The Relationship Between Muscle Capacity Utilization During Gait and Pain in People With Symptomatic

Knee Osteoarthritis

by

Emma Victoria Tung

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# Author's Declaration

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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# Abstract

Muscle capacity refers to an individual's ability to utilize their muscle strength and power in order to efficiently and effectively complete physical activities (Brady & Straight, 2014). Muscle capacity is associated with an individual's physical function (Brady & Straight, 2014), as it incorporates the utilization of skeletal mass during physical tasks (Woods et al., 2011). In fact, age-related declines in both muscle strength and power have been observed to influence changes in physical activity (Doherty et al., 1993; Newman et al., 2006; Woods et al., 2011). Muscle capacity plays an important role in maintaining an individual's health and wellbeing during aging.

This study explored the relationship between pain and muscle capacity utilization during walking in older adults with knee osteoarthritis (OA). A convenience sample of 23 participants (15 females and eight males) with symptomatic knee OA completed this study [age 67 (±8) years, body mass index 29.7 (±3.9) kg/m$^2$, gait speed 1.25 (±0.25) m/s]. Muscle capacity utilization was measured by calculating the ratio of the external peak knee flexion moment measured using gait analysis, to the maximum voluntary isometric contraction (MVIC) of the quadriceps measured on a dynamometer. This ratio reflects the proportion of maximal knee extensor capacity that was used during level walking. Pain was measured using the Knee Osteoarthritis Outcome Score (KOOS), a self-report questionnaire used for evaluating knee pain for people with OA. A higher KOOS score indicates less pain, whereas a lower KOOS score indicates more severe pain.

A series of multiple linear regressions were used to determine the relationship between pain and muscle capacity utilization, after adjusting for age, sex, body mass index (BMI), and gait speed as covariates. Results showed that there was no relationship between pain and muscle capacity utilization ($p>0.05$). However, female participants demonstrated lower MVIC ($p<0.001$) compared to males.

Accordingly, a trend was observed such that females required a greater muscle capacity utilization to complete gait compared to males.

In conclusion, muscle capacity utilization was not associated with pain during walking in people with knee OA. Although the results of this study are insignificant, future work should further explore sex differences using a greater sample size and activities of daily living (ADLs).

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# List of Abbreviations

| | |
|---|---|
| 6MW | Six-Minute Walk |
| ADLs | Activities of Daily Living |
| AGEs | Advanced Glycation End-Products |
| ACR | American College of Rheumatology |
| BMI | Body Mass Index |
| CVD | Cardiovascular Disease |
| CCCARE | Centre for Community, Clinical and Applied Research Excellence |
| EMG | Electromyography |
| GBD | Global Burden of Disease |
| ICC | Intraclass Correlation Coefficient |
| JRFs | Joint Reaction Forces |
| KL | Kellgren Lawrence |
| KAM | Knee Adduction Moment |
| KFM | Knee Flexion Moment |
| KOOS | Knee Osteoarthritis Outcome Score |
| LR | Likelihood Ratio |
| MRI | Magnetic Resonance Imaging |
| MVIC | Maximum Voluntary Isometric Contraction |
| NHANES | National Health and Nutrition Examination Survey |
| NHEFS | NHANES Epidemiologic Follow-up Study |
| NSAIDs | Non-Steroidal Anti-Inflammatory Drugs |
| OA | Osteoarthritis |
| POHEM-OA | Population Based Health Micro-Simulation Model of OA |
| SD | Standard Deviation |
| WOMAC | Western Ontario and McMaster Universities Osteoarthritis Index |

# Introduction

## The Burden of Knee OA

Osteoarthritis (OA) is a progressive, degenerative disease of the synovial joints that causes pain, swelling, stiffness, diminished range of motion and functional disability. This disease is the most common form of arthritis, affecting millions of people worldwide (Badley & DesMeules, 2003; Bombardier, et al., 2011; Canadian Institute for Health Information, 2018). In 2010, 4.4 million Canadians were living with OA; simulations show this number is expected to reach over 10.4 million people by 2040 (Bombardier, et al., 2011). In 2012, over one-quarter (26.6%, 95% confidence interval) of the world-wide population over 45 years of age was diagnosed with OA and the proportion of OA in Canada is projected to increase from 13.8% to 18.6% in the next two decades (Sharif et al., 2015; Turkiewicz et al., 2014). At a global level, the results showed that there were approximately 303.1 million (95% UI 273.3-338.6 million) prevalent cases of hip and knee OA. This was a 9.3% (95% UI 8%-10.7%) increase from 1990 to 2017 (Safiri et al., 2020). In addition, OA accounted for approximately 14.9 million (95% UI 13.4-16.7 million) incident cases globally, an increase of 8.2% (95% UI 7.1%-9.4%) between 1990 and 2017 (Safiri et al., 2020).

While previously we believed that OA occurred when the cartilage in a joint wears down over time, resulting in a gradual loss of its protective and "cushioning" (force-dissipating) effects on the joint, recent advances in the field identify that OA is a much more complex disease. OA affects all of the tissues in and around a synovial joint, including the articular cartilage, subchondral bone, ligament and muscle. OA initially presents itself as a molecular derangement of the joint tissues, consisting of cell stress and the degradation of the extra-cellular matrix. This is followed by anatomic and/or physiologic

derangements of the joint, including articular cartilage loss, bone remodeling, osteophyte formation, and joint inflammation (OARSI, 2016).

OA affects the knee (likely due to its weight bearing role) more than any other joint in the body, accounting for over 50% of all OA cases diagnosed (Turkiewicz et al., 2014). This percentage is observed in people diagnosed exclusively with knee OA, as well as those with combinations of knee and another joint OA. By 2032, the prevalence of OA affecting the knee is projected to increase from 13.8% to 15.7% in the over 45 age group (Turkiewicz et al., 2014). Knee OA has been associated with mobility limitations and difficulties in physical function, such as walking, getting in and out of a car and climbing up and down stairs (Ling et al., 2003; Rejeski et al., 1995).

Additionally, knee OA presents an economic burden for individuals suffering from the disease (Cross et al., 2014; Gupta et al., 2005; Sharif et al., 2015). Indirect employment costs (days missed, reduced productivity, and unemployment due to OA) accounted for 32.9% of the total economic burden for participants younger than 65 years (Gupta et al., 2005). Furthermore, to estimate the future direct cost of OA in Canada, Sharif and colleagues (2015) used a population-based health micro-simulation model of OA (POHEM-OA). According to the POHEM-OA projections, from 2010 to 2031, the hospitalization costs of hip/knee total joint replacement (TJR) surgeries would increase from $720 million dollars to almost $2.8 billion dollars (Sharif et al., 2015). Almost 95% of the hospitalization cost was due to hip and knee TJR surgeries and 5% due to other hospital procedures for people with OA (Sharif et al., 2015). Hip and knee TJR surgeries are increasing by the number in Canada (Bombardier, et al., 2011; Canadian Institute for Health Information, 2018; Sharif et al., 2015). Specifically, the number of knee replacements in Canada increased by 15% between 2011-2017 (Canadian Institute for Health Information, 2018). Knee replacements increased from 58,138 to 67,169 surgeries in Canada (Canadian

Institute for Health Information, 2018).  This increase in the number of knee replacements is one of the main reasons for the increase in the cost of hip/knee TJR surgeries; another reason being the high average cost because of high inflation rate for procedure and prosthesis cost specific to this type of surgery (Canadian Institute for Health Information, 2018).

## Risk Factors of Knee OA

Some people are more likely than others to develop knee OA (OARSI, 2016).  The most prevalent risk factors for developing knee OA are older age, female sex, obesity and muscle weakness (Castell et al., 2015; Misra et al., 2015).  As described below, these risk factors increase the likelihood for OA incidence. These risk factors may also contribute to OA progression (that is, worsening disease).

### Age

There is no doubt that aging is a significant risk factor for knee OA.  The Framingham Osteoarthritis Study showed the prevalence of radiographic OA increased with each decade of life from 33% among those age 60–70 years to 43.7% among those over 80 years of age (Felson et al., 1987).  As the Canadian population ages, OA prevalence is expected to increase and be highest among those over the age of 70 years (Bombardier, et al., 2011).  In 2010, approximately 49% of seniors over the age of 70 years are expected to be living with symptomatic OA (Bombardier, et al., 2011).

Similar to most aging-related health conditions in older adults, the increased risk of knee OA that occurs with aging likely results from an age-related loss in the ability of cells and tissues in the body to maintain homeostasis, particularly when put under physical stress.  Aging introduces vulnerabilities to a joint and makes it susceptible to OA.  For example, there is a greater loss in the number of chondrocytes in the cartilage of older adults diagnosed with OA than in healthy older adults (Anderson

& Loeser, 2010).  These cartilage cells, which are responsible for the synthesis and breakdown of this smooth and elastic tissue, do not replicate and therefore decrease in number with aging.

One of the best studied aging-related matrix protein modification in cartilage is the formation of advanced glycation end-products (AGEs).  AGEs are produced from the spontaneous non-enzymatic glycation of proteins that occurs when reducing sugars (such as glucose, fructose or ribose) react with lysine or arginine residues.  Because the articular cartilage has a relatively low turnover rate, it is particularly susceptible to AGE formation.  Type II collagen, the most abundant matrix protein in cartilage, has a half-life that has been calculated to be over 100 years.  The accumulation of AGEs in cartilage has been suggested to play a role in the development of OA and has been found in both knee and ankle cartilage (Anderson & Loeser, 2010).

Magnetic Resonance Imaging (MRI) studies have shown that knee cartilage thins with aging, particularly at the femoral and patellar articular surfaces, suggesting a gradual loss of cartilage matrix with aging (Anderson & Loeser, 2010).  Excessive or abnormal mechanical stresses accentuate this loss of cartilage, thus playing a key role in the development of knee OA (Laslett et al., 2016).  Wluka et al., (2002) were able to show that people with symptomatic knee OA experienced a loss of total tibial cartilage at a rate of 4.4% to 6.2% per year.  This is nearly double the rate of cartilage loss in healthy older adults without knee pain (Hanna et al., 2005; Wluka et al., 2004).  Another study by Wluka et al., (2006) used a larger sample size of 78 people with symptomatic knee OA and a longer follow-up period of 4.5 years.  The results from this study showed that over 4.5 years, tibial cartilage declines at an average rate of 4% per year (Wluka et al., 2006).

Physical function and ability to perform activities of daily living (ADLs) decrease with age among people living with knee OA (Liikavainio et al., 2008). People with knee OA exhibited significantly poorer physical function, reflected by walking, stair-climbing, dressing, and sit-to-stand tasks, compared with age- and sex-matched control subjects. (Liikavainio et al., 2008). Additionally, Bartley and colleagues (2016) found that older adults with knee OA have a lower mechanical pain threshold in the quadriceps and epicondyle than middle aged adults with knee OA. The authors examined the differences in pain between middle aged (45-56 years of age) and older aged (57-85 years of age) people with knee OA, using questionnaires and experimental pain outcomes. These findings are interesting because the authors attribute their results to the differences in physical activity between the two age groups. A decrease in physical activity in older adults may lead to the lower pain threshold and disability – since movement during physical activity has the potential to evoke pain in people with knee OA (Bartley et al., 2016).

Sex

OA occurs in women 60 years of age (13-16%) more so than men (10-12%) in the same age group (Turkiewicz et al., 2014; Zhang & Jordan, 2010). The prevalence of this disease in the hand, hip, and knee also appear to increase rapidly in women after 50 years of age. This increase is less apparent in men, although they have a higher prevalence of the disease before the age of 50 (Arden & Nevitt, 2006). For knee OA, a longitudinal study showed that women have a 1.8 times greater risk of developing this condition than do men (Felson et al., 1997). In 2010, the prevalence of knee OA was higher in females (mean 4.8%; 95% uncertainty interval (UI) 4.4% to 5.2%) than in males (mean 2.8%; 95% UI 2.6% to 3.1%) worldwide (Cross et al., 2014).

Sex hormones likely impact the onset of OA in women.  There is growing evidence that sex hormones, specifically estrogen, play an important role in maintaining the homeostasis of articular tissues and the joint itself (Roman-Blas et al., 2009; Srikanth et al., 2005).  The presence of estrogen in women prior to menopause influences bone metabolism by resulting in greater bone mass and greater tolerance to mechanical stress on the cartilage of the joint (Felson & Nevitt, 1998; Hannan et al., 1990; Roman-Blas et al., 2009).  At menopause, the presence of estrogen is reduced among women.  There is a dramatic rise in OA prevalence among postmenopausal women, suggesting that there is a link between OA and loss of ovarian function (Roman-Blas et al., 2009).  This hormonal shift puts women at a greater risk of OA incidence, as a lack of this sex hormone is associated with progressive cartilage degradation and high subchondral bone loss (Anderson & Loeser, 2010; Felson & Nevitt, 1998b; Roman-Blas et al., 2009).  Interestingly, older studies have linked higher bone mineral density of the hip or spine to the development of knee OA in women but not men (Arden & Nevitt, 2006; Hannan et al., 1993), but this phenomenon is likely just a reflection of the presence of osteophytes and may not signal OA disease (Arden & Nevitt, 2006).

In the US, women with arthritis report greater prevalence of activity and work limitations, psychological distress, and severe joint pain than their male counterparts (Theis et al., 2007).  More than 10% of all American women older than 18 years of age report arthritis-attributable activity limitation, whereas the same is true for only 7% of men (Theis, et al., 2007).

## Obesity

Obesity is a prominent risk factor in the development of knee OA.  In a population-based cohort of greater than 1.7 million, a dose-response relationship existed between obesity and knee OA incidence, where a body mass index (BMI) >35 kg/m$^2$ had a 4.7-fold elevated risk (Reyes et al., 2016).

People who are obese increase their relative risk (RR) of developing knee OA to 4.55 (95% CI 2.90 to 7.13, $p$<0.001) (Zheng & Chen, 2015).  In fact, the risk of knee OA increases by 35% (95% CI 1.18 to 1.53, $p$<0.001) with a 5 kg/m$^2$ increase in Body Mass Index (BMI).  Obesity is an independent predictor of knee OA risk regardless of the study country, sample size, and gender (Zheng & Chen, 2015).

The mechanisms by which obesity promotes OA are complex and are still being explored; however, there is evidence that obesity compromises joint health through at least three mechanisms (Browning & Kram, 2007; Dumond et al., 2003; Messier, 2009; Messier et al., 2005, 2013; Runhaar et al., 2011).  First, people with obesity walk with greater knee joint loads than healthy weight adults (Browning & Kram, 2007; Messier et al., 2005).  A study by Browning and Kram (2007) found that obese individuals exerted 60% greater vertical ground reaction forces compared to normal weighted people. In obese adults, excessive biomechanical stress in the knee is a likely factor for the pathogenesis and progression of knee OA  (Messier et al., 2005).  The increased load magnitude bourn by the knee can cause a higher risk of knee OA, as inflammation in the joint is a common result of excessive biomechanical stress (Browning & Kram, 2007; Messier et al., 2013).  Second, inflammatory markers such as interleukin-6 (IL-6) are associated with the development of knee OA (Messier et al., 2013). Additionally, the polypeptide leptin, encoded by the obese gene, has been found to be overexpressed in the knee joint of obese people with knee OA, and contributes to the development of OA (Dumond et al., 2003).  In people with OA, leptin was found in cartilage and osteophytes, with the pattern and level of leptin expression being associated with the severity of cartilage degradation (Dumond et al., 2003).  In normal, healthy cartilage, chondrocytes infrequently produce leptin, which suggests that the presence of leptin in people with obesity reflects OA disease (Dumond et al., 2003).  Third, obesity can alter movement patterns of everyday movements (Messier, 2009; Runhaar et al., 2011). For example, obese

individuals have a tendency to take shorter steps, perhaps to reduce the load in the knee joint (Messier, 2009). However, this adjustment can cause a reduction in knee extensor torque, resulting in a dominant knee flexor torque during walking (Messier, 2009). This switch can cause an increase in hamstring muscle activity to provide knee joint stability – resulting in a decrease in quadriceps muscle activity (Messier, 2009). Quadriceps weakness is a significant factor in the development of knee OA (Segal et al., 2010; Segal & Glass, 2011; Slemenda et al., 1998), therefore the decrease in quadriceps activity during walking in obese individuals can put them at a greater risk for developing this disease.

The relationship between obesity and disability in OA has been explored previously (Cimmino et al., 2005; Dumond et al., 2003; Ettinger et al., 1994; Jordan et al., 1996; Marcum et al., 2014; Marks, 2007; Misra et al., 2015). People with OA and higher BMIs reported more pain than those with lower BMIs ($p<0.05$) (Marks, 2007). Specifically, Ettinger and colleagues (1994) looked at the association between obesity, knee OA and long-term disability using data from the National Health and Nutrition Examination Survey, 1971-1975 (NHANES I), and the NHANES Epidemiologic Follow-up Study, 1982-1984 (NHEFS). This data set included 4,059 participants between 45-74 years old. To assess physical function, the participants were asked to answer a 26-question physical function questionnaire, consisting of modified, selected questions from the Fries Functional Disability Scale for Arthritis (Health Assessment Questionnaire), the Rosow-Breslau Scale, and the Katz Activities of Daily Living Scale (Ettinger et al., 1994). The authors found that knee OA and obesity were each significantly associated with poorer physical function, with odds ratios of 4.3 and 1.7, respectively. Their study also found that when obesity was combined with knee OA, the odds ratio for poorer physical function increased to 9.8 (Ettinger et al., 1994). It is clear that obesity is significantly associated with functional impairments and disability amongst people with knee OA.

## Loss of Muscle Function

Poor quadriceps muscle function is a common trait amongst people diagnosed with knee OA (Segal & Glass, 2011; Segal et al., 2010; Segal et al., 2009; Slemenda et al., 1997, 1998). Loss of muscle function can be characterized using measures of strength, where strength loss is measured as a reduction in the maximum force produced by the muscle at a given time, which depends on the muscle force-length relationship (Metter, et al., 2004). Liikavainio and colleagues (2008) showed that healthy controls showed higher knee extension ($p<0.05$) and flexion ($p<0.001$) torques than the people with knee OA.

Knee extensor weakness is likely a risk factor for the initiation (and perhaps progression) of damage to articular cartilage and other tissues in the knee with OA (Slemenda, et al., 1997), particularly amongst women. Segal and colleagues looked at the effect of quadriceps weakness on joint space narrowing, which is a structural marker frequently observed in knee OA (Segal et al., 2010). They found a significant relationship ($p=0.04$) between quadriceps weakness and future patellofemoral joint space narrowing in women, demonstrating that muscle weakness is a risk factor for the development of radiographic knee OA (Segal et al., 2010; Segal et al., 2009)

The mechanisms by which muscle weakness increases the risk for the onset of knee OA in women is multifactorial. The quadriceps muscle is a primary contributor to both functional knee joint stability and knee joint loading. Specifically, in the lower extremity, the knee joint requires dynamic restraining mechanisms to counteract external forces acting on the knee to maintain dynamic joint stability (Segal et al., 2010; Wikstrom, et al., 2006). Dysfunction in quadriceps muscle strength can result in the inability to control and withstand submaximal forces, causing dynamic knee joint instability and an increased risk of damage to the knee joint (Segal & Glass, 2011; Wikstrom et al., 2006).

Weakness of the quadriceps can alter contact stress in the knee joint, leading to degradation of the articular cartilage and contribute to knee OA (Segal & Glass, 2011; Segal et al., 2010).

Several mechanisms have been suggested to cause muscle weakness in knee OA. These mechanisms include disuse atrophy of the muscles; reflex inhibition of muscles moving the affected joint due to joint pain; and incapability to fully activate the quadriceps femoris muscle resulting in the decreased force production (Bennell et al., 2008, 2013). Muscle weakness in the quadriceps has been attributed to altered afferent input from the diseased joint and consequent reduction in efferent motor neuron stimulation of the lower extremity (Slemenda et al., 1997). In people with knee pain, muscle weakness contributed more to disability than the severity of pain or radiographic changes in the knee (Slemenda et al., 1998). This weakness in knee extensor strength appears to be independent of age, sex and body weight (Slemenda, et al., 1997).

Strengthening the quadriceps and hamstrings improves and maintains knee joint stability and mobility, and increases tolerance of pain in people with knee OA (Coudeyre et al., 2016; Fitzgerald, 2005; O'Reilly et al., 1997; Slemenda et al., 1997). Muscle strengthening for knee OA rehabilitation has a significant effect on pain management and disability (Aguiar et al., 2016; Coudeyre et al., 2016; Fransen et al., 2015). For example, Aguiar and colleagues (2016) examined the effects of a resistance training protocol, designed for people with knee OA, that included strengthening the quadriceps, hamstrings, abdominal, and gluteus medius and maximus muscles on disability and functional limitations. This 12 week program improved functional performance ($p < 0.001$), increased gait speed ($p < 0.001$), reduced pain ($p < 0.001$) and improved quality of life (Aguiar et al., 2016). Furthermore, a decrease in strength is a significant predictor for frailty and ADLs disability (Vermeulen, et al., 2011). Thus, strong evidence shows that a loss of quadriceps strength is a risk factor for knee OA among

women, and this weakness is associated with worse clinical outcomes including impaired mobility, greater pain and greater risk for frailty.

## Implications of Living with Knee OA

Knee OA has a profound impact on daily living, including chronic pain, disability, and co-morbidity and mortality. Pain is a multifaceted, subjective phenomenon that is influenced by biological, psychological and social factors (Neogi, 2013). Many pain-related conditions resolve over time; however, OA is a disease that does not resolve. Numerous studies have demonstrated that there is a discordance between radiographic measures of joint degeneration and clinical pain in individuals with knee OA (Bedson & Croft, 2008). This discordance suggests that there is a range of underlying mechanisms explaining structural and clinical manifestations of knee OA. A study by Bastick et al., (2016) aimed to examine knee pain of 705 people with symptomatic knee OA, over a course of five years. These researchers found that 56% of their sample experienced a constant mild or moderate pain trajectory over the five years.

While knee pain may not correlate with structural deterioration in knee OA, people with knee OA who experience pain appears to also experience accelerated structural progression (Wang et al., 2018). In people with both radiographic knee OA and symptomatic knee OA, pain was associated with cartilage loss in the knee joint (Wang et al., 2018). Pain can lead to the avoidance of physical activity and social participation in people with knee OA (Darlow et al., 2018). The quality of life for those with knee OA is often reduced due to the anticipation of increased pain leading to activity limitation – both physically and socially (Darlow et al., 2018). It is clear that there is an underlying relationship between pain and the progression of knee OA, and this relationship significantly impacts the quality of life for

individuals with the disease. However, little research has been done on whether pain is merely a symptom of knee OA or an important factor contributing to the progression of this disease.

Greater severity of knee OA is, not surprisingly, associated with lower quality of life and worsening disability. A qualitative study by MacKay, et al. (2014) explored the perceived consequences and implications of people with OA in between the ages 35-65 years. Many of these participants found that OA not only altered their physical performance but also their social lives (friends, family and work) and their emotional outlook. Participants stated that knee OA affected how they viewed their bodies and themselves. In their daily lives, these experiences translate into fatigue and disability (Botterman et al., 2016; Safiri et al., 2020; Veronese et al., 2016). A considerable number of people with hip or knee OA experience elevated levels of fatigue at an early stage of OA (Botterman et al., 2016). Interestingly, Botterman and colleagues also determined that comorbidity, medication use, and female sex were significantly associated with elevated fatigue in early stages of OA. These findings are consistent with how comorbid diseases, like OA, negatively impact the physical and mental health of people (Botterman et al., 2016).

In fact, the burden of OA on disability is documented on a global scale. A study by Safiri et al. (2020) examined the worldwide burden of OA using the results from the Global Burden of Disease (GBD) Study in 2017. This study included 195 countries and territories, and systematically studied 359 diseases and injuries, and 282 causes of death (Safiri et al., 2020). Nearly 9.6 million (95% UI 4.8 to 19.1) people, globally, were living with disabilities due to OA in 2017 (Safiri et al., 2020).

People with OA are at increased risk of death due to medical morbidities associated with OA (Veronese et al., 2016). People with OA have reported a higher presence of frailty, cardiovascular and

metabolic diseases – these may be important confounders in explaining the relationship between OA and mortality (Veronese et al., 2016). The results from a meta-analysis by Veronese et al. showed that people with OA are known to have high levels of cardiovascular disease (CVD), an increased inflammatory profile and low levels of physical activity, all of which may predispose people with OA to premature mortality.

## Is Gait a Pathway to Disability Due to Knee OA?

Reduced gait speed is an important measurement by which OA increases the risk of disability. Gait speed is an important component to an individual's quality of life and daily living. Gait speed can predict important outcomes such as disability, institutionalization, ability to live independently (Cesari, 2011). Gait speed reflects an individual's well-being and physical function, and a slow gait speed might indicate a sub-clinical impairment in health status (Abellan Van Kan et al., 2009).

Compared to their healthy counterparts, reduced gait speed has been consistently observed in people with knee OA (Bejek, et al., 2006; Bindawas, 2016; Landry, et al., 2007; Marcum et al., 2014; White, et al., 2013; Zeni & Higginson, 2009). White and colleagues (2013) used a sample of 4,179 participants from the Osteoarthritis Initiative cohort study and found those with symptomatic knee OA had an almost nine-fold risk of a fast decline trajectory of gait speed compared with people with neither pain nor radiographic knee OA. Additionally, Marcum and colleagues (2014) were interested in evaluating gait speed and its ability to predict frailty, disability risk, and mortality in the elderly. This cross-sectional study recruited 190 community-dwelling adults aged older than 50 years with knee OA, to identify correlations between reduced gait speed in older adults with chronic pain and knee OA. The results of this study showed that knee pain, age, depressive symptoms, catastrophizing, a number of comorbidities, and opioid use were negatively associated with gait speed ($p<0.05$). It is clear that people

with knee OA and frail older adults show a reduction in gait speed; however, our understanding of why gait speed is reduced in knee OA remains unclear.

A reduction in walking speed is likely a method used by people with medial compartment knee OA to reduce the loads at the knee (Bejek et al., 2006; Landry et al., 2007; Marcum et al., 2014; Zeni & Higginson, 2009). A study by Schnitzer et al., (1993) looked at the use of non-steroidal anti-inflammatory drugs (NSAIDs) in people, with knee OA who experience knee pain, to observe alterations in gait. This study found that the use of NSAIDs reduced pain and increased knee external adduction and external flexion moments during gait – suggesting that pain is a mechanism for altered gait patterns observed in people with knee OA. However, Schnitzer and colleagues (1993) did not account for the effect of gait speed. To investigate this relationship further, Henriksen et al. (2010) adjusted for walking speed, and found that pain was still associated with increased knee moments. Additionally, Zeni & Higginson (2009) found differences in self-selected walking speed between people with severe OA and the healthy control group ($p$= 0.008), where the group of individuals with OA had significantly slower self-selected walking speeds than the healthy control group. These studies provide compelling evidence that altered gait observed in knee OA are, indeed, effective at minimizing pain by offloading the knee (Henriksen et al., 2010; Schnitzer et al., 1993; Zeni & Higginson, 2011).

In fact, altered loading of the knee is associated with the onset and progression of the disease (Manal et al., 2015a). Much research has demonstrated differences between lower limb joint moments during walking in people with knee OA compared with healthy controls (Astephen, et al., 2008; Bennell et al., 2011; Brisson et al., 2017; Chang et al., 2015; Chehab et al., 2014; Favre & Jolles, 2016; Foroughi et al., 2009; Hurwitz et al., 1998; Ro et al., 2019; Simic, et al., 2011; Simic, et al., 2011; Teng et al., 2015; Zeni & Higginson, 2011). Inverse dynamics estimates the forces and moments acting on each body

segment from kinematics, anthropometric data and all external forces acting on the segment (Shimokochi et al., 2009). Joint moments are calculated as a product of the joint segments' moment of inertia and the joint's angular acceleration (Winter, 2009). An example of internal three dimensional (3-D) knee joint moments measured during walking can be seen in the study by Eng & Winter, (1995) (Figure 1). These knee joint moment curves are reported as internal moments which are equal and opposite to external moments. Joint moments represent a net of all internal (e.g., muscle, ligament) and external moments acting at a joint (Winter, 2009). It is important to emphasize that these moments are net values.

In knee OA, knee joint moments are most commonly measured in the frontal and sagittal plane, yielding knee adduction moments (KAM) and knee flexion moments (KFM), respectively.
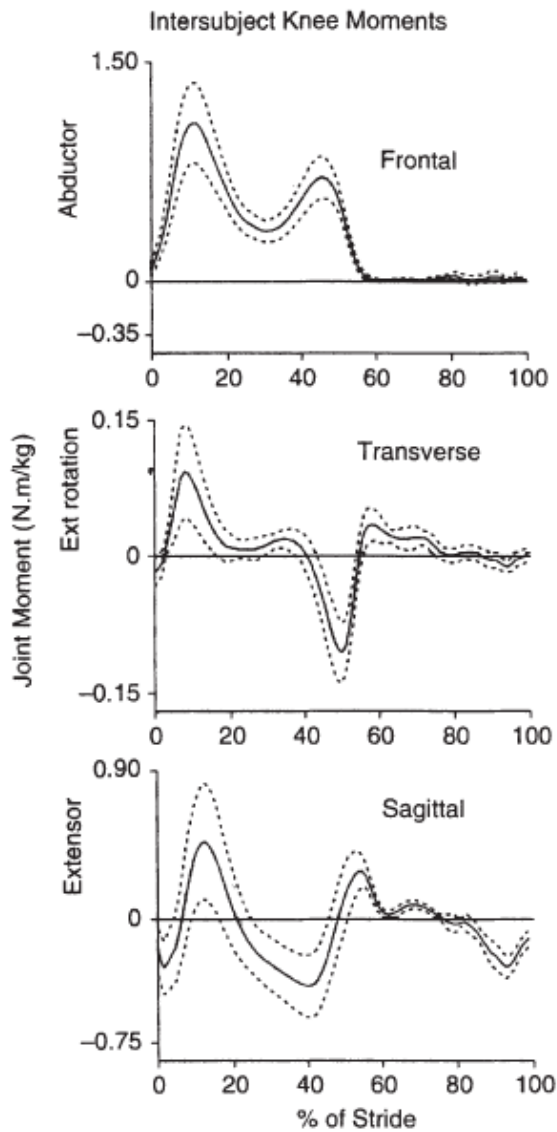
*Figure 1. Intersubject averaged internal knee joint moments normalized to body mass (Nm/Kg) versus. normalized stride in the frontal (top), transverse (middle), and sagittal (bottom) planes by Eng and Winters (1995). Solid lines represent average ensemble curves and dotted lines represent one standard deviation.*

Previous research considers KAM as a reflection of the ratio of medial to total tibiofemoral contact force (Moyer et al., 2014). Meanwhile, KFM is reflective of all agonist and antagonist muscle forces crossing the knee in the sagittal plane. An elevated KAM is implicated in knee OA (Astephen, et al., 2008; Bennell et al., 2011; Brisson et al., 2017; Chang et al., 2015; Favre & Jolles, 2016; Foroughi et al., 2010; Huang et al., 2008; Simic, et al., 2011; Zeni & Higginson, 2011). In a computational modeling study, Manal et al., (2015) demonstrated that KAM and KFM account for more than 85% of variance in peak medial compartment loading of the knee; thus, purporting that changes in KFM and KAM will subsequently affect joint loading of the knee. This altered loading could effectively disrupt the joint cartilage's ability to regenerate and withstand cyclic loading – leading to more severe cartilage damage (Chehab et al., 2014). Peak KAM measured during walking is associated with varus knee joint malalignment as well as the severity of knee OA (Chang et al., 2015; Foroughi et al., 2009, 2010; Hurwitz et al., 1998). However, there is a lack of evidence on whether people with less severe knee OA have a greater KAM compared to age-matched healthy controls (Foroughi et al., 2009), which raised questions about whether KAM was a major risk factor in the development of knee OA (Foroughi et al., 2009). Since that review, several cohort studies have shown that a larger KAM predicted future cartilage loss in people with knee OA, providing consistent evidence that KAM is likely an important contributor to knee OA progression. For example, Chang et al., (2015) demonstrated that KAM peak and impulse were associated with worsening of medial tibiofemoral bone marrow lesions over two years in 204 people with knee OA. Brisson et al., (2017) showed that while KAM peak and impulse were associated with reductions in cartilage volume over 2.5 years

There is some data to support that KFM is an important factor in the development of knee OA (Brisson et al., 2017; Manal et al., 2015; Walter et al., 2010). A study by Chehab, et al., (2014)

demonstrated KFM predicted reduced cartilage thickness over five years in 16 people living with knee OA. The results of this study suggested that KFM has an important influence on joint load that influenced disease progression. However, longitudinal studies with larger samples have not confirmed this finding. For example, Chang et al., (2015) did not find see an association between peak KFM and disease progression outcomes two years later (Chang et al., 2015). Similarly, Brisson et al., (2017) found that, while KAM peak and impulse predicted future cartilage loss, KFM (peak and interactions) did not increase the variance explaining the changes in medial tibial cartilage volume over time ($p$>0.05) in 52 people with knee OA. The inconsistensies between these studies may be explained by the knee OA severity of the participants. In the study by Chehab et al., (2014), more than half (56.3%) of the participants had mild knee OA (Kellgren-Lawrence (KL) grade ≤ 2). Meanwhile, in the study by Brisson et al., (2017) the majority (63%) of participants had moderate knee OA (KL grade ≥ 3). This could mean that KFM is more a more sensitive or important marker during the milder or earlier stages of the disease. A reduction in KFM may represent a compensatory strategy for this altered loading that requires less quadriceps force during walking, perhaps in order to reduce joint loading and joint pain (Zeni & Higginson, 2011). This strategy may be a consequence of persistent quadriceps weakness in people with knee OA (Slemenda et al., 1997). Currently, there is little research on the use of KFM, during gait, as a risk factor for knee OA. The studies that do explore the association between KFM and knee OA yield inconsistent results.

Researchers have observed higher ankle moments and lower hip moments in people with knee OA compared to healthy adults (Ro et al., 2019; Zeni & Higginson, 2011). A study by Ro et al. (2019) looked at the effects of knee OA on hip and ankle gait mechanics. The researchers observed smaller hip and ankle range of motion in people with knee OA compared to the healthy control group (Ro et al.,

2019). Additionally, sagittal moments of the hip and ankle were smaller in the knee OA group than the control group (Ro et al., 2019). Interestingly, the frontal hip moments were smaller in the knee OA group, but the frontal ankle moments were 50% higher in the knee OA group than the control group (Ro et al., 2019). These results are consistent with what clinicians observe in people with knee OA, as these people are often seen walking with decreased range of motion at the hip, knee and ankle joints (Ro et al., 2019). The results of this study show that the presence of knee OA can alter the mechanics of the hip and knee joints during walking. Such changes are important as they can be risk factors for subsequent development of secondary arthritis (i.e. hip and ankle OA) as well as increased pain (Ro et al., 2019; Zeni & Higginson, 2011).

A significant relationship existed between pain and altered gait mechanics in individuals with knee OA; however, conflicting results from these studies do not provide a clear understanding of whether, or how, these factors interact (Bindawas, 2016; Boyer & Hafer, 2019; Heiden et al., 2009; Henriksen et al., 2010; Maly et al., 2008; Messier et al., 1992; Nebel et al., 2009; Ro et al., 2019; Robbins et al., 2011). In a cross-sectional study, Heiden et al. (2009) examined the gait adaptation patterns observed in people with radiographic knee OA. The results showed that increased pain coincided with a decreased external knee adduction moment. However, another cross-sectional study by Maly et al., (2008) used a sample of people with radiographic medial knee OA, and found no relationship between mean peak KAM and pain. Experimental studies provide a different perspective on the role of pain in gait mechanics. Henriksen et al. (2010) replicated the pain symptoms common with knee OA on the healthy participants by administering an isotonic saline injection to the infrapatellar fat pad. Introducing knee pain reduced peak moments in the frontal and sagittal planes, producing gait adaptations in healthy controls that were similar to those with knee OA, even after adjusting for walking speed

(Henriksen et al., 2010). Few studies have explored the longitudinal effects of pain on gait mechanics. White et al., (2013) looked at the effects of knee OA and pain on gait speed over four years. These researchers found that people with symptomatic knee OA were at a higher risk of a decline in gait speed than those with pain alone (White et al., 2013). There is currently, very little information on the underlying mechanisms of pain and its effect on gait mechanics (Bedson & Croft, 2008; Kidd, 2012; Preece et al., 2016). With the exception of gait speed, we do not know much about how pain affects gait.

## Does Knee OA Affect Muscle Capacity Utilization During Gait?

Muscle capacity refers to an individual's ability to utilize their muscle strength and power in order to efficiently and effectively complete physical activities (Brady & Straight, 2014). Muscle capacity is associated with an individual's physical function (Brady & Straight, 2014), as it incorporates the utilization of skeletal mass during physical tasks (Woods et al., 2011). In fact, age-related declines in both muscle strength and power have been observed to influence changes in physical activity (Doherty et al., 1993; Newman et al., 2006; Woods et al., 2011). Muscle capacity plays an important role in maintaining an individual's health and wellbeing during aging.

Healthy older adults tend to utilize close to their maximal torque-producing capabilities of the knee musculature when performing activities of daily living (Hortobagyi, et al., 2003). For example, Hortobagyi et al., (2003) set out to compare the relative effort necessary for older adults (n=14, mean age 74 years) versus younger adults (n=13, mean age 22 years) to perform ADLs such as ascending and descending stairs, and transitioning sit-to-stand. "Relative effort" was represented as the ratio of the knee joint moment required to perform ADLs relative to the maximal joint moment achieved during a maximal effort isometric contraction. Compared to young adults, older adults had significantly lower

maximal knee joint moments and utilized higher relative effort to complete these ADLs. This high relative effort in older adults is due to significantly reduced maximal force-generating capability of knee musculature.

Currently, there is little information on how knee OA affects this relative effort, that is, *muscle capacity utilization*, during activities of daily living – specifically walking. The study by Hortobagyi et al., (2003) provides great information on the difference in muscle capacity between healthy young and old adults. However, it is necessary to explore muscle capacity utilization in knee OA. Because knee OA is characterized by lower muscle strength (Segal & Glass, 2011), it is possible that there is a greater muscle capacity utilization in people with knee OA compared to healthy aging adults. Muscle capacity utilization during gait in people with knee OA is unexplored.

## Knowledge Gaps

1) People with knee OA have demonstrated altered gait mechanics compared to healthy controls. It is possible that people with knee OA have lower muscle capacity in the musculoskeletal system than their healthy counterparts for two reasons. First, adults with knee OA consistently demonstrate lower muscle strength and power. Second, adults with knee OA alter their gait kinetics to "offload" the knee joint surfaces, thereby, "using up" a portion of their muscle capacity. Previous research (Hortobagyi, et al, 2003) showed that this lower capacity within the musculoskeletal system was associated with a greater relative effort required to complete basic activities of daily living in healthy older adults compared to young adults. Yet, there is little research exploring how much muscle capacity people, living with knee OA, use during activity, or

whether pain is associated with this capacity. A decrease in gait speed and a decrease in muscle capacity utilization may be compensatory actions for joint pain in those with knee OA.

2) There are currently inconsistent findings regarding the associations of pain with knee biomechanics in knee OA. It is argued that altered gait mechanics in adults, with knee OA, may act as a stimulus for pain and/or be altered as part of a motor system response to joint pain. There is a need to understand if the proportion of musculoskeletal capacity used during activity is related to knee joint pain among individuals with knee OA. This response may shed light on understanding both the mechanisms by which pain interferes with daily activities in people living with knee OA. Understanding this relationship will be useful in the development of treatment for knee pain in people with knee OA. Treatment in early stages in the disease, as well as, over the course of disease progression is important in preventing cartilage degradation and is likely to have a significant impact on reducing the disease burden.

## Purpose

The purpose of this study is to investigate the association of pain with muscle capacity utilization during walking in older adults with knee OA.

## Objective

This study seeks to identify a significant relationship between muscle capacity utilization (that is, knee flexor moment normalized to MVIC) with Knee Osteoarthritis Outcome Score (KOOS) pain scores in older adults with knee OA.

## Hypothesis

Adults with symptomatic knee OA will display a positive correlation between pain and knee muscle

capacity utilization during walking.

# Methodology

## Study Design

This is an observational, cross-sectional study of individuals with knee OA. Participants completed one test session. During this session, participants completed measurements of physical capacity (knee strength and gait analysis), and completed a self-reported tool reflecting pain (KOOS). Participants also undertook measurements for covariates and descriptors (Table 1).

A human ethics review for this study has been approved by the University of Waterloo's Research Ethics committee. Written, informed consent was provided by all participants.

*Table 1. Table of variables and measurements used in this study.*

| Dependant Variable: | KOOS Pain Score |
|---|---|
| Independent Variables: | Muscle capacity utilization (KFM per MVIC) |
| Covariates: | Age |
| | Sex |
| | BMI |
| | Gait speed velocity |

## Participants

This study recruited adults with symptomatic knee OA. All participants were community - dwelling men and women that were 50 years of age and older and who meet the American College of

Rheumatology (ACR) criteria for clinical knee OA (Altman et al., 1986). The ACR clinical criteria require knee pain on most days of the week and at least three of the following: (i) greater than 50 years of age; (ii) less than 30 minutes of morning stiffness; (iii) crepitus with active range of motion; (iv) bone enlargement; (v) bone tenderness to palpation; and (vi) no signs of inflammation (warmth, swelling). Additionally, all participants were required to have a BMI of less than 35 kg/m$^2$ (below "severe" obesity) (Reyes et al., 2016), and able to jog five meters, walk a city block and climb stairs in a reciprocal fashion. Severe obesity can introduce other health conditions (high blood pressure, high cholesterol, type 2 diabetes, heart disease, stroke) (Reyes et al., 2016) that may impact the results of this study.

The exclusion criteria for all participants included a self-reported history of patellofemoral symptoms; self-reported fractures due to osteoporosis; diagnosis of other forms of arthritis (e.g., rheumatoid, psoriatic); active non-arthritic knee disease (e.g., gout); diagnosis of other non-arthritic knee or hip diseases, conditions that might be exacerbated by the protocol (e.g., unstable angina); neurological conditions such as a stroke; and current/past use of intra-articular therapies or knee surgeries. Participants were excluded if they have a skin allergy to medical tape, use an adaptive aid such as a cane or cannot climb two flights of stairs safely. Lower extremity trauma within the previous three months, ipsilateral hip or ankle conditions, radiation (e.g., cancer treatment) and pregnancy were also exclusion criteria. Individuals who have undergone knee surgery or other significant surgical or other health problems that would affect their walking ability were excluded from participating.

Participants were recruited using poster advertisements placed in the Waterloo, Ontario community, including the University of Waterloo campus and the Centre for Community, Clinical and Applied Research Excellence (CCCARE). These posters included the laboratory name (Mobilize Laboratory), as well as the telephone number and email and invited potential participants to contact a

researcher with questions or interest in participating.  As well, recruitment was facilitated by newspaper advertisements ("Coffee News"), social media (e.g., Mobilize laboratory Facebook page), and the Waterloo Research Aging Pool (WRAP).  Once a potential participant contacted the researcher via email or telephone, the researcher informed the potential participants about the details of the study, and screened them for the inclusion and exclusion criteria.

## Dependent Variable

### Knee Pain Over the Past Seven days

Knee pain was measured by using the Knee Injury and Osteoarthritis Score (KOOS).  The KOOS is a self-report questionnaire used for evaluating knee pain for people with OA in research and clinical settings.  The KOOS is a 42-item questionnaire that covers an individual's pain, symptoms, ADL, sport/recreation activities and quality of life.  The test asks participants to choose from standardized answers for each question in the form of five Likert boxes.  A final score is calculated, where a 0 indicates extreme symptoms and 100 indicates no symptoms.  The KOOS is located in Appendix 1.  The KOOS questionnaire showed high construct validity with other pain measures (SF-36) (physical function versus activities of daily living, r=0.57, physical function versus sport and recreation function, r=0.47, bodily pain versus  pain, r=0.46) (Roos et al., 1998; Roos & Toksvig-Larsen, 2003; Ware et al., 1993) as well as high intraclass coefficient (ICC) (ICC >0.75) (Collins et al., 2011; Roos et al., 1998; Roos & Toksvig-Larsen, 2003)

## Independent Variables

### Knee Extensor Strength

Muscle strength was measured using a Biodex Dynamometer (Biodex System 3, Shirley, MA, USA). Participants were seated in the Biodex such that the axis of flexion and extension at the knee is aligned with the axis of the dynamometer. In this position, the participant was secured with Velcro straps at their chest, waist, and lower shank to minimize extraneous movements. The more symptomatic leg was tested. The knee angle was set to 60 degrees, for optimal muscle length and maximal force production (Haffajee et al., 1972). The weight of the lower-limb and dynamometer attachment was summed and recorded to correct torque data for gravity (Brisson, 2017).

Quadricep muscle strength were recorded as the maximal voluntary isometric contraction (MVIC) achieved for the knee extensor muscles. Participants received a period before the collection started to practice performing submaximal contractions. Once the participant felt comfortable, they were asked to perform three knee flexions and three knee extensions at maximal effort, alternating between extension and flexion for each trial. The participants contracted for five seconds, and rested in between trials for 60 seconds (Brisson, 2017). Participants were also given verbal encouragement to flex and extend their knee. This MVIC data provides an indication of how much torque (Nm) an individual can produce at a specific knee angle and muscle length (60 degrees). Strength data from participants can be compared with normative data to see if an individual is above or below average extensor strength. The mean of the three peak knee extensor torques, during isometric contractions, was used to represent the participant's peak knee extensor strength output.

Torque measurements produced by the Biodex system, using isometric mode, have demonstrated excellent reliability (ICC = 0.99) and instrument validity with a measurement error of <1% difference between trials (Drouin, et al., 2004). An example of muscle strength output on the Biodex can be found in Figure 2, where Torque (Nm) is displayed as a function of Time (seconds) during isometric contractions of the knee. The participant was asked to extend (positive portion of the y-axis) and flex (negative portion of the y-axis) their knee for five seconds per contraction.

Low scores indicate that the participant is deficient in producing muscle strength and power; they are unable to generate enough force at a given joint angle and resistance. Muscle weakness can cause an increased risk for injuries, and is more common amongst people with OA (Liikavainio et al., 2008).
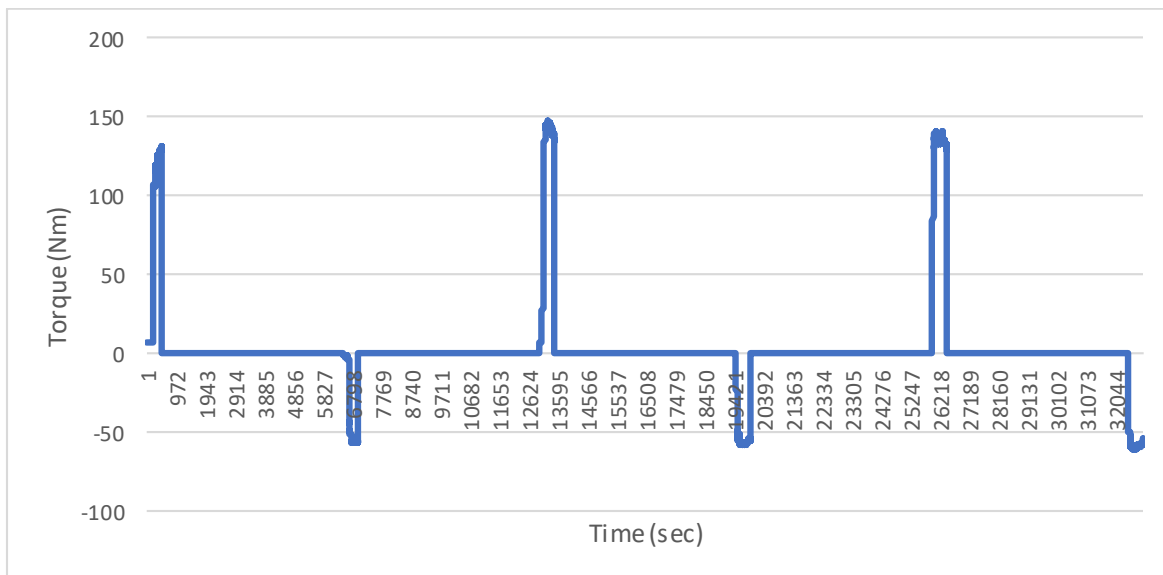


*Figure 2. Time (s) versus. Torque (Nm) of the right knee flexion and extension during isometric contractions on a Biodex Dynamometer. Positive values represent torque during knee extension; negative values represent torque during knee flexion. The three peak values for knee extension were averaged to produce a mean peak knee extensor torque value used in data analysis. These example contractions were performed on a 20-year-old, healthy male who is right-hand dominant.*

## Knee Flexor Moment During Gait

Motion analyses was used to examine joint moments in the knee during gait at a self-selected speed. Participants were asked to wear shorts and be barefoot whilst walking. Rigid bodies were made up of three Infra-Red Emitting Diodes (Northern Digital Inc., Waterloo, ON, Canada), arranged in triads (Figure 4). These were affixed to the sacrum, lateral side of the mid-thigh, mid-shank and anterior aspect of the foot. Additionally, 26 imaginary markers were digitized; the landmarks of these markers are in Table 2. Three-dimensional kinematics were recorded with a four-camera bank (12 cameras) high-speed motion capture system (Optotrak Certus, Northern Digital Inc., Waterloo, ON, Canada) using a sampling frequency of 100Hz and kinetics were collected with a floor-embedded force plate (OR6-7-1000, Advanced Mechanical Technology, Inc., Watertown, MA, USA) using a sampling frequency of 3600Hz.
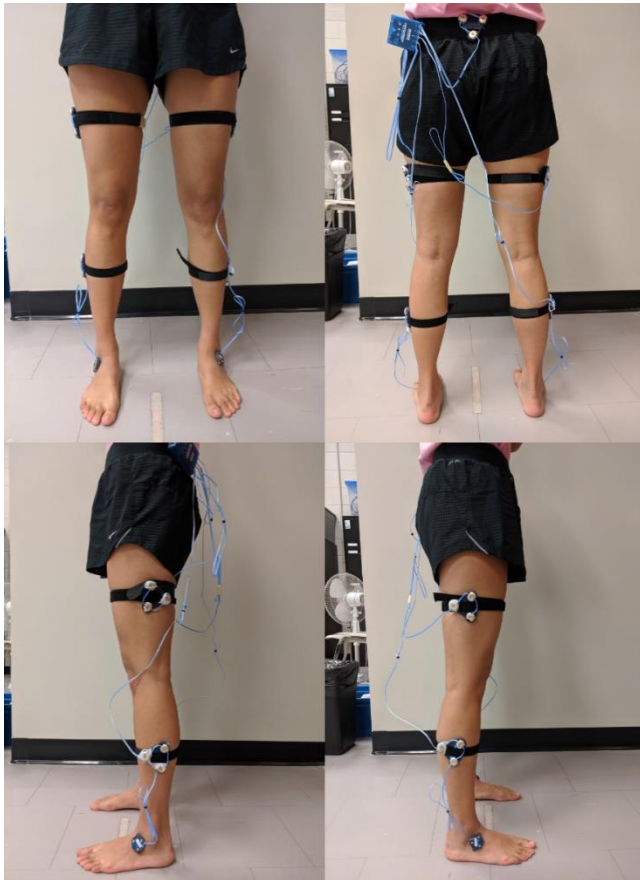
*Figure 3. Placements of the rigid bodies for the thigh, calf and foot on the right and left leg.*

*Table 2. List of imaginary markers used for gait analysis, with corresponding landmarks and rigid bodies.*

| Imaginary Marker Number | Imaginary Marker Landmark | Rigid Body |
|---|---|---|
| 1 | (L) Fibular Head | (L)Calf |
| 2 | (L) Tibial Tuberosity | (L)Calf |
| 3 | (L) Lateral Malleolus | (L)Calf |
| 4 | (L) Medial Malleolus | (L)Calf |
| 5 | (L) Dorsal 2nd Metatarsal Head | (L)Foot |
| 6 | (L) Achilles Tendon Insertion | (L)Foot |
| 7 | (L) Dorsal 5th Metatarsal Head | (L)Foot |
| 8 | (L) Dorsal 1st Metatarsal Head | (L)Foot |
| 9 | (L) PSIS | Sacrum |
| 10 | (R) PSIS | Sacrum |

| Imaginary Marker Number | Imaginary Marker Landmark | Rigid Body |
|---|---|---|
| 11 | (L) ASIS | (L)Thigh |
| 12 | (L) Greater Trochanter | (L)Thigh |
| 13 | (L) Lateral Epicondyle | (L)Thigh |
| 14 | (L) Medial Epicondyle | (L)Thigh |
| 15 | (R) Fibular Head | (R)Calf |
| 16 | (R) Tibial Tuberosity | (R)Calf |
| 17 | (R) Lateral Malleolus | (R)Calf |
| 18 | (R) Medial Malleolus | (R)Calf |
| 19 | (R) Dorsal 2nd Metatarsal Head | (R)Foot |
| 20 | (R) Achilles Tendon Insertion | (R)Foot |
| 21 | (R) Dorsal 5th Metatarsal Head | (R)Foot |
| 22 | (R) Dorsal 1st Metatarsal Head | (R)Foot |
| 23 | (R) ASIS | (R)Thigh |
| 24 | (R) Greater Trochanter | (R)Thigh |
| 25 | (R) Lateral Epicondyle | (R)Thigh |
| 26 | (R) Medial Epicondyle | (R)Thigh |

Abbreviations: (R)= right, (L)= left, PSIS= posterior superior iliac spine, ASIS= anterior superior iliac spine

Motion data produced by the Optotrak has been shown to demonstrate excellent repeatability and high precision when used for gait analysis (Maletsky et al., 2007; Mazumder et al., 2007). Maletsky and colleagues (2007) experimented on different degrees of rotations and translations of the rigid body clusters to see if these differences affect the precision and repeatability of the Optotrak system for gait analysis. The researchers tested the precision and accuracy of the Optotrak system and set out to find how many changes in rotation and translation could be made to the rigid bodies whilst maintaining a 95% repeatability. They found that a 10-degree rotation demonstrated a bias of 0.05 degrees and a 95% repeatability limit of 0.67 degrees. In addition, they found a 10 mm translation demonstrated a bias of 0.3 mm and a 95% repeatability limit of 29 mm. Thus, the researchers were able to demonstrate that a high level of accuracy can be achieved while using the Optotrak system for gait analysis.

Gait data were processed using commercial software (Visual 3D, C-Motion, Inc., Germantown, MD, USA). Marker and force plate data were filtered using a second-order low-pass Butterworth bidirectional filter with 6 Hz cut-off. This cut-off frequency was chosen based on existing literature for kinematic gait analysis (Antonsson & Mann, 1985; Schreven et al., 2015). A Butterworth filter was chosen for this analysis because it provides the best frequency response, without compromising the time domain. Therefore, with a Butterworth filter, the pass-band ripple in the time-domain is optimized for frequency with the content being preserved. The raw data was filtered using a dual-pass, rather than a single-pass because the dual pass filter corrects for phase shifts. External ankle, knee and hip moments were calculated using a three dimensional floating axis coordinate system – consistent with ISB standards Wu et al., (2002).

Internal joint moments and curves were calculated using Visual 3D. The KFM curves in Figure 4 are of an older adult with unilateral, painful knee OA. External peak KFM are the same magnitude as the internal peak knee extensor moments. External knee flexion moments are represented on the positive y-axis; meanwhile, external knee extension moments are represented on the negative y-axis in Figure 4. During gait, the quadriceps must balance the external KFM with internal knee extension moment. By doing so, the activation of the quadriceps impart a compressive force across the tibiofemoral joint, thus, increasing the articular cartilage contact force in the knee joint (Creaby, 2015). The KFM curves in Figure 4 demonstrate a reduction in peak KFM during the first peak (stance phase) between the right and left knee, where the left knee is more symptomatic. Previous research has suggested that this reduction in peak KFM may be a strategy for people with knee OA to reduce compressive forces at the knee (Astephen, et al., 2008).
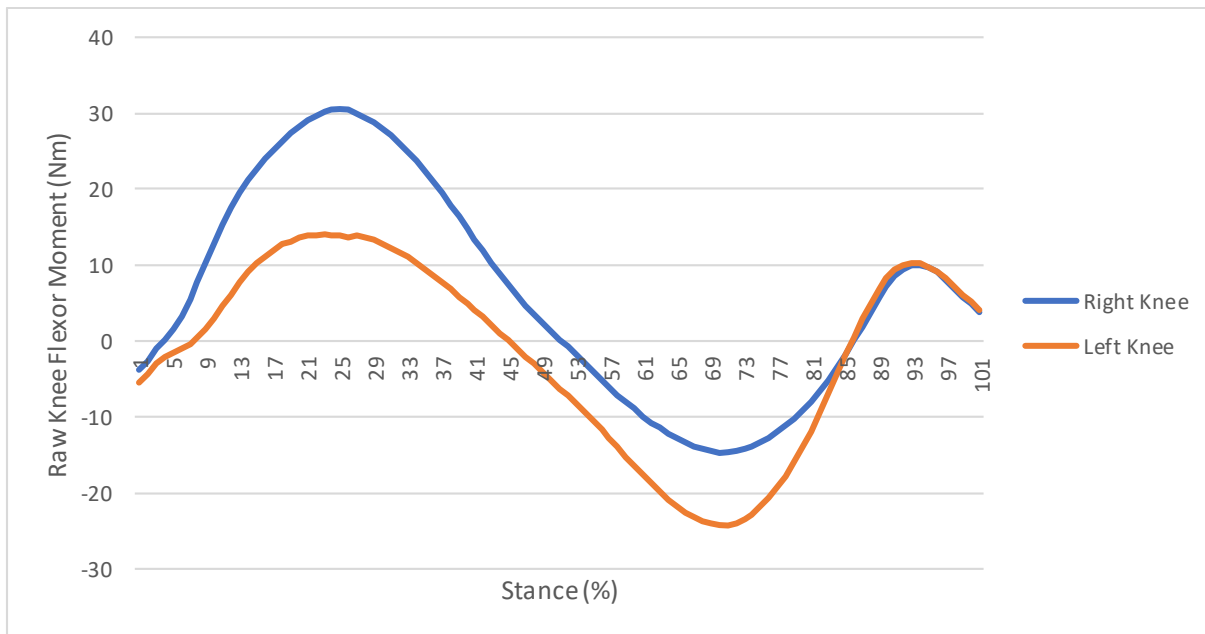
*Figure 4. Raw knee flexor moment versus. stance for the left and right knee joint in an older adult with knee osteoarthritis in the sagittal plane. Where the left knee is represented by the orange curve and the right knee is represented by the blue curve. The participant is a 68-year-old female with a BMI of 28.6, who suffers from knee OA, where their left knee is symptomatic. Their KOOS Pain subscale score is 59% indicating moderate pain.*

## Muscle Capacity Utilization

Knee flexor moments are presented using three methods: KFM unnormalized, KFM normalized to body mass, and KFM normalized to MVIC. Muscle capacity utilization is represented in the third method, where KFM values are normalized to the participant's MVIC. This measurement is the ratio of KFM required during walking, relative to the maximal knee flexor moment achieved during MVIC. This method has been used in previous research to demonstrate the amount of muscle capacity used to complete ADLs (Hortobagyi, et al., 2003).

## Covariates

### Age

Age of the participants was obtained by verbally inquiring by the researcher and then filled out in a Participant Data Collection Form (Appendix 2).

### Sex

Sex of the participant was obtained by verbally inquiring by the researcher and then filled out in a Participant Data Collection Form (Appendix 2).

### Body Mass Index

BMI of the participant was obtained by measuring the participant's height and weight, and then calculated and filled out in a Participant Data Collection Form (Appendix 2). Participants were asked to remove their shoes and socks while height and weight were measured; they remained wearing t-shirt and shorts.

### Gait Speed

Gait speed was measured using the Six Minute Walk test (6MW) to describe the physical function of this sample. Before testing started, the researchers ensured that the walkway was free from traffic and obstacles. The walkway was a pre-determined hallway in the building of Lyle Hallman South at the University of Waterloo. This hallway is indoor, well-lit, and tiled. The participant was asked to wear comfortable walking footwear. Participants were also asked to walk as fast as they can, but in a safe manner. Rest periods were allowed, but were included in the time (Dobson et al., 2013). Furthermore, standardized verbal encouragement was provided at one minute intervals (Dobson et al., 2013).

The 6MW test produces scores with excellent test-retest reliability (ICC =0.991) (Ateef et al., 2016). In addition, the test positively correlated with all KOOS subscales (symptoms, activities of daily living, pain, sports, and quality of life) and had a very strong correlation with knee OA disease severity (Ateef et al., 2016).

## Statistical Analyses

Tests of normality were conducted to ensure the data meet the assumptions required by linear regression. Independent samples t-tests were also performed to examine the differences between female and male participants using the following predictors: age, body mass, height, BMI, 6MW distance, gait speed, MVIC, KFM unnormalized, KFM per Kg, KFM per MVIC and KOOS pain score.

Linear regression analysis was performed using pain as the dependent variable. Four different models were created to explore the relationship of muscle capacity utilization with pain. First, a covariate model was built. Age, sex, BMI and gait speed influence pain and therefore were, a priori, included as covariates in the analyses. Older adults present greater pain symptoms, more persistent pain, and greater pain-related disability than younger adults (Bartley et al., 2016; Van Baar et al., 1998). In addition, research has consistently showed that there is a greater pain prevalence among women relative to men (Bartley & Fillingim, 2013). Additionally, numerous studies have demonstrated that there is a positive correlation between experienced pain and BMI (Hitt et al., 2007; Seaman, 2013; Somers et al., 2011; Zahorska-Markiewicz et al., 1983). Finally, previous research has also showed that knee pain is associated with decreased gait speed in adults with knee OA (Bindawas, 2016; Nebel et al., 2009). These existing relationships justify the selection of age, sex, BMI and gait speed as covariates.

The second model added the peak KFM, in addition to the covariates, to determine whether the external knee flexor moment peak during walking explained additional variance in pain. The third model used the covariates, followed by the peak KFM normalized to body mass as predictors in the model. This normalization to body mass is a traditional technique to account for body size when reporting moments of force (Winter, 2009). Finally, the fourth model used the covariates, followed by the peak KFM normalized to MVIC. This final variable, the peak KFM normalized to MVIC, represents the utilization of muscle capacity required during gait.

Statistical analyses were conducted in RStudio (RStudio: Integrated Development for R. RStudio, PBC, Boston, MA, USA). Data was tested for normality using Shapiro-Wilk test. For the linear regression analyses, data was entered so that all the predictor variables were weighted equally. In addition, t-tests were two-tailed with a statistical significance set at $p < 0.05$. Regression analyses were one-tailed with statistical significance set at $p < 0.05$. Outliers were examined using leverage versus standardized residuals plots.

*Table 3. A series of linear regression analyses was used to explore predictors of knee pain, measured using the KOOS pain subscale, as the dependent variable in women with clinical knee OA. Four different models of pain were created. The first model was a covariate model. Models 2, 3 and 4 explore whether the addition of KFM (Nm), KFM (Nm/kg) or KFM (Nm/MVIC) added variance, over and above the covariate model, respectively. KFM (Nm/MVIC) presents a representation of how much muscle capacity is used during gait.*

| Models | Predictors | | Dependent |
|---|---|---|---|
| Base Model | Step 1 (Covariates) <br> • Age <br> • Sex <br> • BMI <br> • Gait speed | | KOOS Pain |

| Models | Predictors | | Dependent |
|---|---|---|---|
| Model 2 | Step 1 (Covariates) <br> • Age <br> • Sex <br> • BMI <br> • Gait speed | Step 2 <br> KFM Peak (Nm) | KOOS Pain |
| Model 3 | Step 1 (Covariates) <br> • Age <br> • Sex <br> • BMI <br> • Gait speed | Step 2 <br> KFM Peak (Nm/kg) | KOOS Pain |
| Model 4 | Step 1 (Covariates) <br> • Age <br> • Sex <br> • BMI <br> • Gait speed | Step 2 <br> KFM Peak (Nm/MVIC) <br> (Muscle Capacity Utilization) | KOOS Pain |

Abbreviations: BMI = Body Mass Index, KFM = Knee Flexion Moment, KOOS = Knee Osteoarthritis Outcome Score, MVIC = Maximum Voluntary Isometric Contraction

## Results

Of the 23 participants, the mean age was 67 ±8 years, the mean BMI was 29.7 ±3.9 kg/m$^2$. This sample consisted of 15 female participants and eight male participants. Shapiro Wilk Test of Normality was conducted on each variable and repeated for all participant data (n=23), only females (n=15) and only males (n=8). Results of these tests revealed that data are normally distributed. In addition, independent samples t-tests were run to examine differences between males and females. These tests revealed a significant difference between height and MVIC means for females and males ($p$= 0.019, $p$=4.60E-08, respectively). However, no significant differences between males and females were seen in the other variables.

Regression diagnostics revealed no outliers that are influential and outside of Cook's Distance, thus no data points and participants have been excluded.  No association was observed between covariates, age, sex, BMI and gait speed, and KOOS pain ($R^2$= 0.120, *p*=0.66).

## KFM Unnormalized

The addition of KFM unnormalized variable in the covariate model yielded a $R^2$=0.129 (*p*=0.77). The addition of the KFM unnormalized variable increased the $R^2$ value by 0.009.  To test if this 0.9% in explained variance was significant, a likelihood ratio (LR) test was performed.  The LR test yielded *p*=0.64; therefore, no association was observed between measures of KFM unnormalized and KOOS pain.

## KFM Per Body Mass

The addition of KFM normalized to body mass variable in the covariate model yielded a $R^2$=0.123 (*p*=0.79).  The addition of the KFM per kg variable increased the $R^2$ value by 0.003.  The LR test yielded *p*=0.78, showing that the increase of 0.3% in explained variance by the addition of KFM per kg was not significant.  Therefore, no association was observed between measures of KFM per kg and KOOS pain.

## KFM Per MVIC

The addition of KFM normalized to MVIC variable in the covariate model yielded a $R^2$=0.145 (*p*=0.72).  The addition of the KFM per MVIC variable increased the $R^2$ value by 0.025.  The LR test yielded *p*=0.42, showing that the increase of 2.5% in explained variance by the addition of KFM per MVIC was not significant.  Therefore, no association was observed between measures of KFM per MVIC and KOOS pain.

*Table 4. Means, standard deviations, minimum and maximum values for each variable. As well as t-values, 95% confidence intervals and p-values for independent t-tests between males and females for each variable.*

| Variable | All | | | | Female | | | | Male | | | | T-Test | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Mean | SD | Min | Max | Mean | SD | Min | Max | Mean | SD | Min | Max | t-value | 95% Confidence Interval | p-value |
| Age (yr) | 67 | 8 | 50 | 79 | 65 | 6 | 50 | 77 | 70 | 10 | 56 | 70 | -1.50 | (-11.78, 1.92) | 0.15 |
| Body Mass (Kg) | 83.3 | 13.9 | 64.7 | 111.2 | 79.3 | 13.9 | 64.7 | 96.8 | 90.9 | 14.2 | 68.7 | 111.2 | -2.02 | (-23.45, 0.31) | 0.056 |
| Height (m) | 1.67 | 0.09 | 1.5 | 1.85 | 1.64 | 0.08 | 1.5 | 1.85 | 1.74 | 0.08 | 1.59 | 1.8 | -2.98 | (-0.17, -0.030) | 0.0071 |
| BMI (Kg/m^2) | 29.73 | 3.91 | 23.8 | 36 | 29.53 | 3.5 | 24.64 | 36 | 30.08 | 3.8 | 25.83 | 35.53 | -0.31 | (-4,18, 3.09) | 0.76 |
| MVIC (Nm) | 116.75 | 44 | 56.3 | 216.4 | 100.83 | 42.69 | 60.35 | 202.07 | 146.61 | 22.61 | 56.27 | 216.37 | -2.69 | (-81.14, -10.43) | 0.014 |
| 6MW Distance (m) | 449.6 | 89.9 | 315.2 | 712.5 | 436.9 | 96.9 | 315.2 | 712.5 | 473.5 | 71.2 | 351.3 | 506.2 | -0.93 | (-118.76, 45.52) | 0.4 |
| Velocity (m/s) | 1.25 | 0.25 | 0.88 | 1.979 | 1.21 | 0.27 | 0.88 | 1.98 | 1.32 | 0.2 | 0.98 | 1.41 | -0.94 | (-0.33, 0.132) | 0.36 |
| KOOS Pain Score | 65.8 | 19.2 | 19.4 | 97.2 | 65.9 | 17.6 | 19.4 | 97.2 | 65.6 | 24.7 | 38.9 | 91.7 | 0.035 | (-17.59, 18.19) | 0.97 |
| KFM unnormalized (Nm) | 30.01 | 17.51 | 4.15 | 78.29 | 28.91 | 13.76 | 4.15 | 78.29 | 32.08 | 24.05 | 4.25 | 53.68 | -0.43 | (-19.43, 13.09) | 0.69 |
| KFM-Mass (Nm/Kg) | 0.34 | 0.18 | 0.04 | 0.809 | 0.34 | 0.15 | 0.04 | 0.81 | 0.34 | 0.24 | 0.05 | 0.56 | -0.10 | (-0.18, 0.16) | 0.92 |
| KFM-MVIC (unitless) | 0.27 | 0.15 | 0.05 | 0.69 | 0.30 | 0.16 | 0.06 | 0.69 | 0.22 | 0.14 | 0.05 | 0.37 | 1.10 | (-0.065, 0.21) | 0.28 |

Abbreviations: SD = Standard Deviation, Min = Minimum Value, Max = Maximum Value, BMI = Body Mass Index, MVIC = Maximum Voluntary Isometric Contraction, 6MW = The Six Minute Walk Test, KOOS = Knee Osteoarthritis Outcome Score, KFM = Knee Flexion Moment

*Table 5.  Relationships of baseline covariates (age, sex, body mass index, and gait speed) and predictors [and trends] (KFM unnormalized, KFM per Kg and KFM per MVIC) with the dependent variable KOOS Pain score (n = 23).*

| Predictors | Unstandardized β coefficient | 95% CI | $R^2$ | *p* value |
|---|---|---|---|---|
| **Covariates only** | | | 0.120 | 0.66 |
| Age | 0.84 | (-0.56, 2.24) | | |
| Sex | 6.87 | n/a | | |
| Body mass index | 1.62 | (-1.15, 4.39) | | |
| Gait Velocity | 15.22 | (-23.59, 54.036) | | |
| **Covariates + KFM unnormalized** | | | 0.129 | 0.77 |
| Likelihood Ratio Test | | | | 0.64 |
| Age | 0.78 | (-0.68, 2.25) | | |
| Sex | 6.63 | n/a | | |
| Body mass index | 1.36 | (-1.78, 4.51) | | |
| Gait Velocity | 13.80 | (-26.81, 54.42) | | |
| Knee Flexor Moment (raw) | 0.11 | (-0.48, 0.70) | | |
| **Covariates + KFM Normalized to Body Mass** | | | 0.123 | 0.79 |
| Likelihood Ratio Test | | | | 0.78 |
| Age | 0.81 | (-0.67, 2.28) | | |

| Predictors | Unstandardized β coefficient | 95% CI | R² | p value |
|---|---|---|---|---|
| Sex | 6.47 | n/a | | |
| Body mass index | 1.52 | (-1.45, 4.50) | | |
| Gait Velocity | 14.32 | (-26.48, 55.12) | | |
| Knee Flexor Moment (per kg) | 6.15 | (-47.50, 59.80) | | |
| **Covariates + KFM Normalized to MVIC** | | | 0.145 | 0.72 |
| Likelihood Ratio Test | | | | 0.42 |
| Age | 0.85 | (-0.57, 2.28) | | |
| Sex | 9.89 | n/a | | |
| Body mass index | 1.94 | (-1.04, 4.92) | | |
| Gait Velocity | 16.39 | (-23.32, 56.09) | | |
| Knee Flexor Moment (per MVIC) | -20.39 | (-82.02, 41.25) | | |

Abbreviations: MVIC = Maximum Voluntary Isometric Contraction, KFM = Knee Flexion Moment
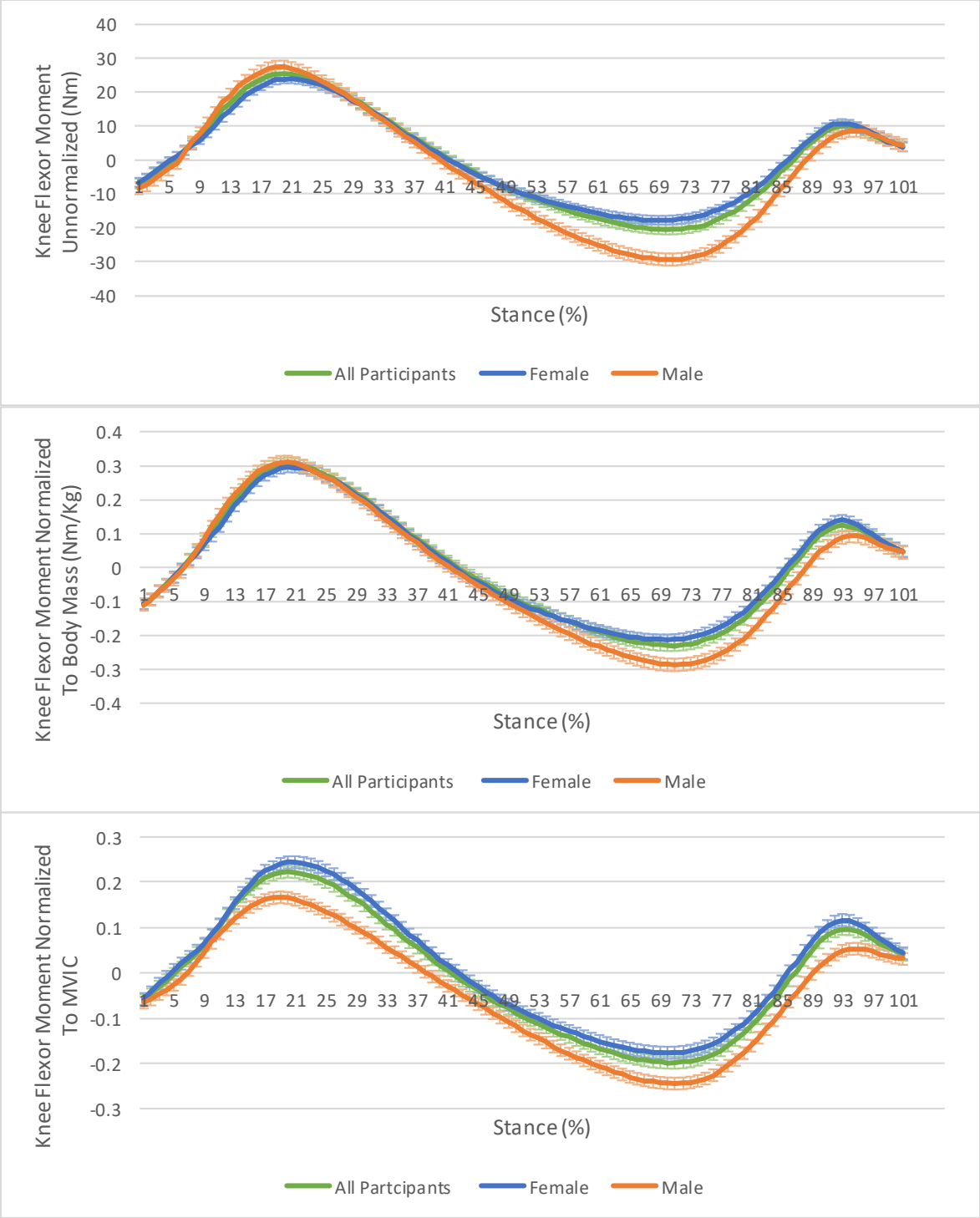
*Figure 5. Averaged ensemble waveforms for all participants, only females and only males for KFM unnormalized (Nm), KFM per Kg (Nm/Kg) and KFM per MVIC (unitless) versus stance phase (%).*
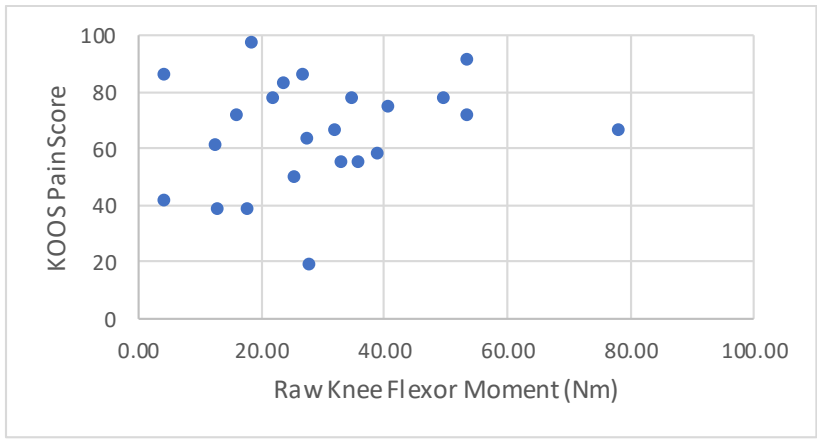
*Figure 6.  Raw knee flexor moment versus.  KOOS pain scores for all participants*
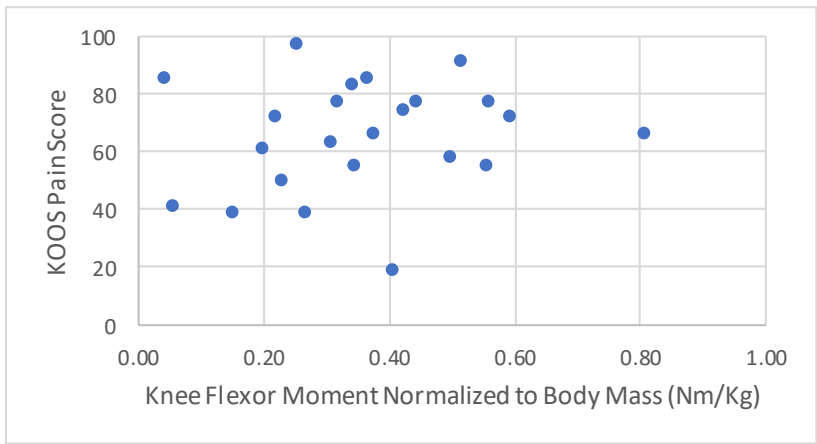


*Figure 7.  Knee flexor moment normalized to body mass versus.  KOOS pain scores for all participants.*
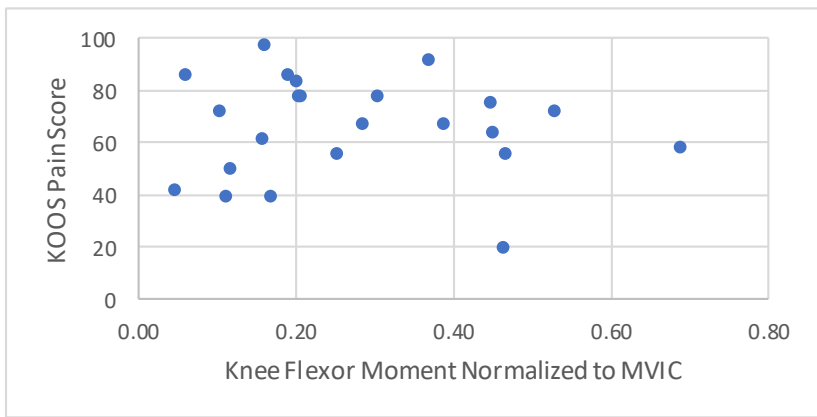


*Figure 8.  Knee flexor moment normalized to MVIC versus.  KOOS pain scores for all participants.*

## Discussion

The objective of this study was to explore the relationship between pain and muscle capacity utilization during walking in older adults with knee OA. To measure muscle capacity utilization, this study normalized KFM during gait by mean peak knee extensor MVIC. This method of measuring muscle capacity utilization provides insight into how much effort an individual requires to complete a task. While this measure of muscle capacity utilization (that is, KFM per MVIC) explained more variance in pain than the KFM unnormalized, or normalized to body mass, muscle capacity utilization during level walking was not significantly related to pain in this sample of older adults with knee OA. However, while not a primary goal of this study, trends in the data could point to sex differences in muscle capacity utilization among those with OA, where females in the current sample appeared to use a greater proportion of KFM during level walking. This potential sex difference likely reflects that females produced lower MVICs than males ($p < 0.05$), consistent with the literature. Although this study was not designed to identify sex differences, these results should be considered as a focus for future work. This work identifies that KFM through different normalization strategies enabled comparisons based on muscle capacity.

### Muscle Capacity Utilization and Pain

Muscle capacity utilization was not related to KOOS pain in this study. Previous work has demonstrated that healthy older adults utilized more muscle capacity during ADLs than healthy young adults (Hortobagyi et al., 2003). Hortobagyi and colleagues measured "relative effort", which the authors defined as the percentage of joint moment relative to maximal joint moment, an approach similar to our muscle capacity utilization calculation. Nonetheless, there were differences in the

methods between the work conducted by Hortobagyi and our study. Hortobayi and colleagues measured maximal leg strength in supine position with a leg press machine using knee flexion angles 15°, 30°, 45°, 60° and 74° (where 0° is full knee extension) (Hortobagyi et al., 2003). In contrast, we quantified knee extensor strength using MVIC measured using a Biodex system at 60° knee flexion. To the best of our knowledge, no other studies have explored relative effort or muscle capacity utilization in OA.

This study extends the use of muscle capacity by exploring whether pain is experienced during walking, and if this pain is associated with how much muscle capacity is being used. It is possible that pain could reduce muscle activation (Lewek et al., 2004; Rafsanjani et al., 2017; Sharma et al., 2017) , and/or cause co-activation of muscles (Hortobágyi et al., 2005; Patsika et al., 2014; Preece et al., 2016). People with symptomatic knee OA have been observed to experience difficulty being able to fully activate their quadriceps muscle (Lewek et al., 2004) and exhibit abnormal muscle activation profiles (Preece et al., 2016) . This abnormal muscle activity may be the consequence of pain, or fear of further injury and pain (Lewek et al., 2004) – making it more difficult and requiring more effort for muscles to support daily activities. The fear of further injury and increased pain can deter people from participating in physical activity, causing their muscles to weaken even more (Fitzgerald, 2005). It is also possible that quadriceps muscle weakness (Segal et al., 2010; Segal & Glass, 2011; Segal et al., 2009), a common observation in older adults with knee OA, may reduce the amount of dynamic support available to the knee joint (Segal et al., 2010; Zeni & Higginson, 2011), thereby, increasing the likelihood of joint injury and subsequent pain. Joint degeneration and structural damage, associated with knee OA, have been shown to lead to failure of voluntary muscle activation and arthrogenic muscle inhibition (Lewek et al., 2004), that results in abnormal afferent information sent to the alpha motoneuron - leading to reduced

muscle activation (Hopkins & Ingersoll, 2000; Lamy et al., 2008; Lewek et al., 2004). It is clear that a reduced muscle capacity, can be attributed to both activation deficits and atrophy. Initial pain can lead to a decrease in physical activity, causing weakness, joint damage, decreased muscle activation, reduced muscle capacity and eventually more pain. It is likely that this is a vicious cycle and that pain is associated with muscle capacity in both directions. Individuals who experience pain will likely experience muscle weakness.

## Pain in Knee OA

The mean KOOS pain scores for the current sample (65.8 ± 19.2 for all participants, 65.9 ± 17.6 for females and 65.6 ± 24.7 for males) were lower, indicating more pain intensity and frequency, compared to normative data collected in healthy adults (ages 18-101 years) (Baldwin et al., 2017). The International Association for the Study of Pain defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage" (Nicholson, 2006).

Pain was the focus of the current study because of its impact in knee OA. Pain associated with knee OA decreases quality of life, reduces physical activity, and often requires medication. Pain is associated with greater cartilage loss in the knee joint in people with radiographic and symptomatic knee OA (Wang et al., 2018). Pain can also lead to an avoidance of social participation (Darlow et al., 2018; Keefe et al., 1987). Keefe et al., (1987) found that knee joint pain caused guarded and hesitant movement during activities of daily living. Pain is also associated with functional knee limitation and less participation in physical activities. Functional limitations developed and followed a very similar trajectory of pain (concordance of 94%) -- indicating that people experienced these two outcomes very similarly (Radojčić et al., 2020). In addition, Song et al., (2018) found that knee pain levels had a strong

negative relationship with moderately intense physical activities. People with more severe knee pain spent less time in moderate physical activity, compared to people with no knee pain. Lastly, people with knee OA commonly use pharmacologic agents to reduce pain. Acetaminophen is one of the most common drugs (ACR, 2000); although it is one of the safest agents, it is also associated with clinically adverse events. Hepatic toxicity is rare but possible for people taking greater doses for more severe pain (ACR, 2000). Acetaminophen is also weakly associated with end-stage renal disease (ACR, 2000). Oral NSAIDs are also commonly administered to help people with OA manage their pain (Pelletier et al., 2016). However, oral NSAID treatment is associated with a three-fold to five-fold increase in the risk of upper gastrointestinal complications, including peptic ulcer perforation, obstruction, and bleeding (ACR, 2000; Pelletier et al., 2016).

People with knee OA demonstrate adaptations in the presence of pain; for example, pain may be a trigger that signals to the motor control to reduce the load on the joint. Henriksen et al., (2010) showed that experimentally induced pain reduced range of motion of the knee flexors/extensors in participants with induced pain compared to the control and sham groups. Such findings are consistent with others that examined the effects of experimental pain on knee mechanics during walking (Seeley et al., 2013). The reduced range of motion may be a protective mechanism to mitigate pain. In addition, pain is one of the most common reasons why people seek healthcare. A study from the World Health Organization conducted surveys across 15 centers in Asia, Africa, Europe and the Americas. Across all centers, 22% of primary care patients reported persistent pain to their doctor (Gureje et al., 1998). Symptoms from OA and joint disorders were the second most common reason for people to visit their doctors in a defined population in the USA in 2005-2009 (St. Sauver et al., 2013)

In this study, we were unable to show a relationship between pain and muscle capacity utilization ($p>0.05$). Moderate and severe pain has been associated with KFM during gait in a study by O'Connell et al., (2016). In the O'Connell (2016) study, researchers grouped the participants by pain severity: no pain (n=18), mild pain (n=27) and moderate/severe pain (n=22). The findings of the O'Connell (2016) study show that people with knee OA, who experience moderate/severe pain during walking, generated a mean peak KFM during midstance of 0.25 (± 0.24) Nm/kg – significantly different from the no pain group who generated a mean peak KFM during midstance of -0.01 (± 0.39) Nm/kg. To our knowledge, this is the O'Connell (2016) study is the only study that has shown a significant association between pain and KFM during gait. It is interesting to note that the participants in the current study generated higher mean peak KFM values than all three groups in the O'Connell (2016) study. Normalizing KFM to MVIC to yield muscle capacity did not meaningfully improve the association with pain. There could be a number of reasons: It is important to note that we did not distinguish between nociceptive and neuropathic pain in this study. Nociceptive pain is pain that is caused by tissue damage or potentially tissue-damaging stimuli (e.g. pain after surgery, arthritis pain) (Nicholson, 2006). Meanwhile, neuropathic pain is pain that is chronic, initiated by nervous system lesions or dysfunction of the nervous system (Nicholson, 2006). It is also possible that the pain measure, which asks participants to respond based on their experience pain over the last seven days, did not match their pain experienced during the gait trials where KFM was assessed.

## Muscle Capacity in Knee OA

Since knee OA is characterized by lower muscle strength (Segal & Glass, 2011), it is possible that people with knee OA utilize more of their muscle capacity than healthy aging adults. Utilizing more muscle capacity suggests an increase in the individual contributions of internal structures (muscles,

ligaments, cartilage) in order to withstand typical loads encountered in daily living, work and recreation (Bennell et al., 2008). A study by Segal et al., (2010) examined the relationship between quadriceps strength and the progression of knee OA in people with known risk factors for knee OA. In this Segal (2010) study, the quadriceps strength means for males and females are 125.7 (± 41.4) Nm and 72.0 (± 24.0) Nm, respectively. Both female and males in the current study generated greater quadriceps strength than the participants in the Segal (2010) study.

Muscle capacity is an important measure as weakness is a disease risk for knee OA. Quadriceps weakness increases the risk of disease development, especially in women (Alnahdi et al., 2012; Segal et al., 2010; Slemenda et al., 1997). Isometric quadriceps strength deficits in people with knee OA range from 10% to 56%, and isometric hamstring strength deficits range from 4% to 35% (Alnahdi et al., 2012). Quadriceps strength is related to the rate of lower extremity loading in healthy women; participants with weaker quadriceps have higher loading rates (Alnahdi et al., 2012; Slemenda et al., 1997). Higher loading rates may initiate knee OA or cause progression of existing disease (Alnahdi et al., 2012; Slemenda et al., 1997). Slemenda (1997) showed a relationship between lower quadriceps peak torque and women with radiographic knee OA. Segal (2010) also showed that greater knee extensor strength is associated with a decrease in risk for symptomatic knee OA.

In addition to disease risk, muscle capacity can also be an important measure for OA progression. Muscle weakness contributes to disease progression in people living with knee OA. Segal et al., (2010) examined the relationship between knee joint space narrowing and quadriceps weakness, over the course of 30 months, to assess the effects of quadriceps weakness on disease progression. Researchers found a significant relationship between patellofemoral joint space narrowing and quadriceps strength in women (Segal et al., 2010).

Several studies have found a disassociation between loss of muscle mass and loss of muscle strength (Barbat-Artigas et al., 2011; Newman et al., 2006; Visser et al., 2000). This suggests that merely assessing body composition or a cross-sectional area of the muscle may be an inadequate measure to ascertain information regarding physical function in older adults. Measuring muscle capacity utilization may yield more insight into functional performance. Individuals with knee OA have demonstrated quadriceps weakness associated with functional limitations (Bacon et al., 2019; Sharma et al., 2001, 2003) – suggesting that muscle capacity is vitally important to functional performance and the execution of ADLs. A study by Bacon (2019) found quadriceps strength thresholds for functional tasks (20 m walk test, sit-to-stand test, and answered questions from WOMAC) in women with knee OA. The Bacon (2019) study found strength thresholds at 57 Nm for the 20-m walk and 32 Nm for the five times sit-to-stand test for women with knee OA. Individuals, who performed below the thresholds, demonstrated stronger relationships between strength and functional abilities. Individuals, who performed above the threshold, demonstrated weaker relationships between strength and functional abilities. These thresholds in strength may help in identifying individuals at the brink of disability, and who may benefit from strengthening exercises to improve overall function (Bacon et al., 2019). Individuals above threshold should focus on maintaining strength (Bacon et al., 2019). Sharma et al., (2003) conducted a three-year longitudinal cohort study investigating factors contributing to poor physical functioning in 257 patients who had knee OA. They found that reduced absolute quadriceps and hamstrings strength increased the likelihood of poor physical functioning. The measurements used in the Sharma (2003) study were: the time needed to perform five repetitions of rising from and sitting down in a chair. It is possible that the participants in this study are stronger than those in previous studies (Segal et al., 2010), suggesting that the participants found walking an easier task, using relatively little muscle

capacity. This may be another explanation as to why we did not see a relationship between pain and muscle capacity during walking.

Low muscle capacity may be the reason why people are less active and participate less in their daily lives. Brady et al., (2014) have proposed an integrated model for the assessment of physical function that includes the variables: body composition (skeletal muscle mass, fat mass), physical activity and exercise (resistance training, and aerobic training), and muscle capacity (leg strength, and leg power). These authors suggest that it is a combination of all three variables that leads to a decrease in physical function in an individual's daily life. It is possible that physical activity, body composition and muscle capacity together synergistically affect physical function in older adults (Brady & Straight, 2014). With age, changes in body composition (increase in adiposity and decrease in muscle mass) and muscle capacity (decrease in strength and power) occur (Brady et al., 2014). According to the model by Brady and colleagues, since quality of body composition and muscle capacity decreases with age, the need for physical activity must increase in order to maintain physical function. However, the age-related changes in these variables make it difficult to participate in physical activities, making them more prone to functional disabilities. These individuals may be in a vicious cycle where they are not strong enough to be mobile, ultimately making them weaker.

## KFM During Gait

Net joint moments are calculated as a product of the joint segments' moment of inertia and the joint's angular acceleration, and reflect a summation of all moments, including those produced by agonist and antagonist muscles crossing that joint (Winter, 2009). A KFM represents the net moments crossing the knee joint in the sagittal plane. In this study, the mean peak KFM normalized to body mass for all participants was 0.36 (± 0.18) Nm/Kg. These peak moments are lower than the mean peak KFM

demonstrated in the Brisson et al., (2017) study of 0.57 (± 0.21) Nm/Kg. It is important to note that the sample recruited in this study had a mean age of 67 (± 8) years, meanwhile the Brisson (2017) study used a sample with a mean age of 61 (± 6.9) years. In addition, based on the mean gait speeds, the participants in this study walked slower than the participants in the Brisson (2017) study. Participants in this study are older and experienced more pain than the Brisson (2017) study, explaining the difference in peak moments between the two studies. It is possible that the lower KFM observed in this study is due to muscle co-activation.

Peak KFM is a significant predictor for medial contact force in the knee during walking (Manal et al., 2015). Manal and colleagues (2015) demonstrated that including the peak KFM in an electromyography (EMG) driven model provided a more accurate indication of peak medial contact force than the input of peak KAM alone. It is possible that joint reaction forces (JRFs) can damage articular structures in unhealthy knees but are likely to help condition cartilage in healthy knees. Human chondrocytes significantly increase during cyclic compression loading (Becker et al., 2013), displaying how healthy cartilage requires loading to maintain its ability to sustain load (Becker et al., 2013). People with knee OA may not be able to tolerate such loads, as their articular cartilage is degenerated from the disease (Bennell et al., 2011; Brisson et al., 2017; Hanna et al., 2005; Mora et al., 2018; Wluka et al., 2002; Wluka et al., 2006).

KFM has been explored as a potentially important element in abnormal and/or cumulative knee loading that is implicated in knee OA disease (Chehab et al., 2014; Creaby, 2015). Creaby et al., (2013) found a significant association between higher knee joint reaction forces and higher KFM. The risk of structural deterioration associated with disease progression in medial knee OA has been linked to higher mechanical loading of the joint during walking (Bennell et al., 2011; Miyazaki et al., 2002). In addition,

Chehab et al., (2014) found an association between changes in medial tibial thickness (marker for OA progression) and KFM over five years in older adults with knee OA. However, there are also several studies that found no association between KFM and knee OA risk or progression (Bennell et al., 2011; Brisson et al., 2017; Chang et al., 2015). This inconsistency may be due to the differences in sample sizes. The Bennell (2010) study (n = 144), the Brisson (2017) study (n = 53) and the Chang (2015) study (n = 204) examined knee moments in larger samples than the Chehab (2014) study (n = 16). One explanation for these inconsistent results may be that KFM has demonstrated questionable ICCs (Brisson et al., 2018). In fact, results from the Brisson (2018) study showed lower ICCs for KFM in people with knee OA than in a healthy population. The instability and unreliability of KFM measurements may explain the inconsistent evidence linking KFM with knee OA.

## What Impacts KFM?

The magnitude joint moments of force increase as gait speed increases (Winter, 1983, 2009). A study by White & Lage (1993) demonstrated that changes in gait speed (by changing cadence and stride length) affects the magnitude of joint moments. Increasing gait speed is associated with an increase in magnitude in joint moments in people with knee OA (Landry et al., 2007). Participants in the current study demonstrated a mean gait speed of 1.25 (± 0.25) m/s from the 6MW test, which is slower than normative reference values of healthy older adults (Dobson et al., 2013). Since a faster walking speed has been shown to increase knee joint moments, muscle capacity utilization will also increase. A study by Hafer & Boyer (2020) found that functional demand (peak KFM divided by MVIC) was greater in less active older adults than young adults and increased with walking speed. However, gait speed while measuring KFM was not included in this analysis, as participants were asked to walk at a self-selected speed.

The muscular demand required to complete a task impacts the required knee joint moments. A study by Luepongsak et al., (2002) described and compared knee and hip moments across ADLs (standing, walking, bending, chair rise, stair descent) in older adults. For KFM, the authors found that stair descent generated the largest moments (7.14 % Bodyweight × Height). Walking generated greater moments compared to chair rise, bending and standing. However, this is inconsistent with an older study by Jeversusevar et al., (1993), where they compared sagittal knee moments during ADLs (gait chair rise, stair ascent, stair descent) in people with knee arthroplasty and healthy controls. For this study, they also found that (in both groups) stair descent generated the largest moments; however, they saw that walking generated the lowest moments (in both groups).

Co-activation is likely a major mechanism for joint stabilization, load distribution, and movement control during gait in knee OA (Astephen, et al., 2008; Astephen Wilson et al., 2011; Baratta et al., 1988; Brenneman et al., 2016; Busse et al., 2006; Hortobágyi et al., 2005; Hubley-Kozey et al., 2008; Rutherford et al., 2012; Segal et al., 2015; Smith et al., 2020, 2019; Stevens et al., 2003). Muscle co-activation is the simultaneous activity of agonist and antagonist muscles (Smith et al., 2019). There are currently inconsistent findings on whether co-activation impacts KFM. According to a study by Heiden et al., (2009), when people with knee OA were compared to the healthy controls, they exhibited increased levels of net muscle activity and co-activation while still having similar joint moments and posture (Heiden et al., 2009). However, Hortobágyi et al., (2005) have shown a relationship between muscle co-activation and stiffness of the knee joint. Their findings suggest that co-activation is necessary to stiffen the knee (reducing knee motion and stabilizing the joint) and concurrently lowering the KFM (Hortobágyi et al., 2005). Importantly, without EMG data in the current sample, there is no way to know how active the quadriceps and hamstrings were during walking, and whether these

opposing muscle groups acted concurrently. Since co-activation was not considered in this analysis, we do not know if it will impact net joint moments; thus, muscle capacity utilization may be underestimated in this study.

Previous research has been conducted to examine muscle capacity during ADLs (Samuel et al., 2013). These researchers used the term "functional demand", defined as the muscle moment generated during a task divided by the maximum isometric strength (expressed as a percentage). The Samuel (2013) study observed mean knee extensor demands of: 72.8% for chair rise, 69% for chair sit down, 103% for stair ascent, 120% for stair descent and 101% during gait. It is important to note that these values are higher than what was observed in this study and what has been reported in previous studies (Hortobagyi et al., 2003; Reeves et al., 2008, 2009). Hortobagyi et al., (2003) observed mean knee extensor demand of: 78% for stair ascent, 88% for stair descent, 80% for chair rise, and did not include gait. Muscle capacity utilization observed in this study was much lower than the existing literature; however, Samuel (2013) and Hortobagyi (2003) recruited healthy older adults. The presence of knee OA may contribute to the poorer muscle capacity utilization seen in this study.

In the current study, females used 32 ± 17% and males used 19 ± 17% of their muscle capacity during walking. This observation likely reflects that walking requires about the same level of demand for successful performance, but females demonstrated lower MVIC values and therefore lower peak muscle capacity than males. It is interesting to note that females have a greater prevalence and severity of knee OA compared to males (Turkiewicz et al., 2014; Zhang & Jordan, 2010). It is possible that a greater utilization of muscle capacity to perform ADLs increases the risk of incident or progressive OA. To date no one has investigated this phenomenon.

## Limitations

This study is a secondary analysis of existing data collected for another purpose. This secondary analysis reflects an alternate thesis plan as a result of the COVID-19 pandemic placing restrictions on face-to-face data collection. This secondary analysis means that muscle capacity utilization was only measured during gait, instead of also collecting data on other ADLs that required greater utilization of muscle capacity. Also, in light of COVID-19, a relatively small sample size was used to address the research question. A sample size calculation was conducted after the analysis to determine how many participants would be required to achieve significance between pain and muscle capacity for future research. An effect size of 0.07, calculated from the $R^2$ values yielded by the statistical analyses in this study, and a Type 1 error of 0.05 were used. A minimum of 120 participants will be required to yield 80% power capable of detecting significant change. In addition, while collecting data, it was not known whether the participants experienced nociceptive or neuropathic pain. Therefore, the association between pain and muscle capacity utilization may be more difficult to find. Furthermore, this analysis did not include EMG to determine whether co-activation influenced KFM; therefore, the muscle capacity utilization being observed may be underestimated. Additionally, there may be more factors that affect an individual's muscle capacity such as muscle quality (volume of muscle and muscle mass) and metabolic components that influence strength and power. These factors were not considered in this current study, but will allow researchers to better understand muscle capacity.

## Future Work

Future research should include sex differences in the analysis. The significant differences observed in muscle strength output between males and females suggest that females must utilize a greater proportion of their muscle capacity than males to conduct ADLs and other activities. It would be

interesting to incorporate muscle capacity utilization and the study of ergonomics by measuring muscle capacity during work-related tasks. Future work should explore these sex differences in muscle capacity to identify cause and/or presence of disability. This research should examine the influence of hormones and body composition differences in males and females to investigate if utilizing more muscle capacity could increase the risk or progression of knee OA. Furthermore, age may influence the relationship between pain and muscle capacity utilization, therefore future work should examine this relationship with a younger and older cohort. In addition, muscle capacity utilization in people with OA should be measured using more demanding ADLs to compare with existing literature on healthy controls. Since this study only considered strength measurements, future work should also include measurements of power, as muscle capacity utilization is influenced by both strength and power. Power production and absorption should be analyzed during ADLs and isotonic and/or isokinetic muscle contractions can be measured on the Biodex Dynamometer. Next, since body composition, physical activity and muscle capacity are synergistic, levels of physical activity may have an important influence on OA. Additionally, future work should consider how muscle quality is associated witch muscle capacity by normalizing MVIC to muscle volume unit. Future work should also consider levels of physical activity as a covariate. Lastly, future work should consider a longitudinal study on the relationship between pain and muscle capacity utilization to understand how the progression of knee OA affects this relationship.

## Conclusion

This work has demonstrated the importance of pain and muscle capacity utilization for knee OA. Although the results of this study did not find a relationship between pain and muscle capacity utilization, future research should aim to pursue these measurements when evaluating knee OA, as this relationship still remains unclear. Muscle capacity utilization may be an important tool for identifying disability in people with knee OA, and understanding what factors influence muscle capacity utilization may help individual's break the vicious cycle of pain and weakness.

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# Appendices

Appendix 1.  KOOS Data Collection Form

# Knee injury & Osteoarthritis Outcome Score

This survey asks for your view about your knee.  This information will help us keep track of how you feel about your knee and how well you are able to perform your usual activities.

Answer every question by ticking the appropriate box, only <u>one</u> box for each question.  If you are unsure about how to answer a question, please give the best answer you can.

## <u>Symptoms</u>
These questions should be answered thinking of your knee symptoms during the **last week**.

S1.    Do you have swelling in your knee?

| Never | Rarely | Sometimes | Often | Always |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

S2.    Do you feel grinding, hear clicking or any other type of noise when your knee moves?

| Never | Rarely | Sometimes | Often | Always |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

S3.    Does your knee catch or hang up when moving?

| Never | Rarely | Sometimes | Often | Always |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

S4.    Can you straighten your knee fully?

| Always | Often | Sometimes | Rarely | Never |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

S5.    Can you bend your knee fully?

| Always | Often | Sometimes | Rarely | Never |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

## Stiffness

The following questions concern the amount of joint stiffness you have experienced during the **last week** in your knee. Stiffness is a sensation of restriction or slowness in the ease with which you move your knee joint.

S6.     How severe is your knee joint stiffness after first wakening in the morning?

| None | Mild | Moderate | Severe | Extreme |
|------|------|----------|--------|---------|
| ☐ | ☐ | ☐ | ☐ | ☐ |

S7.     How severe is your knee stiffness after sitting, lying or resting **later in the day**?

| None | Mild | Moderate | Severe | Extreme |
|------|------|----------|--------|---------|
| ☐ | ☐ | ☐ | ☐ | ☐ |

## Pain

P1.     How often do you experience knee pain?

| Never | Monthly | Weekly | Daily | Always |
|-------|---------|--------|-------|--------|
| ☐ | ☐ | ☐ | ☐ | ☐ |

What amount of knee pain have you experienced the **last week** during the following activities?

P2.     Twisting/pivoting on your knee

| None | Mild | Moderate | Severe | Extreme |
|------|------|----------|--------|---------|
| ☐ | ☐ | ☐ | ☐ | ☐ |

P3.     Straightening knee fully

| None | Mild | Moderate | Severe | Extreme |
|------|------|----------|--------|---------|
| ☐ | ☐ | ☐ | ☐ | ☐ |

P4.   Bending knee fully

| None | Mild | Moderate | Severe | Extreme |
|------|------|----------|--------|---------|
| ☐    | ☐    | ☐        | ☐      | ☐       |

P5.   Walking on flat surface

| None | Mild | Moderate | Severe | Extreme |
|------|------|----------|--------|---------|
| ☐    | ☐    | ☐        | ☐      | ☐       |

P6.   Going up or down stairs

| None | Mild | Moderate | Severe | Extreme |
|------|------|----------|--------|---------|
| ☐    | ☐    | ☐        | ☐      | ☐       |

P7.   At night while in bed

| None | Mild | Moderate | Severe | Extreme |
|------|------|----------|--------|---------|
| ☐    | ☐    | ☐        | ☐      | ☐       |

P8.   Sitting or lying

| None | Mild | Moderate | Severe | Extreme |
|------|------|----------|--------|---------|
| ☐    | ☐    | ☐        | ☐      | ☐       |

P9.   Standing upright

| None | Mild | Moderate | Severe | Extreme |
|------|------|----------|--------|---------|
| ☐    | ☐    | ☐        | ☐      | ☐       |

**Function, daily living**

The following questions concern your physical function.  By this we mean your ability to move around and to look after yourself.  For each of the following activities please indicate the degree of difficulty you have experienced in the **last week** due to your knee.

A1.   Descending stairs

| None | Mild | Moderate | Severe | Extreme |
|------|------|----------|--------|---------|
| ☐ | ☐ | ☐ | ☐ | ☐ |

A2.   Ascending stairs

| None | Mild | Moderate | Severe | Extreme |
|------|------|----------|--------|---------|
| ☐ | ☐ | ☐ | ☐ | ☐ |

A3.   Rising from sitting

| None | Mild | Moderate | Severe | Extreme |
|------|------|----------|--------|---------|
| ☐ | ☐ | ☐ | ☐ | ☐ |

A4.   Standing

| None | Mild | Moderate | Severe | Extreme |
|------|------|----------|--------|---------|
| ☐ | ☐ | ☐ | ☐ | ☐ |

A5.   Bending to floor/pick up an object

| None | Mild | Moderate | Severe | Extreme |
|------|------|----------|--------|---------|
| ☐ | ☐ | ☐ | ☐ | ☐ |

A6.   Walking on flat surface

| None | Mild | Moderate | Severe | Extreme |
|------|------|----------|--------|---------|

☐   ☐   ☐   ☐   ☐

**A7.   Getting in/out of car**
None        Mild        Moderate        Severe        Extreme
☐           ☐           ☐               ☐             ☐

**A8.   Going shopping**
None        Mild        Moderate        Severe        Extreme
☐           ☐           ☐               ☐             ☐

**A9.   Putting on socks/stockings**
None        Mild        Moderate        Severe        Extreme
☐           ☐           ☐               ☐             ☐

**A10.  Rising from bed**
None        Mild        Moderate        Severe        Extreme
☐           ☐           ☐               ☐             ☐

**A11.  Taking off socks/stockings**
None        Mild        Moderate        Severe        Extreme
☐           ☐           ☐               ☐             ☐

**A12.  Lying in bed (turning over, maintaining knee position)**
None        Mild        Moderate        Severe        Extreme
☐           ☐           ☐               ☐             ☐

**A13.  Getting in/out of bath**
None        Mild        Moderate        Severe        Extreme

☐      ☐      ☐      ☐      ☐

A14. Sitting

| None | Mild | Moderate | Severe | Extreme |
|------|------|----------|--------|---------|
| ☐ | ☐ | ☐ | ☐ | ☐ |

A15. Getting on/off toilet

| None | Mild | Moderate | Severe | Extreme |
|------|------|----------|--------|---------|
| ☐ | ☐ | ☐ | ☐ | ☐ |

A16. Heavy domestic duties (moving heavy boxes, scrubbing floors, etc)

| None | Mild | Moderate | Severe | Extreme |
|------|------|----------|--------|---------|
| ☐ | ☐ | ☐ | ☐ | ☐ |

A17. Light domestic duties (cooking, dusting, etc)

| None | Mild | Moderate | Severe | Extreme |
|------|------|----------|--------|---------|
| ☐ | ☐ | ☐ | ☐ | ☐ |

## Function, sports and recreational activities

The following questions concern your physical function when being active on a higher level. The questions should be answered thinking of what degree of difficulty you have experienced during the **last week** due to your knee.

SP1. Squatting

| None | Mild | Moderate | Severe | Extreme |
|------|------|----------|--------|---------|
| ☐ | ☐ | ☐ | ☐ | ☐ |

SP2.  Running

| None | Mild | Moderate | Severe | Extreme |
|------|------|----------|--------|---------|
| ☐ | ☐ | ☐ | ☐ | ☐ |

SP3.  Jumping

| None | Mild | Moderate | Severe | Extreme |
|------|------|----------|--------|---------|
| ☐ | ☐ | ☐ | ☐ | ☐ |

SP4.  Twisting/pivoting on your injured knee

| None | Mild | Moderate | Severe | Extreme |
|------|------|----------|--------|---------|
| ☐ | ☐ | ☐ | ☐ | ☐ |

SP5.  Kneeling

| None | Mild | Moderate | Severe | Extreme |
|------|------|----------|--------|---------|
| ☐ | ☐ | ☐ | ☐ | ☐ |

## Quality of Life

Q1.  How often are you aware of your knee problem?

| Never | Monthly | Weekly | Daily | Constantly |
|-------|---------|--------|-------|------------|
| ☐ | ☐ | ☐ | ☐ | ☐ |

Q2.  Have you modified your life style to avoid potentially damaging activities to your knee?

| Not at all | Mildly | Moderately | Severely | Totally |
|------------|--------|------------|----------|---------|
| ☐ | ☐ | ☐ | ☐ | ☐ |

Q3.  How much are you troubled with lack of confidence in your knee?

| Not at all | Mildly | Moderately | Severely | Extremely |
|------------|--------|------------|----------|-----------|

☐ ☐ ☐ ☐ ☐

Q4.   In general, how much difficulty do you have with your knee?

| None | Mild | Moderate | Severe | Extreme |
|------|------|----------|--------|---------|
| ☐ | ☐ | ☐ | ☐ | ☐ |

***Thank you very much for completing all the questions in this questionnaire***

Appendix 2. Participant Data Collection Form

# Basic Measurements

Participant should be barefoot, wearing shorts.

| Age | | | |
|---|---|---|---|
| Sex | | | |
| Mass (kg) | | | |
| Height (m) | | | |
| Body Mass Index (kg/m$^2$) | | | |
| Dominant Leg (R/L) | | | VL (GT-LC) |
| Involved Leg (R/L) | | | |