women are the strength deficits in the knee muscles.

5.4 Peak Knee Varus Angular Velocity Versus Knee Muscle Strength

The main purpose of this study was to determine the relationship between the pKVAV ("varus thrust") and knee muscle strength measures. This study showed that there was no strong association between pKVAV and the three knee muscle strength measures. Even though all the correlations were negative indicating that a high pKVAV is associated with lower knee muscle strength, the range of the correlation values were very low and not significant (-0.04 to -0.2) (Table 4.3a). Thus the second hypothesis was rejected with no significant relationship found between the maximum quadriceps, hamstrings and plantarflexor isometric strength and the pKVAV in both asymptomatic

controls and moderate knee OA group. Results were non-significant after adjusting for walking speed and sex as well. Additionally, a part of this objective was to determine if radiographic severity as determined by KL scores in the moderate OA group has an influence on this relationship. Likewise, KL scores had no influence on the knee muscle strength-pKVAV relationship.

Thus these results do not support our hypothesis. Chang et al.,2010 examined participants with a visually identified varus thrust with and without radiographic knee OA showing that greater quadriceps strength reduced the odds of varus thrust (OR=0.96) only in those without knee OA (Chang et al.,2010). This could mean that as knee OA is complex in nature a relationship for a single factor such a quadriceps strength and varus thrust cannot be explained as easily as it can in those without knee OA. In the current study, though non-significant, the knee muscle strength (quadriceps and plantarflexors) in the asymptomatic group was able to explain more variability than the OA group when predicting the pKVAV (varus thrust). Varus thrust being a prompt, one time dynamic instability during gait may require more than just strong knee muscles especially in those affected by the disease process. It may depend on the how efficient these muscles are able to 'switch on' at the appropriate time either prior to or during destabilization reflecting adequate neuromuscular protection. However, the ability to adequately recruit and activate depends on the strength of the muscles, where deficient muscle have compromised voluntary and reflex motor control (Hurley, 1999 & 2003). Thus, compromising the adequate functioning of the three sub-systems (active, passive and neural) that maintain joint stability (Panjabi, 1992). Several studies have looked at the neuromuscular activation patterns using EMG across the disease severity (Childs et

al., 2004; Rutherford at al., 2011 & 2013; Hubley-Kozey et al., 2006; Zeni et al., 2009). Collectively they have shown greater activation in the lateral quadriceps and hamstrings in knee OA during gait with an increasing trend as the severity increases. Moreover since these activations are greater during the phase where varus thrust is usually apparent, it would be expected for them to control the thrust. However, it is unclear whether these activation patterns in the deficient knee OA muscles are sufficient to control the abrupt change in the knee varus angle. Neuromuscular activation patterns may help to shed some light on the work of knee muscles during a varus thrust. Quite recently in a 12 week intervention study comparing neuromuscular versus quadriceps strengthening exercises conducted on knee OA participants, it was found that pain associated with a visually observed varus thrust was alleviated with neuromuscular exercises and not quadriceps strengthening (Bennell et al.,2015). Despite no indication if the varus thrust reduced post intervention, it does illustrate that neuromuscular control may have a role to play.

5.5 Peak Knee Varus Angular Velocity Versus Biomechanical gait variables

The third objective of this study was to determine the association between pKVAV and the frontal plane moments (KAM: peak and impulse) and sagittal plane angular displacement variable (KFA range). Consistent with the literature the first peak KAM was significantly higher by 16% in the moderate OA group (Miyazaki et al.,2002;Bennell et al.,2011;Hatfield et al.,2013; Astephen et al.,2008;Mundermaan et al.,2004). The mean relative peak KAM found in this study were similar to those reported for the knee OA population in a few studies (Astephen et al.,2008; Rudolph et

al.,2007;Henrikson et al.,2010;Zeni et al.,2009;Gok et al.,2002) however, they were higher compared to some other studies (Messier et al.,2005;Maly et al.,2015). The probable reason for discrepancies could be due to variability in the walking speed as the peak KAM is found to be sensitive to walking speed (Robbins & Maly, 2009). A comparatively faster ambulating group may have resulted in higher peak KAM measures in the current study. Also, the current study had participants walk with shoes as opposed to the Maly et al., 2015 study, which may have had an influence on the peak KAM (Shakoor & Block, 2006).

Categorizing by sex, OA men had a significantly higher peak KAM than controls. A higher peak KAM in OA men compared to OA women and asymptomatic men is consistent with the findings of Morrow and Kaufman, 2012 and Sims et al., 2009. Interestingly, though there were no significant differences in the peak KAM between asymptomatic and OA women, OA women did have a lower peak KAM compared to OA men consistent with the findings by McKean et al., 2007.

A high peak KAM has been previously found to be associated with a visually identified (Chang et al., 2004; Hunt et al., 2011) and quantified (Kuroyanagi et al., 2012) varus thrust. The current findings do indicate a significant relationship between the pKVAV and peak KAM in the asymptomatic controls and moderate OA group and thus are in agreement with the literature. Also, the peak occurs around the same time within the gait cycle as a varus thrust. As previously noted, the peak KAM has been frequently reported as a biomechanical marker for disease progression and its association with the pKVAV in the moderate OA group supports the possibility of varus thrust contributing to disease progression and hence making it as a clinically relevant variable.

Interestingly, the relationship was stronger in the asymptomatic group (r = 0.54) compared to the moderate OA group (r = 0.22). The positive relationship for both groups indicate that a high pKVAV was associated with a high peak KAM. Also, in the asymptomatic group almost 30% of the variance was explained by pKVAV but in the OA group walking speed was the biggest contributor explaining about 7% of the variance. Peak KVAV explained less than 5 % of the variance in the OA group (Table 4.5). Studies which have looked at varus thrust and peak KAM mainly examine those with knee OA. Thus, it is not clear why the relationship would be stronger for the control group, but likely related to the greater valgus-varus range during early stance for the asymptomatic group.

Like the peak KAM, the KAM impulse has also been associated with knee OA progression, structurally and towards TKA (Hatfield et al., 2014; Bennell et al., 2011) and is gaining importance as it represents the duration as well as the magnitude of loading over the entire stance phase. Consistent with the literature, the mean relative KAM impulse measures were significantly greater in the moderate OA group compared to the asymptomatic controls (Bennell et al., 2011; Thorp et al., 2006).

Categorizing by sex, the KAM impulse was significantly higher in OA men and women compared to asymptomatic controls consistent with the whole group findings. A high KAM impulse along with a lower first peak KAM in OA women is consistent with previous findings that suggests sustained loading patterns in women as found by McKean et al., 2007.

The pKVAV and KAM impulse were not related to each other in either group (Table 4.5). Adjusting the multivariate regression models resulted in about 19 % of the

variance explained by the three variables (pKVAV, walking speed and sex) in the asymptomatic group, with sex and walking speed explaining the greatest variance at approximately 8% each and hence pKVAV explained only about 3% of the variance. In the OA group, while significant, the variance explained by all the three variables was about 10% with walking speed being the only significant and biggest contributor explaining about 7% of the variance. This result supports the stated hypothesis for this objective. The contribution of walking speed was similar in both groups which makes sense as KAM impulse represents the magnitude and duration of loading during the entire stance phase and not a single point early in stance as is the case with pKVAV and also supports previous findings that KAM impulse is sensitive to walking speed (Robbins & Maly, 2009). The higher overall variance explained in the asymptomatic controls was primarily due to the greater contribution of sex in the asymptomatic group compared to the moderate OA group. The probable reasons for this may be the significant differences in the KAM impulse measures between sexes only in the asymptomatic group and greater number of women (2:1 ratio) in this group.

The KFA range was significantly greater in the asymptomatic controls compared to the moderate OA group which is consistent with the literature (Kaufmann et al., 2001;Astephen et al.,2008;Zeni et al.,2009;McCarthy et al.,2013; Childs et al.,2004; Lewek et al 2004). The lower KFA range during early stance is thought to be indicative of either reduced quadriceps activation in response to minimize pain, increased co-activation between the quadriceps and hamstrings or as a result of strength deficits in the quadriceps muscles which is a characteristic of the OA group as mentioned earlier.

The dynamic change in the frontal plane varus angle, varus thrust is found to occur during early mid-stance or during the weight bearing phase of the gait cycle. The hypothesis was that a negative relationship would exist between the KFA range and pKVAV, indicating a greater pKVAV would be associated with a lower KFA range within 30% of the gait cycle. Thus, coinciding with the theory that a varus thrust is visible during weight-bearing with the knee in extension. However, the results did not support the stated hypothesis as a positive weak correlation between the KFA range and pKVAV was found for the asymptomatic group (r=0.26) suggesting that a greater KFA range was associated with a faster pKVAV. Adjusting the multivariate regression models resulted in approximately 36% of the variance explained by all the three variables (pKVAV, walking speed, and sex) in the OA group, with the biggest contribution by walking speed explaining about 24% of the variance and only 1.5% explained by pKVAV. In contrast in the asymptomatic group, pKVAV and walking speed explained only about 7% and 4% of the variance in the KFA range-pKVAV relationship respectively. This indicates a weak association between pKVAV and KFA range. As indicated in Table 4.4c, walking speed and KFA range in the moderate OA group had a moderately positive relationship (r=0.49), suggesting that a high KFA range is associated with a faster walking speed. This may explain the high contribution of walking speed on the KFA range-pKVAV relationship in the moderate OA group. The effect of walking speed on the KFA has been previously found by Landry et al., 2007 where an increase in walking speed resulted into an increase KFA during stance in both asymptomatic controls and OA groups. In the current study, walking speed did have a significant effect on the pKVAV-KFA range relationship in the asymptomatic group

(R^2=3.8%) as well but the effect was stronger in the moderate OA group. The similar effect of sex on the model in both groups can be explained by the significant sex differences found in the KFA range. OA women had a significantly lower KFA range compared to OA men and asymptomatic women. A small sagittal plane knee excursion in OA women is consistent with the literature (McKean et al., 2007).

In summary, the current study was consistent with the literature in finding a significant positive relationship between peak KAM and pKVAV (”varus thrust”) in both asymptomatic and moderate OA groups, but the variance explained in the unadjusted and adjusted asymptomatic model was higher than the OA group. Also, the adjusted moderate OA model indicates that factors other than walking speed and sex were likely more important. The pKVAV and KAM impulse were not associated in either group and to our knowledge this is the first study to show the relationship between the KAM impulse and “varus thrust”. However, unlike the peak KAM which approximately coincides with the pKVAV, the KAM impulse is a magnitude and duration measure over the entire stance phase. Thus, does not theoretically coincide with the single point appearing dynamic varus thrust and hence, the lack of association with a varus thrust does seem reasonable. Lastly, adjusted KFA range-pKVAV relationship was best explained in the moderate OA group, with walking speed being a significant contributor. In the asymptomatic model, though pKVAV had a significant contribution, sex was the biggest contributor in this group. This could indicate that sex differences are possibly important factors that need to be considered.

CHAPTER 6: CONCLUSION

The main objective of this thesis was to determine the association between an objective measure of "varus thrust" and knee muscle (quadriceps, hamstrings and plantarflexors) strength in knee OA with a view to better direct conservative management strategies to reduce the presence of a "varus thrust". To do this we examined two objectives methods that use a frontal plane angular velocity measure to assess varus thrust; the Chang method (pKVAV) and the Takigami method (absolute angular velocity). Regression analysis showed that there was a weak to no association between the two methods and thus cannot be used interchangeably. While the Chang method is more computationally complex, it has been clinically validated and quantified and thus, it was used as the objective measure to quantify varus thrust to address the two main objectives in this thesis. While only one study has shown that lower quadriceps strength is a risk factor for varus thrust (Chang et al., 2010) in asymptomatic participants, this was the first to look at the role of all three knee muscles and varus thrust in both asymptomatic and moderate OA groups. Contrary to the hypothesis, the results showed no significant association between the maximum torque of all three knee muscles and pKVAV. Lastly, varus thrust has been associated with disease progression and frontal plane moment features (KAM) has been related to various OA processes. The peak KAM has previously been related to varus thrust (Chang et al., 2004; Kuroyanagi et al., 2012; Hunt et al., 2011) but the current study is the first to look at the relationship between an objective measure of "varus thrust" and KAM impulse. Finally, this study looked at the relationship between the sagittal plane angular displacement (KFA range) and an objective measure of "varus thrust" as a result of the

reduced knee flexion excursion coupled with compromised stability in knee extension found in knee OA. The key findings related to the overall objective of improving our understanding about varus thrust are as follows:

Key Findings related to general demographics and descriptive data:

- Significant differences in age, BMI and walking speed between asymptomatic and moderate OA participants. More profound differences seen between OA and asymptomatic women.
- Significant strength deficits in all three knee muscle groups in the moderate OA group compared to asymptomatic controls. OA women had significantly reduced knee muscle strength.
- pKVAV, a measure of "varus thrust", was significantly higher in asymptomatic women compared to asymptomatic men. While there were no significant differences between the two groups, it was higher in the asymptomatic group. Likewise the absolute angular velocity was significantly higher in asymptomatic women compared to OA women and though not significant it was higher in the asymptomatic group.
- The pKVAV was not influenced by radiographic disease severity as measured by KL scores.
- Significant differences in the frontal plane moments and sagittal plane angular displacement variables was observed. OA participants had a higher peak KAM, KAM impulse and lower KFA range as compared to asymptomatic controls.

6.1: Summary

Objective 1: Determine the association between two methods that utilize frontal plane knee varus angular velocity measures as an objective measures of varus thrust.

The results of this objective indicate that the two methods were not well correlated and hence cannot be used interchangeably in both asymptomatic controls and moderate OA participants. This could indicate that the Takigami et al., 2000 method may not actually quantify a clinical varus thrust. The Chang method was validated against a visually observed varus thrust whereas the Takigami method was not. However, in context of applying the methods both studies lacked details regarding their quantifying measures that may have opened room for misinterpretations and errors. Thus, it is not conclusive to say that the Takigami et al., 2000 method does or does not capture a varus thrust. However, due to the clinical validation of the Chang method it was used as an objective measure of "varus thrust" in the remaining objectives.

Objective 2: To determine the relationship between an objective measure of "varus thrust" and knee muscle strength (quadriceps, hamstrings and plantarflexors).

Quadriceps, hamstrings and plantarflexor muscle groups have been theorized to control the dynamic varus thrust with lower quadriceps strength reported as a risk factor for varus thrust (Chang et al., 2010). The overall rationale behind this objective was to better understand the role of knee muscle strength and its association with varus thrust. This understanding may provide an insight in developing strategies to reduce the appearance of the dynamic thrust as the Bennell et al. (2015) study has shown that the presence of varus thrust does have implications on the type of therapy. The results of

this study revealed no associations between the quadriceps, hamstrings and plantarflexor muscle groups individually and the pKVAV ("varus thrust") in both asymptomatic controls and moderate OA participants. This may indicate that the maximal muscle strength may not be the key in understanding varus thrust control. Muscle activation patterns and EMG profiles may provide a better understanding of the knee muscles involved in controlling varus thrust and factors such as sex differences must be considered. However, this study was consistent with the literature in observing reduced knee muscle strength (quadriceps, hamstrings and plantarflexor muscle groups) being more significant in women as opposed to men and in the moderate OA group as compared to controls. This indicated that if strength deficits are to be determined as a factor in disease initiation and progression, all three muscle groups should be taken into consideration.

A part of this objective was to determine if radiographic severity as measured by KL scores had an influence on the knee muscle strength-pKVAV relationship in the moderate OA group. Likewise, the results indicated that there was no significant influence of the KL scores on the knee muscle strength-pKVAV relationship. As mentioned earlier the KL scores had no effect on the pKVAV measures as well. This was not in agreement with that reported in the literature, that is, varus thrust was influenced by disease severity where the prevalence of varus thrust was higher among those with a higher KL score (Chang et al., 2010; Takigami et al., 2000; Iijima et al.,2015; Kuroyanagi et al.,2012).

Objective 3: To determine the relationship between an objective measures of "varus thrust" and the frontal plane moment (KAM peak and impulse) and sagittal plane angular displacement (KFA range).

The peak KAM and KAM impulse have both been associated with OA initiation and progression. In turn varus thrust has been associated with the peak KAM as well as OA progression but no study has examined whether there was a relationship between varus thrust and KAM impulse. The rationale behind this objective was to support the earlier findings between varus thrust and peak KAM and to further determine the association with KAM impulse. As expected, pKVAV and peak KAM had significant associations in both groups. However, surprisingly this association was stronger in the asymptomatic group. In contrast and in support with the hypothesis, pKVAV was found to have no effect on the KAM impulse. Alternatively, walking velocity was found have a greater influence on the pKVAV-KAM impulse relationship. This makes sense as the KAM impulse represents the magnitude and duration of loading during the entire stance and thus, an association with the pKVAV which occurs at a single point during stance would be surprising. On the other hand, the first peak KAM represents a single point loading which coincides with the pKVAV.

Lastly, the third part of this objective was to determine associations between the pKVAV and KFA range in early stance (from heel strike to maximum within 30% of the gait cycle). The overall rationale being that varus thrust is apparent during weight-

bearing when the knee is in extension and reduced knee flexion excursion along with structural changes is observed in knee OA. Despite finding reduced knee flexion excursion patterns among the knee OA individuals, no associations were found between the KFA range and KAM impulse. Walking speed had a greater influence on the KFA range rather than the pKVAV in the OA group. This could indicate that adopting knee flexion strategies to reduce the appearance of varus thrust may not be the best mode of treatment and in fact may cause more damage to the joint structures.

6.2 Limitations And Future directions

6.2.1 Limitations

There are a few limitations associated with this study that must be taken into consideration when understanding and interpreting the results of this study.

1) The current thesis was based on the method proposed by Chang et al., 2013 who quantified varus thrust by calculating the time derivative of the frontal plane knee angle during the stance phase of the gait cycle. However, the method described was not in thorough detail that may have left room for misinterpretations. This may be one of the reasons for observing higher pKVAV compared to those reported by Chang et al., 2013. Also, the participants in the current study were not visually observed for a clinical varus thrust due to lack of quality videotape data and thus, the method used in this study could not be clinically validated. This has to be taken into consideration when interpreting the results as there is no concrete guarantee that a high pKVAV will be

correlated to a varus thrust. While this might be the case, the varus thrust literature has indicated that high peak varus angle or high peak varus angular velocity during early stance is a measure of varus thrust.

2) Like the pKVAV, misinterpretations in calculating the absolute angular velocity as understood from the method suggested by Takigami et al., 2000 in quantifying varus thrust could also be expected. Three markers were to be identified in order to calculate the absolute angular velocity by the above method. Of the three markers only the lateral malleolus was an IRED marker whereas the ASIS and tibial tuberosity were identified as virtual markers determined during the standing calibration. Virtual markers are identified by marking the bony landmarks using a digitizer probe. Since, the current dataset ranges over a decade, errors associated in locating the bony landmarks especially ASIS, which is at times difficult to palpate owing to central obesity, could be possible. However, the absolute angular velocities observed in the current study were close to those reported by Takigami et al., 2000. So to some extent the current study was close in achieving similar absolute angular velocity measures in spite of differences in methodologies and demographics. However, the Takigami method was not validated against a clinical varus thrust

3) The current study calculated the 3D joint angles using Cardan-Euler angles following an YZX rotation sequence. According to this sequence, the rotation first occurs around the medio-lateral axis, followed by the antero-posterior axis

and then the vertical axis. Thus, the frontal plane movement which occurs about the coronal axis is now not truly coronal but in an orientation relative to the medio-lateral axis. Thus, varus thrust which is clinically visible in the frontal plane, 2-dimensionally, may not be truly represented by the frontal plane angle as calculated by the Cardan-Euler angles. However, even though this does not affect the interpretation of the pKVAV with a varus thrust, it should be taken into consideration.

It has been indicated that abduction-adduction angles are significantly prone to error due to the definition of the medio-lateral axis and thus, could be of a similar magnitude to the measurement error associated with kinematic cross-talk and skin artifact (Piazza and Cavanagh, 2000). However, these errors are more profound with higher knee flexion angles and in the latter stages of the gait cycle. Thus while a potential limitation, the measures in the present study were found in early stance where knee flexion is minimal. Furthermore, a reliability study showed a 0.5 degree difference in the abduction-adduction angles between days with principal components that captured differences having ICCs of .74 or higher (Robbins et al.,2013).

6.2.2 Future Directions

1) The current study used an established validated method to quantify varus thrust among asymptomatic and moderate OA individuals with the primary aim being to look at the relationship between knee muscle strength and the varus thrust quantifying method. As indicated in chapter 4, we found no association between

the knee muscle strength and the varus thrust quantifying method. However, it does not rule out the role of muscle in controlling frontal plane movement. Future studies should make the use of surface electromyography to look at the knee muscle activation patterns during a varus thrust. Also, along with looking at the muscle activation patterns among those with a high pKVAV, a comparison should be made with a visually apparent varus thrust. This is will provide a better understanding of the knee muscles, varus thrust quantifying method and a clinical varus thrust.

2) As mentioned earlier varus thrust could result as a consequence of neuromuscular failure. Neuromuscular failure could occur in response to pain, knee effusion and muscle fatigue. Studies have shown an association between varus thrust and pain (Lo et al., 2012; Bennell et al., 2015). The use of rehabilitation techniques like neuromuscular exercises has reduced pain in those with varus thrust (Bennell et al., 2015), but did not change the clinical varus thrust. Likewise in addition to looking at the role of knee muscles, determining if muscle fatigue post long duration activities induces a varus thrust can also help understand varus thrust and thus, further strengthen its association with knee OA progression.

Clinically this study indicates that there is no simple method to quantify varus thrust in a clinical setting since there was a weak to no association between the computationally complex Chang method and the comparatively simpler Takigami method. Since there was no association between the isometric knee muscle strength of

the three knee muscles and varus thrust, a focus on knee muscle strengthening alone may not be the best management strategy in reducing the presence of varus thrust. Factors other than isometric muscle strength such as high frontal plane moments, walking velocity and sex differences are better associated with varus thrust. The pKVAV was positively associated with the peak KAM supporting previous literature and identifying and controlling varus thrust early in the disease can reduce the overall medial compartment load and thereby disease progression. Lack of associations between KFA range and pKVAV indicate that future research should determine strategies other than "a flexed knee" gait pattern to reduce the appearance of a varus thrust, as this strategy could increase joint loading and do more harm than good.

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APPENDIX 1 RADIOGRAPH GRADING SCORES

Participant baseline knee radiographs obtained for this study were standard, weight-bearing in both anterior-posterior and lateral views. Each radiograph was scored by a high volume orthopaedic surgeon using the Kellgren and Lawrence scoring system (KL scores) ((Kellgren & Lawrence,1952) to classify the overall radiographic severity and the Scott Feature Based score system (Scott et al.,1993) for the medial and lateral compartment joint space narrowing scores.

The Kellgren and Lawrence scoring system established in 1957 is still the most widely used classification of radiographic knee OA as indicated by the World Health Organisation, 2002. According to the Kellgren and Lawrence scoring system (KL scores) osteoarthrosis is divided in five grades: 0) absence, I) doubtful, II) minimal, III) moderate IV) severe.

These are based on the following changes seen on observing the knee radiographs:

Grade 0: Normal, no changes

Grade I: doubtful narrowing of joint space and possible osteophytic lipping

Grade II: definite osteophytes, definite narrowing of joint space

Grade III: moderate multiple osteophytes, definite narrowing of joint space, some sclerosis and possible deformity of bone contour

Grade IV: large osteophytes, marked narrowing of joint space, severe sclerosis and definite deformity of bone contour

Unlike the KL scores which does not provide a clear indication of disease progression with respect to joint space narrowing that is KL score III represents a wide range of JSN and thus in spite of progression there is no change in the KL score (Kapoor and Mahomed, 2015). The Scott Feature Based score system when used in combination with KL scores provide a more comprehensive indication of the disease severity. Scott Feature Based score system for the medial and lateral compartment joint space narrowing scores is divided in 4 scores as given below. Each joint compartment is graded separately. This study included those participant who had a higher medial joint space narrowing compared to the lateral joint space.

Grade 0: Normal, no narrowing

Grade 1: Minimal but definite narrowing

Grade 2: Moderate narrowing

Grade 3: Severe narrowing, “bone on bone”

APPENDIX 2 : ANALYZING THE SEX DIFFERENCES IN THE PKVAV MEASURES BETWEEN THE ASYMPTOMATIC AND MODERATE OA GROUPS.

The current study had an equal distribution of sexes in the asymptomatic and moderate OA group. As a result, each group was categorized by sex for further analysis. In order to further explore the sex differences found in the pKVAV measures, frontal plane knee angle and knee angular velocity waveforms were plotted for each sex in each group.

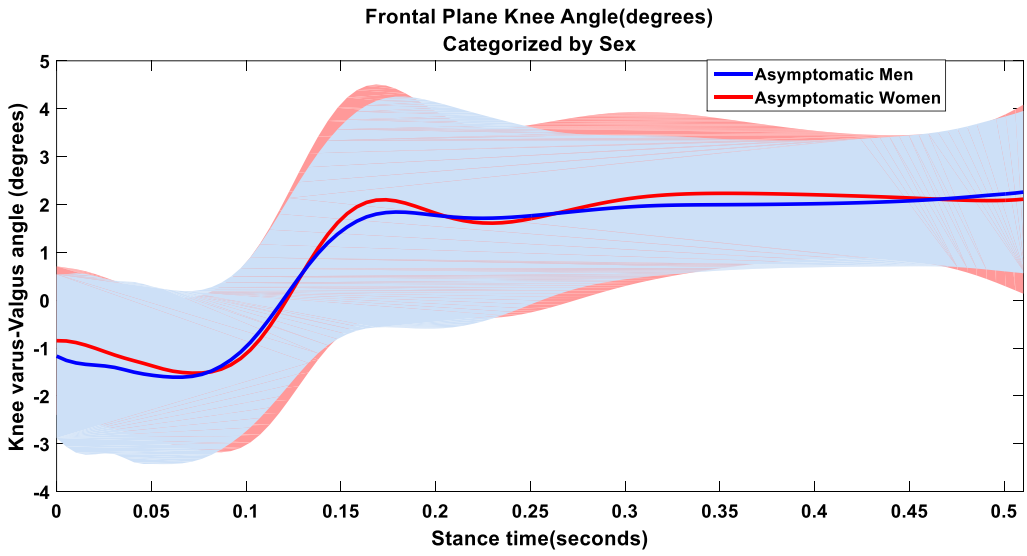

Figure A2.1a: Ensemble average of the frontal plane knee angle (degrees) with the standard deviation (shaded) comparing asymptomatic men (blue line and blue shading) and women (red line and pink shading)

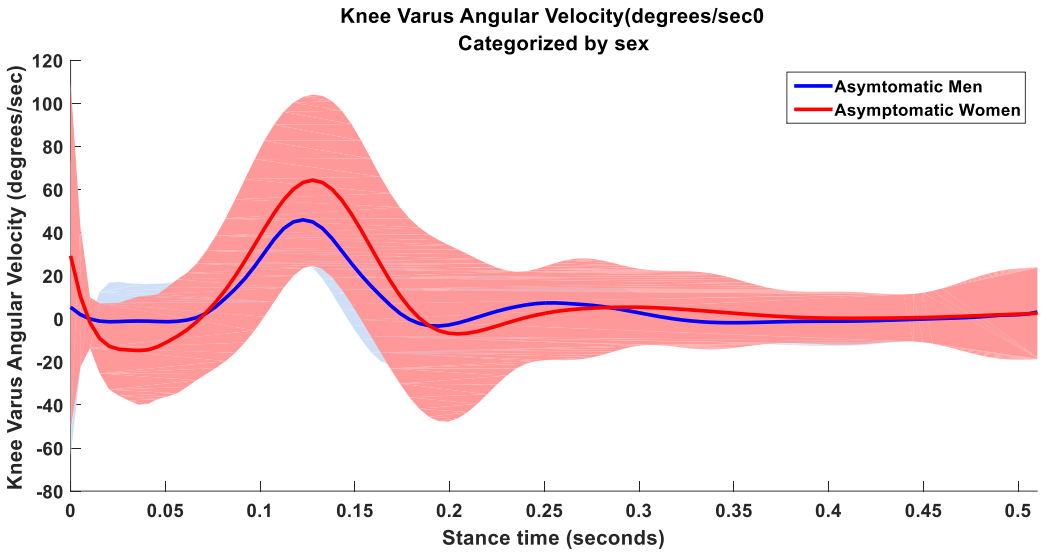

Figure A2.1b: Ensemble average of the KVAV (degrees) with the standard deviation (shaded) comparing asymptomatic men (blue line and blue shading) and women (red line and pink shading)

As seen in Figure A2.1a, qualitatively asymptomatic men and women have a similar knee varus-valgus angle during early stance. However, women seem to have a higher peak knee varus angle compared to men. The KVAV waveforms seen in Figure A2.1b indicate that asymptomatic women have a higher pKVAV than men thereby in conjunction with the findings in Table 4.2.

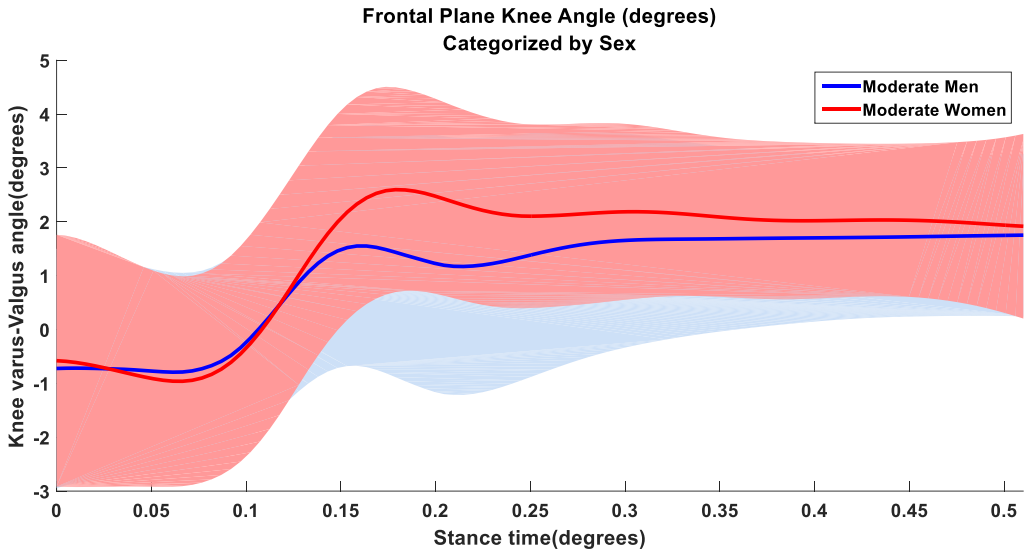

Figure A2.2a: Ensemble average of the frontal plane knee angle (degrees) with the standard deviation (shaded) comparing moderate OA men (blue line and blue shading) and women (red line and pink shading)

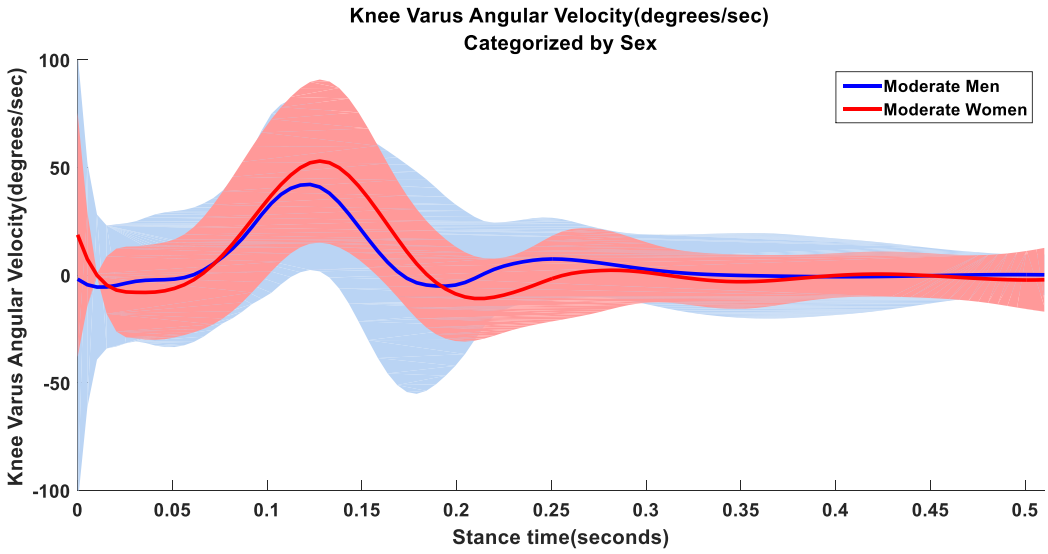

Figure A2.2b: Ensemble average of the KVAV (degrees) with the standard deviation (shaded) comparing moderate OA men (blue line and blue shading) and women (red line and pink shading).

Qualitatively, OA women do seem to have a higher peak knee varus angle as compared to OA men (Figure A2.2a). Likewise the pKVAV in OA women appears to be greater than OA men (Figure A2.2b). This finding was not significant according the analysis in Table 4.2.

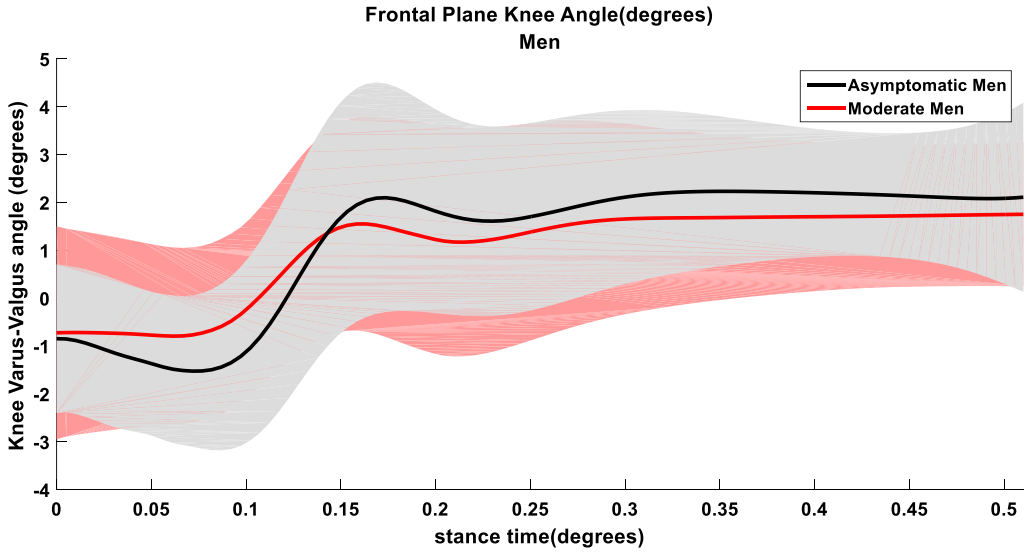

Figure A2.3a: Ensemble average of the frontal plane knee angle (degrees) with the standard deviation (shaded) comparing asymptomatic men (black line and grey shading) and moderate OA men (red line and pink shading)

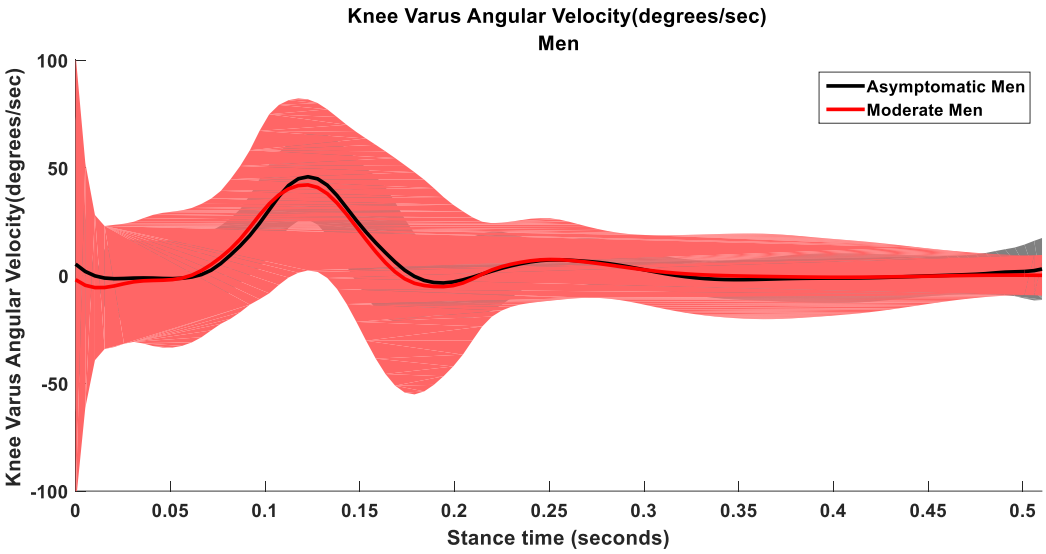

Figure A2.3b: Ensemble average of the KVAV (degrees) with the standard deviation (shaded) comparing asymptomatic men (black line and grey shading) and moderate OA men (red line and pink shading)

Figure A2.1a compares the frontal plane angle between asymptomatic men and OA men. Interestingly, the greater initial valgus deflection seen in asymptomatic men coincide with the findings for the asymptomatic whole group in the current study. Asymptomatic men seem to show a greater valgus to varus change as compared to OA men. As for the KVAV waveforms, no apparent difference can be visualized between the two groups, with similar peaks for both groups (Figure A2.3b).

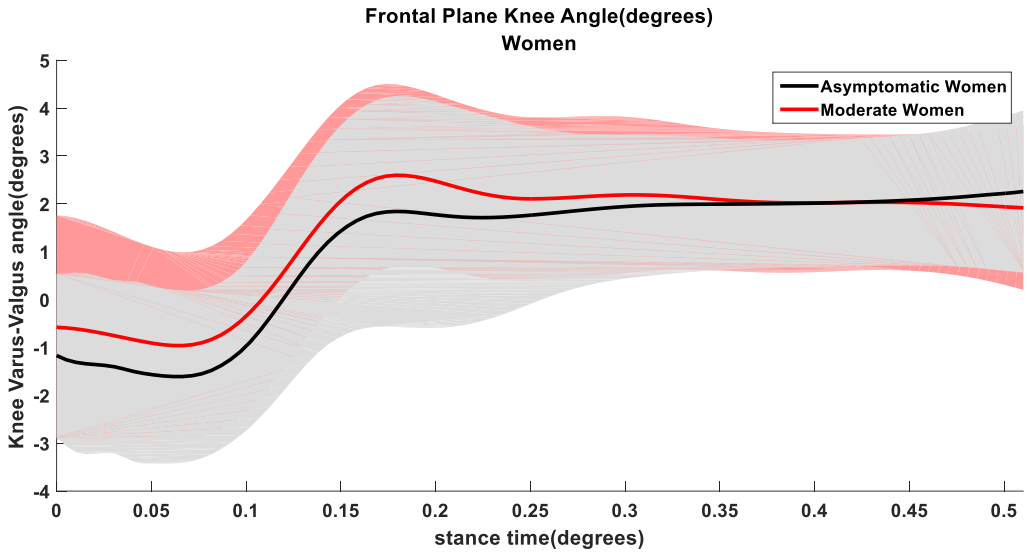

Figure A2.4a: Ensemble average of the frontal plane knee angle (degrees) with the standard deviation (shaded) comparing asymptomatic women (black line and grey shading) and moderate OA women (red line and pink shading)

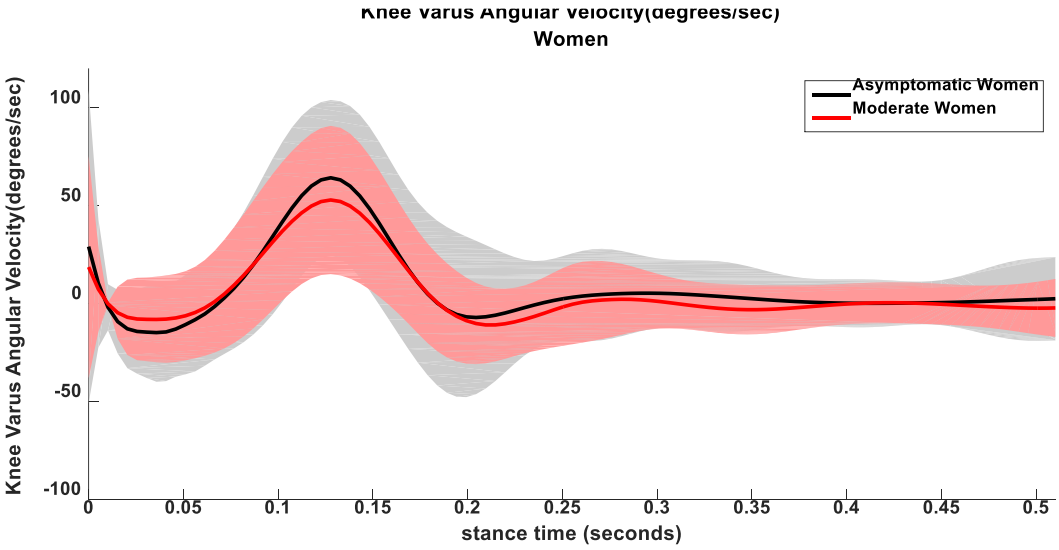

Figure A2.4b: Ensemble average of the KVAV (degrees) with the standard deviation (shaded) comparing asymptomatic women (black line and grey shading) and moderate OA women (red line and pink shading)

Qualitatively, OA women have a higher overall knee frontal plane waveform. The peak knee varus angle in OA women seems to be higher than asymptomatic women. However, the peak valgus angle in asymptomatic women seem to be higher than OA women (Figure A2.4a). This may indicate a difference in the valgus to varus change between asymptomatic and moderate OA groups. The pKVAV in asymptomatic women des seem to be higher than OA women (Figure A2.4b) but as indicated in Table 4.2, this difference was not significant.

Except for the peak knee varus angle, there doesn't seem to be a distinct differentiation between men and women in both groups. However, differences in the frontal plane knee angle and KVAV do seem to appear when comparing between the two groups. The distinct knee valgus deflection seen in the asymptomatic group as opposed to the OA group does indicate that the asymptomatic group had a greater valgus-varus range of motion. However, the OA group in this study was medial and hence, lack of motion in the valgus direction may not be surprising.

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